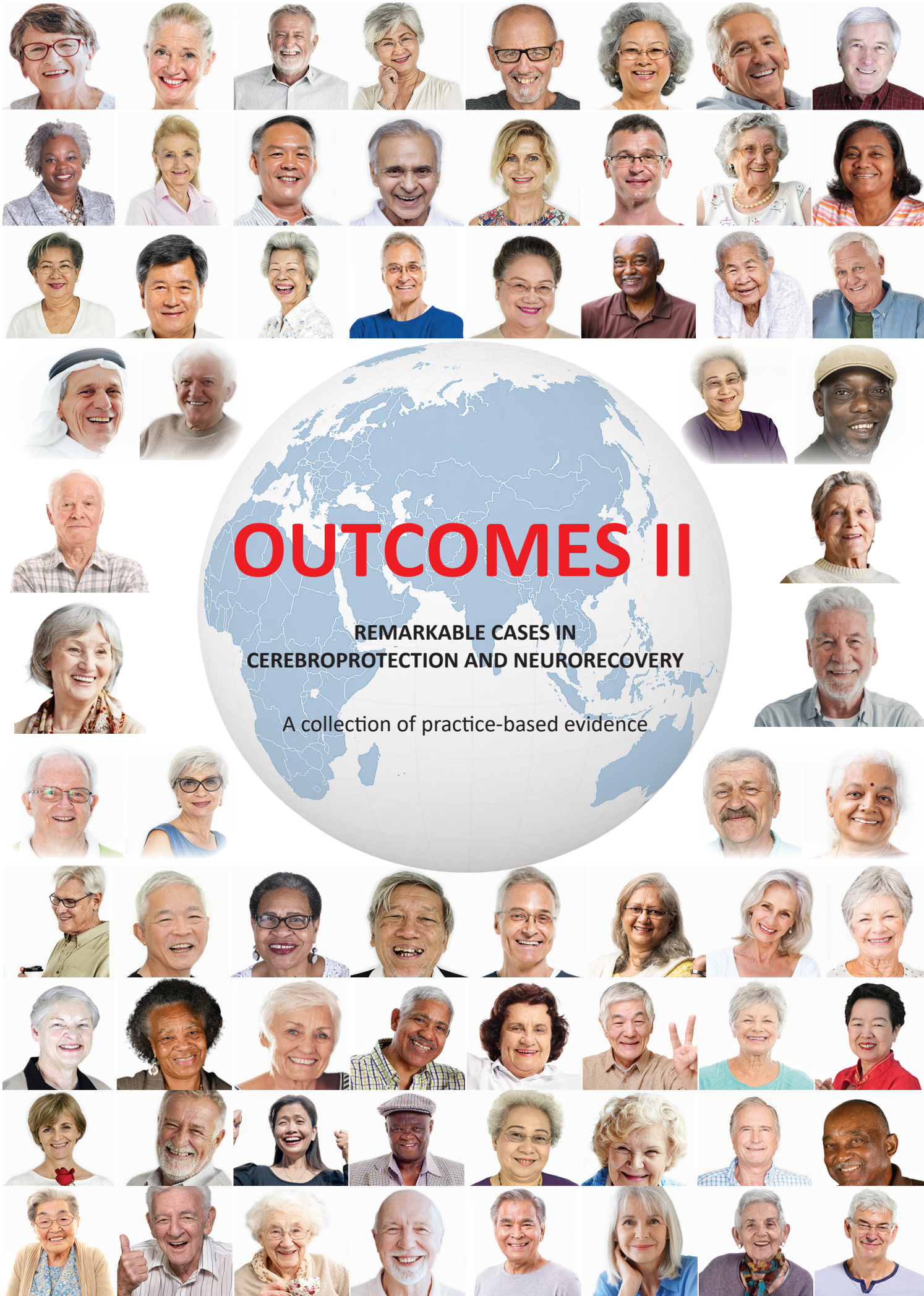




Outcomes II

Remarkable Cases in Cerebroprotection and Neurorecovery

A collection of practice-based evidence

“The **good** physician treats the disease;
the **great** physician treats the patient who has
the disease.”

Sir William Osler (1849-1919)

Founding Professor of Johns Hopkins Hospital

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Austria

Foreword

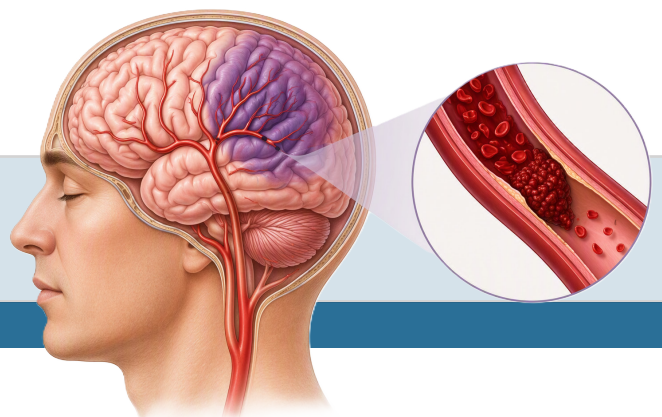
Participating in the development of stroke medicine over several decades, I have especially followed the development of therapeutic concepts and new pharmacological agents. The overall aim for these therapies was to improve outcomes after acute neurological injury. Many approaches and substances have been developed and undergone clinical testing during my time. Among these, the clinical development and use of Cerebrolysin for enhanced recovery after brain damage has been of particular interest and has, almost singularly, withstood the test of time.

What makes the case collection *Outcomes II* particularly interesting is its broad representation. The 45 reports presented in this book come from different clinical settings and from physicians working in different parts of the world. They illustrate the differing settings in which Cerebrolysin has been used to enhance recovery after neurological injury. These cases showcase applications at different stages of disease, combined with varying treatment concepts and offer a glimpse into a wide range of clinical realities.

Of course, individual case reports cannot replace evidence from controlled clinical trials. Their value lies in a complementary role: they provide a window into a real-world clinical practice and illustrate vividly how therapeutic concepts are applied to individual patients. Furthermore, they can be used for generating new questions that deserve further investigation.

I am therefore pleased to see this broad international experience brought together in a single volume. This experience builds on a broader body of evidence, including numerous randomized clinical trials and its inclusion in international clinical guidelines and recommendations. I hope that these cases will stimulate further discussion, encourage further clinical research and, above all, contribute to improve outcomes for patients affected by stroke and traumatic brain injury.

Acute Ischemic Stroke





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Advances in reperfusion therapies have transformed the management of acute ischemic stroke, however, many patients continue to develop irreversible brain injury despite successful recanalization. Moreover, the majority of patients either present beyond the therapeutic time window or have contraindications to intravenous thrombolysis or endovascular thrombectomy. This challenge remains particularly relevant in low- and middle-income countries, where access to reperfusion therapies may be limited. For these patients, treatment relies on optimized stroke unit care, careful management of physiological parameters, neuro-rehabilitation and secondary prevention – and evidence-based cerebroprotective treatment.

Ischemic brain injury continues to evolve beyond the initial vascular occlusion through a complex cascade of secondary pathological processes—including excitotoxicity, oxidative stress, neuroinflammation, mitochondrial dysfunction and apoptosis—contributes to the progression of tissue injury within the ischemic penumbra. As many of these mechanisms remain active for hours to days after stroke onset, they represent a therapeutic window for interventions aiming to protect vulnerable neurons and support the brain's intrinsic repair processes.

The goal of cerebroprotection is to complement standard treatment, particularly early mobilization and -rehabilitation, by limiting secondary injury and promoting neurological recovery. Preclinical studies have demonstrated that it exerts neurotrophic factor-like effects, modulates neuroinflammation, reduces excitotoxic and oxidative damage, promotes neuronal survival and enhances neuroplasticity and synaptic remodeling. Together, these mechanisms provide a biological rationale for investigating its use in patients with acute ischemic stroke.

The cases presented in this chapter illustrate a range of patients who received Cerebrolysin in addition to standard stroke care because they were not eligible for reperfusion therapy. Although individual case reports cannot establish treatment efficacy, they provide valuable insights into real-world clinical practice and demonstrate how cerebroprotective strategies may be integrated into comprehensive stroke management. Collectively, these cases highlight the ongoing need to explore treatment approaches that not only preserve vulnerable brain tissue but also maximize the potential for functional recovery.



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...with high-dose anti-thrombotic treatment

Abstract

This clinical case is an example of a potential synergistic neuroprotective interaction of Cerebrolysin and high doses of aspirin. The case describes the significant recovery of neurological deficits in a patient with moderate ischemic stroke (NIHSS 12 points) caused by right posterior cerebral artery thrombosis (RPCAT) after treatment with Cerebrolysin in combination with high dose of aspirin. Within 7 days after the initiation of the treatment regimen, the NIHSS score improved to 3 points and a control MRI that was performed on the 10th day after stroke, showed a significant decrease of the ischemic area and cerebral edema zone. It further might have an evidence that the combination of Cerebrolysin with high-dose aspirin is safe and might have a synergistic effect in the treatment of ischemic stroke.

Keywords: aspirin, cerebrolysin, ischemic stroke, posterior cerebral artery thrombosis

Introduction

Acute ischemic stroke is the second leading cause of death and one of the most common causes of adult disability worldwide.¹ Thrombolytic therapy within 4.5 hours after stroke onset can significantly reduce mortality and morbidity. However, the effect is negligible after 4.5–6 hours and useful for only a small portion of patients. [1] Therefore, many therapeutic strategies have been developed targeting the pathophysiological cascade that starts with ischemia and ultimately leads to irreversible tissue damage. [2] One of the most effective neuroprotective drugs used in the acute phase of ischemic stroke is Cerebrolysin, which consists of low molecular weight peptides and free amino acids and has been shown to exert both neuroprotective and neurotrophic effects. [1–4] A meta-analysis of these studies confirmed the beneficial effect of Cerebrolysin on the early recovery of neurological deficits in patients with acute ischemic stroke. [1,5,6] Acetylsalicylic acid (aspirin) is widely used as secondary preventive drug in stroke therapy. In ischemic stroke, aspirin in high doses of 160–326 mg is used to achieve antithrombotic as well as neuroprotective effects. [7] Antithrombotic treatment is an effective management tool for acute ischemic stroke and early secondary prevention as it reduces the risk of recurrent ischemic stroke with a low risk of hemorrhagic complications. [7] The combination of high doses of aspirin and Cerebrolysin may have a potential effect in cases of ischemic stroke.

Patient Information

A 72-year-old male patient, left-handed, was taken to the hospital by ambulance with complaints of weakness in the left extremities, left-sided visual field loss, speech impairment, nausea, and dizziness which appeared immediately after awakening. The patient had a history of arterial hypertension (grade 2, risk 4) which was not properly controlled by antihypertensive medication. As the exact time of stroke onset was not known, the patient was not eligible for thrombolytic therapy.

Clinical Findings

Upon admission, vital signs showed an increase in blood pressure (180/110 mm Hg), while the heart rate (65 bpm) and the respiration rate (18 per minute) were within normal limits. The neurological examination revealed the following features: transcortical sensory aphasia, left-sided homonymous hemianopia, mild left-sided central facial nerve palsy, moderate dysarthria, left-sided central hypoglossal nerve palsy, mild left-sided hemiparesis (4/5), a pathological Babinski sign on the left, and left-sided hemilateral hemihypesthesia. The NIHSS score was 12 points. The mRS score was 2.

Diagnostic Assessment

The laboratory and instrumental examinations were made after the patient's admission to the neurological unit in order to identify possible causes of the disease, as well as to exclude other pathologies with similar clinical features.

Blood tests revealed relative and absolute monocytosis, absolute basophilia, platelet size decrease, increased levels of total and conjugated bilirubin, an increase in pro-thrombin time as well as an increased fibrinogen level. In addition, an increase in total cholesterol level (6.7 mmol / L) was observed, which, according to the SCORE table for European regions indicates a very high risk of developing fatal cardiovascular diseases for this patient ($\geq 10\%$).⁸

The patient underwent brain magnetic resonance imaging, on which the diffusion restriction zone without clear contours and smoothing of the adjacent furrows was found in the right temporo-occipital region, measuring 30 × 90 × 40 mm (Figure 1).

A focus with similar characteristics was also visualized in the right thalamus. MRI data confirmed the clinically diagnosed cerebral infarction in the RPCAT basin.

Subsequently, the patient underwent ultrasound examination of the brachiocephalic arteries, which revealed stenosis of the bifurcation of the right common carotid artery (30–40%) and the left common carotid artery (30%).

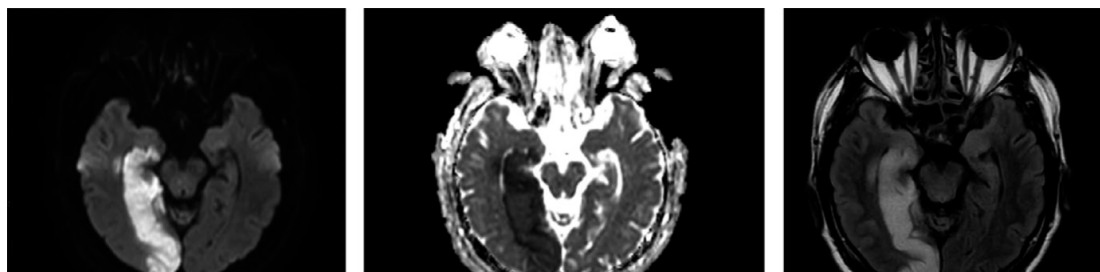


Figure 1: MRI images of the brain in axial projection with an edema and ischemia zone in the right posterior cerebral artery blood supply area.

Therapeutic Intervention

After hospitalization of the patient in the stroke unit, antithrombotic and neuroprotective therapy was initiated: 30ml Cerebrolysin intravenously once daily for 16 days and oral administration of high-dose aspirin (326 mg) once daily for 9 days, followed by low dose Aspirin (75 mg). In addition, the patient received basic stroke therapy in accordance with the AHA-ASA recommendations and the clinical protocol of the Ministry of Health of the Republic of Belarus. For the concomitant hypertension, candesartan (8 mg once daily) and indapamide (2.5 mg once daily) were administered. Due to the fact that the patient has a very high risk of developing fatal cardiovascular diseases, atorvastatin (40 mg once daily) was prescribed to lower cholesterol levels. Furthermore, the patient received gastroprotection, with 20mg pantoprazole once daily during the entire course of treatment.

Follow-up and Outcome Section

Within 7 days after the initiation of the treatment regimen, the NIHSS score improved to 3 points, with remaining signs and symptoms of partial hemianopsia, hemiataxia, and mild central facial nerve palsy. The modified Rankin scale score (mRS) was 1 point. A control MRI was performed on the 10th day after stroke, which indicated a significant decrease of the ischemic area and cerebral edema zone (Figure 2).

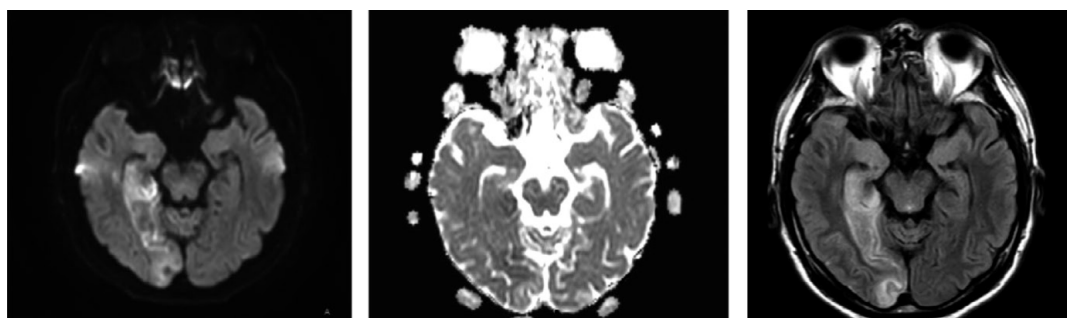


Figure 2: MRI images of the brain in axial view 10 days after stroke.

At the time of the patient's discharge and after the last dose of Cerebrolysin on day 16 after stroke, the neurological status further improved and the residual deficits were limited to a partial left-sided homonymous hemianopsia and a positive pathological Babinski reflex on the left. The NIHSS score further improved to 1 point, mRS score remained at 1 point.

Discussion

This case is an example of a combination widely used: aspirin and the neuroprotective drug Cerebrolysin which can be applied in other similar cases. It further provides evidence that the combination of Cerebrolysin with high-dose aspirin is safe and might have a synergistic effect in the treatment of ischemic stroke.

The clinical effectiveness of Cerebrolysin has repeatedly been demonstrated in randomized double-blind placebo-controlled multicenter studies.[1,2] A meta-analysis confirms previous evidence that Cerebrolysin has a beneficial effect on early global neurological deficits in patients with acute ischemic stroke.[5] These underlying mechanisms of Cerebrolysin are associated with the inhibition of calpain and consequently the stabilization of neuronal cells and with the induction of neuronal sprouting and neurogenesis. It has also been shown to affect a number of signaling pathways including the phosphatidylinositol 3-kinase (PI3)/AKT pathway, the glycogen synthase kinase 3 beta (GSK3 β) pathway, the Sonic hedgehog (Shh) pathway, and other pathways, which are responsible for the formation and maintenance of the blood- brain barrier integrity.[4]

Antithrombotic treatment is an effective management tool for acute ischemic stroke and early secondary prevention as it reduces the risk of recurrent ischemic stroke with a low risk of hemorrhagic complications. This effect is mediated by inhibition of COX-1 in the platelets preventing their adhesion to the vascular wall, as well as by the inhibition of acetylation of coagulation proteins which ultimately increases the rate of fibrinolysis. [7] The neuroprotective effect of aspirin occurs once the blood flow in the thrombosed vessel is restored and is due to its inhibition of COX- 2 in brain tissue, a decrease of NOTCH-1 gene expression as well as IL-6 levels, which downregulates neuroinflammation.[9,10] Furthermore, aspirin has also been shown to interact with the ischemic cascade on the level of glutamate and to significantly decrease its levels post-stroke.[9]

Therefore, the combined treatment of ischemic infarction with the simultaneous use of high-dose aspirin and Cerebrolysin should act synergistically and contribute to a more complete neurological deficit recovery through the combined neuroprotective and neurotrophic effects of both agents. It further provides evidence that the combination of Cerebrolysin with high-dose aspirin is safe and might have a synergistic effect in the treatment of ischemic stroke.

The use of Cerebrolysin in combination with high doses of aspirin may have been the main reason for the almost complete remission of neurological deficit in the patient with moderately severe stroke in the right posterior cerebral artery basin, which clearly justifies the further use of this combination in prospective studies and clinical practice.

CASE SUMMARY



Patient

- 72 years
- Acute ischemic stroke



Challenge

- Moderate stroke with aphasia and hemiparesis



Treatment

- Cerebrolysin 30 mL/day IV × 16 days + high-dose aspirin



Outcome

- NIHSS 12 → 1
- mRS 2 → 1
- Significant reduction of ischemia/edema on MRI



Take Home Message

Cerebrolysin combined with high-dose aspirin (326 mg) was well tolerated and associated with marked neurological improvement, with no clinically significant adverse drug interactions observed.

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...in post-percutaneous coronary intervention after right ACA territory infarction

Abstract

Periprocedural ischemic stroke is an uncommon but potentially devastating complication of coronary angiography and percutaneous coronary intervention (PCI). We describe the case of a 68-year-old man who developed an acute right anterior cerebral artery (ACA) infarction approximately 24 hours after elective coronary stenting. He presented with dense left-sided hemiplegia, with muscle strength graded 0/5 in both the upper and lower limbs, an initial National Institutes of Health Stroke Scale (NIHSS) score of 8, and a modified Rankin Scale (mRS) score of 5. Reperfusion therapy was not pursued following multidisciplinary clinical assessment. Following neurology consultation, the patient was managed conservatively with dual antiplatelet therapy, Cerebrolysin, citicoline, and an early structured physiotherapy program. Serial neurological assessments demonstrated progressive recovery, with complete neurological and functional improvement by day 42 that remained stable at 90-day follow-up. No adverse effects related to Cerebrolysin were observed during treatment. This case highlights the favorable clinical recovery that may be achieved with comprehensive multidisciplinary stroke care and raises interest in the possible adjunctive role of neurotrophic therapy in post-stroke rehabilitation.

Keywords: Periprocedural ischemic stroke, Percutaneous coronary intervention (PCI), Cerebrolysin, Rehabilitation

Introduction

Stroke after cardiac catheterization and PCI is rare, with reported incidence rates ranging from approximately 0.1% to 0.4%, but it remains one of the most serious procedural complications because of its association with significant disability and mortality. [1,2] Proposed mechanisms include thromboembolism from catheter manipulation, embolization of aortic atherosclerotic debris, vascular injury, and procedure-related thrombosis. [1,2]

Management of ischemic stroke in the early post-PCI setting can be particularly complex. Recent arterial access, ongoing antiplatelet therapy, and concerns regarding bleeding risk may influence decisions regarding thrombolytic or endovascular reperfusion therapy. [3]

Cerebrolysin is a peptide-based neurotrophic agent that has been studied as an adjunctive treatment in ischemic stroke recovery. Experimental and clinical studies have suggested possible cerebroprotective and neurorestorative effects through modulation of neuroplasticity, reduction of excitotoxic injury, and support of neuronal survival pathways. [4,5,7] Several clinical trials and meta-analyses have evaluated its potential role in improving neurological recovery after ischemic stroke. [4-6]

We present a case of post-PCI right ACA territory ischemic stroke in a patient who experienced marked neurological recovery following conservative management, early rehabilitation, and administration of Cerebrolysin.

Case Presentation

A 68-year-old man with a history of hypertension, hypothyroidism, chronic smoking, and ischemic heart disease was admitted for elective coronary angiography and percutaneous coronary intervention (PCI). His regular medications included aspirin, candesartan (Atacand), and levothyroxine (Thyroxin). Clopidogrel had been added four days prior to admission in preparation for coronary stent placement. Coronary angiography and PCI were completed successfully without immediate procedural complications.

Approximately 24 hours later, on 3 December 2025, the patient developed sudden weakness affecting the left upper and lower limbs. Neurological examination demonstrated dense left hemiplegia with Medical Research Council (MRC) muscle power graded 0/5 in both limbs. Initial stroke assessment demonstrated a moderate-to-severe neurological deficit, with a National Institutes of Health Stroke Scale (NIHSS) score of 8 and a Modified Rankin Scale (mRS) score of 5, indicating significant functional impairment at presentation. Brain magnetic resonance imaging (MRI) demonstrated an acute ischemic infarction involving the right ACA territory.

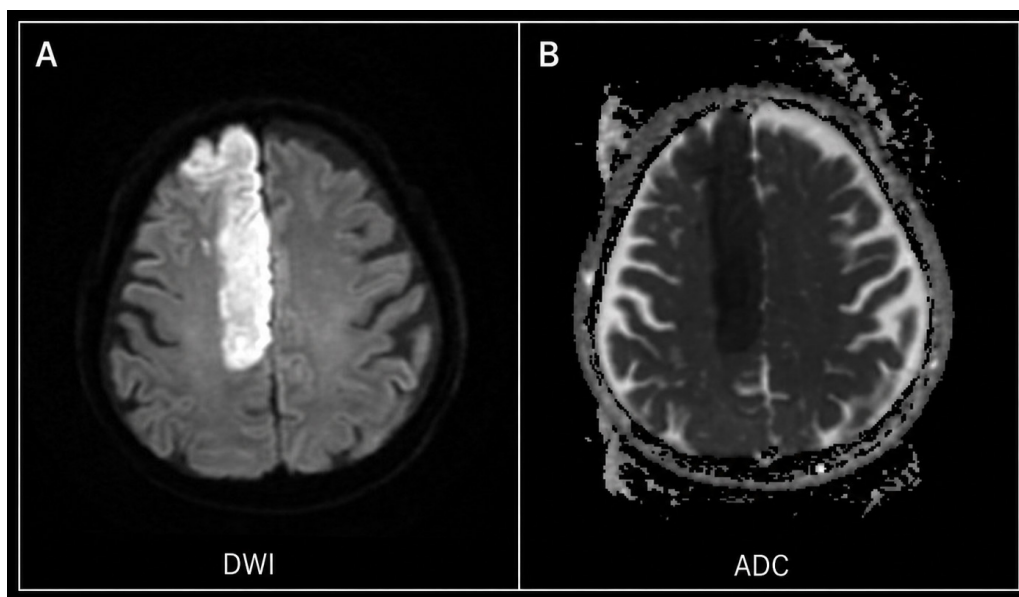


Figure 1: Brain MRI Diffusion-weighted imaging demonstrating an acute infarction involving the medial aspect of the right frontal lobe with hemorrhagic transformation noted (anterior cerebral artery infarction) (A), with the corresponding diffusion restriction on ADC sequences (B).

Based on the temporal relationship to PCI and the patient's vascular risk profile, the stroke was considered most consistent with a catheterization-related embolic ischemic event in the setting of underlying atherosclerotic disease. Blood pressure during the acute phase remained stable at 120/74 mmHg.

The patient was evaluated jointly by the neurology and cardiology teams. Intravenous thrombolysis and endovascular intervention were ultimately not pursued following individualized assessment in the context of recent PCI and ongoing dual antiplatelet therapy. Dual antiplatelet therapy with aspirin and clopidogrel was continued because of the recent coronary stent placement.

On 4 December 2025 (day 1 after stroke onset), Cerebrolysin therapy was initiated at a dose of 30 mL diluted in 250 mL normal saline and administered intravenously over approximately 1.5 to 2 hours daily for 14 consecutive days. This dosing approach has been described in previous stroke studies. [4,5] The patient also received Citicoline (Somazina) for one month, in addition to a structured physiotherapy program that was initiated 48 hours after symptom onset and continued throughout follow-up. No infusion reactions or treatment-related adverse effects were observed during hospitalization.

Clinical Course and Outcomes

By week 1 (9 December 2025), the patient had already demonstrated noticeable neurological improvement. The left arm showed persistent drift, while the left leg demonstrated movement but not yet against gravity. NIHSS improved from 8 to 4, and mRS improved to 4.

At week 2 (14 December 2025), further recovery was observed. The left arm continued to demonstrate mild drift, and the left leg was able to move with some effort against gravity. NIHSS improved further to 3, while mRS remained 4.

At day 42 (11 January 2026), neurological examination showed complete recovery without residual motor deficit. Both NIHSS and mRS scores improved to 0. This full neurological and functional recovery remained stable at 90-day follow-up (24 February 2026).

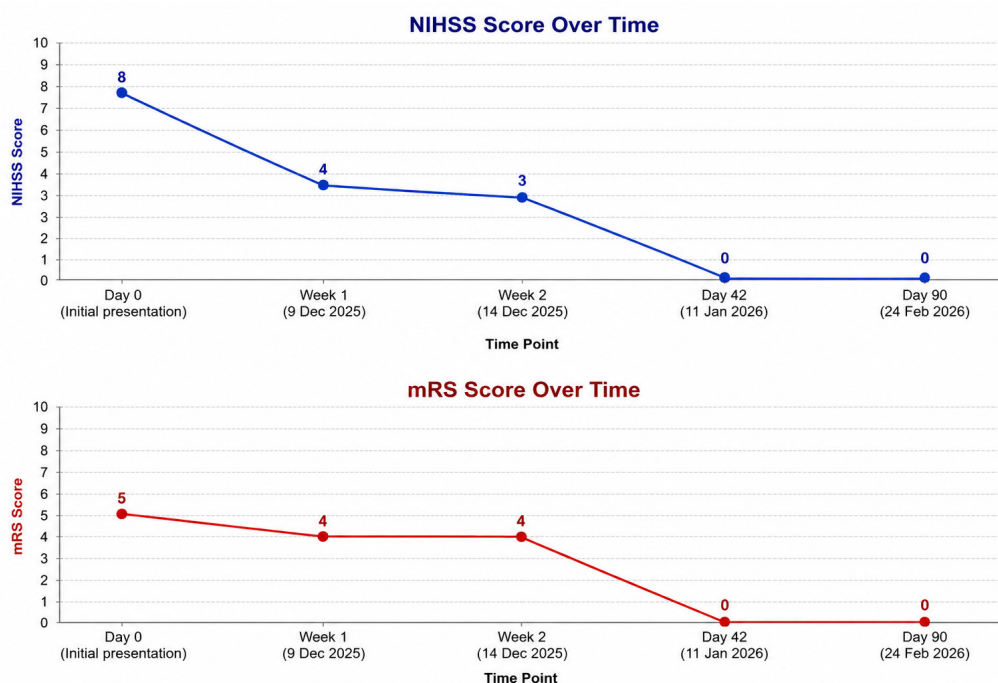


Figure 2: NIHSS Score and mRS Score over time.

Discussion

Periprocedural ischemic stroke remains one of the most concerning complications of coronary catheterization and PCI because of its potential for severe long-term disability and increased mortality. [1,2] The present patient had several recognized vascular risk factors associated with post-catheterization stroke, including advanced age, hypertension, smoking, and diffuse atherosclerotic disease. [1,2]

ACA territory infarctions classically produce contralateral lower-limb-predominant weakness, although larger infarcts may also present with severe hemiparesis and significant functional impairment. [3] Despite presenting with dense hemiplegia and substantial disability at onset, this patient experienced progressive neurological recovery over the following weeks, ultimately achieving complete functional independence.

Cerebrolysin has been evaluated in multiple randomized trials investigating recovery after ischemic stroke. [4-6] In the CARS trial, patients treated with Cerebrolysin in combination with rehabilitation demonstrated improved motor recovery compared with placebo-treated patients undergoing rehabilitation alone. [4] Meta-analyses have also suggested a potentially favorable effect on neurological recovery while maintaining an acceptable safety profile. [5] Proposed mechanisms include cerebroprotection, enhancement of synaptic plasticity, stimulation of neurogenesis, and reduction of secondary neuronal injury. [7]

Although the present case occurred in the setting of a periprocedural stroke following PCI, the potential role of Cerebrolysin is not necessarily limited to this specific clinical context. The proposed cerebroprotective and neurorestorative mechanisms of Cerebrolysin target biological processes involved in ischemic brain injury, including cerebroprotection, neuroplasticity, neurogenesis, and modulation of secondary neuronal damage, which are largely shared across ischemic stroke etiologies. [8]

The exact contribution of Cerebrolysin in this case cannot be determined. Spontaneous neurological recovery, early supportive care, and structured rehabilitation likely all played important roles in the favorable outcome

observed. Nevertheless, the relatively rapid improvement following initiation of therapy was clinically notable. Early physiotherapy may also have contributed substantially to recovery, as timely rehabilitation is recommended to improve functional outcomes after ischemic stroke. [3] While conclusions regarding efficacy cannot be drawn from a single case, this report adds to the existing clinical experience evaluating multimodal approaches to stroke rehabilitation.

Conclusion

We describe a case of right ACA territory ischemic stroke occurring after elective coronary catheterization and PCI in a 68-year-old patient with multiple vascular risk factors.

The patient was managed conservatively with dual antiplatelet therapy, rehabilitation, citicoline, and early Cerebrolysin administration, and he demonstrated complete neurological and functional recovery by day 42, which remained sustained at 90-day follow-up.

Although causality cannot be established from a single case report, this case supports continued investigation into the potential adjunctive role of Cerebrolysin in ischemic stroke recovery.

CASE SUMMARY



Patient

• 68 years • Right ACA territory infarction after periprocedural ischemic stroke



Challenge

• Dense hemiplegia after coronary stenting



Treatment

• Cerebrolysin 30 mL/day IV x 14 days + physiotherapy



Outcome

• NIHSS 8 → 0 • mRS 5 → 0 • Complete recovery by day 42



Take Home Message

Ischemic stroke after PCI is an uncommon but potentially devastating complication requiring rapid multidisciplinary assessment and individualized multimodal management, particularly when standard reperfusion therapies are not feasible.



BENJAMIN WY LO 
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China

...after acute brain injury

Abstract

Cerebrolysin is a peptide-based neurotrophic preparation with neuroprotective and neuroplastic effects that may support recovery after acute brain injury. We present two institutional cases illustrating its use as an adjunct to intensive neurocritical care and rehabilitation. The first case involved a 64-year-old woman with severe traumatic brain injury after a fall, requiring decompressive craniectomy and ventriculostomy, followed by a 14-day Cerebrolysin course. At 3 months, she was ambulatory with a stick and functionally near-independent (Modified Barthel Index 91/100). The second case involved a 60-year-old man with acute right M1 occlusion treated with thrombolysis and thrombectomy, followed by a 3-week Cerebrolysin course. At 8 months, he was ambulatory with a quadripod, cognitively preserved (HK-MOCA 26/30), and functionally improving (FIM 75/100). These cases highlight favorable recovery trajectories after severe neurological injury when Cerebrolysin is incorporated into multidisciplinary neurorehabilitation pathways.

Keywords: Cerebrolysin, traumatic brain injury, ischemic stroke, neurorehabilitation, thrombectomy, craniectomy

Introduction

Cerebrolysin is a peptide-based neurotrophic preparation shown to mitigate secondary neuronal injury through modulation of neuroinflammation, enhancement of neuronal survival, promotion of synaptogenesis, and support of cerebral plasticity [1, 2]. Clinical evidence supports its use as an adjunct to rehabilitation after stroke. The CARS trial demonstrated improved upper-extremity motor recovery when Cerebrolysin was combined with standard rehabilitation [3], while the ESCAS study reported improved verbal recovery when paired with speech therapy [4]. Current European Academy of Neurology guidelines recommend Cerebrolysin as an add-on therapy to standard early rehabilitation after acute ischemic stroke [5].

This report presents two institutional cases—one traumatic brain injury and one ischemic stroke—illustrating meaningful functional recovery after integration of Cerebrolysin into neurocritical care and rehabilitation pathways.

Case 1: Traumatic Brain Injury

A 64-year-old woman was admitted to Queen Mary Hospital on 10 June 2025 after falling down four steps and striking her forehead. On admission, her Glasgow Coma Scale (GCS) score was 14. Cranial CT demonstrated right frontal and left temporal contusions, traumatic subarachnoid hemorrhage, subdural hematoma, and non-depressed left linear skull and middle fossa skull base fractures.

Her neurological status deteriorated over the following 48 hours, with GCS declining to E2V2M5, prompting decompressive craniectomy and ventriculostomy on 12 June 2025. She was managed in the neurosurgical intensive care unit and received a 14-day course of Cerebrolysin as adjunctive neurorecovery support.

Subsequently, she underwent cranioplasty on 12 September 2025. At 3 months post-injury, the patient had achieved substantial recovery. She was able to walk with a stick, perform activities of daily living with only standby or mild assistance, and reached a Modified Barthel Index of 91/100, indicating near independence.

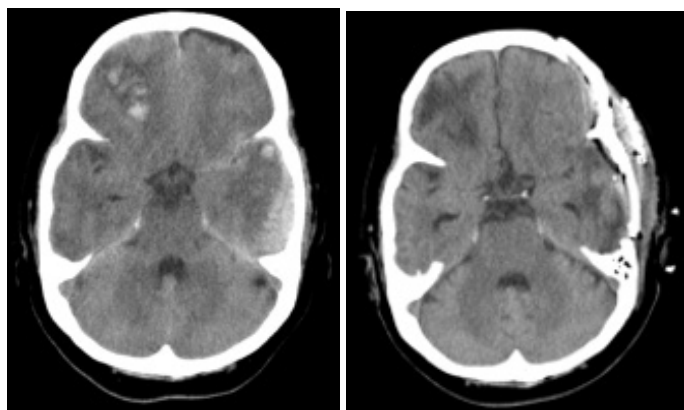


Figure 1: Cranial CT findings in Case 1 (traumatic brain injury).

Case 2: Acute Ischemic Stroke

A 60-year-old man was admitted through Queen Mary Hospital's Green Channel stroke service on 21 December 2024 after returning from Mainland China with sudden onset left hemiplegia and hemineglect.

Initial imaging confirmed right M1 middle cerebral artery occlusion, with NIHSS 16 and ASPECTS 9. Intravenous thrombolysis was administered, followed by successful intra-arterial thrombectomy with complete reperfusion (TICI 3) performed 5.5 hours after symptom onset.

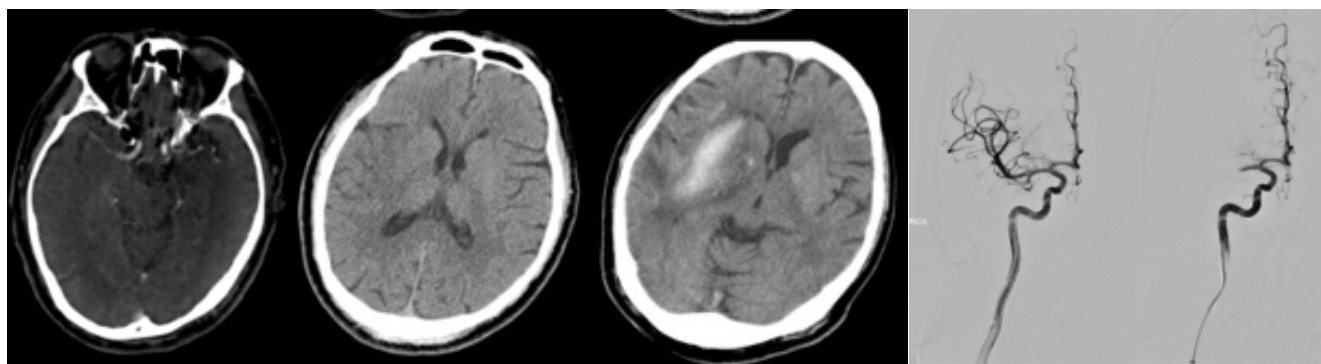


Figure 2: Acute imaging findings and post-treatment imaging in Case 2 (acute ischemic stroke).

Post-procedural CT showed right putaminal reperfusion injury, and the patient was managed in the neurosurgical ICU. The putamen is a structure located deep within the brain's basal ganglia, highly sensitive to changes in oxygen and blood flow. A 3-week course of Cerebrolysin was administered during the acute recovery phase. He subsequently entered an intensive rehabilitation pathway that included conventional therapy and robotic rehabilitation for left hemiparesis.

At 8 months post-stroke, the patient was able to walk with a quadripod, with progressive improvement in left-sided motor deficits. Cognitive screening showed preserved cognition with HK-MOCA 26/30, and functional assessment demonstrated continued recovery with FIM 75/100.

Follow-Up Outcomes

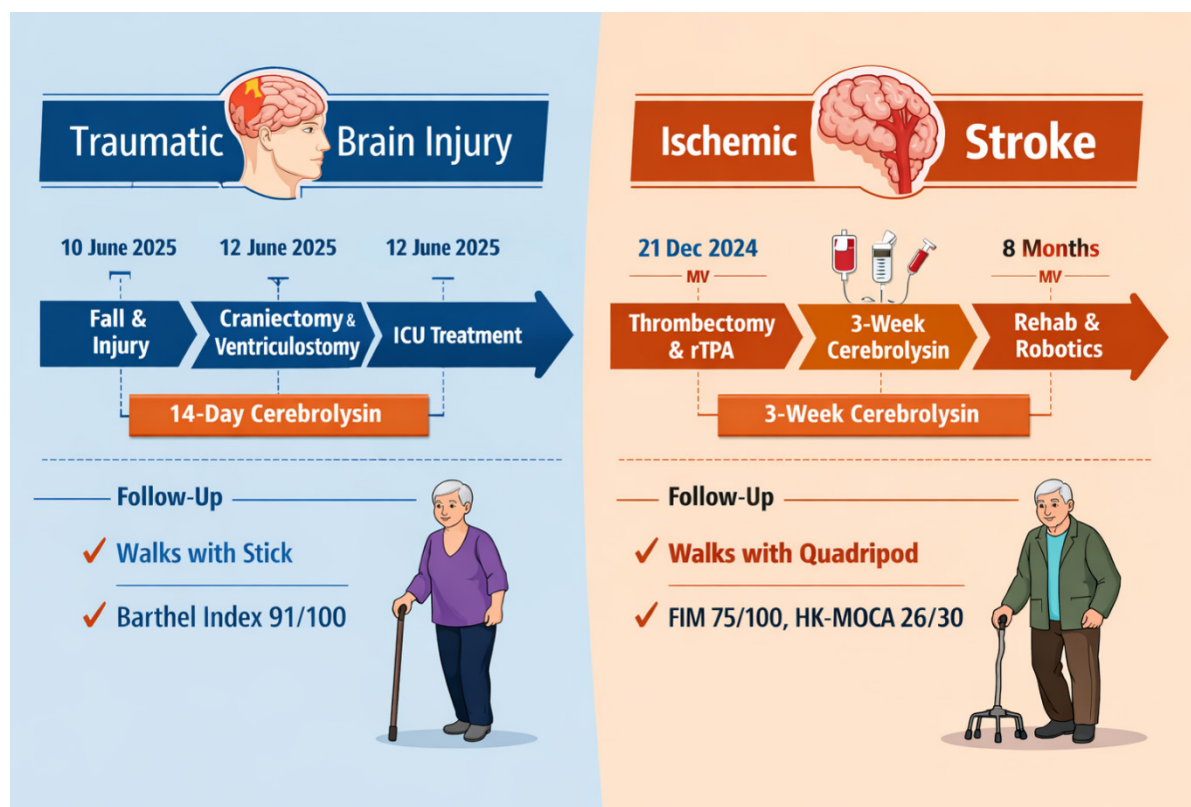


Figure 3: Clinical timeline and follow-up overview of the two reported cases.

Discussion

These two institutional cases demonstrate meaningful recovery trajectories after severe acute brain injury when Cerebrolysin is integrated into multidisciplinary neurocritical care and rehabilitation.

The first case is notable for the degree of functional recovery achieved after multicompart ment traumatic brain injury requiring decompressive surgery. Despite initial neurological deterioration, the patient progressed to near-independent ambulation and self-care within three months.

The second case illustrates substantial recovery after large vessel occlusion stroke, despite severe initial deficits and reperfusion injury. Early reperfusion therapy restored cerebral blood flow, while adjunctive Cerebrolysin may have supported neuronal recovery during the vulnerable post-ischemic period. The favorable cognitive and motor outcomes at 8 months suggest effective integration of pharmacological neurorecovery support with advanced rehabilitation technologies, including robotic therapy.

Although causal attribution cannot be established in a case series, both patients showed recovery trajectories exceeding what is often expected after the severity of their initial presentations. These cases support the concept that Cerebrolysin may be a valuable adjunct within structured neurorehabilitation pathways across different forms of acquired brain injury.

Conclusion

This two-patient case series demonstrates favorable long-term functional recovery after severe traumatic brain injury and large vessel ischemic stroke when Cerebrolysin was incorporated into acute neurocritical care and multidisciplinary rehabilitation. These institutional experiences support further use and study of Cerebrolysin as an adjunctive neurorecovery strategy in both traumatic and vascular brain injury.

CASE SUMMARY

 Patient • 64 years • Severe TBI	 Patient • 60 years • Right M1 occlusion stroke
 Challenge • Neurological deterioration requiring craniectomy	 Challenge • Severe hemiplegia and hemineglect
 Treatment • Cerebrolysin 30 mL/day IV x 14 days + neurocritical care	 Treatment • Cerebrolysin 30 mL/day IV x 21 days + IVT + EVT
 Outcome • BI 91 • walks with stick	 Outcome • MoCA 26 • FIM 75 • walks with quadripod
 Take Home Message Favorable recovery is feasible after severe TBI and severe AIS when Cerebrolysin is integrated as an adjunct into multidisciplinary neurocritical care and rehabilitation.	



ROMANY HOSNI GABRA



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...in metabolic emergencies due to high-temperature zone exposure

Abstract

Heat exposure and dehydration may contribute to ischemic stroke risk, particularly in vulnerable older adults with vascular and metabolic comorbidities. We report the case of a 65-year-old man from Upper Egypt, a region characterized by prolonged high ambient temperatures, who presented 96 hours after sudden onset of impaired consciousness and left-sided weakness. Initial brain computed tomography (CT) was unremarkable despite severe neurological deficits, including Glasgow Coma Scale (GCS) score of 8/15, left hemiplegia, and left upper motor neuron facial weakness. Diagnostic work-up showed no hemorrhage, no early visible infarction, no carotid plaques, and no atrial fibrillation on electrocardiography. Clinical suspicion favored acute ischemic stroke in the setting of dehydration, hypertension, diabetes, and likely low-flow cerebral hypoperfusion.

The patient was treated conservatively because he was outside the reperfusion window. Management included dual antiplatelet therapy, cautious intravenous hydration, glycemic control, physiotherapy, and adjunctive Cerebrolysin 30 mL daily for 7 days. By discharge, GCS improved to 13/15, motor deficits regressed substantially, and follow-up CT demonstrated a right parietal hypodense infarct corresponding to the clinical syndrome. At short-term follow-up, the patient was ambulatory with mild support. This case highlights the importance of recognizing dehydration and environmental heat as potentially modifiable contributors to stroke in climate-stressed regions and illustrates the value of structured supportive neurorecovery strategies.

Keywords: ischemic stroke; dehydration; heat exposure; Cerebrolysin; neurorecovery;

Introduction

Stroke remains a major cause of disability and mortality in low- and middle-income countries. In Upper Egypt, prolonged periods of high temperature may increase the burden of dehydration, hemoconcentration, metabolic instability, and systemic hypoperfusion, all of which may precipitate ischemic cerebrovascular events in susceptible individuals. This risk may be amplified in older adults with hypertension and diabetes mellitus. The present report describes a delayed-presenting ischemic stroke in a patient from a high-temperature climate region whose initial CT was negative despite severe focal deficits. The case is presented in accordance with the CARE reporting guideline, with emphasis on diagnostic evolution, conservative acute management, and early neurorecovery.

Patient Information

A 65-year-old man presented to the emergency department of Assiut University Hospital with a 4-day history of sudden impaired consciousness and left-sided weakness. He had a history of moderately controlled hypertension treated with ramipril 2.5 mg daily and recently diagnosed type 2 diabetes mellitus controlled on metformin 1000 mg/day. No previous stroke, malignancy, atrial fibrillation, or other major debilitating illness

was reported.

The history obtained from relatives suggested recent exposure to hot weather conditions with insufficient fluid intake before symptom onset, raising suspicion of dehydration as a precipitating factor.

Clinical Findings

On admission, blood pressure was 155/90 mmHg and random blood glucose was 180 mg/dL. Neurological examination revealed marked impairment of consciousness with GCS 8/15, complete left hemiplegia, and left upper motor neuron facial weakness. The presentation was highly suggestive of right hemispheric acute ischemic stroke.

Timeline

Table 1: Clinical timeline and therapeutic interventions from symptom onset to follow-up.

Time point	Clinical event
96 hours before admission	Sudden impaired consciousness and left hemiparesis progressing to hemiplegia
Day 0	Admission, negative initial CT, supportive stroke management initiated
Days 1–7	Dual antiplatelet therapy, hydration, glycemic optimization, Cerebrolysin, physiotherapy
Day 5	Initiation of assisted mobilization and range-of-motion exercises
Day 7	Clinical improvement; repeat CT showed right parietal hypodensity
1 month	Continued outpatient neurorecovery treatment and follow-up

Diagnostic Assessment

The differential diagnosis at presentation included acute ischemic stroke with delayed radiological visibility, metabolic encephalopathy, postictal deficit, and less likely intracranial hemorrhage. The severe focal neurological syndrome strongly supported a vascular event.

Routine laboratory investigations were within acceptable limits apart from mild hyperglycemia. Electrocardiography showed no atrial fibrillation. Carotid duplex ultrasonography demonstrated no significant plaques or hemodynamically relevant stenosis. No evidence suggested tumor, infection, or another structural brain lesion.

The initial CT being negative despite profound deficits was interpreted as consistent with either an early ischemic lesion below CT sensitivity or delayed radiographic evolution. Repeat CT after 7 days demonstrated a rightparietal hypodense area, confirming ischemic infarction and matching the patient’s left-sided deficits.

Therapeutic Intervention

Because the patient presented well beyond the thrombolysis and thrombectomy windows, conservative stroke management was pursued.

Treatment included aspirin 162 mg once daily plus clopidogrel 75 mg once daily. Careful intravenous hydration was initiated with 250 mL normal saline/day and 250 mL of 5% glucose/day, with attention to avoid fluid overload. During hospitalization, glycemic control was optimized using short-acting insulin, later transitioned back to oral therapy under diabetology follow-up.

As an adjunctive neurorecovery strategy, Cerebrolysin 30 mL intravenous infusion once daily was administered for 7 days. Piracetam 1200 mg/day intravenously was also prescribed. Physiotherapy focusing on passive range-of-motion exercises began early and progressed to assisted mobilization from day 5 onward.

After discharge, the patient continued rehabilitation and received weekly Cerebrolysin 25 mL intravenous infusions for 1 month as part of the local neurorecovery protocol.

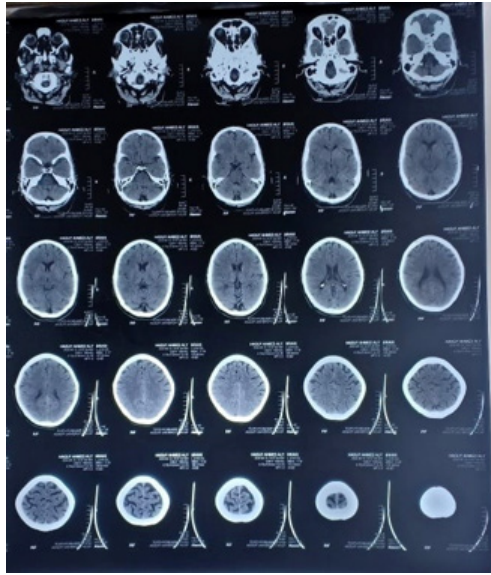


Figure 1: Initial non-contrast CT brain showed no hemorrhage and no clearly visible acute infarction. Given the environmental context, age, diabetes, and presumed inadequate hydration, the most likely mechanism was low-flow ischemia or dehydration-associated cerebral hypoperfusion superimposed on chronic vascular risk factors.

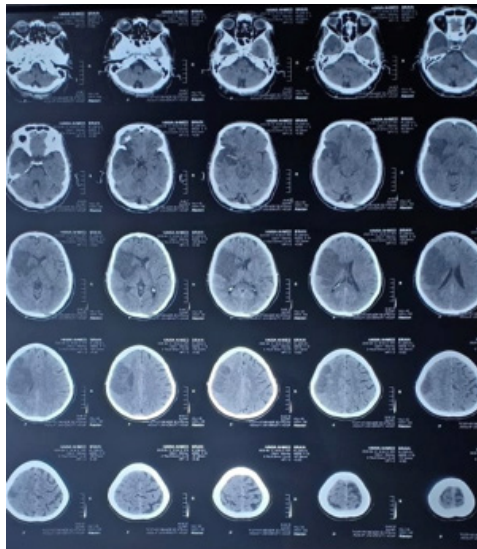


Figure 2: CT at the time of discharge with hypodense area and resolution of most symptoms

Follow-up and Outcomes

Clinical recovery was notable within the first week. By discharge, the patient's GCS improved from 8/15 to 13/15. Motor recovery progressed from complete left hemiplegia to the ability to walk with mild support. Facial weakness and overall responsiveness also improved.

The repeat CT on day 7 confirmed a right parietal infarct, while the clinical trajectory suggested substantial salvage of functionally impaired but viable tissue (Figure 2).

Planned follow-up included serial neurological assessment, risk-factor optimization, diabetic monitoring, and repeat CT every 90 days during the first year. According to the patient and family, functional recovery continued over subsequent follow-up visits.

Discussion

This case illustrates several clinically relevant themes in neurorecovery-oriented stroke care. First, dehydration and heat exposure may act as underrecognized triggers of ischemic stroke in regions with extreme climate conditions. In Upper Egypt, sustained high temperatures, excessive sweating, and inadequate fluid intake may promote hemoconcentration, endothelial dysfunction, and reduced cerebral perfusion, especially in older adults with hypertension and diabetes.

Second, the case demonstrates the well-recognized mismatch between early CT findings and clinical syndrome. A normal initial CT does not exclude ischemic stroke, particularly in delayed or small cortical infarctions, and repeat imaging remains essential when clinical suspicion is high.

Third, the favorable recovery observed here likely reflects a combination of factors: preserved collateral circulation, cautious rehydration, metabolic stabilization, antiplatelet treatment, and early mobilization. The adjunctive use of Cerebrolysin was incorporated as part of the neurorecovery protocol to support neuroplasticity, reduce secondary neuronal injury, and enhance functional restoration. Although causality cannot be established in a single case, the temporal association between treatment initiation and rapid neurological improvement is clinically noteworthy.

The case also supports the concept that climate-related metabolic stressors may produce stroke syndromes indistinguishable from other ischemic mechanisms. Therefore, clinicians working in hot environments should actively evaluate hydration status, renal perfusion, glycemic control, and recent environmental exposure when managing cryptogenic or low-flow stroke presentations.

The main limitation of this report is the absence of magnetic resonance imaging and perfusion-based vascular characterization, which would have better defined lesion timing and mechanism. Nevertheless, the clear clinikoradiological evolution and functional recovery make the case valuable for educational neurorecovery literature.

Conclusion

Dehydration and heat exposure can trigger ischemic stroke in vulnerable adults, even with initially normal imaging. Prompt supportive care, metabolic optimization, and early neurorehabilitation can yield substantial recovery, underscoring the need for awareness in climate-stressed regions.

Patient Perspective

The patient and family expressed satisfaction with the recovery trajectory, particularly the regained ability to walk with mild assistance after severe initial deficits. They agreed to long-term monitoring and preventive follow-up.

CASE SUMMARY	
 Patient	• 65 years • Acute Ischemic Stroke
 Challenge	• Impaired consciousness and hemiplegia
 Treatment	• Cerebrolysin 30 mL/day IV x 7 days + Piracetam + Physiotherapy
 Outcome	• GCS 8 → 13 • Hemiplegia markedly improved
 Take Home Message	Heat-related dehydration is a modifiable risk factor for stroke that underscores the importance of early metabolic optimization to prevent or limit secondary neurological injury.



VIEN C LE 

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...with intra-arterial infusion of autologous bone marrow mononuclear cells

Abstract

We present a patient with severe middle cerebral artery occlusion who received an intra-arterial infusion of autologous bone marrow stem cells combined with Cerebrolysin IV. The patient was evaluated before and after treatment using the National Institutes of Health Stroke Scale, the Medical Research Council Muscle Scale, Modified Brunnstrom Classification, Barthel Index and modified Rankin Scale. After the therapy, the patient showed good outcome with functional as well as neurological improvements especially in terms of functional motor recovery without any side effects. Further controlled studies are needed to find possible side effects and establish net efficacy.

Keywords: Stem cell therapy, cerebrolysin, ischemic stroke

Introduction

Ischemic stroke, of all strokes, is a major cause of serious long-term disability and the therapeutic efficacy of medical treatment is usually very limited.¹ In particular, large middle cerebral artery (MCA) infarction poses an increased risk of mortality (by 17%) and severe disability (by 50%) compared to other infarcts.² One of the most encouraging innovative treatment options is restorative therapy using stem cell replacement in the injured cerebral tissues. Although evidence of the beneficial effects of stem cells in animal stroke models is growing, there is a lack of clinical data.³⁻⁵

Cerebrolysin is a neuropeptide preparation with neuro-protective and neurorestorative effects. In stroke patients with severe motor impairment, patients receiving intravenous infusions of Cerebrolysin had significantly better improvements in motor function compared with those who do not receive Cerebrolysin.⁶ This case report presents the good outcome of a patient with MCA occlusion after intra-arterial infusion of autologous bone marrow stem cell (BMSC) combined with Cerebrolysin.

Case Report

A 58-year-old man with a medical history of hypertension and hyperlipidemia was admitted to our stroke center 1 day after a sudden left-sided weakness and facial drooping. Physical examination showed clouding of consciousness, hemineglect and left-sided hemiparesis. The initial NIHSS score⁷ was 17. He was bedridden and required constant nursing care and attention, corresponding with modified Rankin Scale (mRS) of 5. Head magnetic resonance imaging (MRI) on day 14 after stroke onset (pre-therapy) showed a large hyperintensity lesion on diffusion-weighted imaging (DWI; Figure 1(d)) and hypointensity on the apparent diffusion coefficient (ADC) image (Figure 1(e)) in the right hemisphere consistent with an acute infarct.

Magnetic resonance (MR) angiography revealed occlusion at the M1 segment of the right MCA (Figure 1(f)). Patient received medical treatment according to the American Heart Association and the American Stroke Association (AHA/ASA) stroke guideline.

In total, 14 days after stroke onset, the patient still showed severe disability: left-sided hemiparesis (upper extremity: MRC grade 1; lower extremity: MRC Grade 2)^{8,9} and there was no movement in the patient's hands and fingers (MBC Grade 1).^{10,11} The patient was not able to sit on the bed and required constant nursing care (mRS 5).¹² He still had unilateral neglect and some symptoms of right hemispheric damage. The patient scored 12 on the NIHSS and 10 on the Barthel Index (BI) scales.

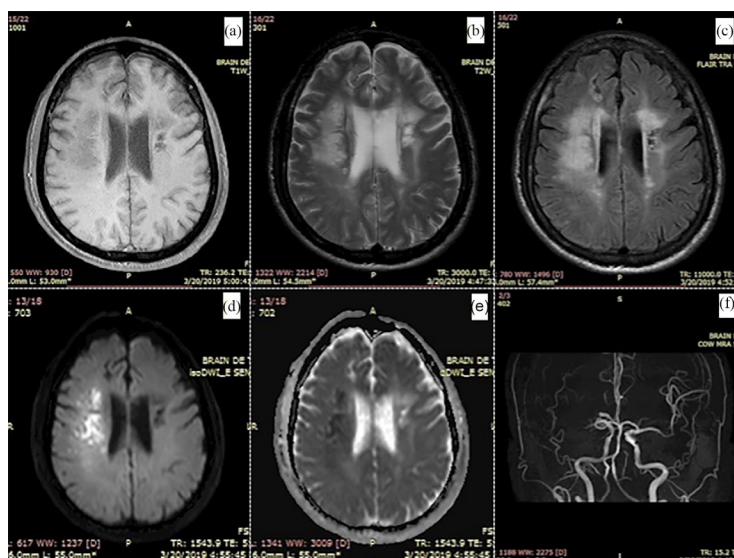


Figure 1: Head MRI at day 14 from stroke onset (pre-therapy) showed a large hyperintensity lesion on DWI (d), T2W (b), T2FLAIR (c) images and hypointensity on ADC (e), T1W (a) images in the right hemisphere. MR angiography revealed occlusion at the M1 segment of the right MCA (f).

We decided to offer the patient the following treatment:

- Intra-arterial infusion of 1×10^6 autologous bone marrow mononuclear cells (BMMCs), infused through the internal carotid artery, using digital sub-traction angiography;
- A 10-day treatment course with daily intravenous infusion of 20 mL of Cerebrolysin, repeated every month for the first 6 months after the stroke.

After infusion of BMMCs, the patient was evaluated every hour for the first 24 h for vital signs, any neurological deterioration as well as anaphylactic reactions, and then every day for the following week. The patient was discharged on day 28.

Table 1: NIHSS, MRC grade, BI and mRS score over time.

Scale	Baseline	Day 14 (Pre-therapy)	Day 45	Day 105	Day 195
NIHSS (all items)	17	12	4	3	3
MRC grade (upper extremity)	-	1	5	5	5
MRC grade (lower extremity)	-	2	5	5	5
MBC (hand)	-	1	5	5	5
Barthel index	-	10	75	90	90
mRS	-	5	3	2	2

BI: Barthel Index;13 MBC: Modified Brunnstrom Classification;10,11 MRC: Medical Research Council;8,9 mRS: modified Rankin Scale;12 NIHSS: National Institutes of Health Stroke Scale.7

On day 45 after stroke, which corresponds to day 30 after infusion of BMMCs and initiation of Cerebrolysin treatment, the patient showed remarkable improvements, in particular, in terms of motor function recovery. Motor strength was 5/5 for both upper and lower extremities, and the patient was able to walk without assistance. He had regained motor function in his hands and fingers almost completely and was able to hold objects in his hand (MBC 5). However, certain neurological sequelae could be observed, such as facial palsy, dysarthria and neglect—corresponding to an NIHSS score of 4. The patient required help with certain daily

activities, such as showering and climbing stairs, and also had cognitive deficits, corresponding to an mRS of 3 and a BI score of 75 (Table 1).

On day 105, corresponding to day 90 after initiation of BMMC and Cerebrolysin treatment, further improvements were observed, especially in terms of cognitive function. The patient was able to carry out daily activities corresponding to an mRS of 2 and a BI score of 90. The patient still had some remaining signs of cognitive decline resembling mild cognitive impairment (MCI), neglect and facial paralysis. The NIHSS score was 3 (Table 1).

At the final examination on day 195 (day 180 after therapy), no further improvement could be observed. The patient was stable, with assessment scales remaining the same as on day 105 (NIHSS 3, mRS 2 and BI 90; Table 1). Head MRI showed a hypointense lesion on DWI and hyperintense lesion on ADC, with the dimensions of 23 × 53 × 20 mm (Figure 2), having reduced in size compared to day 14 (30 mm × 55 mm × 25 mm; Figure 1). During and after using this therapy, we found no adverse effects, which are related to the techniques as well as cell therapy. Study testing disclosed no safety concerns. Serial physical exams and blood testing did not disclose any significant findings.

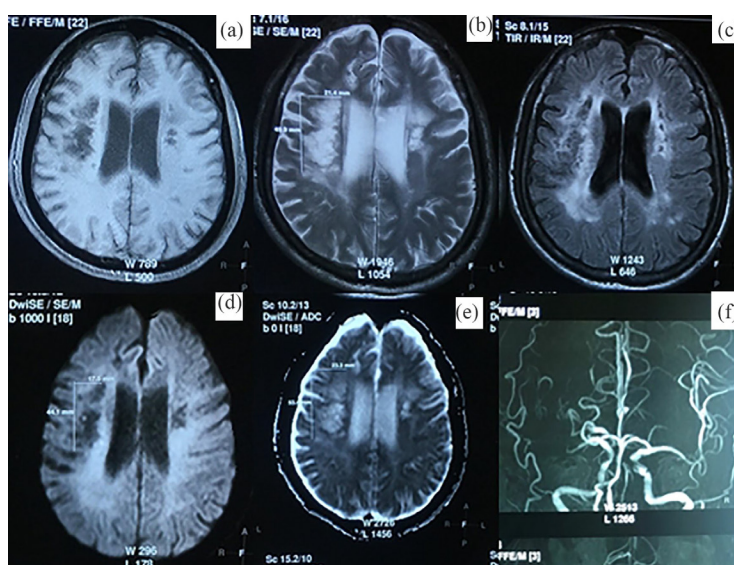


Figure 2: Head MRI at day 195 from stroke onset (6 months after therapy) showed a large hyperintensity lesion on ADC (e), T2 W (b), T2FLAIR (c) images and hypointensity on DWI (d), T1 W (a) images in the right hemisphere. MR angiography revealed occlusion at the M1 segment of the right MCA (f).

Discussion

Normally, the prognosis of patients with a large MCA infarction is very poor. Even with the current optimal medical treatment, MCA infarction may lead to death in 17% of cases, and survivors frequently suffer from long-term severe disability (50%), especially in the motor and speech function.² Unfortunately, the survivors have no effective treatment available other than neurorehabilitation in order to improve neurological functions. In recent years, steady progress in the clinical applications of regenerative medicine has occurred for a variety of diseases. Cell transplantation has emerged as a promising treatment for stroke recovery. Depending on this approach, we have decided to use this new therapy for patient.

In our case study, BMSCs were infused for patient at day 17 from the onset corresponding to subacute stage of cerebral infarction. We selected this time window upon revision of preclinical trials and clinical trials.^{5,14} Also, stroke patients are liable for deterioration in early days either by the effect of cerebral edema or hemorrhagic transformation. Finally, some patients with ischemic stroke have spontaneous recovery, therefore, we selected the subacute stage to be sure that the patient has stable deficit due to ischemic stroke.

After the therapy, the patient showed remarkable outcome. His improvements manifested most clearly in terms of motor function, especially the recovery of the motor function in the hand. It is well known that the

recovery of motor function in upper extremities, particularly in the hand, is harder to achieve compared to in lower extremities due to its complex structure, specialized functions.¹⁵ Jang et al. investigated the motor outcomes in 23 patients with a complete middle cerebral artery territory infarct, about 70% of these patients were able to walk independently after 3–6 months, but no patient achieved functional hand recovery.¹⁰

As mentioned earlier, while many treatment methods have been developed, there is a lack of effective therapies that can facilitate the recovery of patients from subacute phase post-stroke, and rehabilitation is the only method that is known to contribute to the functional recovery. Several rehabilitation measures, such as robotic rehabilitation therapy and mirror therapy, have been reported to be effective in improving hand function of stroke survivors with severe sequelae.^{16,17} Apart from their individual impact, research shows that exercise enhances the effect of stem cells by helping the mobilization of local stem cells and encouraging angiogenesis. Hence, the concept of neuroregenerative rehabilitation therapy (NRRT) is becoming a potential research direction in the hope of finding a more effective approach to treat stroke sequelae.¹⁸

In terms of the safety of the therapy, patient was closely followed during and after the treatment (6 months), no side effect was noted. We chose autologous BMSCs for treatment because they are easily accessible through the aspiration of the bone marrow, can be isolated from patients themselves thereby bypassing the ethical problems and can easily be administered to the patients for autotransplantation. Furthermore, some studies have demonstrated the safety and advantages of this kind of stem cell.^{4,5} We referred to the dose of BMSCs based on a number of previous studies and the results of these studies showed that they did not find any dose-response association, raising doubt about cause and effect relationship between BMSCs and outcome.^{4,5} Previous research has shown that Cerebrolysin is safe and has positive effects on neurorecovery after various types of brain lesions such as ischemic stroke and brain trauma.^{6,19–21}

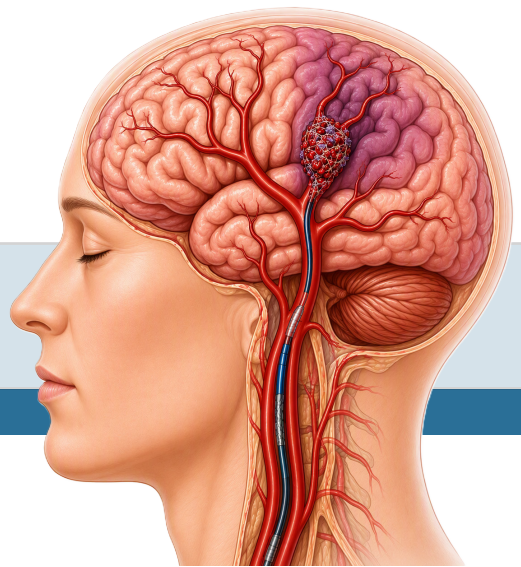
Conclusion

In conclusion, intra-arterial infusion of BMSCs combined with long-term concomitant treatment of Cerebrolysin over 6 months appeared to be safe therapy without adverse effects in our case. Functional and neurological improvement, especially in terms of functional motor recovery, were initially observed in this patient who initially had a very poor prognosis due to the MCA occlusion. To corroborate our findings, larger and controlled clinical studies should be initiated to further investigate the efficacy and safety of BMSCs therapy combined with Cerebrolysin in the treatment of disability in ischemic stroke.

CASE SUMMARY	
 Patient	• 58 years • Large MCA infarction (M1 occlusion)
 Challenge	• Severe disability, bedridden, neglect and hemiparesis
 Treatment	• Cerebrolysin 20 mL/day IV x 10 days (repeated monthly for the first 6 months after the stroke) + autologous bone marrow cell infusion
 Outcome	• NIHSS 12 → 3 • mRS 5 → 2 • BI 10 → 90
 Take Home Message	In large MCA infarction, combining autologous bone marrow-derived cell therapy with Cerebrolysin may offer a promising restorative approach beyond standard care, with substantial functional improvement and no treatment-related adverse effects observed in this case.

CERECAP Program

Cerebrolysin **RE**canalization **A**nd **P**erfusion





NATAN BORNSTEIN 

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INTRODUCTION

The role of Cerebrolysin as adjunct treatment...

The introduction of intravenous thrombolysis and mechanical thrombectomy has revolutionized the treatment of acute ischemic stroke. For many patients, timely recanalization offers the best opportunity to salvage threatened brain tissue and improve functional outcomes. Yet, despite successful restoration of blood flow, a considerable proportion of patients fail to achieve the recovery expected from technically successful reperfusion. This discrepancy has shifted attention from reopening the occluded artery alone to preserving the integrity of the neurovascular unit, the downstream microcirculation and protecting the brain throughout ischemic injury, reperfusion, and subsequent recovery.

Among the determinants of successful recovery, the blood–brain barrier (BBB) has emerged as a critical therapeutic target. Ischemia disrupts the BBB, leading to increased vascular permeability, inflammatory cell infiltration, cerebral edema, and hemorrhagic transformation. Although recanalization restores perfusion, it does not immediately reverse these pathological processes and may, in some circumstances, aggravate tissue injury through reperfusion-associated oxidative stress, inflammation, and further disruption of the neurovascular unit. Consequently, BBB dysfunction and the complex pathophysiological processes associated with reperfusion injury are increasingly recognized as important contributors to futile reperfusion.

These concepts have also been highlighted in a recent publication in the *Journal of Stroke and Cerebrovascular Diseases*, which discusses the need to complement successful recanalization with therapeutic strategies addressing the biological consequences of ischemia and reperfusion.¹ Such considerations have stimulated interest in adjunctive therapies that stabilize the neurovascular unit while supporting neuronal survival and repair. Cerebrolysin is a multimodal neurobiological agent with anti-inflammatory, anti-excitotoxic, antioxidant, and anti-apoptotic properties. Its broad mechanistic profile suggests that it may have the potential to attenuate several components of reperfusion injury, including oxidative stress, inflammatory activation, and BBB disruption. Experimental and emerging clinical evidence further suggests that Cerebrolysin may preserve BBB integrity, potentially limiting vascular leakage, cerebral edema, and hemorrhagic transformation after reperfusion. By preserving the neurovascular environment, Cerebrolysin may also facilitate neuroplasticity during post-stroke recovery.

The patients presented in this chapter all underwent successful evidence-based reperfusion treatment with intravenous thrombolysis, mechanical thrombectomy, or both. Nevertheless, their treating physicians recognized that restoring cerebral blood flow is only one component of optimal stroke management. In these cases, Cerebrolysin was introduced as adjunctive therapy with the aim of supporting the neurovascular unit and potentially addressing pathological mechanisms associated with ischemia and reperfusion injury, while promoting recovery following recanalization. While these observations cannot replace evidence from randomized clinical trials, they illustrate the practical application of a multimodal cerebroprotective strategy alongside current standards of acute stroke care.



ALEX CHANG

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...in the management of MCA re-occlusion after EVT resulting in divergent outcomes

Abstract

Background: Hemorrhagic transformation and incomplete clinical recovery remain important limitations after endovascular thrombectomy (EVT), even when angiographic reperfusion is successful. Adjunctive cerebroprotective treatment strategies have been applied, while achieving conclusive evidence remains under investigation.

Case presentation: A 63-year-old woman with vascular risk factors and suspected atrial fibrillation experienced two contralateral middle cerebral artery (MCA) occlusion strokes within approximately 3 months. During the first episode, EVT failed to achieve immediate angiographic reperfusion, but the patient subsequently recovered with good functional outcome. During the second episode, near-complete reperfusion was achieved after EVT, but the patient developed severe hemorrhagic deterioration and ultimately died. The two events differed in adjunctive post-EVT management.

Conclusion: This same-patient case illustrates divergent outcomes after two MCA occlusion episodes treated with EVT. The observation does not establish causality, but supports further investigation of adjunctive neuroprotection after EVT in high-risk cardioembolic MCA infarction.

Keywords: acute ischemic stroke; endovascular thrombectomy; Cerebrolysin; atrial fibrillation; hemorrhagic transformation; reperfusion injury

Introduction

Endovascular thrombectomy (EVT) is the standard treatment for acute ischemic stroke caused by anterior-circulation large-vessel occlusion. Although successful reperfusion improves functional outcomes, angiographic success does not always translate into neurological recovery. Reperfusion injury, blood–brain barrier disruption, hemorrhagic transformation, and delayed neuroinflammation may contribute to poor outcomes despite technically successful EVT.^{4,5}

Patients with atrial fibrillation and cardioembolic MCA occlusion are at particularly high risk because they often present with large thrombus burden and require early anticoagulation while remaining vulnerable to hemorrhagic transformation.^{4,6} Adjunctive neuroprotective therapies that preserve neurovascular integrity have therefore attracted interest, although clinical evidence remains limited.^{5,7} Cerebrolysin is a multimodal peptide preparation with neurotrophic and neuroprotective properties. In the CEREHETIS trial 8, early Cerebrolysin added to intravenous thrombolysis was reported to reduce symptomatic hemorrhagic transformation and early neurological deficit.^{6,9}

We report a patient who experienced two contralateral MCA occlusion strokes within approximately 3 months. Despite opposite angiographic outcomes after EVT, the clinical courses were markedly different, providing a unique within-patient observation that may generate hypotheses regarding adjunctive post-EVT neuroprotection.

Patient Information

A 63-year-old woman had a history of hypertension, dyslipidemia, prediabetes with HbA1c 6.2%, and suspected Af, with family reporting prior anticoagulant use with edoxaban 30 mg once daily. Her premorbid functional status was independent in activities of daily living. She experienced two separate MCA territory ischemic stroke episodes within approximately 3 months.

First stroke episode: right MCA occlusion with failed immediate angiographic reperfusion

On July 27, 2024 the patient developed acute left-sided weakness and slurred speech. On admission (NIHSS 11), rtPA 0.9 mg/kg was administered. During thrombolysis, her left-sided weakness progressed to Medical Research Council (MRC) grade 0 and she was transferred to our institution for EVT evaluation.

On arrival at ER, neurological examination showed severe right hemispheric stroke syndrome (NIHSS 21). Noncontrast CT and CT angiography/perfusion demonstrated right M1 occlusion, right MCA territory ischemic changes with ASPECTS 8 and a perfusion mismatch of 26 mL. The occlusion was considered to have a large thrombus burden.

EVT was performed using multiple techniques because of refractory right M1 occlusion. Aspiration thrombectomy was first attempted with a RED 72 reperfusion catheter for 3 passes, followed by stent retriever thrombectomy using a 5 × 22 mm Embotrap device for 3 passes. Balloon angioplasty with a 2.5 × 10 mm Euphora balloon was also attempted for 3 inflations. However, right MCA occlusion persisted.

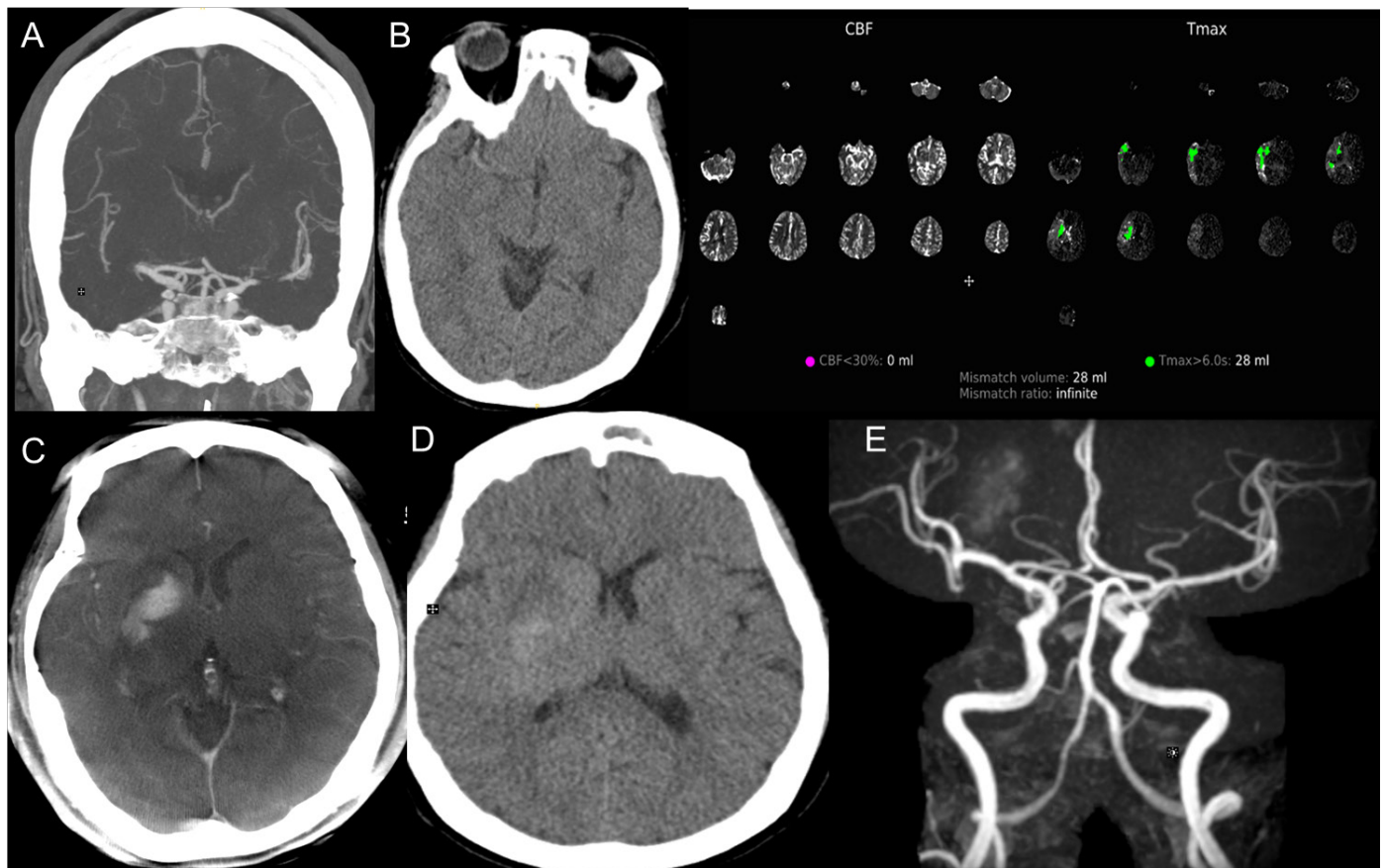


Figure 1: First right MCA occlusion episode: persistent occlusion after EVT followed by delayed complete recanalization. **A)** Initial coronal CT angiography shows right M1 occlusion. **B)** Initial noncontrast CT and CT perfusion demonstrate ASPECTS 8 with a perfusion mismatch, including Tmax >6 seconds volume of 28 mL and CBF <30% volume of 0 mL. **C)** Post-EVT DynaCT obtained after failed reperfusion shows right basal ganglia hyperdensity, compatible with contrast staining and/or early hemorrhagic transformation. Cerebrolysin was initiated shortly after EVT with a 50 mL intravenous loading dose, followed by 30 mL/day for 10 days. **D)** Follow-up noncontrast CT approximately 10 hours after EVT shows persistent evolving right MCA infarction, with ASPECTS decreasing from 8 to 7. **E)** Follow-up magnetic resonance angiography shows delayed complete recanalization of the right M1 segment.

Adjunct pharmacological treatment included intra-arterial tirofiban (3 mL bolus diluted in 20 mL normal saline, followed by infusion of 47 mL in 200 mL normal saline at 10 mL/hour). Due to persistent right M1 occlusion, a Solombra maneuver was performed with deployment of a stent retriever across the occluded segment and

continuous infusion of heparinized saline (3000 units heparin in 1000 mL normal saline) through the aspiration catheter for approximately 10 minutes before retrieval. Activated clotting time was 250 seconds initially and 256 seconds post-procedure. Despite extensive mechanical and pharmacological measures, final reperfusion remained mTICI 0. Postoperatively, the patient was managed in a neurocritical care setting. With persistent mTICI 0 occlusion, systolic blood pressure was maintained below 180 mmHg. Follow-up CTA at ~10 hours showed persistent total right MCA occlusion with ASPECTS decline to 7. Antiplatelet therapy (aspirin, clopidogrel) was withheld due to ongoing occlusion. Enoxaparin was initiated 12 hours post-EVT (1 prefilled syringe every 12 hours for 7 days). Subsequent MRI angiography demonstrated spontaneous complete recanalization of the right M1 segment, and apixaban 5 mg twice daily was restarted.

Cerebrolysin was administered early after EVT with a 50 mL intravenous loading dose (diluted in 70 mL normal saline) within 3 hours, followed by 30 mL/day intravenously for 10 days. The course was complicated by mild right basal ganglia hemorrhagic transformation without clinical deterioration. The patient improved and achieved mRS 2 at 3 months.

Second stroke episode: contralateral left MCA occlusion with near-complete reperfusion but fatal hemorrhagic deterioration

Approximately 3 months after the first stroke, while receiving apixaban 5 mg twice daily, the patient developed sudden falling down, dense right hemiplegia, and left gaze deviation during a rehabilitation program. Initial assessment showed NIHSS 20. Imaging demonstrated a left MCA territory acute ischemic stroke with ASPECTS 9. EVT was performed for the second occlusive event. Aspiration thrombectomy was performed twice using a React™ 71 catheter. A Solumbra technique using a Tiger17 device was then performed twice, with removal of a long clot. Final angiography demonstrated near-complete reperfusion, documented as mTICI 2c. Immediate DynaCT showed minimal subarachnoid hemorrhage.

In contrast to the first episode, intra-arterial tirofiban and heparinization were not administered, and Cerebrolysin was not given postoperatively. Aspirin and clopidogrel were not administered. Six hours after the procedure, the patient developed severe hemorrhagic deterioration. Surgical intervention with craniotomy was required 7 days later. Despite intensive management, the patient ultimately died.

Table 1: Comparison of therapeutic interventions and outcomes across two consecutive stroke events.

	First	Second
Cerebrolysin	✓	X
IA tirofiban	✓	X
Heparinized aspiration	✓	X
Reperfusion	TICI 0	mTICI 2c
Hemorrhagic transformation	Mild	Severe
Outcome	mRS 2	Death

Discussion

This case presents a rare within-patient comparison of two contralateral MCA-LVO stroke episodes treated with EVT but followed by markedly different clinical outcomes. The first episode resulted in good functional recovery despite failed immediate angiographic reperfusion (TICI 0), whereas the second achieved near-complete reperfusion (mTICI 2c) but was followed by early hemorrhagic deterioration and death. This observation highlights that angiographic success alone does not necessarily determine clinical outcome after EVT.

The findings should be regarded as hypothesis-generating only. They do not demonstrate that Cerebrolysin

prevented hemorrhagic transformation during the first episode or that its absence contributed to the fatal outcome during the second. Hemorrhagic transformation after ischemic stroke is multifactorial, reflecting interactions among reperfusion injury, blood–brain barrier (BBB) disruption, infarct evolution, antithrombotic therapy, hypertension, and procedural factors.^{4,5} The two stroke episodes also differed in hemisphere, timing, procedural findings, anticoagulation status, and reperfusion success. Notably, minimal subarachnoid hemorrhage was already present on immediate DynaCT after the second EVT, suggesting early vascular injury or reperfusion-related tissue fragility before clinical deterioration.⁴

Nevertheless, the within-patient comparison reduces some interindividual biological variability because the patient's vascular risk factors and suspected atrial fibrillation were shared across both episodes. The favorable recovery after an initially unsuccessful thrombectomy, followed by delayed spontaneous recanalization, raises the possibility that factors beyond angiographic reperfusion—including thrombus resolution, microvascular integrity, neurovascular stability, and tissue resilience—may influence recovery after EVT.⁵

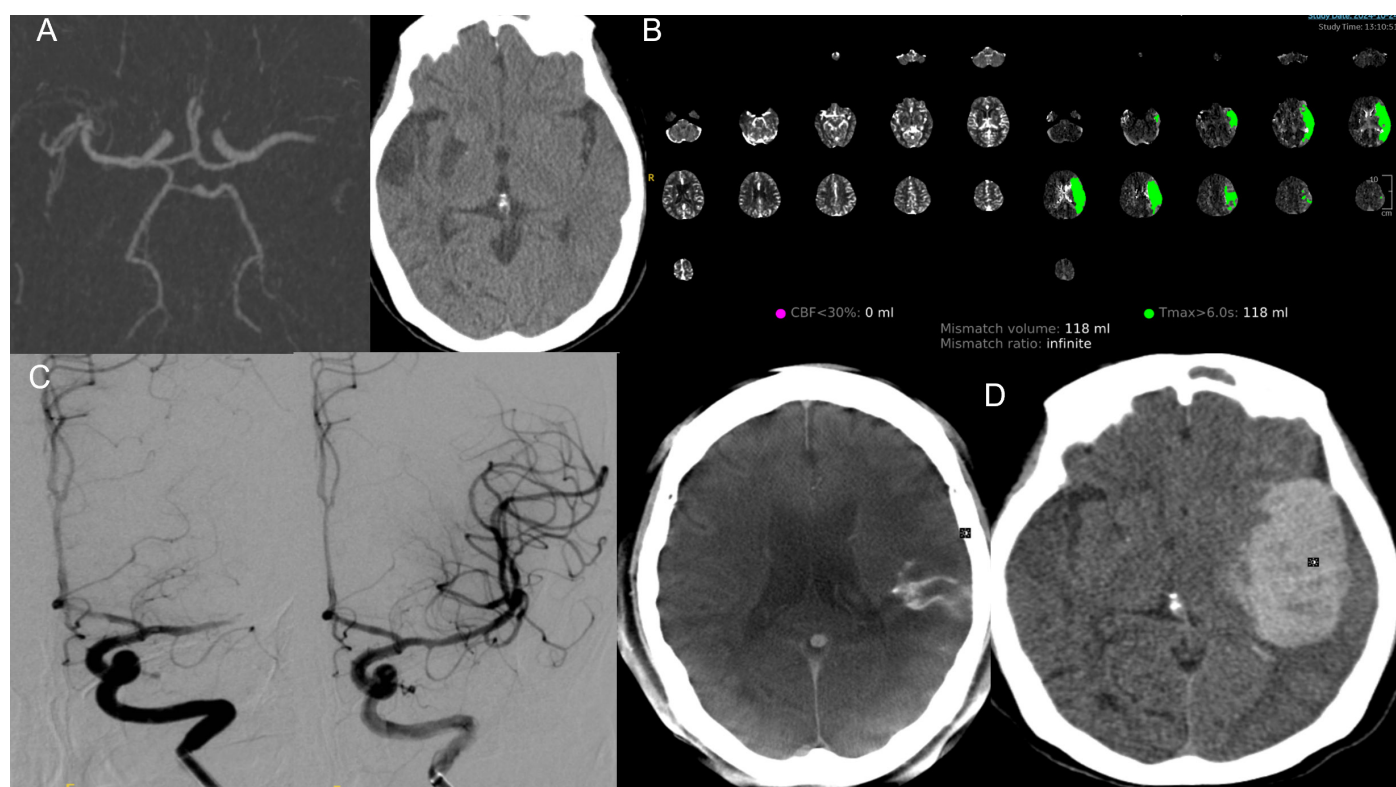


Figure 2: Second left MCA occlusion episode: near-complete reperfusion followed by early hemorrhagic deterioration.

A) Initial vascular imaging and noncontrast CT demonstrate left MCA occlusion with ASPECTS 9. **B)** Initial CT perfusion shows a large perfusion mismatch, with $T_{max} > 6$ seconds volume of 118 mL and $CBF < 30\%$ volume of 0 mL. **C)** Digital subtraction angiography demonstrates distal left MCA occlusion before thrombectomy and near-complete reperfusion after EVT, with final mTICI 2c. **D)** Immediate post-EVT DynaCT shows left hemispheric hyperdensity, compatible with contrast staining and/or early subarachnoid hemorrhage; follow-up CT 6 hours later demonstrates severe left intracerebral hemorrhage with mass effect.

Cerebrolysin has proposed multimodal cerebroprotective effects, including stabilization of the neurovascular unit, attenuation of BBB disruption, anti-inflammatory activity, and promotion of neuronal repair.^{6,8} In the CEREHETIS trial, early Cerebrolysin added to intravenous thrombolysis was associated with reduced early neurological deterioration and symptomatic hemorrhagic transformation, although no consistent long-term functional benefit was demonstrated.⁸ Subsequent post-hoc analyses suggested that these effects may be greater in patients at high risk of hemorrhagic transformation and may facilitate earlier transition to anticoagulation, although these findings remain exploratory and were derived from IVT-treated rather than EVT-treated patients.^{6,9}

Evidence specific to EVT is emerging. A propensity-matched observational study reported improved 12-month functional outcomes in patients receiving adjunctive Cerebrolysin after EVT, but these findings require confirmation in randomized trials.⁷ Together with growing interest in adjunctive neuroprotection during EVT,

these studies support the concept that post-EVT recovery may depend not only on successful recanalization but also on preservation of neurovascular integrity.^{5,7}

This report has several limitations. As a single-patient observation, it cannot establish causality. The two stroke episodes differed in vascular territory, thrombus characteristics, procedural course, reperfusion status, and adjunctive management. Important variables, including collateral status, thrombus composition, perfusion characteristics, blood pressure variability, and the combined use of tirofiban, heparin, enoxaparin, and Cerebrolysin during the first episode, preclude attribution of the outcome to any individual intervention.

Despite these limitations, the case illustrates the potential discordance between angiographic reperfusion and clinical recovery after EVT. It supports further prospective investigation of adjunctive neuroprotective strategies, including Cerebrolysin, in carefully selected patients with cardioembolic large-vessel occlusion who are at increased risk of hemorrhagic transformation.^{5,7}

Conclusion

This same-patient case report describes two contralateral MCA occlusion strokes treated with EVT and followed by sharply contrasting outcomes. The first right M1 occlusion, despite failed immediate reperfusion, was followed by delayed complete recanalization and meaningful recovery after intensive adjunctive therapy including early Cerebrolysin. The second left MCA occlusion, despite near-complete reperfusion, was complicated by early hemorrhagic deterioration and death without Cerebrolysin. The observation is not causal but is hypothesis-generating. In light of emerging data on hemorrhagic transformation risk after reperfusion therapy and exploratory EVT cohorts using adjunctive Cerebrolysin, further prospective study of post-EVT cerebroprotection appears warranted in high-risk AF-related MCA infarction with large thrombus burden and competing hemorrhagic and recurrent embolic risks.⁷⁻⁹

CASE SUMMARY



Patient

- 63 years
- Two MCA occlusion strokes within 3 months



Challenge

- Recurrent cardioembolic large-vessel stroke, High risk of hemorrhagic transformation



Treatment

- Stroke 1: Cerebrolysin 50 mL loading dose, then 30 mL/day IV x 10 days + EVT
- Stroke 2: EVT



Outcome

- Stroke 1: • mRS 2 at 90 days, • Delayed complete recanalization
- Stroke 2: • Severe hemorrhagic deterioration • Death



Take Home Message

Successful EVT restores cerebral perfusion, but preservation of neurovascular integrity remains critical; early adjunctive Cerebrolysin may help mitigate reperfusion-related injury and hemorrhagic transformation, supporting safer neurological recovery after recanalization.



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...in the management of severe MCAO after EVT

Abstract

Acute ischemic stroke (AIS) due to middle cerebral artery (MCA) occlusion presents usually with a severe neurological deficit associated with poor clinical outcome and many sequels, which affect significantly quality of life after stroke. In case of AIS in dominant hemisphere, the related severe aphasia also occurs very often. Despite of early treatment with endovascular mechanical thrombectomy (MT), not many patients achieve a good three-month functional outcome. We present a case of 58-year old male without previous medical history, who was admitted for AIS due to left MCA occlusion. Patient presented with severe right hemiparesis and global aphasia (NIHSS 15). The stroke onset was unknown and brain MRI showed acute and subacute ischemic changes in left MCA territory with MCA occlusion. Patient underwent MT with complete recanalization of MCA, however he did not improve immediately. Thus, after control brain CT, the Cerebrolysin treatment was started (50 ml for 10 days) with intensive rehabilitation (RHB) incl. speech therapy, which continued at RHB department subsequently. Patient was discharged home after three weeks. After three months, he presented with a very mild motor aphasia only (NIHSS 1). This case documents well the benefit of adjunct Cerebrolysin treatment with combination of intensive RHB in severe AIS.

Keywords: Acute ischemic stroke, middle cerebral artery occlusion, aphasia, mechanical thrombectomy, Cerebrolysin

Introduction

Acute ischemic stroke (AIS) due to middle cerebral artery (MCA) occlusion presents usually with severe neurological deficits associated with poor clinical outcome and many important sequels, which affect the quality of life significantly. In case of AIS in the dominant hemisphere, a related severe aphasia also occurs very often and contributes to poor outcome and leads to further social isolation.

Currently, endovascular mechanical thrombectomy (MT) is recommended as a standard treatment of MCA occlusion and it may be considered also in selected patients with unknown stroke onset based on neuroimaging findings [1, 2]. Despite a great technical success of MT with high recanalization rates, not all patients achieve excellent or good functional outcome after three months. Intensive rehabilitation incl. speech therapy became an important part of stroke therapy and recent research focuses on possibilities to support neurogenesis and regeneration of damaged neurons with activation of restoration processes called as “neuroplasticity” [3].

We present a case of severe AIS due to MCA occlusion treated with MT and followed with intensive RHB supported by adjunct Cerebrolysin treatment, according to CARE case reporting guideline criteria.

Patient Information

A 58-year old male was admitted in the morning at our comprehensive stroke center for acute severe right hemiparesis with a global aphasia; National Institutes of Health Stroke Scale (NIHSS) was 15. The time of stroke onset was unknown; patient was last seen healthy in the evening a day before admission by neighbors. He has no medical history and he did not use any medication regularly.

Clinical findings

On arrival at the emergency department, the patient presented with severe right hemiparesis, lesion of the right facial nerve and with a global aphasia (NIHSS 15). Blood pressure was 140/80 mmHg, sinus rhythm (87/min) was detected on ECG. Blood level of glucose was 6.3 mmol/L.

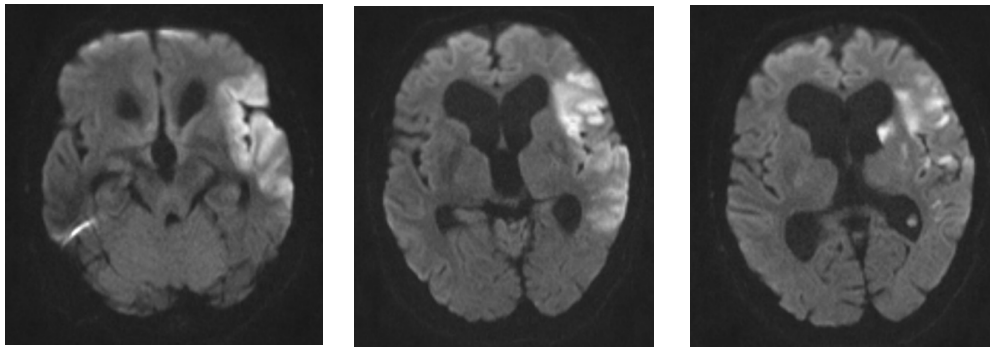


Figure 1: Acute ischemic changes in left MCA territory on DWI

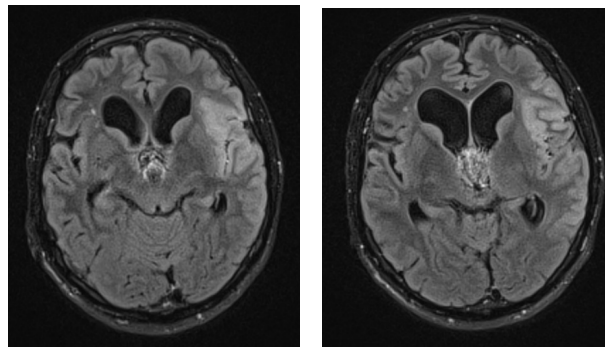


Figure 2: Acute ischemic changes in left MCA territory on FLAIR

Diagnostic Assessments

Brain MRI showed large acute ischemic changes in the left MCA territory on DWI (Figure 1) and some of them were visible also on FLAIR (Figure 2). MR angiography showed left MCA occlusion in M1 segment (Figure 3).

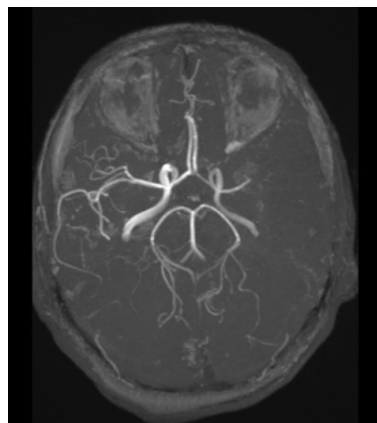


Figure 3: MR angiography of occluded left MCA in M1 segment.

Therapeutic Intervention

After brain MRI, the patient underwent endovascular MT with successful recanalization of the occluded MCA (Figure 4). After the intervention, the patient was admitted at ICU in our comprehensive stroke center and no early clinical improvement was observed at admission. A control brain CT performed after 24 hours showed acute ischemic changes in the left MCA territory with hemorrhage (Figure 5). Aspirin (100 mg per day) was administered for secondary prevention. Intensive RHB incl. speech therapy was started in combination with the adjunctive Cerebrolysin treatment; a dose of 50 ml of Cerebrolysin per day was administered for 10 days.

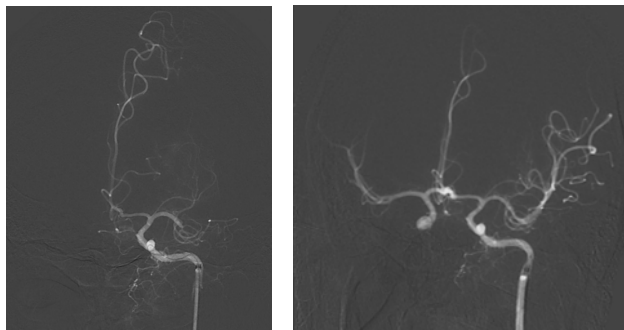


Figure 4: MT of occluded MCA on angiograms.

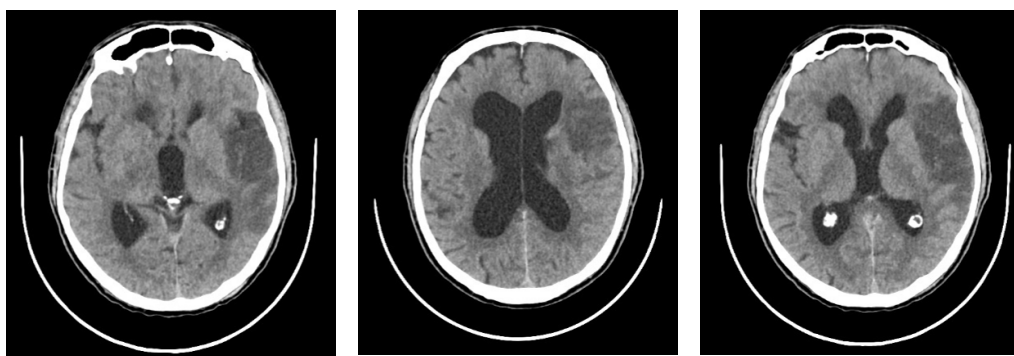


Figure 5: Control brain CT after 24 hours.

Follow-up

No complications were observed during the hospitalization at ICU, and the patient improved after two weeks into severe motor aphasia with moderate right hemiparesis (NIHSS 7). He underwent diagnostic setting to assess the etiology of stroke: transesophageal echocardiography with normal findings and 24-hour ECG Holter monitoring without detection of paroxysmal atrial fibrillation (AF). The patient presented with normal levels of blood pressure, LDL-c was 2.9 mmol/l and he received statin (40 mg per day). Ultrasound of carotid arteries showed mild to moderate atherosclerotic (AS) plaques in both internal carotid arteries (Figure 6).

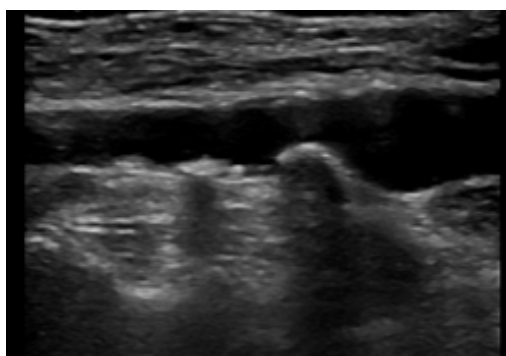


Figure 6: AS plaques in internal carotid artery

The patient was transferred to the rehabilitation department of our hospital, where intensive RHB incl. speech therapy was continued. He was discharged home after three weeks. At discharge, he presented with mild motor aphasia and very mild right hemiparesis: NIHSS 3, modified Rankin scale (mRS) score: 2, Barthel index:

95. He continued with outpatient RHB and speech therapy and underwent a four-week ECG Holter monitoring for screening subclinical AF.

Three-month outcome

At three-month follow-up, the patient presented with very mild motor aphasia without impairment on right limbs; NIHSS: 1, mRS: 1, Barthel index: 100. He had already returned back to his work at the same position (technician). Etiology of AIS was graded as cryptogenic embolic stroke of undetermined source.

Discussion

AIS due to MCA occlusion is usually associated with severe neurological deficit and many patients have poor clinical outcome with serious sequels despite early treatment with MT [4]. Specific intensive rehabilitation is very important for recovery after stroke and recent research has shown that the main goal is a reorganization of neuronal networks damaged by ischemia – neuroplasticity [5,6]. Metabolic, inflammatory and genetic processes, which are associated with neuroplasticity, are mostly present in the first 30 days after ischemic damage [7,8].

Cerebrolysin has shown its positive effect on neuroplasticity and neurogenesis after ischemic stroke associated with recovery [3,9,10], which was observed in experimental studies and in animal models [11,12]. The results of these studies have also shown, that significant improvement was achieved, if Cerebrolysin treatment was combined with a RHB training program. These findings support the suggestion that Cerebrolysin may affect biological repair and regeneration processes after ischemic stroke [13,14].

The recently published results from the large international prospective multicentric CREGS (Cerebrolysin Registry Study in Stroke) study have shown significant superiority of Cerebrolysin treatment in comparison to standard care in neurological improvement and functional outcome after AIS [15].

In the case presented, the adjunct Cerebrolysin treatment after MT in combination with intensive RHB led to the significant clinical improvement and excellent three-month functional outcome after severe AIS despite large acute ischemic damage due to MCA occlusion.

CASE SUMMARY



Patient

• 58 years • Left MCA occlusion stroke



Challenge

• Global aphasia and severe hemiparesis



Treatment

• Cerebrolysin 50 mL/day IV x 10 days + EVT + rehabilitation



Outcome

• NIHSS 15 → 1 • mRS → 1 • Returned to work



Take Home Message

In dominant-hemisphere AIS, severe aphasia contributes to poor outcomes and social isolation, while Cerebrolysin combined with intensive speech and language rehabilitation may improve clinically relevant recovery.



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...in the management of progressive ACA ischemic stroke following IV thrombolysis

Abstract

Acute ischemic stroke (AIS) may progress despite timely reperfusion therapy, particularly in patients with evolving infarction and persistent hemodynamic compromise. We report the case of a 55-year-old Japanese man with well-controlled hypertension who presented with transient right-sided weakness followed by persistent right arm impairment approximately two hours after symptom onset. Initial neuroimaging demonstrated acute infarction within the left anterior cerebral artery (ACA) territory without evidence of large-vessel occlusion. During diagnostic evaluation, neurological deterioration occurred with worsening right-sided weakness and an NIHSS score of 6. Intravenous alteplase was administered 45 minutes after hospital arrival, resulting in complete initial clinical recovery.

Follow-up imaging at 24 hours demonstrated progression of the ischemic lesion. Standard post-stroke management was initiated, including dual antiplatelet therapy and Cerebrolysin treatment. On day 5, the patient developed recurrent neurological deterioration with severe right lower-limb weakness. Neuroimaging revealed further infarct progression and severe stenosis of the left ACA. Supportive hemodynamic management and continued Cerebrolysin treatment were provided. Progressive neurological recovery subsequently occurred, with motor strength improving from grade 1 on day 15 to grade 4 by day 17. This case illustrates the potential role of adjunctive Cerebrolysin therapy as part of a comprehensive treatment strategy in patients with progressive ischemic stroke despite reperfusion therapy.

Key Words: acute ischemic stroke; anterior cerebral artery infarction; Cerebrolysin; thrombolysis; neurological recovery; progressive stroke

Introduction

Acute ischemic stroke (AIS) remains a leading cause of death and long-term disability worldwide. (1) Although intravenous thrombolysis and endovascular reperfusion therapies have significantly improved outcomes, a substantial proportion of patients experience neurological deterioration or infarct progression despite timely treatment. (2) Ongoing secondary injury mechanisms—including excitotoxicity, oxidative stress, inflammation, and delayed neuronal cell death—may contribute to continued neurological damage after the initial ischemic event. (4)

Anterior cerebral artery (ACA) infarctions are relatively uncommon, accounting for less than 5% of all ischemic strokes. (3) The anterior cerebral artery perfuses the medial frontal and parietal lobes, including the cingulate gyrus and much of the corpus callosum; consequently, infarction in this vascular territory commonly presents with contralateral leg weakness, gait impairment, behavioral changes, and executive dysfunction. (3) In some cases, progressive ischemia related to intracranial atherosclerotic disease or hemodynamic insufficiency may lead to infarct expansion and delayed neurological worsening despite initial clinical improvement. (3)

Cerebrolysin is a neuropeptide preparation with neuroprotective and neurorestorative properties that has

demonstrated beneficial effects on neurological recovery in patients with ischemic stroke. Experimental studies suggest that Cerebrolysin may reduce ischemia-induced injury, enhance neuroplasticity, and support endogenous repair mechanisms. (5) Clinical studies have reported improved functional recovery when Cerebrolysin is administered early after stroke, particularly in combination with standard stroke care and rehabilitation. (5,6)

We report a case of acute left ACA territory infarction treated with intravenous thrombolysis followed by adjunctive Cerebrolysin therapy. Despite initial recovery, the patient developed progressive neurological deterioration associated with infarct expansion before achieving substantial neurological improvement. This case highlights the challenges of progressive ischemic stroke and the potential role of adjunctive neuroprotective strategies in supporting recovery.

Patient Information

A 55-year-old Japanese man presented to the emergency department with acute right lower-limb weakness. Approximately two hours prior to admission, while watching television, he experienced sudden-onset right-sided hemiparesis lasting approximately 30 minutes, followed by partial spontaneous improvement. Residual clumsiness of the right arm and hand persisted at presentation.

His medical history was significant for hypertension that was reportedly well controlled. No additional vascular risk factors, family history, or previous neurological disorders were reported.

Clinical Findings

On admission, blood pressure was 197/136 mmHg and pulse rate was 97 beats/minute with regular rhythm. Neurological examination demonstrated an alert and cooperative patient who was fully oriented. Cranial nerve examination was unremarkable. Motor strength was largely preserved, although mild right-hand clumsiness and impaired right-sided finger-to-nose testing were observed. Sensory function was intact.

During MRI assessment, the patient developed neurological worsening characterized by a decline in right lower-limb strength from grade V to grade II and right upper-limb strength from grade V to grade IV. The NIHSS score increased to 6.

Timeline

Table 1: Clinical course and treatment timeline.

Time Point	Clinical Course and Therapeutic Interventions
Day 0	Sudden-onset right hemiparesis with partial spontaneous improvement; residual right-hand impairment remained. Neurological deterioration occurred; NIHSS score increased to 6. Intravenous alteplase (0.9 mg/kg) administered 45 minutes after arrival. Complete resolution of neurological deficits following thrombolysis.
Day 1	Follow-up MRI demonstrated infarct progression. Standard stroke care and Cerebrolysin 50 mL/day initiated. Please mention early rehabilitation if it happened Applied rehabilitation & blood pressure measurement.
Day 5	Recurrent neurological worsening with severe right leg weakness and dysarthria. MRI showed infarct progression; severe left ACA stenosis identified.
Days 5–12	Intensive hemodynamic support, hydration, and continuation of Cerebrolysin therapy.
Day 15	Motor power improved to grade 1
Day 16	Motor power improved to grade 3
Day 17	Motor power improved to grade 4

Diagnostic Assessment

MRI performed on admission demonstrated acute infarction involving the left ACA territory, specifically the cortical-subcortical region of the left mid-cingulate gyrus.

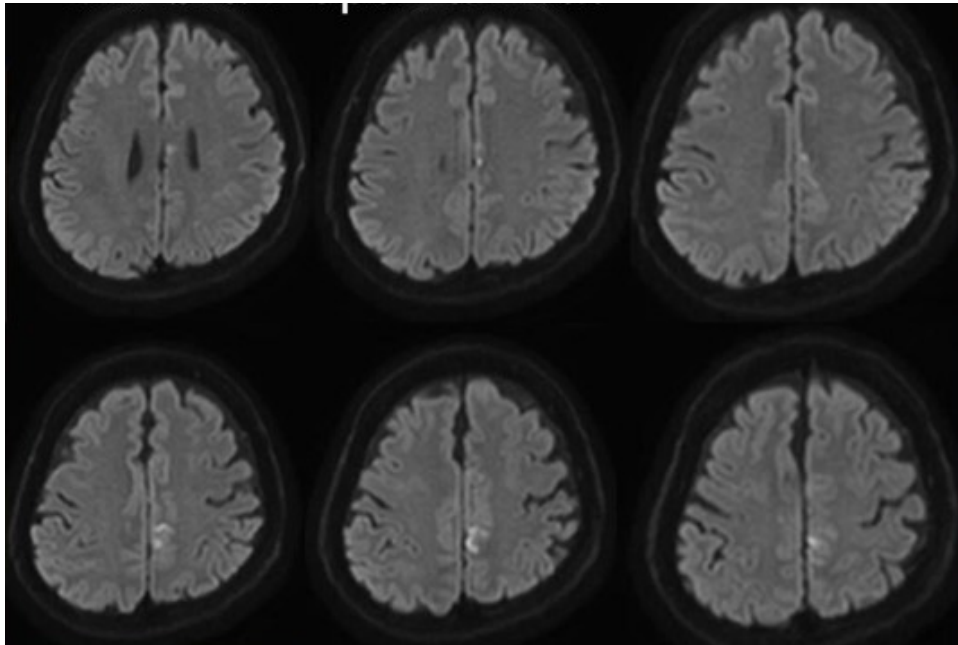


Figure 1: MRI brain upon admission

Magnetic resonance angiography demonstrated no high-grade stenosis or occlusion within the A1–A3 segments of the bilateral ACAs, although reduced flow-related enhancement was observed in the distal ACA branches.



Figure 2: Magnetic resonance angiography upon admission

Follow-up MRI performed 24 hours after thrombolysis demonstrated progression of the infarction involving the left mid-cingulate gyrus and corpus callosum.

Following neurological deterioration on day five, repeat MRI revealed further expansion of the infarction involving the parasagittal frontal and parietal regions, genu, and body of the corpus callosum. Severe stenosis of the left A2 segment was identified.

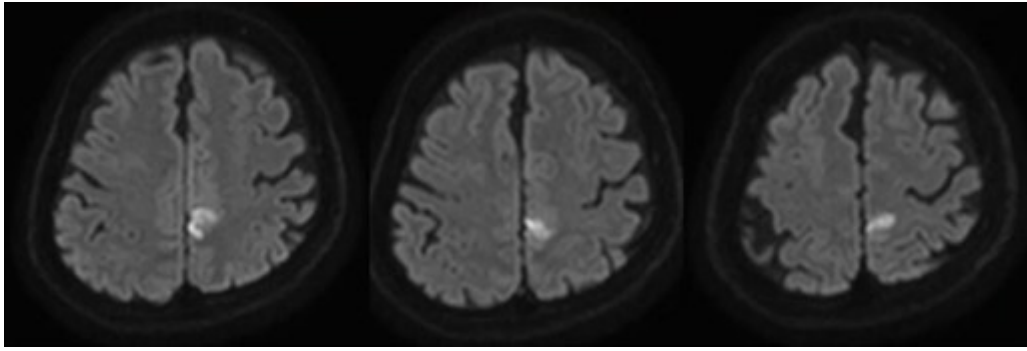


Figure 3: Follow-up MRI on day five

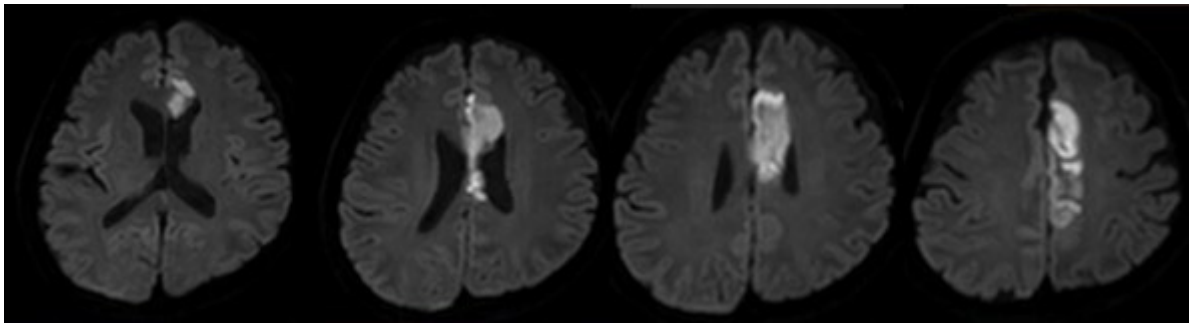


Figure 4: MRI brain on day 7th

Therapeutic Intervention

Intravenous alteplase at a dose of 0.9 mg/kg was administered 45 minutes after hospital arrival. Following treatment, the patient's right-sided weakness completely resolved.

Standard stroke management included close monitoring in the intensive care unit, dual antiplatelet therapy with aspirin and clopidogrel initiated after 24 hours, and strict blood pressure management. Cerebrolysin was initiated on the first day of hospitalization at a dose of 50 mL intravenously once daily.

After recurrent neurological deterioration, management focused on maintaining cerebral perfusion through intravenous fluids, albumin administration, permissive blood pressure management, and continuation of cerebroprotective therapy with Cerebrolysin.

Follow-up and Outcomes

Although the patient initially achieved complete neurological recovery following thrombolysis, recurrent deterioration occurred on day 5 with profound right lower-extremity weakness, mild facial weakness, dysarthria, and psychomotor slowing. Subsequent treatment was associated with gradual neurological improvement. No adverse events related to Cerebrolysin treatment were reported.

Discussion

This case illustrates several clinically relevant aspects of acute ischemic stroke management. Despite timely intravenous thrombolysis and complete initial neurological recovery, the patient experienced progressive infarct expansion and recurrent neurological deterioration associated with severe intracranial ACA stenosis. Such delayed worsening is well recognized in patients with persistent hemodynamic compromise, impaired collateral circulation, or progression of underlying intracranial atherosclerotic disease, emphasizing that successful reperfusion does not completely prevent secondary ischemic injury. (3,4)

Cerebrolysin was initiated within the first 24 hours after stroke onset and continued throughout the patient's subsequent clinical course (How many days) For 18 days. The rationale for early administration is supported by both experimental and clinical evidence indicating that many of the pathophysiological processes responsible for secondary brain injury—including excitotoxicity, oxidative stress, neuroinflammation, apoptosis, and blood–brain barrier (BBB) disruption—are activated shortly after ischemia and continue during the first days following

stroke. (4–6) Beyond its multimodal neuroprotective and neurorestorative actions, Cerebrolysin has been shown in preclinical studies to preserve BBB integrity, reduce vasogenic edema, and attenuate neurovascular unit injury. These observations are complemented by clinical data suggesting that early Cerebrolysin administration is safe following reperfusion therapy and may contribute to reducing complications related to BBB dysfunction, including hemorrhagic transformation, while supporting neurological recovery.

The present case is also consistent with the emerging concept underlying the CERECAP (Cerebrolysin Early RECanalization Adjunctive Program), which evaluates Cerebrolysin as an adjunctive treatment to contemporary recanalization therapies. Rather than targeting a single stroke mechanism, the CERECAP program recognizes that patients undergoing intravenous thrombolysis and/or mechanical thrombectomy represent a biologically heterogeneous population in whom secondary injury pathways remain active despite successful reperfusion. Early adjunctive Cerebrolysin aims to address these shared mechanisms by protecting the neurovascular unit, limiting ongoing tissue injury, and enhancing endogenous recovery processes. Consequently, CERECAP represents an important entry point toward a precision medicine approach in acute ischemic stroke, where patients may be stratified according to imaging characteristics, reperfusion status, vascular pathology, or biological markers to identify those most likely to benefit from adjunctive cerebroprotective therapy.

Although causality cannot be established from a single case, the favourable clinical evolution observed despite documented infarct progression and recurrent neurological deterioration is noteworthy. Recovery occurred in parallel with continued Cerebrolysin administration, comprehensive stroke unit care, optimization of cerebral perfusion, and rehabilitation. This case therefore supports the growing body of evidence suggesting that Cerebrolysin can be safely incorporated into multimodal treatment strategies following recanalization therapy and reinforces the rationale for investigating its efficacy across different ischemic stroke subtypes within structured clinical programs such as CERECAP.

Further prospective studies are needed to determine which patient populations derive the greatest benefit from early adjunctive Cerebrolysin and to define its role within individualized treatment algorithms for acute ischemic stroke.

CASE SUMMARY



Patient

- 55 years
- Progressive left ACA ischemic stroke



Challenge

- Recurrent neurological deterioration despite thrombolysis



Treatment

- Cerebrolysin 50 mL/day IV x 18 days + alteplase + intensive stroke care



Outcome

- NIHSS 6
- Motor strength grade 1 → 4
- Gradual neurological recovery



Take Home Message

Secondary brain injury may progress despite successful reperfusion, therefore early adjunctive Cerebrolysin therapy protects the neurovascular unit, by limiting BBB disruption and reperfusion injury.



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...in the management of acute basilar artery occlusion after EVT

Abstract

Basilar artery occlusion (BAO) is an uncommon yet devastating cause of posterior circulation stroke, frequently resulting in severe disability or death despite successful reperfusion. We describe a 67-year-old woman with multiple vascular risk factors who presented with acute BAO and was treated with intravenous thrombolysis followed by successful mechanical thrombectomy (Thrombolysis in Cerebral Infarction [TICI] grade 3), with adjunctive Cerebrolysin therapy administered subsequently. Rapid neurological improvement was observed within 24 hours, with the National Institutes of Health Stroke Scale (NIHSS) score decreasing from 7 to 2, followed by complete neurological recovery (NIHSS 0) by day 3. Clinical recovery was sustained throughout the 12-month follow-up period, with only mild residual gait disturbance noted at discharge. No adverse events attributable to Cerebrolysin were observed. Successful reperfusion remains the key determinant of outcome in BAO, and no causal inference can be made regarding Cerebrolysin. This case adds to the limited evidence on the use of Cerebrolysin as an adjunct to reperfusion therapy and supports further investigation in controlled studies of posterior circulation stroke.

Keywords: adjunctive therapy, Cerebrolysin, cerebroprotection, posterior circulation stroke, basilar artery occlusion

Introduction

Basilar artery occlusion (BAO) is a rare but devastating subtype of posterior circulation stroke, associated with poor functional outcomes and reported mortality rates approaching 85% in untreated patients [1]. Recent randomized controlled trials (RCTs), including the ATTENTION and BAOCHÉ trials, have shown a benefit of mechanical thrombectomy in selected BAO patients, with intravenous thrombolysis (IVT) used as concomitant therapy [2,3]. Despite successful reperfusion, a substantial proportion of patients have unfavorable outcomes, highlighting an ongoing therapeutic challenge in BAO [2-5].

These limitations have prompted interest in adjunctive neuroprotective strategies to enhance neurological recovery. Cerebrolysin is a neuropeptide preparation with proposed multimodal cerebroprotective and neurotrophic properties and has been investigated as an adjunct to standard stroke therapy. Most clinical evidence comes from studies in anterior circulation stroke, where Cerebrolysin is well tolerated and may be associated with functional benefits [6-12]. However, data on posterior circulation stroke, including BAO, remain limited.

An ongoing prospective study evaluating Cerebrolysin as an add-on therapy for posterior circulation stroke secondary to BAO has been initiated at the Department of Neurology, University Hospital Center Sestre Milosrdnice (ClinicalTrials.gov: NCT06489925). Here, we report a case from this study describing a favorable clinical outcome following intravenous thrombolysis (IVT), mechanical thrombectomy, and adjunctive Cerebrolysin therapy.

Patient Information

A 67-year-old woman with a history of hypertension, dyslipidemia, diabetes mellitus, and chronic right internal carotid artery occlusion following elective endarterectomy presented with acute-onset vertigo and left-sided hemiparesis. There was no previous history of stroke or cognitive impairment. No relevant family history was reported.

Clinical Findings

On admission, the patient was somnolent but arousable, with preserved comprehension and mild dysarthria. Neurological examination revealed left internuclear ophthalmoplegia, vertical nystagmus, mild left-sided hemiparesis, and left-sided dysmetria. The patient was unable to stand or walk without assistance. The NIHSS score was 7. The clinical progression and treatment timeline are presented in Table 1.

Table 1: Clinical progression and treatment timeline

Day	Clinical Course and Key Therapeutic Interventions
Day 0 (~45 minutes before admission)	Sudden onset of left-sided limb weakness, dysmetria, somnolence, dysarthria, and internuclear ophthalmo-plegia. NIHSS score 7.
Day 0 (upon admission)	IV alteplase at a standard dose of 0.9 mg/kg administered within one hour of hospital admission, followed by immediate endovascular mechanical thrombectomy. Cerebrolysin initiated 7 hours after symptom onset at a dose of 30 mL in 250 mL of 0.9% NaCl, administered IV once daily for 14 days.
Day 1	Mild paresis of the left upper limb and dysmetria in the left extremities observed on clinical assessment. NIHSS score 2. ASA 100 mg PO once daily, atorvastatin 80 mg PO once daily, and LMWH 40 mg SC once daily for DVT pro-phylaxis initiated alongside Cerebrolysin. Hyperglycaemia corrected as needed with short-acting subcutaneous insulin. Perindopril/ amlodipine 5mg/ 5mg PO once daily continued without dose adjustment.
Day 3	No neurological deficits detected. NIHSS score 0. Patient mobilized to upright position with physiotherapist assistance.
Day 5	Structured daily neurorehabilitation program (45-60 min) initiated, including coordination, mobility, balance, and activities of daily living (ADL)-focused training.
Day 16	Mild residual gait disturbance noted. mRS score 1. Patient discharged home on ASA 100 mg PO once daily, atorvastatin 80 mg PO once daily, adjusted antidia-betic therapy as per glycaemic control, and continuation of chronic antihypertensive therapy.

NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale; IV, intravenous; PO, per os; SC, subcutaneous; ASA, acetylsalicylic acid; LMWH, low-molecular-weight heparin; DVT, deep vein thrombosis



Figure 1: Non-contrast brain CT showed an encephalomalacia and gliotic scar in the right frontal lobe, consistent with prior ischemic injury

Diagnostic Assessment

Non-contrast brain CT showed no acute ischemia or intracranial hemorrhage, apart from an old encephalomalacic and gliotic scar in the right frontal lobe (Figure 1). CT angiography demonstrated basilar artery occlusion (Figure 2), with thrombus extending into both superior cerebellar arteries, and chronic occlusion of the right common and internal carotid arteries.



Figure 2: CT angiography demonstrated basilar artery occlusion (BAO)

Laboratory evaluation revealed hyperglycemia (11.9 mmol/L); other parameters were within normal limits. Digital subtraction angiography (DSA) demonstrated partial recanalization of the basilar artery after thrombolysis (Figure 3), followed by complete reperfusion—Thrombolysis in Cerebral Infarction (TICI) grade 3 after mechanical thrombectomy (Figure 4).



Figure 3: Digital subtraction angiography (DSA) showing partial recanalization of the basilar artery following thrombolytic therapy

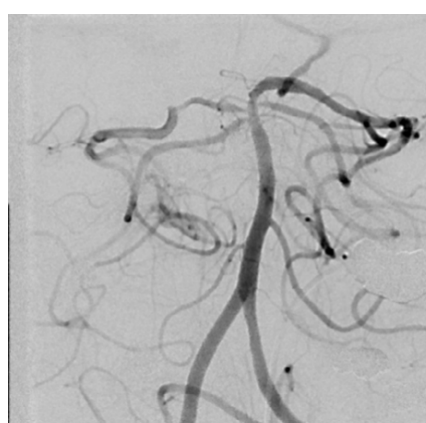


Figure 4: DSA showing subsequent complete recanalization (TICI grade 3) achieved by mechanical thrombectomy

Follow-up brain CT showed acute ischemia in the left anterior cerebellar lobe and superior cerebellar peduncle without hemorrhagic transformation (Figure 5).

A comprehensive post-procedural diagnostic work-up was performed. 24-hour Holter monitoring did not reveal atrial fibrillation or other clinically significant arrhythmias, and transthoracic echocardiography showed no significant structural abnormalities. The transcranial Doppler (TCD) bubble test was negative for right-to-left shunt, with no evidence of a patent foramen ovale or other intracardiac or extracardiac shunt as a potential embolic source. Carotid and vertebral artery Doppler ultrasonography demonstrated chronic occlusion of the right common carotid artery and right internal carotid artery, without evidence of acute or new large-artery pathology.

Therapeutic Intervention

Intravenous (IV) alteplase was administered within one hour of admission and was immediately followed by mechanical thrombectomy. Endovascular thrombectomy was performed via a right transradial approach. A guiding catheter was positioned in the proximal segment of the basilar artery. Angiography demonstrated

partial recanalization of the basilar apex. Mechanical thrombectomy was then performed using a stent retriever in combination with an aspiration catheter, resulting in complete reperfusion (TICI 3). Hemostasis at the right radial puncture site was achieved by manual compression.

Therapy with Cerebrolysin (30 mL diluted in 250 mL saline, IV once daily for 14 days) was initiated 7 hours after symptom onset. The dosing regimen was based on commonly used protocols from previous acute ischemic stroke studies of Cerebrolysin, in which adjunctive Cerebrolysin therapy was typically initiated shortly after reperfusion therapy and administered at a dose of 30 mL IV once daily, with treatment durations ranging from 10 to 21 days in most trials [6-12].

Secondary prevention included acetylsalicylic acid, antihypertensive and lipid-lowering therapy, and prophylactic unfractionated heparin. A structured neurorehabilitation program was initiated on hospital day 5 and provided daily until discharge, with 45–60-minute sessions. The intervention included coordination training (Frenkel exercises and proprioceptive neuromuscular facilitation [PNF] rhythmic stabilization), task-specific training, functional mobility training [bed mobility, transfers, sit-to-stand activities, and fall prevention], and neuromuscular re-education focusing on balance, coordination, weight-bearing, and visual cueing strategies. Patient and caregiver education, as well as an individualized 24-hour rehabilitation program, were also implemented.

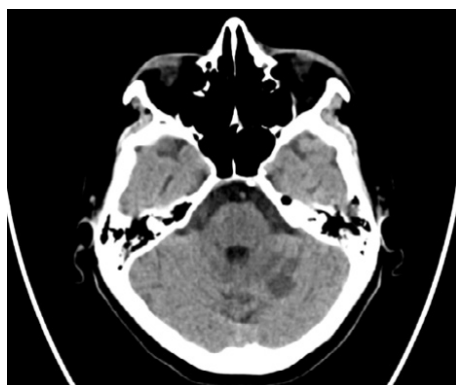


Figure 5: Non-contrast brain CT performed 24 hours after acute treatment, demonstrating acute ischemia in the left anterior cerebellar lobe and left anterior cerebellar peduncle, without evidence of intracranial hemorrhage

Follow-up and Outcomes

At 24 hours, the NIHSS score improved to 2, with mild left upper-limb paresis and dysmetria. By day 3, neurological examination was normal (NIHSS 0). At discharge (hospital day 16), a mild gait disturbance persisted (mRS 1). No adverse effects related to Cerebrolysin were observed. Follow-up at 1, 3, 6, and 12 months demonstrated sustained neurological stability. At the 12-month follow-up, the patient reported intermittent gait unsteadiness and peripheral vascular symptoms, which were managed conservatively.

Discussion

This case illustrates rapid and sustained neurological recovery following successful mechanical thrombectomy for BAO in a patient who also received IVT and adjunctive Cerebrolysin therapy. The patient presented with an NIHSS score of 7 and achieved complete resolution of neurological deficits within 72 hours (NIHSS 0), with only mild residual gait impairment at discharge, resulting in a favorable functional outcome (mRS 1).

Endovascular thrombectomy has been shown to improve functional outcomes in BAO in both observational studies and RCTs. The BASILAR registry reported favorable functional outcomes following reperfusion, while recent RCTs demonstrated higher rates of good functional outcomes compared with medical management [2,3,13]. Both ATTENTION and BAOCHE demonstrated early neurological improvement after thrombectomy. ATTENTION reported lower median NIHSS scores at 24-72 hours (21 vs. 30) and at 5–7 days or discharge (16 vs. 35), while BAOCHE showed higher rates of dramatic early neurological improvement (25% vs 10%) [2,3]. Notably, these trials predominantly enrolled patients with higher baseline neurological severity (NIHSS $\geq$ 10), while data on outcomes in patients with lower NIHSS scores remain limited [2-4].

However, despite the overall benefits of reperfusion therapy, approximately half of the patients with BAO fail to achieve functional independence at 90 days despite successful reperfusion, reflecting the phenomenon of futile recanalization [2-4,13,14]. These variable outcomes have been associated with baseline neurological severity, time to reperfusion, complex vascular anatomy of the posterior circulation, and secondary ischemic injury processes [14-18].

In this context, Cerebrolysin was administered as an adjunctive therapy based on its proposed multimodal neurotrophic and neuroprotective properties, which are thought to reflect general pathophysiological pathways of ischemic brain injury rather than being specific to a particular cerebrovascular territory. Clinical evidence to date has predominantly been derived from anterior circulation stroke populations, and, in the absence of a known circulation-specific mechanism, its potential effects in posterior circulation stroke are hypothesized to be similar. However, this remains unproven [8,10,12,19,20].

Overall, the clinical course observed in this patient is consistent with the favorable end of the outcome spectrum reported after complete (TICI 3) reperfusion in BAO, where early and substantial neurological improvement is commonly driven by restoration of posterior circulation blood flow [2-4,13].

Although adjunctive Cerebrolysin was administered as a cerebroprotective agent, its contribution cannot be disentangled from the effect of complete reperfusion, which remains the primary determinant of outcome. Structured rehabilitation, including coordination, mobility, balance, and activities of daily living (ADL)-focused training, was initiated after early substantial recovery; its contribution to long-term functional stability cannot be excluded. The patient reported rapid symptom improvement and expressed satisfaction with the recovery process, particularly regarding regained mobility and independence.

This case highlights the need for further prospective studies evaluating the use of adjunctive Cerebrolysin alongside standard reperfusion therapies to clarify its potential cerebroprotective role in posterior circulation stroke.

CASE SUMMARY



Patient

• 67 years • Basilar artery occlusion



Challenge

• Posterior circulation stroke with severe disability risk



Treatment

• Cerebrolysin 30 mL/day IV x 14 days + thrombolysis + thrombectomy



Outcome

• NIHSS 7 → 0 • mRS 1 • Sustained recovery at 12 months



Take Home Message

Acute cerebroprotective therapy with adjunctive Cerebrolysin after recanalization in patients with BAO may reduce the risk of treatment while improving chances for improved functional outcome.

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...in a patient treated with tenecteplase

Abstract

Despite high recanalization rates with mechanical thrombectomy (MT), large-vessel occlusion stroke results in death or dependency in over half of patients. Cerebrolysin, a multimodal neuropeptide preparation, may attenuate ischemia–reperfusion injury and support early neurorehabilitation. We report an 88-year-old woman with moderate prestroke disability who presented 2 h after the onset of right hemiparesis and aphasia due to M2 occlusion of the left middle cerebral artery. She received intravenous tenecteplase followed by MT, achieving complete reperfusion after three passes with no direct complications and no immediate clinical improvement. Directly postprocedure, Cerebrolysin 30 mL/day was initiated as adjunctive treatment. Over the next 24 h, neurological deficits gradually resolved with no hemorrhagic transformation or evident infarct on follow-up CT. As the patient did not require early intensive rehabilitation and regained her prestroke functional status, Cerebrolysin was discontinued after three doses. This report is not intended to establish the therapeutic efficacy of short-course adjunctive Cerebrolysin. It illustrates how clinical signals from randomized and observational studies can be interpreted for the purpose of individual therapeutic decisions.

Keywords: Cerebrolysin; functional recovery; intravenous thrombolysis; mechanical thrombectomy; stroke; tenecteplase

Introduction

Stroke remains a leading cause of death and disability worldwide, even with contemporary workflows in well-developed systems with good access to reperfusion therapies [1, 2]. In large-vessel occlusion (LVO) strokes, mechanical thrombectomy (MT) achieves successful recanalization (mTICI 2b–3) in over 80% of patients, but only about 38% regain functional independence [2]. These reflect the complex pathophysiology of ischemia–reperfusion injury, including rapid growth of the ischemic core prior to recanalization, microvascular “no-reflow,” distal microembolization, and disruption of the blood–brain barrier (BBB) [3]. Recent STAIR recommendations have therefore emphasized that future cerebroprotective strategies should be tested as add-ons to timely reperfusion rather than as stand-alone treatments, targeting both neuronal survival and microcirculatory integrity [4]. In parallel, multiple randomized trials and meta-analyses have established tenecteplase as the recommended alternative to alteplase in patients eligible for intravenous thrombolysis (IVT), especially in the 4.5-h time window or considered for MT [5].

We report an elderly patient with moderate prestroke disability treated for acute M2 occlusion with tenecteplase-assisted MT followed by a very early short course of cerebrolysin. While no inference regarding efficacy can be drawn from a single observation,

Our case illustrates how clinical signals from randomized and observational studies can be interpreted for the purpose of individual therapeutic decisions.

Case

An 88-year-old woman was transported by ambulance to the Neurological Emergency Department at 11:57, two hours after sudden-onset right-sided limb paresis and aphasia. Her medical history included untreated hypertension, osteoporosis, and chronic low back pain limiting ambulation (modified Rankin Scale [mRS] score of 3). On admission, she scored 10 points on the National Institutes of Health Stroke Scale (NIHSS): questions and single-step commands (2 + 1), right-sided limb paresis (1 + 1), severe mixed aphasia (2), and right facial nerve palsy with dysarthria (2 + 1). Noncontrast brain computed tomography (CT) at 12:20 showed a hyperdense sign in the left middle cerebral artery (MCA) with no clear early ischemic changes (Alberta Stroke Programme Early CT score of 10, Figure 1). Subsequent CT angiography confirmed the M2 occlusion of a left MCA branch. At that point, the patient was deemed potentially eligible for both IVT and MT.

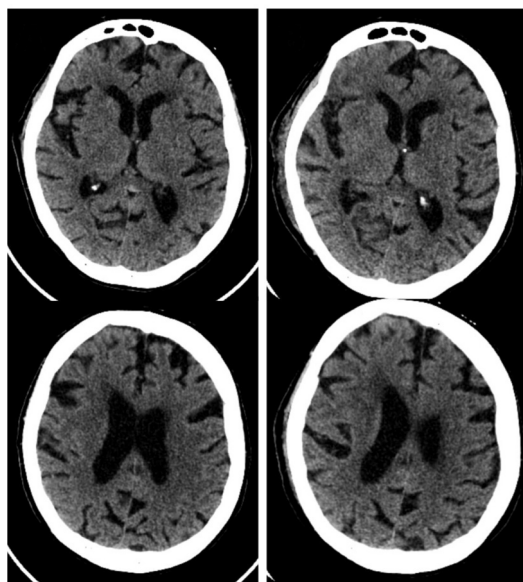


Figure 1: Noncontrast CT on admission (A) and 24 h after reperfusion therapy (B). No hemorrhagic transformation or visible infarction is seen on follow-up CT.

After transfer to a monitored bed (blood pressure 133/70 mmHg and heart rate 80/min) and a point-of-care blood glucose check (134 mg/dL), at 12:36, she received 20 mg of tenecteplase (0.25 mg/kg). The endovascular procedure was started under general anesthesia at 13:15. After three passes (two aspirations with the RED62 catheter, then one combined aspiration thrombectomy with the RED62 catheter and the Solitaire X 3 × 20 mm stent retriever) at 13:44, she achieved complete reperfusion (mTICI 3) with no immediate clinical effect (Figure 2). After return from the angio suite, Cerebrolysin 30 mL intravenously was administered as adjunctive treatment on the basis of a biologically plausible cerebroprotective rationale and available clinical safety data [6, 7]. This decision was made after the procedure and was not part of a predefined protocol. No direct procedural complications or adverse events temporally associated with cerebrolysin were observed.

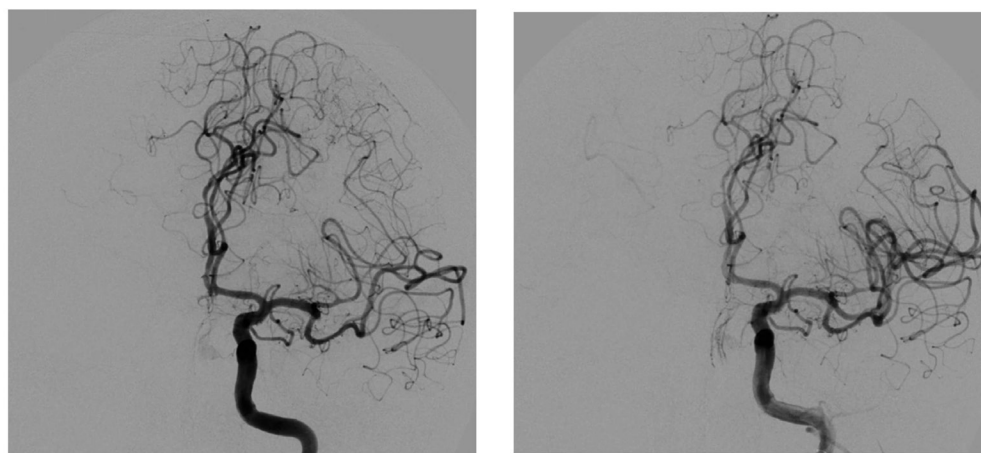


Figure 2: Digital subtraction angiography before thrombectomy (A) and after recanalization (B). The arrow points to the occluded middle cerebral artery M2 branch.

We observed gradual neurological improvement reaching NIHSS 0 by the next morning. Cerebrolysin was discontinued after the third daily dose because the patient had complete neurological recovery, no hemorrhagic

transformation on 24-h CT, and no stroke-related deficit requiring intensive early neurorehabilitation (Figure 1). After a comprehensive diagnostic workup, she was diagnosed with an embolic stroke of undetermined source. The only abnormal laboratory finding was an elevated LDL cholesterol level (150 mg/dL). The patient was discharged home on acetylsalicylic acid and high-dose atorvastatin with no neurological deficits (NIHSS 0, mRS 3). At the 3-month follow-up, her condition remained stable (NIHSS 0, mRS 3).

Discussion

This case report illustrates the safety, feasibility, and potential usefulness of using cerebrolysin as additional therapy in combination with IVT and MT. Cerebrolysin is an intravenously administered mixture of low-molecular-weight peptides and amino acids derived from porcine brain tissue with multimodal actions, including antiexcitotoxic, antioxidative, and anti-inflammatory effect, and promotion of neuroplasticity and synaptogenesis [8]. Cerebrolysin modulates receptors involved in glutamatergic, GABAergic, and cholinergic signaling, corresponding to protective effects against excitotoxicity and apoptosis. Its anti-inflammatory effects are supposed to counteract the destabilization of BBB [7]. Both randomized and nonrandomized studies did not reveal any important safety issues [3, 6, 7, 9–16]. A meta-analysis of 9 randomized trials by Bornstein et al. reported that cerebrolysin initiated within 72 h of stroke onset was associated with better 90-day functional outcomes in patients with moderate-to-severe stroke, without excess serious adverse events [9]. In contrast, the more recent Cochrane meta-analysis was neutral for cerebrolysin and raised concerns about imprecision and risk of bias [10]. The apparent discrepancy stems from methodological differences, namely, imposing the 48 h therapeutic window, that resulted in the exclusion of the positive CARS trials [11]. The 2021 European Academy of Neurology guidelines provide a weak recommendation for its use for at least 10 days as part of early motor rehabilitation after ischemic stroke, especially if NIHSS is ≥ 8 [17]. This concept has been reinforced by the ESCAS trial on poststroke aphasia and in the recently published CREG-2 registry that included patients with baseline NIHSS 8–15 [12, 13].

More directly relevant to our case report, the nonrandomized CEREC-Stroke study showed that patients with baseline NIHSS ≥ 8 and futile recanalization who received 14–21 days of cerebrolysin had lower 12-month mortality (13% vs. 43%) and numerically fewer hemorrhagic transformations (HT, 8% vs 33%) compared with controls [14]. In the randomized CERETIS trial, early addition of cerebrolysin to alteplase significantly reduced the rate of symptomatic intracranial hemorrhage (sICH, 3% vs 9%), but with no clear effect on 90-day functional outcome [15]. A more recent prospective, nonrandomized, blinded-endpoint study (N = 100) focusing on patients undergoing successful MT for anterior-circulation LVO reported that add-on Cerebrolysin initiated ≤ 8 from the onset and continued for 21 days resulted in significantly lower occurrence of HT (14% vs. 40%) and sICH (2% vs. 24%), with a higher proportion of good functional outcome at 90 days (68% vs. 44%) [3]. A similar propensity score matched analysis in cardioembolic LVO also showed lower rates of HT (20% vs 57%) and sICH (3% vs 41%), with a higher proportion of good outcomes (64% vs 35%) and even lower mortality (5% vs 33%) [16]. Taken together, previous studies provide a biologically and clinically plausible rationale for combining cerebrolysin with reperfusion therapy to attenuate reperfusion injury and potentially improve the translation of radiological success into clinical recovery [6, 7].

Our patient differs in several important respects from the populations studied in these trials. Firstly, she represents a clinically relevant but largely underrepresented in trials group of very elderly patients with prestroke dependency not related to neurological deficits. Second, her cerebrolysin regimen was initiated immediately after MT and discontinued after three daily doses, unlike the regular 10–21-day courses used in most studies. Such a schedule may be better suited to targeting early BBB stabilization and reperfusion injury than to longer-term neurorestorative effects. However, direct measures of BBB stabilization were not available in this case.

It is important to note that our patient had several well-established predictors of complete neurological recovery, including early presentation, absence of early ischemic changes on baseline CT, an M2 branch, intravenous tenecteplase before thrombectomy, and complete angiographic reperfusion. Previous controlled studies indicate that very early adjunctive cerebrolysin could have contributed to getting the full potential of recanalization without hemorrhagic transformation [6, 7]. The patient required three passes to achieve

mTICI 3, and her neurological improvement was gradual rather than immediate. Nonetheless, this case cannot determine to what extent cerebrolysin contributed to the clinical or radiological outcome, and further randomized studies are warranted.

Conclusion and Potential Treatment Strategy

Based on available evidence from randomized trials and observational studies, very early initiation of cerebrolysin (30 mL/day i.v.) may be considered as an adjunct therapy to IVT with tenecteplase or alteplase and/or MT in selected cases [3, 6, 7, 14–16]. The intended rationale is two-fold:

- To increase the direct benefit from reperfusion therapy by mitigating ischemia–reperfusion injury and reducing the risk of hemorrhagic transformation;
- To support early recovery and facilitate timely rehabilitation when indicated.

This approach may be most relevant in moderate ischemic stroke (NIHSS 8–15), particularly in patients with cortical deficits, including upper-limb weakness or nonfluent aphasia [7, 9, 11–13]. If clinically significant deficits persist after reperfusion and intensive rehabilitation is required, cerebrolysin may be continued for a conventional 10–21-day course, as suggested by EAN 2021 rehabilitation guidelines [17].

In patients with rapid and near-complete clinical recovery, it seems reasonable to discontinue very early initiated cerebrolysin after 2–3 doses. The present case illustrates the feasibility of such a treatment strategy. However, new data from academic-driven randomized trials are needed to guide decisions in everyday clinical practice.

CASE SUMMARY



Patient

• 88 years • Left MCA (M2) ischemic stroke



Challenge

• Aphasia and right hemiparesis due to LVO stroke



Treatment

• Cerebrolysin 30 mL/day IV x 3 days + TNK + mechanical thrombectomy



Outcome

• NIHSS 10 → 0 • mTICI 3 • No hemorrhagic transformation



Take Home Message

The combination treatment of Cerebrolysin with TNK after thrombectomy is feasible and led to an unexpected fast recovery in a severe stroke patient.

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...to hyperacute cerebroprotection in combination with bridging therapy

Abstract

Background: Bridging therapy with intravenous thrombolysis (IVT) followed by endovascular thrombectomy (EVT) remains a standard reperfusion strategy for acute ischemic stroke (AIS) caused by large-vessel occlusion (LVO). However, hemorrhagic transformation (HT) remains an important complication of reperfusion, prompting interest in adjunctive therapies that may protect the neurovascular unit. Cerebrolysin has demonstrated potential to reduce HT when administered during reperfusion therapy, but clinical experience during bridging therapy remains limited.

Case presentation: We report two patients with anterior circulation LVO who underwent successful bridging reperfusion therapy with complete recanalization (mTICI 3). Both had Alberta Stroke Program Early CT Scores (ASPECTS) of 6 and were classified as having a high predicted risk of HT using the Hemorrhagic Transformation Index (HTI). To the first patient, Cerebrolysin (30 mL intravenously) was initiated concurrently with alteplase and continued for 14 days. Follow-up imaging demonstrated a small infarct without HT, and neurological deficits improved from a National Institutes of Health Stroke Scale (NIHSS) score of 14 before thrombolysis to 4 at discharge. The second patient was treated with standard bridging therapy alone, follow-up imaging demonstrated asymptomatic hemorrhagic infarction type 2, despite a similarly small infarct volume and comparable neurological recovery.

Conclusion: These cases illustrate contrasting radiological outcomes after successful bridging reperfusion in patients with comparable baseline characteristics and predicted risk of HT. Although causal inference cannot be made from two observations, the findings are consistent with previous clinical evidence suggesting that early Cerebrolysin administration may reduce reperfusion-related hemorrhagic transformation. Prospective studies are warranted to evaluate this strategy further.

Keywords: Large-vessel occlusion, thrombectomy, Cerebrolysin, hemorrhagic transformation

Introduction

For patients with acute ischemic stroke (AIS) due to large vessel occlusion (LVO), intravenous thrombolysis (IVT) followed by endovascular thrombectomy (EVT)—bridging therapy—remains a widely used reperfusion strategy despite ongoing debate regarding its benefit over EVT alone. Concerns that IVT may increase hemorrhagic transformation (HT) without consistently improving outcomes have prompted interest in adjunctive therapies to protect the neurovascular unit during early reperfusion [1,2].

Cerebrolysin, a multimodal neurotrophic preparation, has been proposed as an early adjunct to reperfusion therapy with potential protective effects against HT and reperfusion injury. In the prospective randomized CEREHETIS trial, Cerebrolysin initiated concurrently with IVT was associated with reduced HT, suggesting improved blood–brain barrier integrity [3]. Post hoc analyses further supported these findings, showing consistent reductions in hemorrhagic events across risk strata and effects on anticoagulation timing in patients with non-valvular atrial fibrillation (AF) [4,5].

Observational studies of patients undergoing EVT have suggested improved functional outcomes with

Cerebrolysin at 3 and 12 months, including in patients with futile recanalization after IVT, where reperfusion injury may contribute to poor outcome [6–9]. However, real-world experience with Cerebrolysin initiated during the IVT phase of bridging therapy remains limited.

We present two cases of bridging reperfusion therapy illustrating this hypothesis in clinical practice: one with Cerebrolysin initiated concomitantly with IVT as an early adjunctive treatment and one managed without neurotrophic therapy.

Case Presentation

Case 1

Patient Information and Clinical Findings

An 84-year-old woman presented with acute left-sided weakness, sensory loss and dysarthria. Intravenous alteplase had been initiated at a referring stroke centre within two hours of symptom onset. Simultaneously, Cerebrolysin 30 mL diluted in 100 mL saline was administered intravenously through a separate infusion line. Medical history included hypertension, diabetes mellitus, coronary artery disease with previous myocardial infarction and non-valvular atrial fibrillation. Before stroke, her modified Rankin Scale (mRS) score was 1. Neurological examination demonstrated an NIHSS score of 12 on admission (14 immediately before thrombolysis).

Diagnosis

Brain CT excluded intracranial hemorrhage and demonstrated early ischemic changes within the right middle cerebral artery (MCA) territory (ASPECTS 6) with a hyperdense MCA sign. MR angiography and digital subtraction angiography confirmed distal M1 occlusion extending into the M2 branches.

Laboratory investigations showed hyperglycemia, elevated fibrinogen and D-dimer levels, while echocardiography demonstrated ischemic cardiomyopathy with reduced left ventricular ejection fraction (39%). The Hemorrhagic Transformation Index (HTI) score was 4, indicating a high predicted risk of hemorrhagic transformation.

Therapeutic Intervention

Intravenous alteplase (Actilyse®, Boehringer Ingelheim GmbH, Germany) was administered at the standard dose of 0.9 mg/kg within 2 hours of symptom onset. Concurrently, Cerebrolysin® 30 mL diluted in 100 mL of 0.9% normal saline was infused intravenously over 20 minutes through a separate infusion line. Endovascular thrombectomy using a stent retriever achieved complete reperfusion (mTICI 3) with an onset-to-groin puncture time of 330 minutes. Cerebrolysin treatment was subsequently continued for a total of 14 consecutive days.

Follow-up and Outcomes

Twenty-four-hour CT demonstrated a small infarction (7 mL) without hemorrhagic transformation. NIHSS improved to 6 after 24 hours and to 4 at discharge, with an mRS score of 2.

Case 2

Patient Information and Clinical Findings

A 74-year-old man presented with acute right hemiparesis, hemisensory loss and aphasia. Intravenous alteplase was initiated within 1.5 hours after symptom onset. No adjunctive neurotrophic therapy was administered. Medical history included hypertension, coronary artery disease, peripheral arterial disease and previous ischemic stroke. Pre-stroke mRS was 1. Admission NIHSS was 14 (16 immediately before thrombolysis).

Diagnosis

Initial CT demonstrated early ischemic changes within the left MCA territory (ASPECTS 6) without intracranial

hemorrhage. Angiography confirmed distal M1 occlusion extending into M2 branches. Laboratory findings showed mild hyperglycemia. Echocardiography demonstrated ischemic cardiomyopathy with left ventricular ejection fraction of 38%. HTI score was 3, corresponding to a high predicted risk of hemorrhagic transformation.

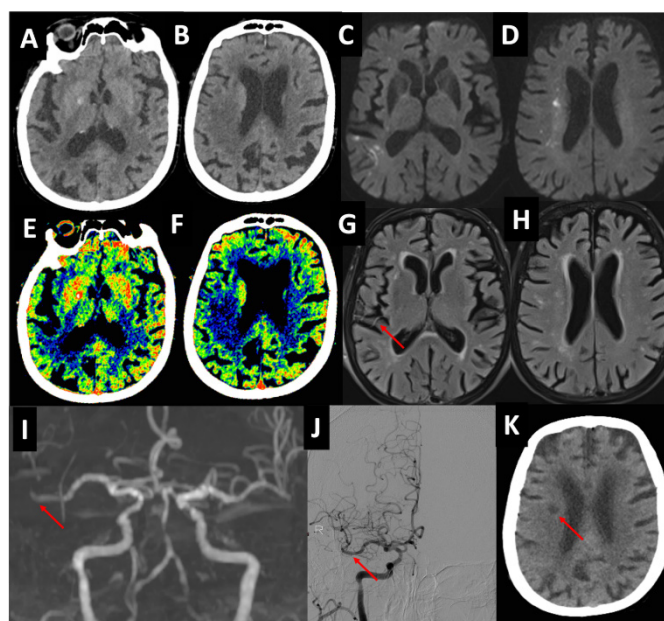


Figure 1: A–B: Baseline non-contrast CT displayed in the conventional brain window (width 100, level 50). Early ischemic changes (subtle hypoattenuation) are difficult to appreciate in the right insular cortex, internal capsule, and M5/M6 cortical regions (ASPECTS 6). C–D: Baseline diffusion-weighted imaging (DWI) demonstrates scattered acute ischemic lesions throughout the right MCA territory. E–F: The same CT sections displayed in the stroke window (width 40, level 40) with a color lookup table (CLUT). Early ischemic changes are more conspicuous, appearing as blue areas. G–H: Baseline fluid-attenuated inversion recovery (FLAIR) images show faint ischemic changes. Severe chronic white matter hyperintensities (Fazekas grade 3) are present. The “spaghetti sign” (red arrow) within the right MCA territory suggests well-developed leptomeningeal collateral circulation. I: Baseline three-dimensional time-of-flight MR angiography demonstrates occlusion (red arrow) of the distal M1 segment extending into the M2 branches of the right MCA. J: Digital subtraction angiography following EVT demonstrates complete reperfusion (red arrow) of the right MCA (mTICI 3). K: Follow-up CT at 24 hours demonstrates a small right MCA territory infarct (infarct volume, 7 mL) without HT (red arrow).

Therapeutic Intervention

Intravenous alteplase was administered at the standard dose of 0.9 mg/kg within 1.5 hours of symptom onset. No adjunctive cerebroprotective therapy was given. Endovascular thrombectomy using a stent retriever achieved complete reperfusion (mTICI 3), with an onset-to-groin puncture time of 350 minutes.

Follow-up and Outcomes

Twenty-four-hour CT demonstrated a 10-mL infarction complicated by asymptomatic hemorrhagic infarction type 2 (HI-2). NIHSS improved to 8 after 24 hours and to 5 at discharge, with an mRS score of 2.

Discussion

Hemorrhagic transformation remains one of the principal limitations of reperfusion therapy despite major advances in endovascular treatment. Recanalization restores cerebral perfusion but may also exacerbate blood–brain barrier disruption, resulting in reperfusion injury and secondary hemorrhage. Consequently, adjunctive therapies capable of protecting the neurovascular unit during early reperfusion are of considerable clinical interest. [1–3]

The two patients presented here shared several important characteristics that make comparison clinically informative. Both had anterior circulation LVO, similar baseline stroke severity (NIHSS 14–16), ASPECTS of 6, successful bridging therapy with complete reperfusion (mTICI 3), and a high predicted risk of hemorrhagic transformation according to the HTI score. [10] Despite these similarities, only the patient who did not receive Cerebrolysin developed radiological hemorrhagic transformation. Although the observed hemorrhage was

asymptomatic, radiographic HT remains clinically relevant because it is associated with larger infarct burden, poorer long-term prognosis in some patients, and may influence decisions regarding initiation of antithrombotic or anticoagulant therapy after stroke. [4,5] The absence of HT in the Cerebrolysin-treated patient therefore represents a potentially meaningful observation. These findings align with previous evidence from the CEREHETIS trial and subsequent observational studies suggesting that early Cerebrolysin administration during reperfusion therapy may reduce hemorrhagic transformation and improve functional outcomes [3–5].

The biological rationale is plausible. Cerebrolysin has been shown experimentally to stabilize the blood–brain barrier, attenuate inflammatory cascades, reduce oxidative stress and support neuronal survival through multimodal neurotrophic mechanisms. Administration during thrombolysis may therefore protect vulnerable brain tissue during the early phase of reperfusion. [3].

The principal limitation of this report is its descriptive nature. Conclusions regarding efficacy cannot be drawn from two patients, and differences in individual vascular or systemic factors cannot be excluded. Nevertheless, both patients underwent the same bridging reperfusion strategy, achieved complete recanalization and had comparable baseline imaging findings and predicted hemorrhagic risk, reducing several important sources of clinical heterogeneity. [10]

These cases therefore complement existing randomized and observational evidence by illustrating the feasibility of initiating Cerebrolysin concurrently with intravenous thrombolysis during bridging therapy and support further prospective investigation of this treatment strategy.

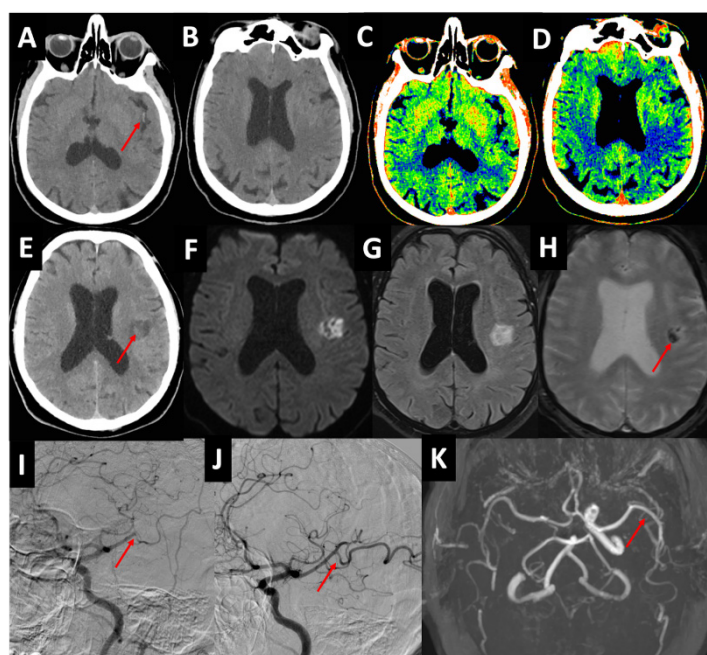


Figure 2: Figure 2. Brain imaging findings in Case 2. A–B: Baseline non-contrast CT displayed in the conventional brain window (width 100, level 50). Early ischemic changes (subtle hypoattenuation) are difficult to appreciate in the left internal capsule and the M3, M5, and M6 cortical regions (ASPECTS 6). A hyperdense left MCA sign (red arrow) is present. C–D: The same CT sections displayed in the stroke window (width 40, level 40) with a color lookup table (CLUT). Early ischemic changes become more conspicuous, appearing as blue areas. E–H: Follow-up imaging at 24 hours. Non-contrast CT (E), DWI (F), FLAIR (G), and T2-gradient recalled echo (H) demonstrate a small left MCA territory infarct (infarct volume, 10 mL). Petechial hemorrhage (red arrow) within the infarcted tissue is consistent with hemorrhagic infarction type 2 (HI-2). I: Baseline digital subtraction angiography demonstrates occlusion (red arrow) of the distal M1 segment extending into the M2 branches of the left MCA. J: Digital subtraction angiography following EVT demonstrates complete reperfusion (red arrow) of the left MCA (mTICI 3). K: Follow-up three-dimensional time-of-flight MR angiography at 24 hours demonstrates a patent left MCA (red arrow).*

Conclusion

This two-case report describes contrasting hemorrhagic outcomes following successful bridging reperfusion therapy in two patients with anterior circulation large-vessel occlusion and a high predicted risk of hemorrhagic transformation. Early administration of Cerebrolysin during intravenous thrombolysis was associated with the

absence of hemorrhagic transformation, whereas standard reperfusion therapy alone resulted in asymptomatic hemorrhagic infarction despite comparable baseline characteristics and complete reperfusion. Although no causal conclusions can be drawn from these observations, they are consistent with accumulating evidence that early cerebroprotective treatment may reduce reperfusion-related injury and justify prospective clinical evaluation.

CASE SUMMARY



Patient

- 84 years
- Large-vessel ischemic stroke



Challenge

- High risk of hemorrhagic transformation



Treatment

- Cerebrolysin 30 mL/day IV x 14 days + bridging therapy (IVT + EVT)



Outcome

- NIHSS 14 → 4
- mRS 2 at discharge
- no hemorrhagic transformation



Take Home Message

Early administration of Cerebrolysin concurrently with intravenous thrombolysis (IVT) in patients with high risk of hemorrhagic transformation (HT) may reduce the likelihood of HT development, as demonstrated by the absence of HT due to its ability to preserve blood–brain barrier integrity

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...with low-dose rt-PA after severe intraventricular hemorrhage

Abstract

Acute obstructive hydrocephalus is a complication of intraventricular hemorrhage, which requires a combination of medical and surgical treatments. We report a clinical case of intraventricular hemorrhage extension secondary to a ruptured arteriovenous malformation, successfully treated with a combination of methods: endovascular embolization of arteriovenous malformation, external ventricular drainage, intraventricular fibrinolysis with low-dose recombinant tissue plasminogen activator, and medical treatment with the neurotrophic drug Cerebrolysin in combination with neurorehabilitation.

Keywords: External ventricular drain, Cerebrolysin, intraventricular hemorrhage, neurology

Introduction

Patients with intraventricular hemorrhage (IVH) due to a ruptured arteriovenous malformation (AVM) with acute obstructive hydrocephalus are at high risk of mortality and poor functional outcome.¹ Treatment is difficult and requires a clinical strategy that combines medical, surgical, and end-ovascular methods.² The high volume of blood in the third and fourth ventricles may cause hydrocephalus; however, insertion of an external ventricular drainage (EVD) is ineffective due to the blood clots formed in the ventricles.³ Intraventricular fibrinolysis via the EVD is known to facilitate the removal of blood from the ventricles and has a good safety profile.⁴ A large amount of blood in the ventricles may damage neurons and the blood–brain barrier, leading to acute hydrocephalus and increased intracranial pressure.⁵ Pharmacological treatment was applied to treat cerebral edema, and the neurotrophic agent Cerebrolysin was used as an add-on therapy to minimize neuronal damage and to stimulate neurorecovery.⁶ Rehabilitation measures followed the recommendations of the AVANT (Austrian Vietnamese Advancement Neurorehabilitation Treatment) program,⁷ with essential exercises to help stroke patients regain independence. We report a case of a patient with acute obstructive hydrocephalus after IVH due to rupture of an AVM, who was successfully treated with the above strategy.

Case Report

A 18-year-old woman with normal medical history suddenly collapsed and was admitted to the emergency department 5 hours after symptom onset. On examination, the patient was found to be in a comatose status, Glasgow Coma Scale (GCS) 7/15 (Table 1), left pupil dilated to 3 mm, right pupil dilated to 2 mm, both pupils non-reactive, with paralysis of all extremities, blood pressure of 140/80 mmHg, pulse rate of 80 bpm, and mild fever of 38°C.

Initial non-contrast computed tomography (CT) scan showed all four ventricles full of blood, the lateral ventricles enlarged, suggestive of obstructive hydrocephalus, and a Graeb score of 12 points (Figure 1(a) and (b)). A CT angiogram done shortly thereafter confirmed an AVM located beside the left lateral ventricle (Figure 1(c) and (d)).

A digital subtraction angiography showed a Spetzler–Martin Grade 3 AVM. The feeding vessels were the branches of the anterior cerebral artery. The size of the nidus was 2 × 2 cm and it drained into the vein of the superior sagittal sinus. Endovascular embolization is most commonly used to reduce the size of the AVM in preparation for surgery; thus, a microcatheter was placed via AVM feeding arteries close to the nidus, and then the embolic agent Onyx was infused in the nidus. As a result, the AVM was fully embolized.

The patient was immediately taken to the operating room and an EVD was placed, intravenous Cerebrolysin 20 mL and mannitol were administered, and the patient's blood pressure was kept below 140/90 , mmHg. The postoperative clinical status of the patient did not improve and a cast was formed in the ventricular system. Ventriculostomy was adequately positioned but demonstrated a poor waveform, and cerebrospinal fluid (CSF) output was judged to be slow at 3 mL/h (Figure 2(a)).

The possible risk of re-hemorrhage and subsequent death was discussed with the family, but the decision to give intra-ventricular thrombolytics due to the high rate of mortality associated with the patient's condition was made. Specifically, the large volume of blood in all four ventricles, the obstructive hydrocephalus, and the poor clinical status worsened the prognosis. We administered 1 , mg of recombinant tissue plasminogen activator (rt-PA) through the EVD and then flushed the EVD with 3 mL of normal saline. After administrating the rt-PA, the ventriculostomy was clamped and the intracranial pressure was monitored closely. After 1 h, the ventriculostomy was opened and allowed to drain at a height of 10 , cm above the patient's ear. Rt-PA was given every 8 h, for a total of seven doses (Figure 2(b)–(d)).

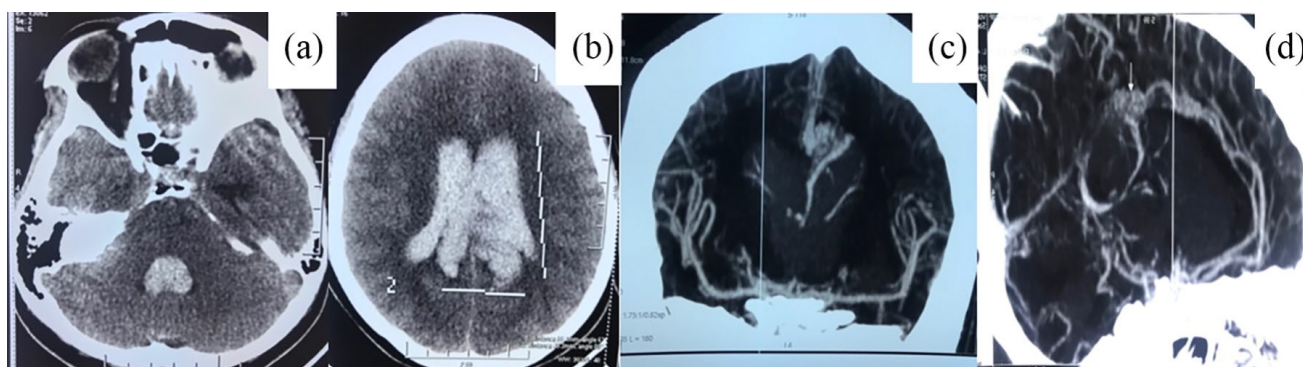


Figure 1: (a, b) Non-contrast CT scan and (c, d) AVM located in the left lateral ventricle.

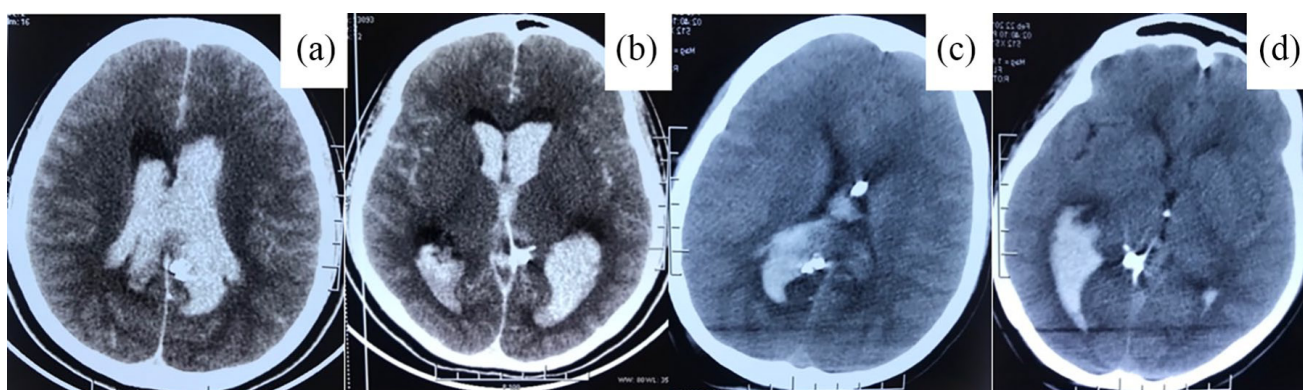


Figure 2: (a) Before treatment; (b) after 5 doses of rt-PA; (c) after 7 doses of rt-PA; and (d) after removal of the drain.

The patient received intensive care and the previously described treatment. Cerebrolysin was administered intravenously at a daily dose of 20 mL for 14 days. A tracheostomy for prolonged ventilation was carried out after 12 days. The patient was also enrolled in a rehabilitation program following the AVANT recommendations. Post-bleed day (PBD) 15: The patient's neurological functions improved (GCS 9, Table 1), she could move both extremities by herself and breathe without mechanical ventilation, and the left pupil dilation decreased to 2 mm and the right pupil dilation to 1.5 mm.

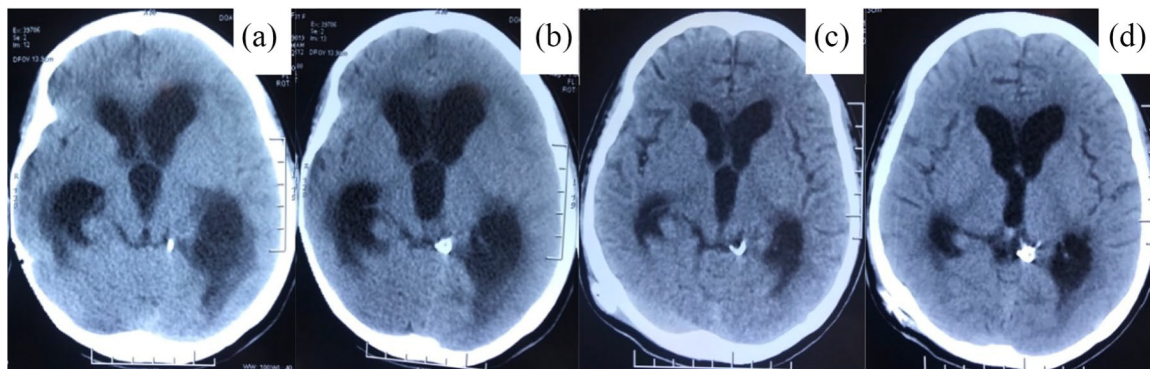


Figure 3: (a, b) Before ventriculo-peritoneal shunt and (c, d) after ventriculo-peritoneal shunt.

Table 1: NIHSS, GCS and mRS scores over time.

Scale	Baseline	Day 15	Day 30	Day 40	Day 60	Day 90
NIHSS	30	20	22	12	2	1
GCS	7	9	8	15	15	15
mRS	-	5	5	4	2	1

PBD 30: The patient developed increased confusion and lethargy, the GCS decreased to 7–8 (Table 1), and the patient was put on mechanical ventilation again. A CT scan of the head showed an acute hydrocephalus (Figure 3(a) and (b)). It was evident that the patient required permanent CSF shunting; consequently, we decided to establish a ventriculo-peri-toneal shunt (Figure 3(c) and (d)). Cerebrolysin 20 mL was administered intravenously daily for another 10, days, from day 31 to day 40. Participation in the AVANT rehabilitation program was interrupted.

PBD 40: The patient's consciousness improved moderately, and she recovered partial motor function with muscle strength of 3/5. She could breathe without mechanical ventilation. The patient continued with the AVANT rehabilitation program.

PBD 60: The patient's mRS (modified Rankin Scale)⁹ was 2 (Table 1); she showed good recovery in terms of com-munication and was able to take care of her daily needs with-out assistance, although she remained unable to resume all her previous activities.

PBD 90: The patient continued improving in motor and speech functions. NIHSS (National Institutes of Health Stroke Scale)¹⁰ assessment showed a score of 0 and the mRS a score of 1 (Table 1). Figure 4 shows that the excess fluid had been drained, and the brain had stabilized.

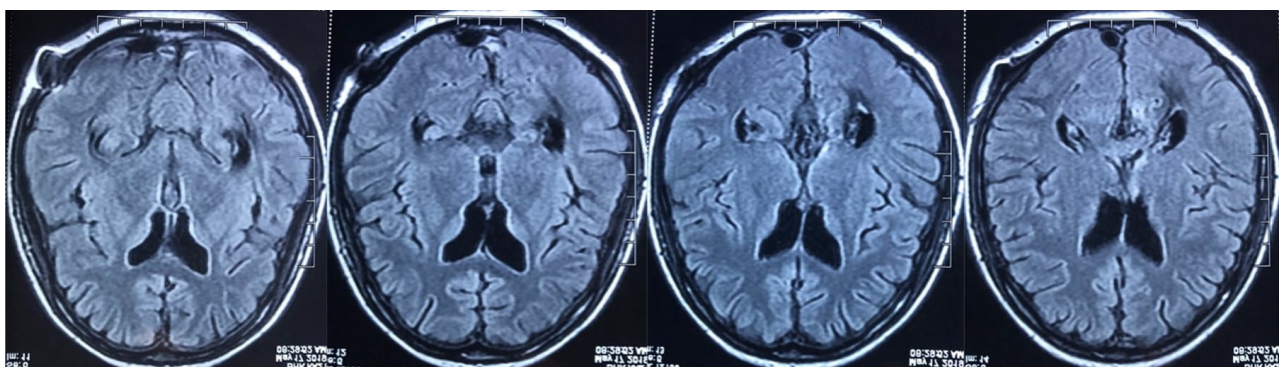


Figure 4: MRI after 90 days.

Discussion

The prognosis for patients with IVH is very poor, with high rates of disability and mortality, in the presence of any IVH up to 50%.¹¹ This high mortality rate is proportional to the amount of ventricular hemorrhage and increases when the third and fourth ventricles are involved.^{12,13} In observational studies, the mortality rate after intracranial hemorrhage from AVM rupture ranges from 12% to 66.7%.^{14,15}

The successful treatment of this case is attributable to a combination of medical, surgical, endovascular, and pharmacological methods. Endovascular embolization of the AVM prior to surgery helped reduce the risk of hemorrhagic complications due to the use of rt-PA. This was followed by the placement of an EVD and administration of rt-PA to remove the blood clot and drain the ventricles. After seven doses of rt-PA, most of the blood was drained from the ventricles, but the patient's clinical status did not improve due to resorptive hydrocephalus and complications. Aiming to reduce complications and to stimulate functional recovery, we decided to apply Cerebrolysin.

Previous research has shown a positive effect on neurorecovery after various types of brain lesions such as ischemic stroke and brain trauma. In addition, the patient received essential neurorehabilitation exercises in accordance with the recommendations of the AVANT program.

Although only little improvement could be seen in the acute phase after seven doses of rt-PA, this case finally resulted in a very positive and unexpected outcome after applying the AVANT neurorehabilitation program in combination with intra-venous Cerebrolysin treatment. The patient was discharged after 54 days and continued to recover with excellent results. By day 90, the patient had an mRS of 1, could walk by herself, showed good speech recovery, and had no signs of local paralysis. The patient was able to carry out daily activities without assistance, such as walking, communicating, and eating.

Conclusion

The combination of medical, surgical, and endovascular methods with pharmacological treatment and a structured rehabilitation program to support neurorecovery was a successful and safe therapeutic strategy, which should therefore encourage further research in the development of a comprehensive treatment strategy for patients with IVH and hydrocephalus.

CASE SUMMARY



Patient

• 18 years • Severe intraventricular hemorrhage due to ruptured AVM



Challenge

• Coma and obstructive hydrocephalus



Treatment

• Cerebrolysin 20 mL/day IV x 14 days + AVM embolization + EVD + rt-PA + rehabilitation



Outcome

• NIHSS 30 → 1 • GCS 7 → 15 • mRS 5 → 1



Take Home Message

Severe intraventricular hemorrhage with acute obstructive hydrocephalus carries high mortality risk, while adjunctive Cerebrolysin with intensive rehabilitation may support neurological recovery.

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...in the management of tandem ICA and MCA occlusion after EVT with residual perfusion deficit

Abstract

Acute ischemic stroke patients may demonstrate persistent tissue-level hypoperfusion despite successful angiographic recanalization after mechanical thrombectomy. We report a 57-year-old man with wake-up stroke due to tandem occlusion of the right internal carotid artery and M1 middle cerebral artery who presented with left hemiparesis, neglect, and dysarthria (NIHSS 7). Imaging demonstrated salvageable penumbral tissue, and the patient underwent intravenous alteplase followed by mechanical thrombectomy with carotid artery stenting, achieving complete angiographic recanalization (TICI 3). However, post-procedural CT perfusion revealed persistent residual hypoperfusion despite macrovascular reperfusion. Adjunctive Cerebrolysin therapy was initiated immediately after the procedure. The patient demonstrated rapid neurological improvement (NIHSS 1 within hours), without treatment-related adverse effects, and was discharged on hospital day 5 with mild residual cognitive deficits. This case highlights the dissociation between angiographic and tissue-level reperfusion after thrombectomy and supports further investigation of adjunctive cerebroprotective strategies guided by post-procedural perfusion imaging.

Key Words: adjunctive therapy; Cerebrolysin; cerebroprotection; anterior circulation stroke; tandem internal carotid artery occlusion; post-thrombectomy CT perfusion; wake-up stroke

Introduction

Endovascular thrombectomy (EVT) has transformed the management of acute ischemic stroke due to large vessel occlusion, with the HERMES collaboration demonstrating successful angiographic recanalization in approximately 71% of treated patients. Despite this success, approximately half of all successfully recanalized patients fail to achieve functional independence at 90 days — a phenomenon termed “futile recanalization.” Multiple mechanisms have been proposed, including microvascular obstruction, distal embolization, no-reflow phenomenon, and reperfusion injury. Post-EVT CT perfusion (CTP) has emerged as a sensitive imaging biomarker to detect tissue-level reperfusion failure even when modified Thrombolysis in Cerebral Infarction (mTICI) scoring suggests complete reperfusion. Persistent $T_{max} > 6$ s hypoperfusion despite TICI 3 grade has been documented in 20–50% of cases, and is independently associated with worse functional outcome. These observations have prompted increasing interest in adjunctive cerebroprotective strategies aimed at enhancing neurological recovery in patients with documented tissue-level reperfusion failure.

Cerebrolysin, a mixture of low-molecular-weight neuropeptides and free amino acids with established neurotrophic properties, includes attenuation of glutamate-mediated excitotoxicity, reduction of oxidative stress, modulation of post-reperfusion inflammatory cascades and promotion of neuroplastic recovery. Clinically it has demonstrated benefits in anterior circulation stroke when used alongside standard reperfusion therapy, with a favorable safety profile.

As part of an ongoing prospective study at the Department of Neurology, Shaare Zedek Medical Center, eligible patients with anterior circulation large vessel occlusion who undergo mechanical thrombectomy (MT) receive adjunctive Cerebrolysin. Here, we report a representative case from this cohort demonstrating dissociation between post-EVT angiographic and tissue-level reperfusion, with favorable clinical recovery following adjunctive Cerebrolysin therapy.

Patient Information

A 57-year-old single man with a history of long-standing severe smoking, peripheral vascular disease, and prior right superficial femoral artery stenting (2021), and with a remote history of substance abuse, presented with acute-onset left-sided weakness consistent with a wake-up stroke. He was not taking any regular medications, including no antiplatelet or anticoagulant therapy. His baseline modified Rankin Scale (mRS) score was 0; he had been fully independent. There was no previous history of stroke, transient ischemic attack, or cognitive impairment. No relevant family history of cerebrovascular disease was reported.

Clinical Findings

The patient had gone to sleep at approximately 02:00 in his usual baseline neurological state. He awoke at approximately 05:00 with sudden onset of left-sided weakness, was unable to rise from bed, and fell while attempting to stand, sustaining a left-sided contusion. He called emergency medical services and was admitted to the emergency department at 08:16.

On admission, the patient was fully alert and oriented to person, place, and time. Vital signs were notable for elevated blood pressure of 190/93 mmHg; heart rate 80 beats per minute; oxygen saturation 99% on room air. Neurological examination demonstrated severe left-sided hemiparesis, with muscle strength graded 3/5 in the left upper limb and 4/5 in the left lower limb, accompanied by left-sided sensory neglect, left central facial palsy, and mild dysarthria. Pupils were equal and reactive, with intact extraocular movements. The NIHSS score on admission was 7.

Timeline

Table 1. Clinical progression and treatment timeline.

Day	Clinical Course and Key Therapeutic Interventions
Day 0	Wake-up stroke with left hemiparesis (NIHSS 7). CT/CTA/CTP demonstrated tandem right ICA–M1 occlusion. Intravenous alteplase followed by MT and carotid stenting achieved TICI 3 recanalization. Post-procedural CTP revealed persistent residual hypoperfusion. Adjunctive Cerebrolysin therapy was initiated.
Days 1–3	Continued adjunctive Cerebrolysin therapy. Sustained motor recovery and mild residual cognitive deficits noted.
Day 5	Discharged with NIHSS 1 on dual antiplatelet, antihypertensive and lipid-lowering therapy; referred to community neurorehabilitation.

Diagnostic Assessment

Non-contrast brain CT excluded intracranial hemorrhage. CT angiography demonstrated tandem occlusion involving the right internal carotid artery (RICA) and the M1 segment with poor distal filling. Pre-procedural CTP (Figure 1) demonstrated a large right anterior circulation perfusion deficit, with Tmax >6 s volume of 74.73 cm³, an ischemic core (rCBF <30%) of 33.23 cm³, a penumbra of 41.5 cm³, and a mismatch ratio of 2.25. These findings indicated the presence of salvageable tissue and supported eligibility for MT.

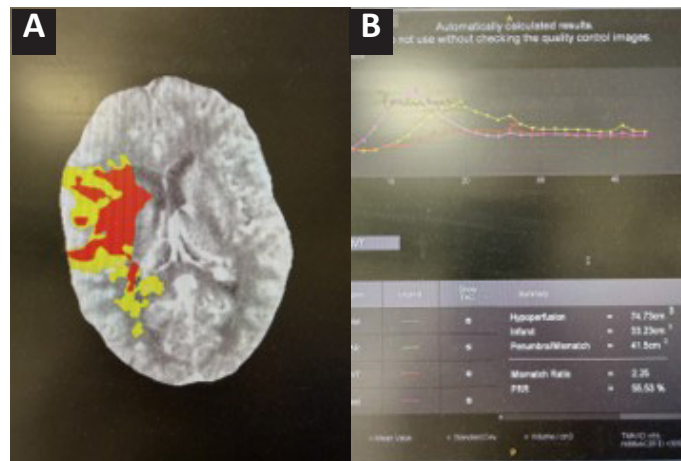


Figure 1: **(A)** Pre-procedural CTP. The color overlay demonstrates a large area of ischemic core (red, rCBF <30%) within the right anterior circulation territory, surrounded by penumbral hypoperfusion (yellow, Tmax >6 s). **(B)** The automated quantitative summary shows a hypoperfusion volume of 74.73 cm³, an ischemic core of 33.23 cm³, a penumbral mismatch of 41.5 cm³, and a mismatch ratio of 2.25.

Digital subtraction angiography (Figures 2) confirmed the tandem occlusion with severely diseased right internal carotid artery and absent intracranial filling on the right side. Following stent placement in the right ICA and MT, complete macrovascular recanalization (TICI grade 3) was achieved. (Figure 2B)

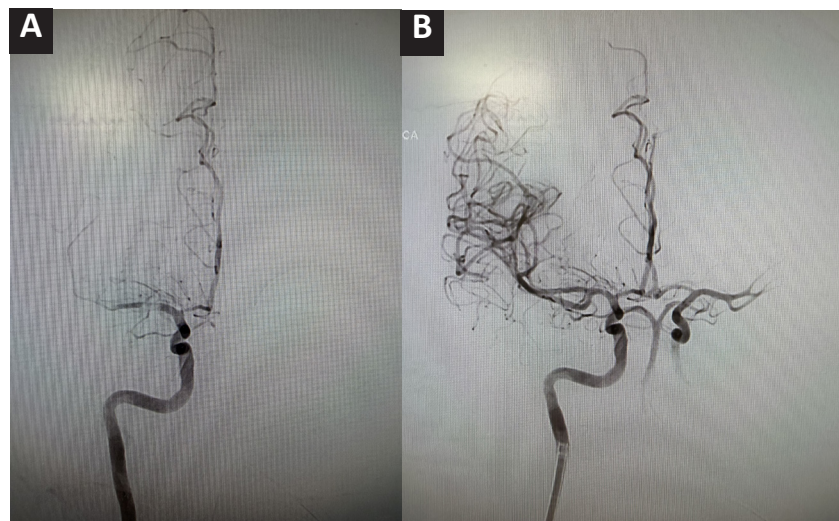


Figure 2: **(A)** Pre-thrombectomy digital subtraction angiography (DSA) demonstrating diseased right internal carotid artery with absent flow into the intracranial circulation, consistent with tandem RICA–M1 occlusion. **(B)** Post-thrombectomy digital subtraction angiography demonstrating complete recanalization (TICI grade 3) of the right anterior circulation following internal carotid artery stenting and MT. Robust filling of the right middle cerebral artery branches is now visible.

Despite the achievement of complete angiographic recanalization, post-procedural CTP performed immediately (Figure 3) demonstrated persistent residual hypoperfusion. (Figure 3B) Scattered residual deficits were present in the right middle cerebral artery territory, indicating that complete angiographic reperfusion did not equate to complete tissue-level reperfusion. This finding identified the patient as a candidate for adjunctive cerebroprotective therapy.

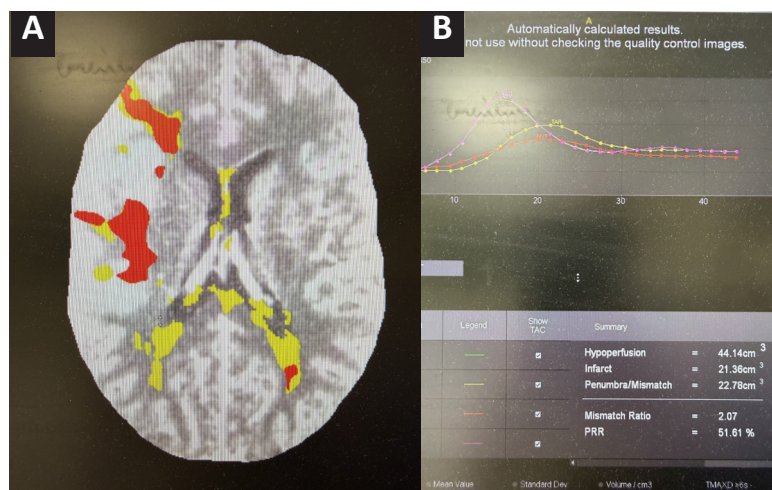


Figure 3: **(A)** Post-procedural CTP color overlay performed immediately after MT. Despite TIC1 3 recanalization, scattered residual ischemic core (red) and penumbra (yellow) persist within the right middle cerebral artery territory, consistent with microvascular reperfusion failure (no-reflow phenomenon). **(B)** Post-procedural CTP automated quantitative summary. Hypoperfusion volume = 44.14 cm³, ischemic core = 21.36 cm³, penumbral mismatch = 22.78 cm³, mismatch ratio = 2.07. Although volumes are reduced compared with the pre-procedural study, significant tissue-level hypoperfusion persists despite TIC1 3 angiographic recanalization.

Follow-up non-contrast brain CT (Figure 4) demonstrated evolution of acute ischemic changes within the right middle cerebral artery territory, without hemorrhagic transformation.

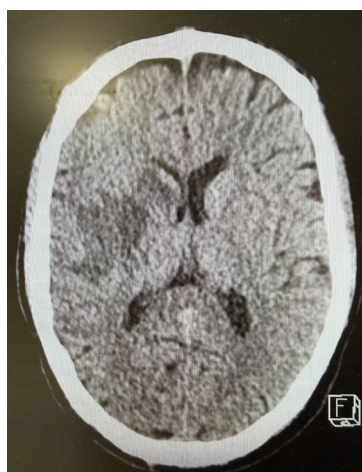


Figure 4: Follow-up non-contrast brain CT performed 24 hours after acute treatment.

Laboratory evaluation revealed admission hyperglycemia; other parameters were within normal limits. Stroke work-up, including transthoracic echocardiography with bubble study and 24-hour Holter monitoring, was unrevealing, and the stroke was classified as cryptogenic.

Therapeutic Intervention

Intravenous alteplase was administered approximately one hour after admission, followed by MT with placement of an internal carotid artery stent. Dual antiplatelet therapy (DAPT) was loaded peri-procedurally with 300 mg clopidogrel and 300 mg aspirin to maintain stent patency.

MT Adjunctive Cerebrolysin (30 mL diluted in 250 mL saline, daily intravenously) was started immediately after MT because of persistent post-procedural perfusion deficits and continued throughout hospitalization.

Secondary prevention measures included continued dual antiplatelet therapy, low-dose ramipril for blood pressure control, and lipid-lowering therapy. A structured neurorehabilitation program was initiated during the hospital stay, with focus on cognitive rehabilitation given the patient's residual deficits.

Follow-up and Outcomes

Immediately following MT, the patient demonstrated dramatic neurological improvement, with the NIHSS

score decreasing from 7 to 1, reflecting full motor and language recovery with only mild residual dysarthria. He was transferred to the Neurology Intensive Care Unit for monitoring. The early hospital course was complicated by brief hemodynamic instability requiring transient noradrenaline support, followed by stabilization and initiation of low-dose ramipril for blood pressure control. Over the subsequent days, motor function remained fully recovered. However, neuropsychological assessment identified mild residual cognitive deficits, specifically affecting short-term memory and executive function. Speech-language and physical therapy assessments confirmed otherwise satisfactory functional recovery. No adverse effects related to Cerebrolysin therapy were observed during the inpatient stay. At discharge on hospital day 5 (31 October 2023), the patient had a discharge NIHSS score of 1, with mild residual cognitive impairment as the primary remaining concern. He was discharged on dual antiplatelet therapy, ramipril, and lipid-lowering therapy, and referred to a community-based neurorehabilitation program with continued cognitive rehabilitation.

Discussion

This case illustrates several critical aspects of contemporary stroke management and provides an important clinical example of the dissociation between angiographic and tissue-level reperfusion that can occur even after technically successful MT.

First, the patient's presentation as a wake-up stroke with tandem right internal carotid artery and M1 segment occlusion represents a clinically challenging scenario requiring imaging-based selection for late-window MT. The presence of a significant pre-procedural ischemic core (33 cm³) accompanied by a favorable mismatch ratio (2.25) supported the decision to proceed with combined intravenous thrombolysis and MT with carotid artery stenting.

Second, and most importantly for this case, the post-procedural CTP findings revealed a clinically significant disparity between the angiographic outcome (TICI grade 3, indicating complete macrovascular recanalization) and the actual tissue-level reperfusion (persistent Tmax >6 s volume of 44 cm³ and residual ischemic core of 21 cm³). This phenomenon — sometimes termed the “no-reflow phenomenon” or microvascular reperfusion failure — has been documented in 20–50% of patients with technically successful thrombectomy and is increasingly recognized as a critical mechanism underlying futile recanalization. Recent systematic reviews have established that post-EVT CTP-defined residual hypoperfusion is independently and consistently associated with worse functional outcome, identifying patients who may benefit from adjunctive cerebroprotective intervention.

Third, despite the substantial residual perfusion deficit on post-procedural imaging, the patient demonstrated dramatic acute clinical improvement (NIHSS 7 to 1) following the procedure. While spontaneous reperfusion of penumbral tissue and early recovery of stunned but viable brain tissue likely contributed to this rapid improvement, the magnitude of clinical recovery in the face of substantial documented residual hypoperfusion raises the possibility of cerebroprotective benefit from adjunctive Cerebrolysin therapy.

Nevertheless, single-case observations cannot establish causality between adjunctive Cerebrolysin and the favorable clinical course. Spontaneous recovery, the contribution of successful reperfusion to penumbral salvage, and structured rehabilitation likely all contributed to the observed outcome. The persistence of mild cognitive deficits at discharge, despite full motor recovery, underscores the multidimensional nature of post-stroke recovery and highlights the importance of comprehensive cognitive assessment beyond standard motor and language scales.

This case also illustrates the value of routine post-procedural CTP as a clinical tool for both prognostication and patient selection for adjunctive therapy. Patients with documented residual tissue-level hypoperfusion despite TICI 3 recanalization represent a clinically and biologically distinct subgroup who may benefit from adjunctive cerebroprotective strategies in addition to standard reperfusion therapy.

Ongoing prospective studies, including those at our institution, are expected to further clarify the therapeutic role of adjunctive Cerebrolysin and other cerebroprotective agents in patients with persistent post-thrombectomy perfusion deficits.

CASE SUMMARY



Patient

- 57 years
- Wake-up stroke (tandem ICA-MCA occlusion)



Challenge

- Residual tissue hypoperfusion despite successful thrombectomy



Treatment

- Cerebrolysin 30 mL/day IV x 5 days + alteplase, thrombectomy and carotid stenting



Outcome

- NIHSS 7 → 1
- Complete motor recovery
- mild residual cognitive deficits



Take Home Message

Patients with documented residual tissue-level hypoperfusion after thrombectomy represent a clinically and biologically distinct patient population, benefitting from adjunctive cerebroprotective strategies with immediate Cerebrolysin administration.



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...in a colon cancer patient suffering from ischemic stroke

Abstract

We present a clinical case of cancer-associated ischemic stroke in a 70-year-old patient with metastatic sigmoid colon cancer. The patient was admitted to the hospital in the hyperacute stage of ischemic stroke caused by thrombosis in the left middle cerebral artery territory, presenting with severe global aphasia and right-sided hemiplegia (NIHSS score: 20). Despite the high risk of hemorrhagic complications associated with malignancy, systemic thrombolytic therapy with alteplase was successfully administered, although hemorrhagic transformation subsequently developed. Early comprehensive rehabilitation and adjunctive therapy with Cerebrolysin (30 ml/day) led to significant regression of neurological deficits. One month after stroke onset, the patient demonstrated almost complete recovery of motor function and substantial speech improvement with no short-term complications related to anticoagulant therapy with apixaban. This case highlights the importance of early diagnosis and a multidisciplinary approach in the management of ischemic stroke in patients with cancer.

Keywords: cancer-associated stroke, ischemic stroke, systemic thrombolysis, alteplase, Cerebrolysin, hemorrhagic transformation, anticoagulant therapy, clinical case.

Introduction

This clinical case is of practical interest because ischemic (IS) stroke occurs relatively frequently in patients with malignant neoplasms. Cancer may provoke ischemic stroke through coagulation disorders leading to hypercoagulability, as well as through intercurrent infections. Typical features of cancer-associated ischemic stroke (CAIS) include multiple infarctions in different vascular territories, markedly elevated D-dimer levels, and the presence of metastases [1]. Arterial hypertension, hyperlipidemia, and congestive heart failure are relatively less common in patients with CAIS than in the general population.

Additional risk factors for CAIS include [2] tumor-associated thrombophilia and coagulopathies, particularly in patients with metastatic or aggressive tumors; cancer progression and the development of new metastases; the use of cytotoxic or hormonal therapies that may affect coagulation; prolonged immobilization, which increases the risk of venous thrombosis; advanced age and comorbid chronic conditions, especially cardiovascular and immune disorders; and vascular embolization by tumor cells. These factors increase the risk of ischemic stroke in patients with cancer and require careful monitoring and timely preventive measures.

Clinical Case

A 70-year-old male patient was brought to the emergency department by ambulance at 07:06 AM. According to his wife, he awoke at around 05:40 in satisfactory condition, but at approximately 06:00 he suddenly became unable to speak and developed weakness in the right limbs.

The medical history included ischemic heart disease and arterial hypertension; however, the patient was

not receiving regular medication, including antithrombotic therapy. He also had sigmoid colon cancer with lung metastases and was receiving combined oncological treatment. Surgical treatment included left lung lobectomy 14 months before stroke onset. The last course of chemotherapy had been completed 4 months before the stroke.

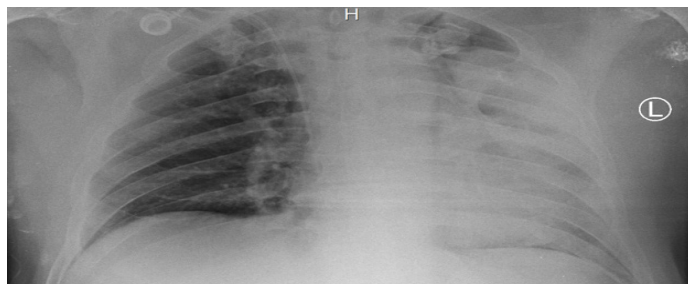


Figure 1: Chest radiograph showing asymmetric lung changes. Right lung: Heterogeneous reduction in aeration, predominantly in the middle and lower zones, with diffuse opacification and no clearly defined focal lesion. The findings are consistent with pulmonary consolidation/infiltration, possibly due to right lower-lobe pneumonia or pleural effusion. Left lung: Increased lucency in the lateral regions, with markedly reduced pulmonary vascular markings, consistent with post-lobectomy changes in the left lung. Additional findings: Pulmonary vascular markings are reduced bilaterally. The hilar structures are poorly defined.

At 07:10, the patient underwent a neurological examination. The patient weighed 102 kg, was 176 cm tall, and had a body mass index (BMI) of 32.9 kg/m². Neurological assessment revealed a Glasgow Coma Scale (GCS) score of 13 and severe global aphasia. No meningeal signs were present. The pupils were equal and reactive to light, and eye movements were full. Examination of the cranial nerves showed flattening of the right nasolabial fold and deviation of the tongue to the right side, while swallowing function was preserved. Motor examination demonstrated decreased muscle tone in the right upper and lower extremities, with complete paralysis (muscle strength 0/5) on the right side. Deep tendon reflexes were increased on the right, and a positive Babinski sign was elicited on the same side. Sensory testing revealed right-sided hemianesthesia. The severity of the stroke was assessed using standardized clinical scales. The patient had a National Institutes of Health Stroke Scale (NIHSS) score of 20, indicating a severe neurological deficit, and a modified Rankin Scale (mRS) score of 5, reflecting severe disability and dependence on assistance for daily activities.

At 07:19, brain CT (Figure 2) showed no intracranial hemorrhage or pathological lesions. The midline structures were not displaced. The basal cisterns were preserved and ventricles were not enlarged. The ASPECTS score was 10. Chest radiography (Figure 1) revealed subtotal heterogeneous opacity of the left lung and increased pulmonary markings on the right side without infiltrative shadows.

Laboratory Findings and Initial Management

Laboratory investigations on admission demonstrated a blood glucose level of 10.1 mmol/L, a platelet count of $140 \times 10^9/L$, a D-dimer concentration of 388 ng/mL, a prothrombin time of 12.5 seconds, a C-reactive protein (CRP) level of 21.9 mmol/L, and an HDL cholesterol level of 0.73 mmol/L.

Based on the clinical presentation and diagnostic findings, the patient was diagnosed with a cryptogenic ischemic stroke in the territory of the left middle cerebral artery. The stroke manifested with global aphasia, right-sided hemiplegia, and right-sided anosognosia in the acute phase. The event occurred in the context of metastatic sigmoid colon cancer, arterial hypertension stage II, and cerebral atherosclerosis.

Given the severity of the neurological deficit and the absence of contraindications, the medical team decided to proceed with intravenous systemic thrombolytic therapy using alteplase. Treatment was initiated at 08:00 with a total dose of 90 mg, consisting of a 9 mg intravenous bolus followed by an 81 mg infusion administered over one hour. The door-to-needle time was 54 minutes.

Clinical Course

One hour after alteplase administration, the patient's neurological condition showed early signs of improvement. The Glasgow Coma Scale score increased from 13 to 14, while the NIHSS score improved from 20 to 18. Fragmented speech emerged, and slight recovery of motor function was noted in the right lower extremity, with muscle strength improving to 1/5.

Twenty-four hours after thrombolytic treatment, further neurological recovery was observed. The patient achieved a GCS score of 15, and the NIHSS score improved to 9. Partial comprehension of speech returned, and strength in the right leg increased to 3/5. Follow-up computed tomography performed 24 hours after thrombolysis demonstrated the development of an ischemic lesion in the left temporoparietal region measuring 30 × 35 mm. Early rehabilitation was initiated within the first 24 hours following stroke onset. The rehabilitation program included proper positioning and mobilization of the patient, physiotherapy, speech therapy, and massage of the affected extremities.

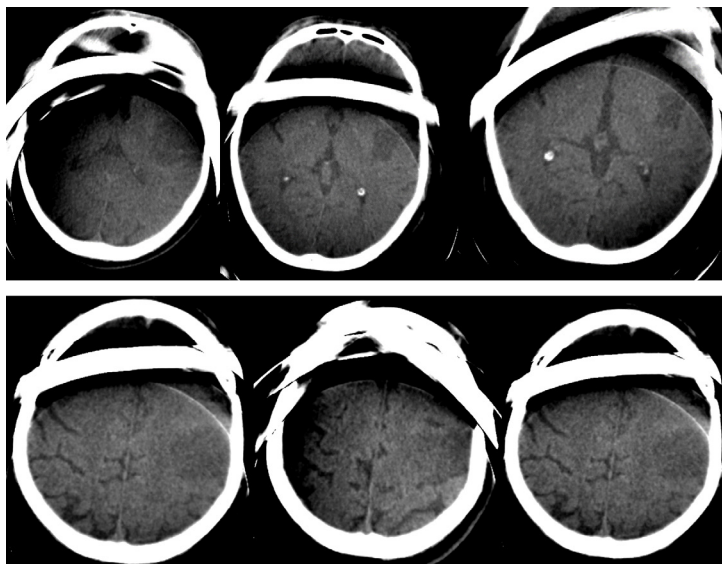


Figure 2: Non-contrast CT of the brain. The examination is significantly limited by severe motion artifacts caused by the patient's agitation. Within the limitations of the study, no definite evidence of intracranial hemorrhage or focal areas of abnormal attenuation is identified. There is no midline shift. The basal cisterns are preserved. The ventricular system is not dilated. ASPECTS: 10.

Three days after thrombolytic therapy, the patient remained clinically stable. To reduce the risk of thromboembolic complications, dalteparin sodium 5,000 IU once daily was initiated. In addition, as part of the early rehabilitation strategy, Cerebrolysin was administered intravenously at a dose of 30 mL/day diluted in 200 mL of saline for ten consecutive days, with the aim of supporting speech recovery and improving motor function of the dominant hand.

Neuroimaging and Additional Investigations

On the seventh day after stroke onset, magnetic resonance imaging of the brain revealed an acute infarction within the territory of the left middle cerebral artery. Imaging also demonstrated cytotoxic edema involving the left temporal and parietal lobes, as well as hemorrhagic transformation along the cortical regions of the infarcted area. Cardiac evaluation with transthoracic echocardiography did not identify a major cardioembolic source. Doppler ultrasonography of the brachiocephalic arteries revealed only mild atherosclerotic stenosis, estimated at 15-20%, at the bifurcation of the left carotid artery. The patient remained hospitalized for a total of 14 days.

Outcome and Follow-Up

At the time of discharge, mild facial asymmetry persisted, together with severe paresis of the right upper extremity and a residual right-sided hemisensory deficit. Nevertheless, substantial neurological improvement had been achieved, with the NIHSS score decreasing to 3 and the modified Rankin Scale score improving to 2. The patient was discharged home on secondary prevention therapy consisting of ramipril 2.5 mg once daily, pantoprazole 20 mg once daily, atorvastatin 40 mg once daily, and apixaban 5 mg twice daily. Despite the presence of hemorrhagic transformation on follow-up imaging, the multidisciplinary medical board considered early anticoagulation to be justified because of the very high risk of recurrent ischemic stroke associated with active metastatic malignancy.

Twenty-six days after discharge, outpatient follow-up demonstrated continued neurological recovery. Only mild residual motor aphasia remained, while no motor, sensory, or coordination deficits were detected on

examination. Functional outcome had further improved, with an mRS score of 1. No short-term complications related to anticoagulant therapy were observed during the follow-up period.

Discussion

Admission within the therapeutic time window allowed systemic thrombolysis with standard-dose alteplase. Given the patient's oncological history, the risk of hemorrhagic complications was considered high, which was later confirmed by MRI findings showing hemorrhagic transformation. Timely medical intervention enabled successful reperfusion therapy and early rehabilitation. The favorable functional outcomes were likely facilitated not only by prompt treatment but also by the early administration of Cerebrolysin at an effective dose of 30 ml/day for 10 days. This therapy may have contributed both to improved rehabilitation potential and to prevention of severe hemorrhagic complications [5,6].

Previous studies suggest that Cerebrolysin reduces the risk of hemorrhagic transformation, including symptomatic hemorrhage [6], through stabilization of endothelial tight junction proteins within the blood-brain barrier [7] and suppression of matrix metalloproteinase activity [8]. These mechanisms may be particularly relevant in patients with cancer, who have a substantially increased risk of hemorrhagic transformation [9]. The multidisciplinary rehabilitation team successfully integrated these therapeutic strategies, leading to significant improvement in speech and motor recovery, a shorter rehabilitation period, and improved quality of life. Notably, the patient periodically resided in Belarus and did not initially speak Russian, although he understood it. After treatment and intensive speech therapy, he was able to speak Russian again.

In conclusion, cancer-associated ischemic stroke requires special attention and careful evaluation by clinicians, who must recognize the high risk of this complication and manage it promptly and effectively, especially in the context of active or progressive malignancy.

CASE SUMMARY



Patient

• 70 years • Cancer-associated left MCA stroke



Challenge

• Global aphasia and right hemiplegia



Treatment

• Cerebrolysin 30 mL/day IV x 10 days + thrombolysis + early rehabilitation



Outcome

• NIHSS 20 → 3 • mRS 5 → 1 • Near-complete motor recovery



Take Home Message

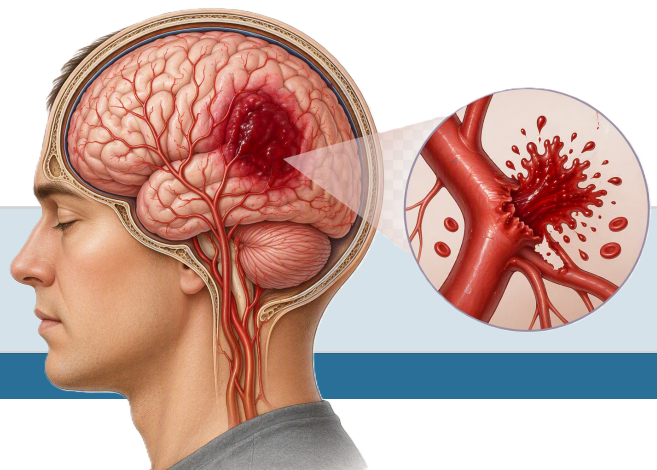
Cerebrolysin, when added to reperfusion therapy and early comprehensive rehabilitation in a patient with active metastatic cancer and severe ischemic stroke with high risk of hemorrhagic complications, was associated with marked motor and speech recovery and a favorable functional outcome.

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Hemorrhagic Stroke





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Hemorrhagic stroke, including intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH), remains among the most severe forms of cerebrovascular disease, with high rates of mortality and long-term disability. Despite important advances in neurocritical care, surgical management and prevention of secondary complications, effective pharmacological strategies that directly promote neurological recovery remain limited. Consequently, there is a continued need to explore therapies that protect vulnerable brain tissue and support recovery after hemorrhagic injury.

The consequences of hemorrhagic stroke extend far beyond the initial bleeding event. In ICH, hematoma formation damages surrounding brain tissue and triggers a cascade of secondary injury mechanisms. In SAH, exposure of the brain to blood products initiates inflammatory responses and contributes to complications such as delayed cerebral ischemia, microvascular dysfunction and impaired neuronal recovery. Across both conditions, shared pathological pathways—including neuroinflammation, oxidative stress, excitotoxicity, mitochondrial dysfunction, blood–brain barrier disruption and apoptosis—contribute to progressive brain injury and may represent important therapeutic targets.

The concept of cerebroprotection is therefore highly relevant in hemorrhagic stroke. Beyond controlling the source of bleeding and preventing complications, therapeutic approaches that limit secondary injury and enhance endogenous repair mechanisms may provide additional opportunities to improve outcomes. Cerebrolysin has attracted interest in this context because of its multimodal biological effects, including modulation of inflammatory responses, reduction of oxidative and excitotoxic damage, support of neuronal survival and promotion of neuroplasticity and synaptic remodeling. These mechanisms provide a rationale for investigating its potential role as an adjunctive therapy in patients recovering from hemorrhagic brain injury.

The growing interest in this therapeutic approach is reflected by clinical development efforts to generate credible evidence, including my own CLINCH study. It was designed to investigate the effects of Cerebrolysin in patients with spontaneous intracerebral hemorrhage. While prospective studies are essential to define the clinical role of cerebroprotective strategies, real-world clinical experience provides valuable insights into their potential application. The cases presented in this chapter illustrate the use of Cerebrolysin in patients with hemorrhagic stroke, including individuals with ICH and SAH, and highlight the broader concept that recovery after brain hemorrhage depends not only on controlling the initial event but also on protecting and restoring the injured brain.



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...in severe dorsal pontine hemorrhage

Abstract

Spontaneous pontine hemorrhage is an uncommon but highly lethal subtype of intracerebral hemorrhage, frequently associated with profound neurological disability and mortality rates exceeding 70% in severe presentations. We report the case of a previously healthy 37-year-old man who presented with abrupt dysarthria, left hemiparesis, vomiting, and focal seizures, followed by progressive decline in consciousness. Early computed tomography demonstrated a 2.9 cc pontine parenchymal hemorrhage related to the basilar territory, without aneurysm or arteriovenous malformation.

The patient required intensive neurocritical care, including mechanical ventilation, strict blood pressure control, hyperosmolar therapy, multimodal sedation, serial transcranial Doppler and optic nerve sheath monitoring, and treatment of transient sedation-associated myocardial dysfunction. As an adjunctive neurorecovery strategy, Cerebrolysin 50 mL intravenously once daily was started within 48 hours and continued for 28 days.

Despite the initially poor prognosis, serial imaging showed no hematoma expansion, hydrocephalus, or ventricular extension, and the patient demonstrated progressive neurological improvement during the ICU stay without adverse events attributable to Cerebrolysin. This case highlights the possible role of prolonged neurotrophic therapy within a highly optimized neurocritical care environment and supports further prospective research on Cerebrolysin in brainstem hemorrhage.

Keywords: pontine hemorrhage; Cerebrolysin; neurocritical care; neurorecovery; neuroplasticity

Introduction

Primary pontine hemorrhage remains one of the most devastating forms of hemorrhagic stroke because of the concentration of cardiorespiratory centers, ascending arousal pathways, and corticospinal tracts within the brainstem. Even small hematomas may cause severe deficits, autonomic instability, and early respiratory failure. Surgical options are often limited, leaving supportive neurocritical care as the cornerstone of treatment.^{1–3}

Cerebrolysin is a peptide-based neurotrophic preparation containing low-molecular-weight peptides and amino acids with proposed neuroprotective and neurorestorative properties. Experimental and clinical literature suggests modulation of apoptosis, neuroinflammation, oxidative stress, synaptic remodeling, and endogenous neurotrophin signaling.^{4–7} Although evidence is stronger in ischemic stroke and traumatic brain injury than in hemorrhagic brainstem lesions, its biological rationale supports exploratory use in carefully selected neurocritical patients.^{8–12}

We present a case of severe spontaneous pontine hemorrhage in a young adult with better-than-expected early neurological recovery after multimodal ICU treatment including 28 days of Cerebrolysin treatment.

Patient Information

A 37-year-old man with no known medical history, vascular risk factors, or previous neurological disease developed sudden dysarthria, diaphoresis, left hemiparesis, and two episodes of vomiting after routine physical activity. He subsequently experienced focal motor seizures without sphincter relaxation and self-presented to the emergency department.

There was no known history of anticoagulant use, illicit drug exposure, trauma, or prior hypertension.

Clinical Findings

On arrival, blood pressure was 215/139 mmHg, heart rate 112 bpm, and respiratory rate 18/min. Neurological deterioration prompted immediate stroke-code activation. Cranial CT performed within 10 minutes showed acute pontine intraparenchymal hemorrhage. CT angiography of the posterior circulation did not identify aneurysm, arteriovenous malformation, or other structural vascular lesions.

Due to worsening level of consciousness and concern for airway compromise, the patient was intubated and transferred to the ICU. Early bedside neuromonitoring with optic nerve sheath diameter and transcranial Doppler suggested intracranial hypertension, with estimated ICP >30 mmHg.

Timeline

Table 1: Clinical course and treatment timeline

Time	Clinical event
Day 0	Sudden dysarthria, left hemiparesis, vomiting, focal seizures
ED (first 10 min)	CT: pontine hemorrhage; CTA negative for vascular lesion
Day 0	IV labetalol bolus and infusion; ICU admission and intubation
First 24 h	Suspected sedation-related myocardial dysfunction; levosimendan and norepinephrine started
<48 h	Cerebrolysin 50 mL IV daily initiated
Days 1–7	Hyperosmolar therapy, multimodal sedation, serial TCD/optic sheath monitoring
ICU course	Tracheostomy for ventilator weaning; refractory hypertension workup and renal embolization
Day 28	Completion of Cerebrolysin course with progressive neurological improvement
ICU discharge	Stable imaging and improved neurological status

Diagnostic Assessment

Follow-up CT confirmed a stable pontine hematoma measuring approximately 2.9 cc without expansion, mass effect, hydrocephalus, or intraventricular extension. Neurosurgical evaluation concluded that surgical intervention was not indicated because of the deep pontine location and absence of hydrocephalus.

During the first ICU hours, the patient developed bradycardia, low cardiac output (cardiac index 1.4 L/min), reduced central venous oxygen saturation (74% to 54%), and left ventricular ejection fraction of 24%. The pattern was considered most consistent with halogenated-sedation-associated myocardial depression, prompting discontinuation of the offending agent and escalation of hemodynamic support.

Persistent severe hypertension during the stabilization phase led to an investigation for secondary causes, which was unrevealing.

Therapeutic Intervention

Initial blood pressure management consisted of IV labetalol bolus followed by continuous infusion, with only partial response. In the ICU, treatment focused on strict cerebral perfusion optimization, invasive airway protection, and mitigation of secondary brain injury.

Hyperosmolar therapy was initiated for suspected intracranial hypertension. The patient received deep

multimodal sedation with fentanyl, midazolam, propofol, and sevoflurane, targeting a Richmond Agitation-Sedation Scale score of -5 and bispectral index values between 37 and 40.

Because of transient myocardial dysfunction, levosimendan and norepinephrine were administered, with vasopressor requirements up to 0.92 mcg/kg/min. Respiratory failure during sedation weaning and thoracoabdominal dissociation led to tracheostomy as part of a planned ventilator liberation strategy.

As adjunctive cerebroprotective therapy, Cerebrolysin, was started within the first 48 hours at 50 mL intravenously once daily for 28 consecutive days. The rationale was to reduce secondary neuronal injury and potentially enhance endogenous neuroplasticity during the acute and subacute phases.

Refractory hypertension later required sodium nitroprusside and oral multidrug therapy. Given persistent instability, the hemodynamics team performed bilateral selective renal artery embolization without immediate complications.

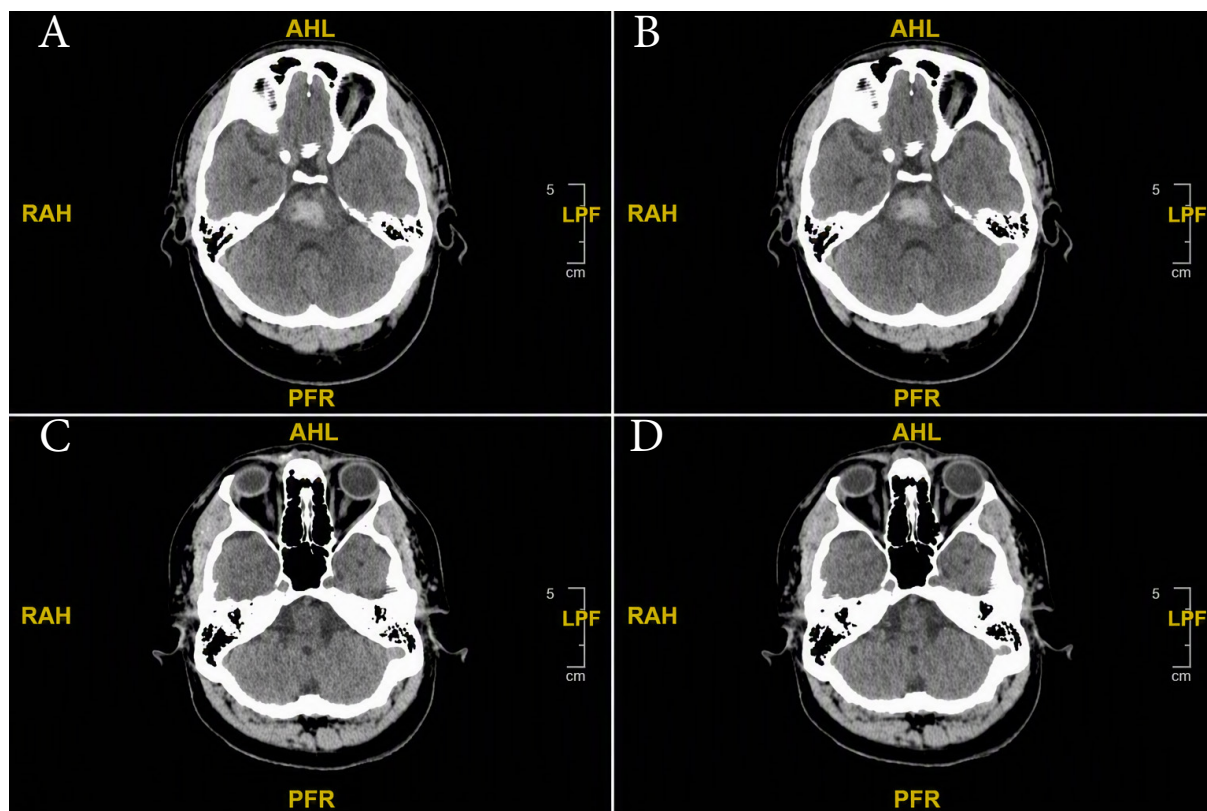


Figure 1: (A, B) Initial non-contrast cranial CT scans obtained at presentation demonstrating an acute pontine intraparenchymal hemorrhage. (C, D) Follow-up CT images obtained during the neurocritical care course showing a stable hematoma without evidence of expansion, hydrocephalus, intraventricular extension, or significant mass effect. The radiological stability of the lesion paralleled the patient's progressive neurological improvement during intensive care treatment.

Follow-up and Outcomes

Serial transcranial Doppler and optic nerve sheath assessments remained stable after initiation of therapy, with no major fluctuations suggestive of worsening intracranial dynamics. Repeat neuroimaging demonstrated persistent but non-progressive pontine hemorrhage.

Over the 28-day ICU course, the patient showed gradual neurological improvement, allowing progressive reduction of sedation and advancement of ventilatory weaning. No renal, hepatic, hematologic, or seizure-related adverse effects attributable to Cerebrolysin were observed.

The patient was discharged from the ICU after completion of the 28-day course with neurological status improved beyond the initial expectation for severe pontine hemorrhage.

Discussion

This case illustrates the potential value of combining meticulous neurocritical care with adjunctive neurotrophic therapy in a lesion classically associated with devastating outcomes. Pontine hemorrhage carries an especially poor prognosis because even limited hematoma volumes may interrupt consciousness pathways, descending motor tracts, and autonomic nuclei.^{1–3}

The favorable evolution in this patient cannot be attributed to a single intervention. Intensive blood pressure control, prevention of hematoma expansion, respiratory support, management of intracranial hypertension, and correction of sedation-related cardiac dysfunction were all likely essential contributors. Nevertheless, the prolonged and early administration of Cerebrolysin may have supported the recovery environment by promoting synaptic plasticity and neuronal survival during the secondary injury cascade.^{4–7}

The proposed mechanisms of Cerebrolysin, including activation of PI3K/Akt and MAPK/ERK signaling, attenuation of oxidative stress, and enhancement of neurotrophin-mediated remodeling, are biologically relevant in hemorrhagic injury, where perihematomal edema, excitotoxicity, mitochondrial dysfunction, and inflammatory signaling contribute to delayed tissue damage.^{4–6}

Human evidence in hemorrhagic stroke remains limited, and current guidelines do not recommend routine use. However, studies in ischemic stroke, traumatic brain injury, and severe disorders of consciousness suggest a favorable safety profile and potential functional benefit when treatment is extended for 10–28 days.^{8–14} This case adds clinically relevant observational evidence in a brainstem hemorrhage setting, where therapeutic options remain scarce.

The main limitation is the inability to isolate the specific effect of Cerebrolysin from the broader multimodal ICU strategy. As a single case, it should be interpreted as hypothesis-generating rather than proof of efficacy.

Conclusion

In this case, a young patient with severe spontaneous pontine hemorrhage experienced meaningful early neurological improvement after optimized neurocritical care combined with 28 days of Cerebrolysin. Although causality cannot be established, the absence of hematoma progression, the favorable safety profile, and the better-than-expected recovery support further controlled studies exploring neurotrophic therapies in brainstem hemorrhage and severe neurorecovery states.

CASE SUMMARY

**Patient**

- 37 years
- Severe pontine hemorrhage

**Challenge**

- Progressive neurological deterioration

**Treatment**

- Cerebrolysin 50 mL/day IV x 28 days + neurocritical care

**Outcome**

- Progressive neurological improvement

**Take Home Message**

Pontine hemorrhage is a neurological emergency requiring early imaging and intensive monitoring, while Cerebrolysin may support neurorecovery as an adjunct to optimized neurocritical care.



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...after aneurysmal subarachnoid hemorrhage (Fisher IV)

Abstract

A case is presented of a 72-year-old female patient with a history of systemic arterial hypertension, who had an acute onset of severe headache, accompanied by vomiting, followed by loss of consciousness. Initial cranial computed tomography showed a Fisher grade IV subarachnoid hemorrhage in the M2 segment of the right middle cerebral artery, accompanied by temporal intraparenchymal hemorrhage, intraventricular hemorrhage, and severe cerebral edema.

During her hospital stay, she developed cardiorespiratory arrest with severe neurological sequelae, requiring advanced management in the intensive care unit with mechanical ventilation, sedation, tracheostomy, and gastrostomy. Serial follow-up studies were performed, documenting a progressive decrease in hemorrhage volume and partial resolution of the edema. On August 28, 2025, endovascular embolization of two aneurysms (middle cerebral artery and internal carotid artery) was performed without complications, with favorable postoperative evolution.

As part of comprehensive management, brain protection treatment with RENACENZ® (Cerebrolysin) was initiated at a dose of 5 mL daily for 20 days, starting on August 28 and continuing until hospital discharge on September 16. Over 45 days of hospitalization, the patient showed progressive improvement, achieving a Glasgow score of 15, limited but present speech, limb movement, and participation in physiotherapy. Comparison between the initial CT scan and the latest follow-up study demonstrated a significant reduction in hemorrhage and partial resolution of the edema.

This case highlights the importance of a multidisciplinary approach, the favorable impact of timely endovascular management, and the role of brain protection therapy in the functional recovery of patients with severe subarachnoid hemorrhage.

Keywords: Subarachnoid hemorrhage, Brain protection, Fisher IV, Cerebrolysin, Endovascular therapy

Introduction

A 72-year-old woman with arterial hypertension and chronic venous insufficiency developed a sudden severe headache on August 2, 2025, reaching 10/10 intensity within minutes and accompanied by two episodes of vomiting followed by loss of consciousness. On admission, she was stuporous, with left hemiplegia and blood pressure of 170/110 mmHg. Non-contrast head CT revealed Fisher grade IV subarachnoid hemorrhage, right temporal intraparenchymal hemorrhage, and cerebral edema (Figure 1).

The patient was considered critically ill with a high risk of complications. Surgical intervention was initially ruled out because of her age and comorbidities, and conservative intensive care management was initiated. Twenty-four hours after admission, she remained deeply sedated (fentanyl and propofol; RASS -4), with non-reactive pupils and invasive mechanical ventilation using lung-protective settings. Hemodynamic support with norepinephrine was required to maintain mean arterial pressure, while Nimodipine was started for

vasospasm prophylaxis. Hyperglycemia was treated with rapid-acting insulin. No active bleeding or fever was detected, cultures were obtained, and a urinary catheter was placed.

During the first week in the ICU, follow-up CT scans on days 4 and 7 demonstrated extensive intraparenchymal hemorrhage with mass effect, midline shift, and left intraventricular hemorrhage (Figure 2).

Case Report

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Timeline

Table 1: Clinical course and treatment timeline

Date	Clinical event
Aug 2, 2025	Thunderclap headache, vomiting, loss of consciousness; CT showed Fisher IV SAH with right temporal hematoma and IVH
Aug 3, 2025	ICU admission, mechanical ventilation, sedation, vasopressor support, nimodipine
Aug 14, 2025	Hypoxia-related cardiorespiratory arrest; ROSC after 4 minutes
Aug 19, 2025	Tracheostomy and gastrostomy
Aug 27, 2025	Endovascular embolization of MCA and ICA aneurysms
Sep 7, 2025	Follow-up CT showed major hemorrhage reduction and edema improvement
Mid-Sep 2025	Discharge to home rehabilitation program

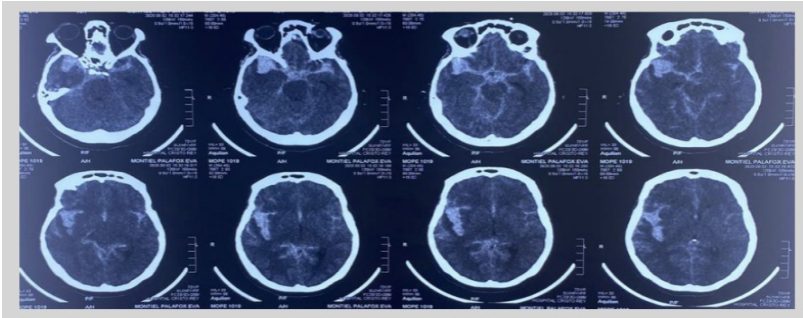


Figure 1: Non-contrast cranial computed tomography. Diffuse Fisher IV subarachnoid hemorrhage is observed, with right temporal intraparenchymal hemorrhage and associated cerebral edema. Findings are consistent with rupture of an aneurysm in the right middle cerebral artery.

On August 14, 2025, after 12 days of ICU management, the patient developed cardiopulmonary arrest secondary to hypoxia caused by a mucus plug and refractory bronchospasm. Advanced resuscitation was performed, achieving return of spontaneous circulation after 4 minutes. She subsequently developed supraventricular tachycardia, requiring amiodarone loading as part of post-arrest management, as well as continued sedation, analgesia, and norepinephrine support. Two weeks after admission, on August 16, 2025, a follow-up non-contrast head CT scan performed after the arrest demonstrated subacute-phase hemorrhage with perilesional edema, without evidence of additional ischemia compared to prior follow-up studies. On August 19, a tracheostomy and gastrostomy were performed to ensure adequate ventilation and nutrition.

After 25 days of in-hospital ICU management, the patient exhibited spontaneous eye opening and normoreactive pupils. As she was hemodynamically stable, it was decided to proceed with an endovascular embolization procedure, successfully treating two aneurysms: one in the right middle cerebral artery (proximal dorsal M2 segment, Raymond-Roy classification II) and another in the ophthalmic segment of the right internal carotid artery (Raymond-Roy IIIA). The procedure was completed without complications (Figure 3).

On August 28, adequate post-embolization evolution was documented, with the patient being alert, exhibiting spontaneous eye opening, normoreactive pupils, and spontaneous movement of the right hemibody. In the following days, the patient remained under ICU monitoring with a favorable clinical course and adequate post-embolization evolution. Due to the initial severity of the clinical presentation and the improvement observed after embolization, treatment with RENACENZ® (Cerebrolysin) was initiated at a dose of 5 ampoules IV (1,076 mg/day) daily for 20 days, beginning on August 28 and continuing until hospital discharge on September 16 as part of a brain protection strategy following the reduction of hemorrhagic volume.

On September 7, 2025, after 36 days of hospital management, a follow-up CT scan showed a decrease in intraparenchymal bleeding, reclassified as Fisher grade I, with findings consistent with favorable progression. The patient was significantly more alert and responsive, with improved mobility. As she remained hemodynamically stable, she was transferred to the general ward, where a physical therapy program was initiated, with active participation from the patient.

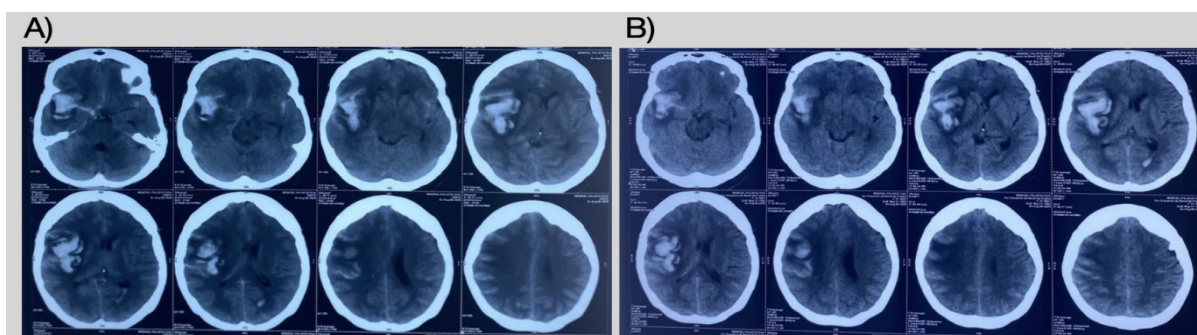


Figure 2: Extensive intraparenchymal hemorrhage in the right temporal lobes (52 31 mm), edema with ventricular obliteration, left intraventricular hemorrhage and poor gray-white matter differentiation, with midline shift. A: August 6,2025 B: August 9,2025

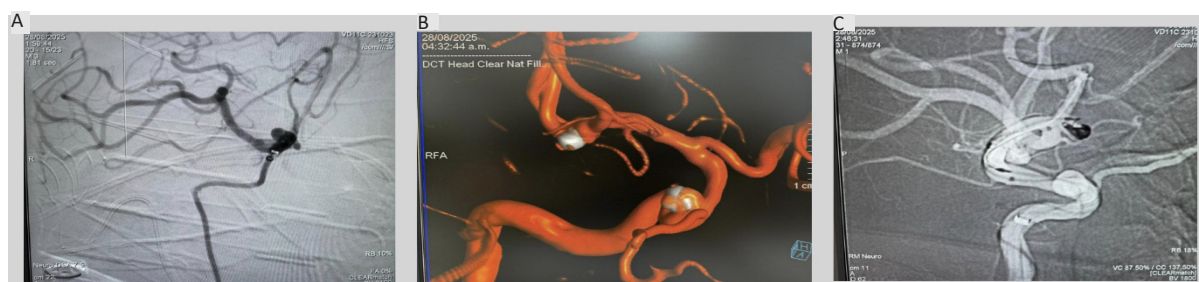


Figure 3: Endovascular procedure performed on August 28,2025

(A) Digital subtraction angiography demonstrating a saccular aneurysm in the M2 segment of the right middle cerebral artery. (B) Three-dimensional reconstruction showing two aneurysms: one in the right middle cerebral artery and another in the ophthalmic segment of the right internal carotid artery. (C) Post-embolization angiographic control evidencing adequate exclusion of the aneurysm with preservation of distal circulation.

Finally, after 45 days of hospitalization, the patient was alert and cooperative, with a Glasgow score of 15 (E4, V4, M6). Speech was limited but present, with preserved naming and repetition. Muscle strength was 4/5 in the right hemibody and 3/5 in the left, without focal seizures. She demonstrated adequate tolerance to enteral feeding via gastrostomy and maintained oxygen saturation above 90% without continuous supplemental oxygen. A final head CT scan, compared with the initial study, showed no evidence of hemorrhage and progressive resolution of edema, findings consistent with clinical improvement (Figure 4). Based on the above, hospital discharge was decided on September 16, 2025, with recommendations for neurological follow-up, intensive physical rehabilitation, and home care.

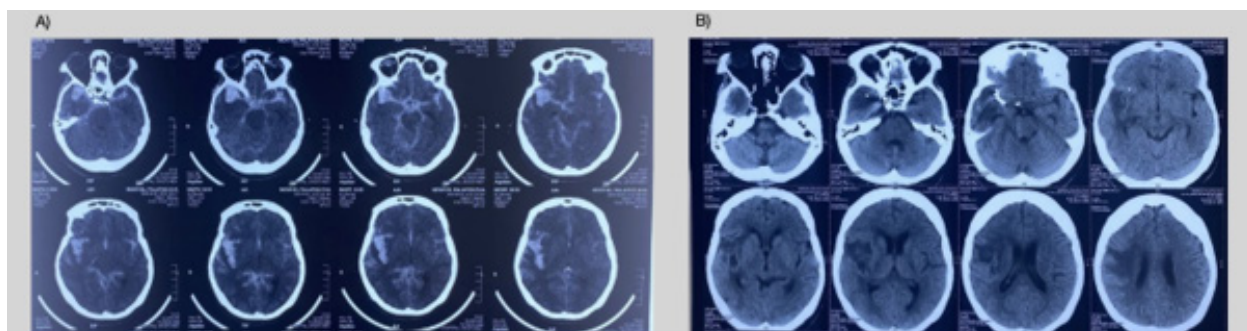


Figure 4: Comparison between CT Studies. (A) Initial CT (08/02/2025): diffuse Fischer IV subarachnoid hemorrhage, large-volume right temporal intraparenchymal hemorrhage, severe cerebral edema, and effacement of cortical sulci are observed. (B) Final follow-up CT (09/07/2025): marked reduction in hemorrhage volume, decreased edema and improved definition of intracranial structures are evident, findings consistent with the patient's clinical improvement (Glasgow 15, active mobility, and participation in physiotherapy).

Discussion

Aneurysmal subarachnoid hemorrhages represent one of the most severe neurological emergencies, with high morbidity and mortality, especially in elderly patients. Multidisciplinary management includes hemodynamic control, prevention of complications, surgical or endovascular treatment, and brain protection strategies. In this case, the patient presented with an extensive and complicated hemorrhage requiring advanced critical care. Fortunately, the initial conservative management allowed for hemodynamic stabilization during the acute phase of the event, leading to a better outcome after endovascular embolization. Combined with supportive care and brain protection therapy, this approach enabled a successful clinical course and outcome despite the initially poor prognosis.

Serial imaging studies were essential to assess the evolution of the hemorrhage, demonstrating a progressive reduction in bleeding, decreased cerebral edema, and improvement in ventricular morphology. The administration of Cerebrolysin, a relatively recent brain protective agent that has shown efficacy in multiple neurological conditions, with emerging evidence indicating a reduction in morbidity in severe subarachnoid hemorrhage as an adjunctive therapy, provided the expected neuroprotective and neurotrophic effects, associated with the patient's documented clinical recovery.

The evolution of this clinical case demonstrates that even in severe scenarios, the combination of an initial intensive conservative approach, allowing the course of vasospasm to stabilize, together with timely subsequent endovascular management and brain protective strategies can significantly improve quality of life and functional prognosis in these patients.

Conclusion

The patient showed a favorable clinical course despite presenting with a complicated Fisher grade IV aneurysmal subarachnoid hemorrhage, which can be attributed to a comprehensive approach that included advanced critical care management, endovascular embolization, and brain protection therapy.

This case illustrates that, even in widely known and extensively studied conditions, whose management is often standardized or, in many cases, limited to supportive measures due to an unfavorable initial prognosis, an intensive and up-to-date multidisciplinary approach that incorporates endovascular treatment and recently

implemented brain protection strategies can significantly impact functional recovery. Therefore, it is essential to remain up to date with these therapeutic advances and integrate them into daily clinical practice, with the aim of optimizing functional outcomes and improving the quality of life of affected patients.

CASE SUMMARY



Patient

• 72 years • Fisher Grade IV aneurysmal subarachnoid hemorrhage



Challenge

• Severe SAH with cerebral edema and loss of consciousness



Treatment

• Cerebrolysin 5 mL/day IV x 20 days + endovascular embolization and intensive care



Outcome

• GCS 15 • Fisher Grade IV → I • Marked hemorrhage and edema reduction on CT



Take Home Message

A coordinated multidisciplinary approach—including critical care, endovascular treatment, cerebroprotection with Cerebrolysin, and early rehabilitation—can improve recovery after severe aneurysmal subarachnoid hemorrhage.

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...in severe basal pontine hemorrhage

Abstract

Primary brainstem hemorrhage carries a poor prognosis, particularly in patients with depressed consciousness, ventilatory failure, and larger pontine hematomas. We report the case of a 53-year-old man with hypertension and chronic kidney disease on hemodialysis who presented with sudden impaired consciousness caused by a 2.6 cm dorsal pontine hemorrhage with early hydrocephalus. After neurological deterioration requiring mechanical ventilation, he underwent intracranial pressure monitoring and received neurocritical care with adjunctive Cerebrolysin for 14 days. His consciousness gradually improved, allowing transfer to rehabilitation and subsequent post-acute neurorecovery care. At three months, he remained awake and interactive despite persistent right-sided paraplegia and follow-up imaging demonstrated complete hematoma resolution without encephalomalacia. This case illustrates meaningful recovery after severe pontine hemorrhage under structured neurocritical and neurorecovery management.

Keywords: Primary brainstem hemorrhage; pontine hemorrhage; intracranial pressure monitoring; Cerebrolysin; rehabilitation

Introduction

Primary brainstem hemorrhage remains a highly devastating neurological emergency compared to other spontaneous intracranial hemorrhages. The outcome is strongly influenced by the initial level of consciousness, need for urgent ventilatory support, hematoma size, and anatomical extension. Although radiological classification systems based on hematoma size, location, and hydrocephalus have been proposed, evidence-based guidance for management, including blood pressure control, surgical intervention and neurorecovery strategies remains limited. We present a case of spontaneous pontine hemorrhage managed conservatively with ICP monitoring and adjunctive Cerebrolysin treatment.

Patient Information

A 53-year-old man presented with a sudden onset of disturbance of consciousness in the morning of admission. His medical history was significant for IgA nephropathy, chronic kidney disease requiring regular hemodialysis, and longstanding hypertension. No recent trauma, anticoagulant exposure, or other precipitating factors were reported.

Clinical Findings

On arrival, the patient was in a confused state with a Glasgow Coma Scale (GCS) score of 10 (E3M5V2). His respiratory rate was 16 breaths per minute, blood pressure was 148/96 mmHg, and both pupils were equal at 2.5 mm and reactive to light. His neurological status subsequently deteriorated to GCS 8 (E3M4V1), prompting endotracheal intubation and mechanical ventilation.

Timeline

Table 1: Clinical course and treatment timeline

Timepoint	Clinical Event
Day 0	CT showed 2.6 cm dorsal pontine hematoma with mild hydrocephalus, Intubation due to neurological deterioration (GCS 8), ICP monitor inserted via right Kocher's point
Days 1–14	Neurocritical care monitoring + Cerebrolysin 30 mL/day
Week 2	Transfer to rehabilitation ward
Discharge	Referral to local post-acute care hospital
3 months	Persistent motor deficits, improvement to GCS 10
Follow-up imaging	Complete hematoma resolution

Diagnostic Assessment

Head computed tomography (Figure 1A) revealed a 2.6 cm hyperdense hematoma predominantly located in the dorsal pons (tegmental region), without extension into the fourth ventricle. Mild dilation of the bilateral lateral ventricles was present, suggesting early hydrocephalus. The lesion size and bilateral tegmental involvement placed the patient in an intermediate-to-high risk prognostic group.

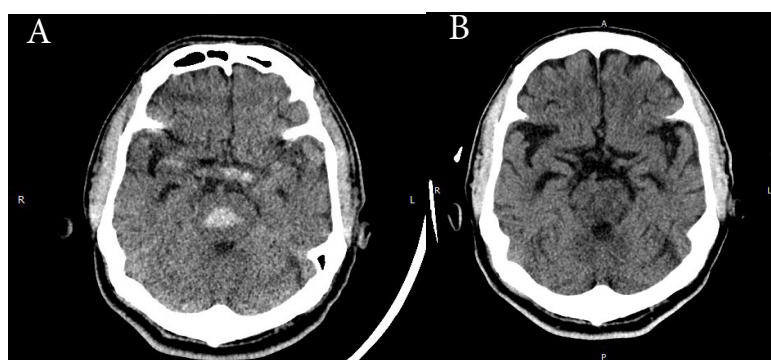


Figure 1. **(A)** Initial CT showing dorsal pontine intracerebral hemorrhage with early hydrocephalus before cerebrolysin treatment. **(B)** Follow-up CT demonstrating complete hematoma absorption without apparent encephalomalacic change (same slice as Figure 1A).

Therapeutic Intervention

After discussion with the family and obtaining consent, an intracranial pressure monitor was implanted through the right Kocher's point. The patient was then admitted to the neurocritical care unit, where he received mechanical ventilation, continuous neurological observation, ICP monitoring, hemodynamic stabilization, and standard conservative intracerebral hemorrhage management. Because of marked fluctuations in consciousness and intermittent apnea during ICU care, Cerebrolysin 30 mL/day was administered for 14 consecutive days as an adjunct neurorecovery therapy.

Follow-up and Outcomes

During the ICU stay, the patient demonstrated marked neurological fluctuation ranging from GCS 3 (E1M2VT) to GCS 10 (E4M6VT). After two weeks, his level of consciousness improved sufficiently to allow transfer to the ward, where rehabilitation was initiated. Following discharge, he was referred to a local hospital for a structured post-acute care program.

Three-month Follow-up

At three-month follow-up, the patient was awake and interactive with a GCS score of 10. However, persistent right-sided paraplegia remained. He continued to require assistance with tracheostomy care, daily activities and mobility support.

Imaging Outcome

Follow-up computed tomography demonstrated complete hematoma resolution without obvious encephalomalacic change (Figure 1B).

Discussion

Brainstem hemorrhage most commonly affects patients aged 40–60 years and is most frequently associated with hypertension. Clinical manifestations include sudden coma, tetraplegia or hemiplegia, respiratory compromise, pupillary abnormalities, and autonomic dysfunction.

Consistent with prior literature, the most important predictors of poor outcome include depressed initial consciousness, large hematoma size, bilateral or basal extension, acute hydrocephalus, and the need for mechanical ventilation.

Although several CT-based classification systems exist, prognosis remains difficult in patients with intermediate features, such as our patient, who had a relatively large 2.6 cm dorsal pontine hematoma with fluctuating neurological examination.

Current guidelines generally discourage surgical evacuation of primary brainstem hematomas, and conservative treatment remains standard. In this context, specialized neurocritical care - including close neurological monitoring, ICP surveillance, and early rehabilitation planning- may be crucial for optimizing recovery.

In this case, adjunctive Cerebrolysin treatment was used as a neurorecovery strategy during the period of neurological instability. While causality cannot be established from a single case, the time course of improvement in consciousness and favorable radiological resolution suggest that multimodal treatment with Cerebrolysin combined with neurocritical support may benefit selected patients whose prognosis is otherwise uncertain.

CASE SUMMARY



Patient

• 72 years • Fisher Grade IV aneurysmal subarachnoid hemorrhage



Challenge

• Severe SAH with cerebral edema and loss of consciousness



Treatment

• Cerebrolysin 5 mL/day IV x 20 days + endovascular embolization and intensive care



Outcome

• GCS 15 • Fisher Grade IV → I • Marked hemorrhage and edema reduction on CT



Take Home Message

A coordinated multidisciplinary approach—including critical care, endovascular treatment, cerebroprotection with Cerebrolysin, and early rehabilitation—can improve recovery after severe aneurysmal subarachnoid hemorrhage.

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...in ICH due to poorly controlled hypertension

Abstract

Background: Poorly controlled long-standing hypertension remains a major cause of spontaneous intracerebral hemorrhage (ICH), particularly in older adults with vascular risk factors such as diabetes mellitus. Early blood pressure control, neurocritical care, and structured neurorehabilitation are essential for functional recovery.

Case presentation: A 65-year-old woman with a 20-year history of diabetes mellitus and poorly controlled hypertension presented with sudden right-sided weakness and mixed aphasia. On admission, her blood pressure was 220/110 mmHg, Glasgow Coma Scale (GCS) score was 7/15, and National Institutes of Health Stroke Scale (NIHSS) score was 23. Brain computed tomography (CT) demonstrated spontaneous intracerebral hemorrhage. She was managed in the intensive care unit with osmotherapy, blood pressure control, supportive anti-hemorrhagic therapy, Cerebrolysin 50 mL/day, and early neurorehabilitation. After 30 days, her GCS improved to 14/15, NIHSS to 7, and she regained assisted ambulation.

Conclusion: This case highlights the importance of rapid recognition of hypertensive ICH, aggressive blood pressure management, multidisciplinary inpatient care, and early rehabilitation. Favorable recovery was observed over one month; however, the contribution of adjunctive neurotrophic therapy should be interpreted cautiously within the context of comprehensive stroke care.

Keywords: Hypertensive crisis; brain imaging; intracerebral hemorrhage; sensory aphasia; neurorehabilitation

Introduction

Hypertension is a leading modifiable risk factor for spontaneous intracerebral hemorrhage and remains a major contributor to stroke-related disability and mortality worldwide. (1,2,8,12) Chronic poor blood pressure control may induce lipohyalinosis, vessel wall fragility, and rupture of small penetrating cerebral arteries. In patients with concomitant diabetes mellitus, vascular endothelial dysfunction and microangiopathy may further increase susceptibility to hemorrhagic stroke.(11)

This report describes the clinical course and short-term recovery of an older woman with hypertensive crisis-related ICH presenting with severe neurological deficits, including hemiplegia and aphasia, who showed marked improvement following neurocritical care, antihypertensive optimization, and rehabilitation.(5,6,7,9,13)

Patient Information

A 65-year-old moderately obese woman presented to the emergency department with sudden onset of right-sided weakness and inability to communicate effectively. Her medical history was significant for type 2 diabetes mellitus for 20 years, treated with glimepiride 5 mg/day, and poorly controlled hypertension treated with bisoprolol 5 mg/day with suboptimal follow-up and adherence. There was no known history of prior stroke, renal disease, anticoagulant use, or other major debilitating illnesses.

Clinical Findings

On arrival, the patient was critically ill. Blood pressure was 220/110 mmHg. Neurological examination revealed a GCS score of 7/15, complete right-sided hemiplegia, right upper motor neuron facial weakness, and mixed motor-sensory aphasia. The NIHSS score was 23, consistent with severe stroke. Her body mass index was mildly elevated.

Diagnostic Assessment

Urgent non-contrast CT brain demonstrated spontaneous intracerebral hemorrhage involving the left cerebral hemisphere, correlating with the patient's aphasia and contralateral hemiplegia (Figure 1). Routine laboratory investigations and physiological monitoring were performed, including blood glucose, renal profile, coagulation parameters, and serial blood pressure measurements. No secondary structural lesion was identified on initial imaging. The clinical and radiological findings were most consistent with hypertensive intracerebral hemorrhage.

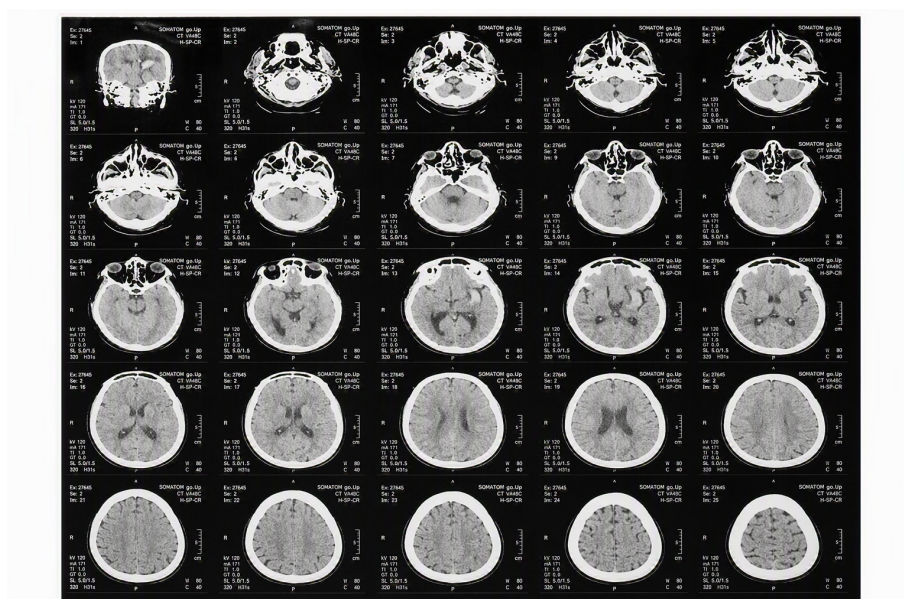


Figure 1: CT at time of admission with ICH

Timeline

Table 1: Clinical course and treatment timeline

Time	Clinical event
Day 0	Sudden right hemiplegia and aphasia; BP 220/110 mmHg; CT confirmed ICH; admitted to ICU
Days 1–9	ICU care with osmotherapy, BP control, Cerebrolysin infusion, monitoring, and early rehabilitation
Day 9	Improved consciousness and stabilization; transferred to regular inpatient ward
Days 10–30	Continued oral antihypertensive combination therapy, Cerebrolysin, and rehabilitation
Day 30	Follow-up CT performed; GCS 14/15, NIHSS 7, ambulatory with mild support
>Day 30	Continued outpatient rehabilitation and follow-up imaging planned

Therapeutic Intervention

The patient was admitted to the intensive care unit for neurocritical monitoring and conservative management. Osmotherapy was initiated using mannitol 10% at 1000 mL/day to reduce cerebral edema. Supportive anti-hemorrhagic therapy included etamsylate 500 mg intravenously twice daily and phytomenadione 10 mg

intravenously every 12 hours. Blood pressure control was prioritized using antihypertensive therapy, later optimized to a combination regimen including a calcium channel blocker, angiotensin receptor blocker, and diuretic.

Adjunctive therapy included Cerebrolysin 50 mL/day by intravenous infusion during hospitalization, followed by continuation for 21 additional days after ICU transfer. Early neurorehabilitation, including mobilization and speech-motor supportive therapy, was initiated during inpatient care and continued after discharge.

Follow-up and Outcomes

The patient remained in the ICU for 9 days, followed by 21 days in the regular inpatient ward. Clinical improvement became evident during the first week, particularly in the level of consciousness and hemodynamic stability. At 30-day follow-up, the patient's GCS had improved from 7/15 to 14/15. Motor recovery was substantial, with the patient able to walk with mild support. The NIHSS improved from 23 to 7, reflecting marked neurological recovery. Blood pressure was well controlled at 125/80 mmHg on combination oral therapy. Follow-up CT showed interval improvement without evidence of hematoma expansion (Figure 2). She was discharged with instructions to continue structured neurorehabilitation, strict blood pressure monitoring, diabetes management, and scheduled neuroimaging follow-up.

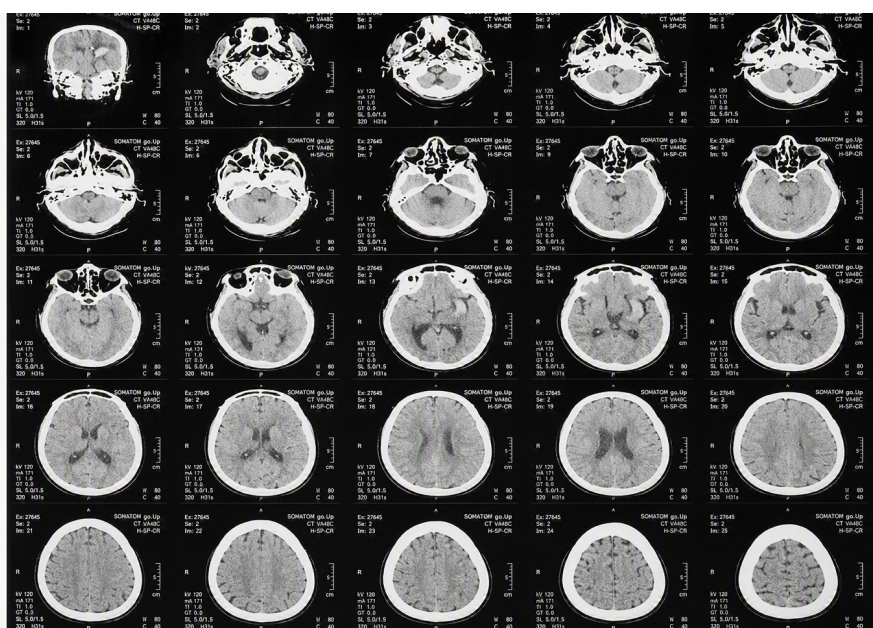


Figure 2: CT after 30-Days Follow-up

Discussion

This case illustrates a classic but severe presentation of hypertensive intracerebral hemorrhage in an older patient with two major vascular risk factors: long-standing hypertension and diabetes mellitus. (1,2,8,11,12) The profound neurological deficits at presentation, including aphasia, hemiplegia, and depressed consciousness, were consistent with a large dominant hemispheric hemorrhage. (1,7,14)

The most important determinant of outcome in this case was likely early stabilization and rapid blood pressure control, which remain the cornerstone of ICH management. (5,6,7) Prevention of hematoma expansion, control of cerebral edema, close neurological observation, and timely rehabilitation all contributed to the favorable short-term outcome. (1,7,9,13)

The patient also received adjunctive Cerebrolysin throughout hospitalization and during the recovery phase. Although improvement was temporally associated with this treatment, causality cannot be established from a single case report, especially in the setting of simultaneous standard stroke management and rehabilitation. (15) Any interpretation of neuroprotective or neuroplastic effects should therefore remain cautious and hypothesis-generating rather than confirmatory.

Another important learning point is the value of early multidisciplinary care. The coordinated involvement of neurologists, intensive care staff, rehabilitation specialists, nursing caregivers, and family support likely facilitated the observed recovery trajectory.(9,15) This case further reinforces the importance of long-term outpatient risk factor control, especially medication adherence and regular blood pressure monitoring, to prevent recurrence.(1,11)

Conclusion

This CARE-compliant case emphasizes that hypertensive crisis–related ICH can present with devastating deficits but may still show meaningful recovery when managed promptly with intensive blood pressure control, neurocritical monitoring, and early rehabilitation. The case also underscores the importance of secondary prevention through strict long-term vascular risk management.

Patient Perspective

The patient’s family reported satisfaction with the rapid hospital response and the progressive improvement in speech, consciousness, and mobility over the admission period. They particularly valued the early transfer from critical care to the ward and the patient’s ability to regain supported walking by one month.

CASE SUMMARY	
 Patient	• 65 years • Hypertensive intracerebral hemorrhage
 Challenge	• Severe hemiplegia and aphasia
 Treatment	• Cerebrolysin 50 mL/day IV × 30 days + neurorehabilitation
 Outcome	• NIHSS 23 → 7 • GCS 7 → 14 • Assisted ambulation regained
 Take Home Message	Rapid blood pressure control and neurocritical care remain the cornerstone of hypertensive intracerebral hemorrhage management; in addition, multimodal pharmacological and rehabilitation therapy contribute largely to improved functional outcome.



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...in ruptured brain arteriovenous malformations

Abstract

Brain arteriovenous malformations (AVMs) are uncommon cerebrovascular lesions that may present with hemorrhage, seizures, or focal neurological deficits. Surgical excision remains an important treatment option for selected patients. This report describes three patients who developed postoperative neurological deficits following complete AVM excision and subsequently received adjunctive intravenous Cerebrolysin therapy. Favorable functional and cognitive recovery was observed during follow-up. Although these findings suggest a potential neurorestorative effect, larger prospective studies are required to determine the efficacy of Cerebrolysin in the postoperative management of AVMs.

Background: Brain AVMs are abnormal vascular connections between arteries and veins without an intervening capillary bed. They commonly present with intracranial hemorrhage, seizures, headache, or focal neurological deficits. Surgical excision provides definitive treatment for appropriately selected lesions. Adjunctive neurorestorative therapies such as Cerebrolysin may potentially enhance postoperative neurological recovery.

Case Series: During a 5-year period at the Department of Neurosurgery, North Okkalapa General Hospital, Yangon, Myanmar, 38 patients with cerebral AVMs were evaluated, and 16 underwent surgical excision. Three patients who developed postoperative neurological deficits received adjunctive intravenous Cerebrolysin according to the institutional protocol. These representative cases are presented to illustrate their clinical course and recovery.

Conclusion: Adjunctive Cerebrolysin therapy following AVM excision was associated with favorable neurological and cognitive outcomes in this small case series. Further controlled studies are needed to clarify its therapeutic role.

Keywords: Brain arteriovenous malformation; neurosurgery; surgical excision; postoperative neurological deficit; Cerebrolysin; neurorestorative therapy; case series

Introduction

Brain arteriovenous malformations (AVMs) are rare congenital vascular lesions characterized by direct communications between arteries and veins without an intervening capillary network. Clinical manifestations include intracerebral hemorrhage, seizures, headache, and focal neurological deficits. Surgical excision remains an established treatment for selected patients, particularly those with accessible ruptured lesions. (2)

The present report describes three patients treated at the Department of Neurosurgery, North Okkalapa General Hospital (NOGH), Yangon, Myanmar, who underwent complete AVM excision and subsequently received adjunctive Cerebrolysin therapy for postoperative neurological deficits. Their clinical outcomes are presented to explore the potential role of neurorestorative treatment in postoperative recovery.

Case 1

A 48-year-old man was admitted to the Neurosurgery Unit of North Okkalapa General Hospital with sudden onset right hemiparesis and reduced consciousness.

Clinical Findings

On examination, his Glasgow Coma Scale (GCS) score was 14/15 with right-sided motor weakness graded as MRC 3/5.

Diagnostic Assessment

Computed tomography (CT) of the head demonstrated a left frontoparietal intracerebral hemorrhage suggestive of a ruptured AVM. Subsequent cerebral angiography confirmed a left frontal paramedian AVM classified as Spetzler–Martin Grade III (S2V0E1).

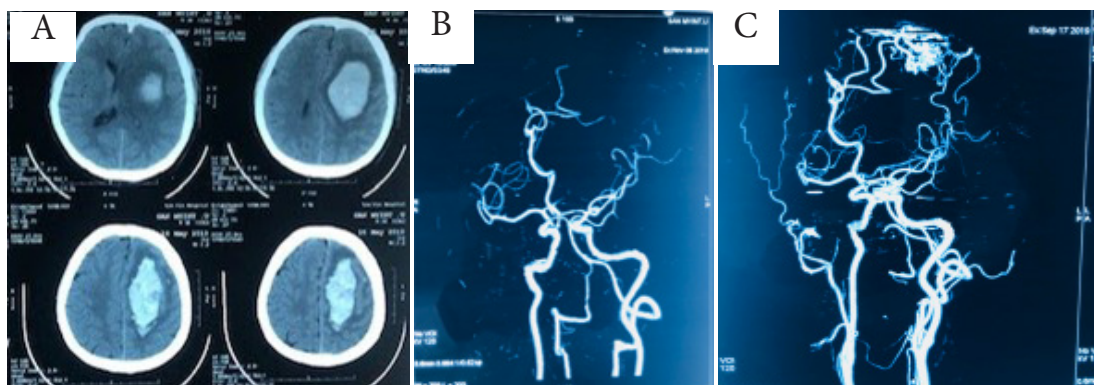


Figure 1: (A) Preoperative CT scan and (B) Preoperative Angiogram (C) Postoperative Angiogram

Therapeutic Intervention

The patient underwent craniotomy with complete excision of the AVM. Postoperatively, standard neurosurgical management was provided together with adjunctive Cerebrolysin administered intravenously at a daily dose of 30 mL diluted in 100 mL normal saline for 10 days. Gradual neurological improvement was observed during recovery.

Follow-Up and Outcomes

The patient was discharged with a GOS score of 4 and improved further to GOS 5 at one-month follow-up. Although he initially required support for ambulation, he regained independent walking ability at one year.

Case 2

A 27-year-old male peasant presented with recurrent seizures occurring two to three times daily over a 12-year period. He had previously been diagnosed with a ruptured AVM at another hospital five years earlier. Neurological examination demonstrated preserved motor strength (MRC 5/5) but revealed mild right-sided tingling and numbness, impaired articulation, and reduced memory function. Contrast-enhanced CT and cerebral CT angiography identified a left sylvian fissure AVM adjacent to the sensory cortex and Wernicke's speech area, classified as Spetzler–Martin Grade III (S2V0E1). The patient underwent successful craniotomy and complete AVM excision. Postoperative management included standard neurosurgical care together with intravenous Cerebrolysin administered at 10 mL every 12 hours for 7 days. Following surgery, improvements were observed in speech articulation and memory function. The patient achieved GOS 5 at discharge and was able to return to work within one month.

Patient Information

A 27-year-old male peasant presented with recurrent seizures occurring 2–3 times daily for 12 years. He had a previous history of ruptured AVM diagnosed at another hospital five years earlier.

Clinical Findings

Neurological examination revealed preserved motor strength (MRC 5/5) with mild right-sided tingling and numbness, impaired articulation, and reduced memory function.

Diagnostic Assessment

Contrast-enhanced CT (CECT) of the head demonstrated a left sylvian fissure AVM adjacent to the sensory cortex and Wernicke's speech area. (Figure 2A) CT cerebral angiography confirmed a left sylvian AVM classified as Spetzler–Martin Grade III (S2V0E1). (Figure 2B)

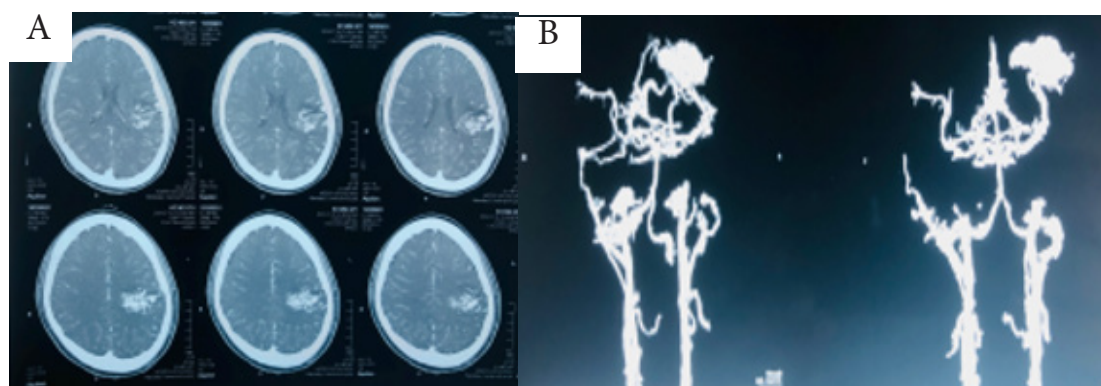


Figure 2 : (A) CECT (Head) and (B) preoperative Angiogram

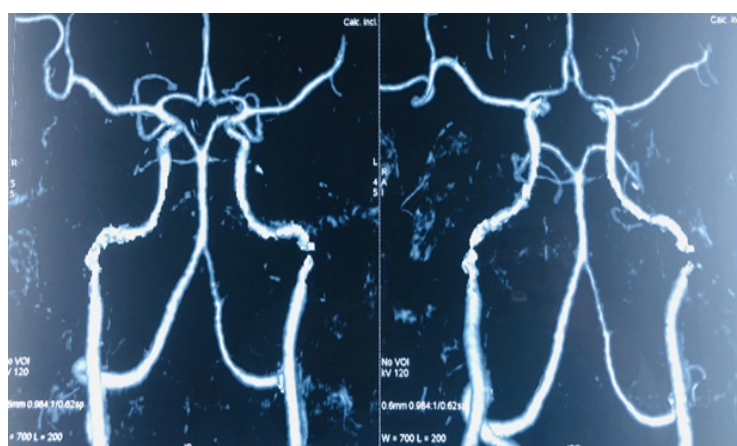


Figure 3: Postoperative cerebral Angiogram

Therapeutic Intervention

The patient underwent craniotomy with complete excision of the AVM.(Figure 3) Postoperatively, standard neurosurgical care was provided together with intravenous Cerebrolysin administered at a dose of 30 mL in 100 mL normal saline every 24 hours for 7 days.

Follow-Up and Outcomes

Postoperative recovery showed improvement in speech articulation and memory function. The patient achieved a GOS score of 5 at discharge and returned to work within one month.

Timeline

Table 1: Clinical course and treatment timeline of Case 2.

Day	Clinical Event
Day 0	Presentation to outpatient department with 12-year history of seizures and previous diagnosis of ruptured AVM
Day 1–5	CECT Head and cerebral CT angiography demonstrated left sylvian AVM adjacent to sensory cortex and Wernicke’s area; Spetzler–Martin Grade III (S2 V0 E1)
Day 30–60 (approx.)	Craniotomy and complete excision of AVM performed on 22 October 2020
Postoperative Day 0–7	Standard postoperative care with daily Cerebrolysin infusion 30 mL in 100 mL normal saline for 7 days
Postoperative Day 7–10	Improvement in articulation and memory; discharged with GOS 5
Postoperative Day 30	Returned to work and resumed normal daily activities

Case 3

A 50-year-old man presented with right-sided weakness, slurred speech, and facial asymmetry. Neurological examination demonstrated dysphasia, right facial palsy, and right hemiplegia with motor power graded as MRC 3/5. Emergency CT imaging revealed a large intracerebral hematoma associated with a ruptured AVM involving the left sylvian region near Broca’s speech area. CT cerebral angiography confirmed a Spetzler–Martin Grade II AVM (S1V0E1). Surgical excision with complete AVM removal was successfully performed. Postoperatively, the patient received standard neurosurgical care and adjunctive Cerebrolysin therapy consisting of 10 mL diluted in 100 mL normal saline every 12 hours for 7 days. Progressive improvement was observed in hemiparesis, dysphasia, and facial palsy during recovery. The patient was discharged with GOS 4 and improved to GOS 5 at one-month follow-up, achieving independent ambulation without assistance.

Patient Information

A 50-year-old man was admitted to the Neurosurgery Unit, NOGH, with weakness of the right side of the body, slurred speech, and right facial asymmetry.

Clinical Findings

Neurological examination demonstrated dysphasia, right facial palsy, and right hemiplegia with motor power graded as MRC 3/5.

Diagnostic Assessment

Emergency CT of the head revealed a large intracerebral hematoma with features suggestive of a ruptured AVM involving the left sylvian region near Broca’s speech area. (Figure 4) CT cerebral angiography confirmed a left sylvian AVM classified as Spetzler–Martin Grade II (S1V0E1). (Figure 5)

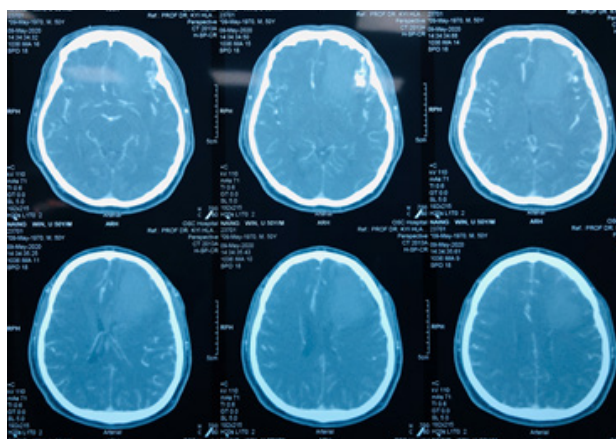


Figure 4: Preoperative CT

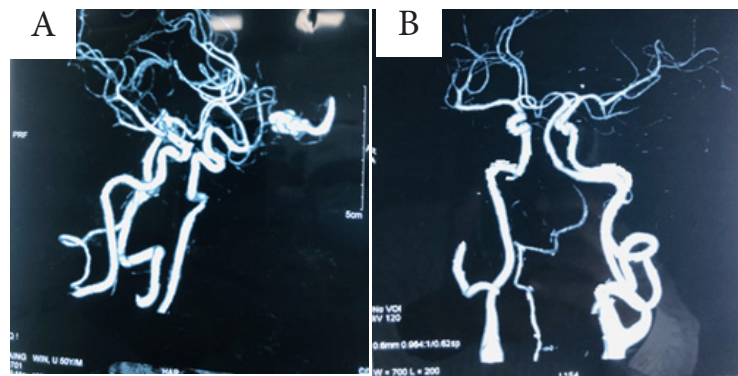


Figure 5: (A) Pre and (B) postoperative Angiogram

Therapeutic Intervention

The patient underwent surgical excision with complete removal of the AVM. Postoperatively, standard neurosurgical care was provided together with intravenous Cerebrolysin administered at a dose of 10 mL diluted in 100 mL normal saline every 12 hours for 7 days.

Follow-Up and Outcomes

Postoperative recovery showed gradual improvement in right hemiparesis, dysphasia and facial palsy. The patient was discharged with a GOS score of 4 and improved to GOS 5 at one-month follow-up, achieving independent ambulation without assistance.

Timeline

Table 2: Clinical course and treatment timeline of Case 3.

Day	Clinical Event
Day 0	Admission with right-sided weakness, slurred speech, and right facial asymmetry
Day 1–3	CT cerebral angiography confirmed AVM in left Broca's speech area; Spetzler–Martin Grade II (S1 V0 E1)
Day 7–14 (approx.)	Craniotomy and complete excision of AVM performed in May 2020
Postoperative Day 0–7	Standard postoperative management plus daily infusions of Cerebrolysin 30 mL in 100 mL normal saline for 7 days
Postoperative Day 7–14	Gradual improvement in hemiparesis, dysphasia, and facial palsy; discharged with GOS 4
Postoperative Day 30	Follow-up demonstrated GOS 5 with independent walking without assistance

Discussion

This case series highlights the clinical presentation, surgical management, and postoperative recovery of patients with ruptured cerebral AVMs treated at a tertiary neurosurgical center in Myanmar. Consistent with previous reports, hemorrhage and focal neurological deficits were the predominant presentations. (2) Most lesions were classified as Spetzler–Martin Grade II or III, supporting microsurgical excision in carefully selected patients with acceptable operative risk. (1)

All patients underwent complete surgical excision with favorable angiographic and functional outcomes. Progressive recovery of motor, speech, cognitive, and memory functions was observed, with improvement in Glasgow Outcome Scale scores and restoration of independence in daily activities. These findings are important because neurological deficits after AVM rupture or surgery may significantly affect long-term quality of life despite complete lesion obliteration. (3)

Adjunctive Cerebrolysin was administered postoperatively in patients with neurological impairment. Previous studies have suggested potential benefits in stroke rehabilitation, traumatic brain injury, and cognitive recovery.

Although evidence in postoperative AVM patients remains limited, the favorable outcomes observed in this series suggest a possible supportive role in neurological recovery.

Improvements were particularly notable in patients with AVMs involving eloquent cortical regions. Cases 2 and 3 showed recovery of speech and memory functions despite lesions adjacent to Wernicke's and Broca's areas, while Case 1 demonstrated substantial motor recovery with eventual independent ambulation. Spontaneous recovery and rehabilitation likely contributed to these outcomes, although adjunctive neurorestorative therapy may also have supported functional improvement.

This study has several limitations, including its small sample size, single-center design, lack of a control group, absence of standardized neurocognitive assessments, and limited follow-up in some patients. Larger prospective controlled studies are needed to better define the efficacy and safety of Cerebrolysin following AVM surgery.

Conclusion

This case series describes the clinical presentation and surgical outcomes of patients with brain AVMs managed at North Okkalapa General Hospital, Yangon, Myanmar. Favorable neurological and functional recovery was observed following complete AVM excision combined with adjunctive Cerebrolysin therapy in selected patients with postoperative neurological deficits.

CASE SUMMARY		
 Patient • 48 years • Ruptured left frontal AVM with intracerebral hemorrhage	 Patient • 27 years • Left sylvian AVM with seizures	 Patient • 50 years • Ruptured left sylvian AVM with hematoma
 Challenge • Reduced consciousness and right hemiparesis	 Challenge • Speech impairment, memory deficits and sensory symptoms	 Challenge • Hemiplegia, dysphasia and facial palsy
 Treatment • Cerebrolysin 30 mL/day IV x 10 days + AVM excision	 Treatment • Cerebrolysin 30 mL/day IV x 7 days + AVM excision	 Treatment • Cerebrolysin 30 mL/day IV x 7 days + AVM excision
 Outcome • GOS 4 → 5 • Independent walking	 Outcome • GOS 5 • Improved speech and memory	 Outcome • GOS 4 → 5 • Improved hemiparesis and dysphasia
 Take Home Message Complete surgical excision of ruptured AVM combined with structured postoperative rehabilitation and adjunct Cerebrolysin therapy can result in excellent functional recovery		



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...in the treatment after poor-grade aneurysmal subarachnoid hemorrhage

Abstract

Introduction: Aneurysmal subarachnoid hemorrhage (aSAH) remains associated with substantial mortality and neurological disability, particularly in patients with poor-grade hemorrhage. Early brain injury, including neuroinflammation, oxidative stress, blood-brain barrier (BBB) disruption, cerebral edema, and neuronal injury, may contribute to secondary neurological damage even after aneurysm occlusion. Cerebrolysin is a multimodal neuroprotective and neurorecovery-oriented agent investigated in several forms of acute brain injury, but its role in aSAH remains insufficiently defined.

Case presentation: A 64-year-old woman with mild, well-controlled hypertension presented after a generalized tonic-clonic seizure and prolonged somnolence. Imaging demonstrated diffuse SAH with associated intracerebral hemorrhage surrounding a ruptured left middle cerebral artery aneurysm, classified as Hunt and Hess grade IV and Fisher grade 4. Following transfer to a tertiary neurovascular center, the aneurysm was successfully occluded using three coils. Standard neurocritical care was initiated, and adjunctive Cerebrolysin therapy was started approximately 2 hours after aneurysm occlusion and within 24 hours of symptom onset, at 30 mL intravenously once daily.

Serial CT showed progressive blood resorption without hydrocephalus or secondary hemorrhagic deterioration. Transcranial Doppler monitoring showed no clinically relevant vasospasm. Sedation was reduced after 72 hours, and the patient regained full consciousness during the following day. She was successfully weaned from mechanical ventilation on day 9, when mild right-sided hemiparesis and expressive aphasia remained. Cerebrolysin was discontinued on day 12, followed by transfer for continued rehabilitation.

Conclusion: Very early adjunctive Cerebrolysin administration after aneurysm occlusion was feasible in this patient with poor-grade aSAH. The favorable early clinical course cannot establish efficacy or causality but supports further investigation of early multimodal cerebroprotection in this setting.

Keywords: aneurysmal subarachnoid hemorrhage; Cerebrolysin; cerebroprotection; blood–brain barrier; early brain injury; intracerebral hemorrhage

Introduction

Aneurysmal subarachnoid hemorrhage (aSAH) is a severe form of acute brain injury associated with substantial mortality and long-term neurological disability, particularly in patients presenting with poor-grade hemorrhage [1]. Following aneurysm rupture, neuroinflammation, oxidative stress, endothelial dysfunction, blood-brain barrier (BBB) disruption, cerebral edema, and neuronal injury develop during the early phase and may subsequently interact with delayed cerebral ischemia and other secondary complications.

Definitive aneurysm occlusion and comprehensive neurocritical care remain central to management [1]. However, securing the aneurysm does not immediately terminate the biological processes initiated by the hemorrhage. This provides a rationale for investigating adjunctive approaches aimed at limiting secondary injury and supporting recovery.

Cerebrolysin is a multimodal preparation with neurotrophic, anti-inflammatory, antioxidant, anti-apoptotic, and neurorepair-associated effects described in preclinical and clinical studies. Although clinical research has focused primarily on ischemic stroke and traumatic brain injury, these properties have also prompted investigation in aSAH [2-4].

We report a patient with poor-grade aSAH and associated intracerebral hemorrhage who received Cerebrolysin very early after successful endovascular aneurysm occlusion.

Case Presentation

A 64-year-old woman with mild, well-controlled arterial hypertension and no other relevant medical history was admitted after a generalized tonic-clonic seizure followed by prolonged somnolence. Imaging demonstrated diffuse SAH with associated intracerebral hemorrhage surrounding a ruptured left middle cerebral artery aneurysm. The hemorrhage was classified as Fisher grade 4 and the clinical presentation as Hunt and Hess grade IV.

The patient was intubated and mechanically ventilated for transfer to a tertiary neurovascular center.

Therapeutic Intervention

Catheter angiography confirmed the aneurysm, which was successfully occluded using three coils. Standard neurocritical care included nimodipine, approximately 72 hours of analgosedation, blood-pressure management, venous thromboembolism prevention, and seizure prophylaxis with levetiracetam. Approximately 2 hours after aneurysm occlusion, and within 24 hours of symptom onset, Cerebrolysin was initiated at 30 mL intravenously once daily and continued for 12 days.



Figure 1. Ruptured left middle cerebral artery aneurysm before and after coiling.

A control CT approximately 24 hours after treatment showed perifocal edema around the intracerebral hematoma, early resorption of the subarachnoid blood, and no hydrocephalus. Serial CT examinations demonstrated continued blood resorption without secondary hemorrhagic deterioration. Transcranial Doppler monitoring showed no evidence of significant vasospasm.

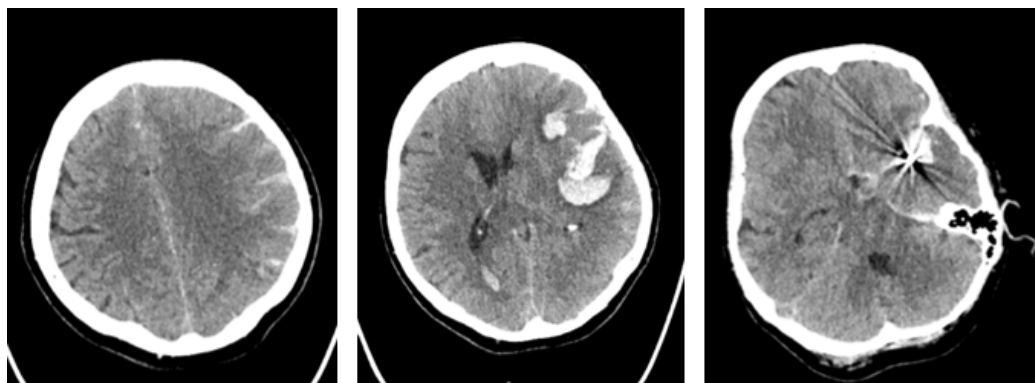


Figure 2. Control CT approximately 24 hours after coiling, showing subarachnoid and intracerebral blood with left hemispheric edema and no radiological signs of hydrocephalus.

After 72 hours, sedation was gradually reduced, and the patient regained full consciousness during the following day. Mild right-sided hemiparesis and disorientation were present. On day 9, she was successfully weaned from mechanical ventilation and demonstrated mild right-sided motor impairment and expressive aphasia. Cerebrolysin was discontinued on day 12, and the patient was transferred to the referring hospital for continued rehabilitation. No adverse event was clinically attributed to Cerebrolysin during the observed period. Long-term functional and cognitive follow-up was unavailable.

Timeline

Table 1: Clinical course and treatment timeline.

Time	Clinical event
Day 0	Seizure, somnolence; CT/angiography: poor-grade SAH, associated ICH and ruptured left MCA aneurysm
Day 0	Hunt–Hess IV; Fisher 4; intubation and transfer
Day 0	Endovascular occlusion using three coils
~2 h after coiling	Cerebrolysin 30 mL IV once daily initiated
Day 1	CT: perifocal edema, no hydrocephalus, early blood resorption
Days 2–3	TCD monitoring without significant vasospasm
Day 4	Fully awake; mild right hemiparesis and disorientation
Day 9	Weaned from mechanical ventilation; mild hemiparesis and expressive aphasia
Day 12	Cerebrolysin discontinued; transfer for rehabilitation

Discussion

This case illustrates that Cerebrolysin could be initiated approximately 2 hours after aneurysm coiling in a patient with poor-grade aSAH and associated intracerebral hemorrhage without interfering with standard neurocritical care. Despite an initial Hunt and Hess grade IV presentation, the patient showed early neurological recovery without hydrocephalus or clinically apparent delayed cerebral ischemia during the monitored period. As an uncontrolled observation, however, the course cannot establish a treatment effect or support a general conclusion regarding safety.

The rationale for early adjunctive treatment relates to the pathophysiology of early brain injury. Aneurysmal SAH triggers endothelial dysfunction, BBB disruption, neuroinflammation, oxidative stress, cerebral edema, and neuronal injury that may persist despite successful aneurysm occlusion. BBB disruption is particularly relevant because endothelial and tight-junction damage increases vascular permeability, contributes to vasogenic edema, and facilitates inflammatory signaling.

Experimental and translational findings suggest that Cerebrolysin may influence some of these pathways. In a human cerebral endothelial cell model, tissue plasminogen activator and fibrin increased endothelial permeability and altered inflammatory mediators and tight-junction proteins; Cerebrolysin attenuated the increase in permeability and partially reversed these changes [3]. Although such findings cannot be directly extrapolated to aSAH, they provide a biological rationale for investigating BBB integrity as a mechanistic endpoint. The absence of hydrocephalus or substantial progression of edema in this patient cannot be attributed to Cerebrolysin.

Clinical evidence in aSAH remains limited. In a randomized, placebo-controlled pilot trial, 50 patients received Cerebrolysin 30 mL/day or placebo for 14 days. Treatment was feasible and well tolerated, but no significant differences were observed in 6-month GOSE, mRS, cognitive outcome, or delayed cerebral ischemia [2]. The study population was predominantly good-grade (60%), with a median modified WFNS grade of II, which limits conclusions for poor-grade aSAH. A subsequent systematic review and meta-analysis reported a possible mortality signal but emphasized the limited evidence base and the need for larger randomized trials [4].

Further research should therefore focus on clinically defined high-risk populations and incorporate both functional outcomes and mechanistic measures of BBB permeability or neurovascular-unit integrity. An ongoing registered trial at our center (ISRCTN16818128) is evaluating adjunctive Cerebrolysin in patients with subarachnoid hemorrhage and an initial Hunt and Hess grade of III or higher. Combination approaches are also hypothesis-generating: a published case report described the feasibility of intraventricular recombinant tissue plasminogen activator combined with Cerebrolysin in severe intraventricular hemorrhage, although efficacy cannot be inferred from a single case [5].

Overall, the present case extends the limited clinical experience with very early Cerebrolysin administration to a patient with poor-grade aSAH. Its value lies in documenting timing, co-administration with standard care, and the early clinical course; it does not demonstrate efficacy or causality.

Strengths and limitations

A strength of this report is the detailed temporal relationship between aneurysm occlusion, very early Cerebrolysin administration, and subsequent clinical evolution. However, the single-case design precludes conclusions regarding efficacy, causality, or general safety. The patient received multiple established treatments, and the absence of significant vasospasm or hydrocephalus may have contributed to the favorable course. No direct assessment of BBB integrity was performed, and long-term functional and cognitive outcomes were unavailable.

Conclusion

Very early adjunctive Cerebrolysin administration after aneurysm occlusion was feasible in this patient with poor-grade aSAH. The favorable early course should be interpreted cautiously because established treatments and the absence of major complications provide alternative explanations. This observation supports further controlled investigation of early multimodal cerebroprotection using functional outcomes together with mechanistic measures of BBB and neurovascular-unit integrity.

CASE SUMMARY



Patient

- 64 years
- Poor-grade aneurysmal subarachnoid hemorrhage



Challenge

- Severe SAH with associated intracerebral hemorrhage and reduced consciousness



Treatment

- Cerebrolysin 30 mL/day IV x 12 days + neurocritical care



Outcome

- Extubated on Day 9
- Conscious and awake by Day 4
- Transferred to rehabilitation with only mild hemiparesis and expressive aphasia



Take Home Message

The treatment with Cerebrolysin after poor-grade aSAH is safe and feasible and resulted in unexpectedly good recovery.

Neurorehabilitation





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Neurorehabilitation is a core component of modern neurological care. After stroke, traumatic brain injury, neurosurgical intervention, or other causes of acquired brain injury, the initial lesion defines only the starting point of recovery. The trajectory that follows is shaped by spontaneous biological repair, neuroplasticity, targeted rehabilitation, patient engagement, and the quality and timing of medical interventions.

Our understanding of neurorehabilitation has advanced considerably over recent decades. Rehabilitation was long delivered as a separate phase that began after acute medical treatment had ended. Current evidence supports an integrated continuum in which acute care and structured rehabilitation act as complementary elements of a unified therapeutic strategy that promotes early neurological recovery. Within this continuum, the timing, intensity, individualization, and biological context of rehabilitation influence its effectiveness.

This integrated model of care is directly relevant to pharmacological approaches intended to support neurorecovery. In ischemic stroke, our exploratory, randomized, placebo-controlled CARS trial evaluated Cerebrolysin combined with standardized motor rehabilitation initiated early after onset and reported improved upper-extremity motor recovery, its primary endpoint, together with a favorable global functional outcome at 90 days. Drawing on this and related evidence, the joint guideline of the European Academy of Neurology and the European Federation of NeuroRehabilitation Societies issued a recommendation for Cerebrolysin (30 mL intravenously for at least 10 days, added to early motor rehabilitation) in patients with moderate-to-severe ischemic stroke. In routine practice, the multinational C-REGS 2 comparative-effectiveness registry found that, in moderate ischemic stroke, Cerebrolysin added to standard care was associated with better functional outcome on the modified Rankin Scale at 90 days. Beyond the motor domain, our randomized, placebo-controlled ESCAS pilot trial reported greater improvement of nonfluent aphasia when Cerebrolysin was combined with speech-language therapy, and the ongoing multicenter, placebo-controlled CODEC trial is evaluating Cerebrolysin for post-stroke cognitive decline.

In moderate-to-severe traumatic brain injury, our randomized, placebo-controlled, single-center CAPTAIN II trial evaluated Cerebrolysin as an adjunct to standard care and reported benefits across a prespecified multidimensional set of functional and neuropsychological outcomes, supporting continued investigation of multimodal approaches to neurorecovery. The ongoing randomized, placebo-controlled C-RETURN trial extends this work in the same population, with global functional outcome at 90 days as the primary endpoint and a large sample of patients.

The cases presented in this chapter illustrate the complexity of neurorehabilitation in real-world clinical practice, where patients differ in lesion characteristics, level of disability, comorbidities, therapeutic window, and rehabilitation potential. These differences call for rehabilitation strategies adapted to the individual patient. Clinical experience must remain closely connected to scientific evidence. Randomized clinical trials are the reference standard for establishing efficacy, and well-documented cases complement them with insight into treatment implementation, patient selection, timing, multidisciplinary care, and outcomes that are underrepresented in controlled research.

The cases collected in this chapter of Outcomes II present neurorehabilitation from the perspective of individual patients and their recovery trajectories. They underline a central principle of contemporary neurorehabilitation: the goal of care is to maximize each patient's recovery of function, independence, and participation in daily life.



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...in different stroke etiologies but identical neurorehabilitation strategies

Abstract

Background: The etiological mechanism of ischemic stroke determines acute management and secondary prevention, whereas functional recovery is shaped primarily by neuroplasticity and structured rehabilitation. We report two patients with mild ischemic stroke caused by markedly different mechanisms but managed using convergent, individualized neurorehabilitation strategies.

Case presentations: A 70-year-old man (NIHSS 5) presented with a right hemispheric ischemic stroke associated with severe (>75%) stenosis of the right internal carotid artery and a probable border-zone atherothrombotic mechanism. He received antiplatelet therapy, high-intensity statin treatment, vascular risk-factor management, and subsequent carotid endarterectomy. A 73-year-old man (NIHSS 4) presented with vertigo, gait instability, and left-sided dysmetria. Brain MRI revealed multiple acute ischemic lesions in supratentorial and infratentorial territories, while echocardiography demonstrated a left ventricular aneurysm with mural thrombus, supporting a cardioembolic mechanism. Oral anticoagulation was initiated. Both patients underwent deficit-oriented, structured neurorehabilitation and received adjunctive Cerebrolysin 30 mL/day, with favorable functional evolution.

Conclusion: These cases illustrate that etiological precision remains essential for secondary prevention, while rehabilitation strategies may converge across different stroke mechanisms. Even in mild stroke, early, individualized, task-oriented rehabilitation should be integrated into a multimodal recovery plan. As descriptive case reports, these observations do not establish treatment efficacy but provide clinically relevant real-world examples of recovery-oriented care.

Keywords: ischemic stroke; border-zone infarction; cardioembolic stroke; neurorehabilitation; Cerebrolysin; case reports

Introduction

Ischemic stroke remains one of the leading causes of long-term disability worldwide, with significant clinical and socioeconomic impact [1]. A key principle in stroke management is the identification of the underlying etiological mechanism, as this determines both acute therapeutic decisions and strategies for secondary prevention [2].

Among the major ischemic stroke subtypes, large artery atherosclerosis and cardio embolism represent two of the most clinically relevant categories. Border zone (watershed) infarcts typically occur at the interface between major cerebral arterial territories and are often associated with hemodynamic compromise, particularly in the presence of significant carotid stenosis [3]. In contrast, cardioembolic strokes result from embolic material originating from the heart and are characterized by abrupt onset and a tendency to involve multiple vascular territories [4].

While this etiological distinction is critical for guiding treatment—antiplatelet therapy and revascularization

in large artery disease versus anticoagulation in cardioembolic stroke—the processes underlying neurological recovery are less dependent on etiology and more closely related to neuroplasticity and functional reorganization [5].

This raises an important clinical question: to what extent do rehabilitation strategies converge despite divergent stroke mechanisms? The present report illustrates this concept through two cases with markedly different etiologies but similar post-stroke recovery approaches.

Case 1

A 70-year-old male, with a history of heavy smoking (75 pack-years) and no prior chronic treatment, presented to the emergency department with neurological symptoms that had developed abruptly more than 12 hours prior to admission. The patient reported impaired coordination of the left upper limb and visual disturbance affecting the left visual field.

On neurological examination, the patient was alert and cooperative, with mild left-sided hemiparesis, more pronounced in the upper limb (MRC 4/5), associated with dysarthria and a positive Babinski sign on the left. A left homonymous hemianopia was also documented. The NIHSS score at admission was 5, indicating a mild stroke.

Initial non-contrast CT revealed a hypodense area in the right parietal region, suggestive of an ischemic lesion. (Figure 1A) Subsequent MRI confirmed an acute infarction in the territory of the right middle cerebral artery. Importantly, CT angiography demonstrated a severe stenosis (>75%) at the origin of the right internal carotid artery. (Figure 1B)

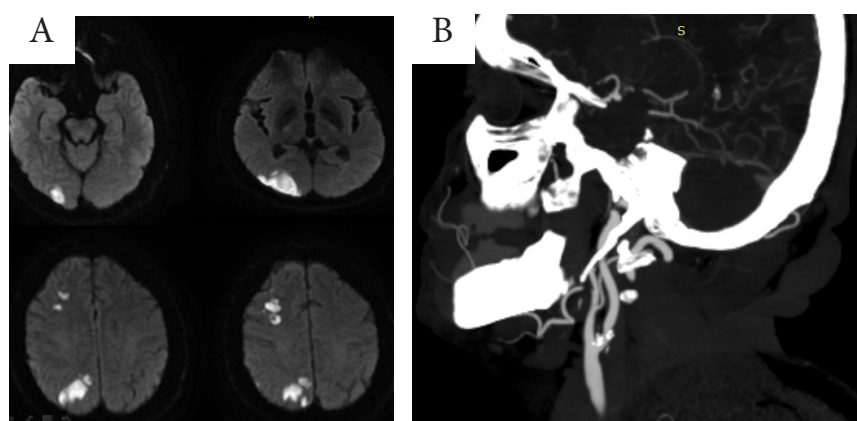


Figure 1: (A) Initial non-contrast CT. (B) Subsequent MRI.

Given the imaging findings and the absence of a cardioembolic source on cardiac evaluation, the stroke was interpreted as being of atherothrombotic origin, with a probable hemodynamic component consistent with a border zone infarction mechanism.

The patient was not eligible for reperfusion therapy due to delayed presentation. Management included initiation of antiplatelet therapy and high-intensity statin, along with strict control of vascular risk factors. In addition, the patient underwent carotid endarterectomy one week after discharge, without perioperative complications.

Beyond etiological treatment, the patient was enrolled in a structured neurorehabilitation program focusing on motor recovery and functional independence. As part of this multimodal approach, adjunctive therapy with Cerebrolysin 30 ml/day was administered for 10 days. Clinical evolution was favorable, with progressive improvement in motor function and partial recovery of visual deficits, allowing the patient to regain functional autonomy in daily activities.

Case 2

A 73-year-old male with a complex cardiovascular history, including prior myocardial infarction, coronary artery bypass grafting, and poorly controlled hypertension, presented with acute onset of vertigo, gait instability, nausea, and vomiting. According to family members, the patient had been asymptomatic approximately seven hours prior to presentation.

Neurological examination revealed a cerebellar syndrome characterized by bilateral horizontal-rotatory

nystagmus, marked gait ataxia, and dysmetria affecting the left side. A mild residual right-sided weakness was also noted, consistent with a prior stroke. The NIHSS score was 4. MRI of the brain demonstrated multiple acute ischemic lesions of small size, distributed across both supratentorial and infratentorial regions, involving different vascular territories. This pattern strongly suggested an embolic mechanism.

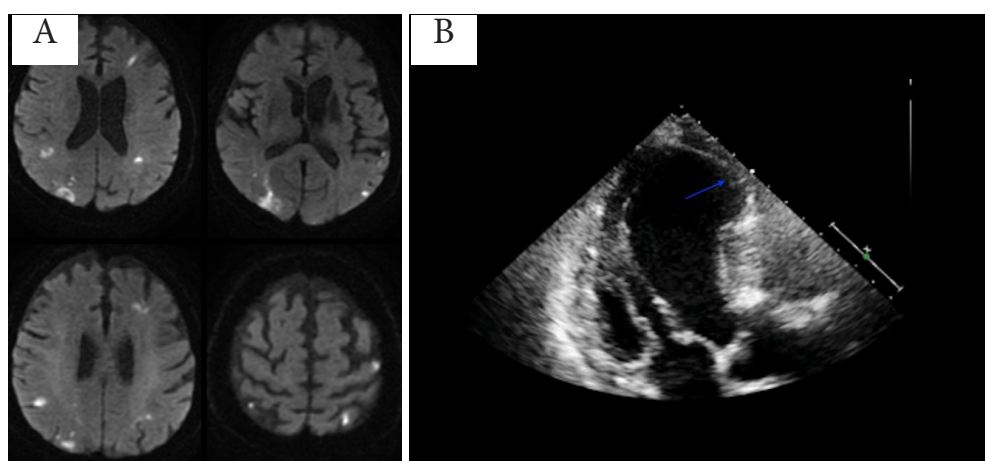


Figure 3: (A) MRI of the brain. (B) Transthoracic echocardiography.

Carotid Doppler ultrasonography did not reveal hemodynamically significant stenosis. However, transthoracic echocardiography identified a left ventricular aneurysm with an associated mural thrombus, providing a clear cardioembolic source. (Figure 3) Based on these findings, the diagnosis of cardioembolic stroke was established. The patient was started on oral anticoagulation as secondary prevention. Similarly to the first case, the patient underwent a structured neurorehabilitation program aimed at improving balance, coordination, and functional mobility. Adjunctive therapy with Cerebrolysin 30 ml/day was also administered. During follow-up, the patient showed gradual neurological improvement, particularly in gait stability and coordination, leading to a significant reduction in disability.

Discussion

These two cases highlight the clinical importance of distinguishing ischemic stroke mechanisms without allowing etiological differences to obscure the shared principles of post-stroke recovery. In the first patient, severe ipsilateral internal carotid artery stenosis supported an atherothrombotic mechanism with a probable hemodynamic component. In the second patient, multifocal acute lesions involving different vascular territories, together with a left ventricular aneurysm and mural thrombus, strongly supported cardioembolism. These distinctions were clinically decisive because they led to different secondary-prevention strategies: antiplatelet therapy and carotid revascularization in the first case, and oral anticoagulation in the second [3,4,6,7].

Despite this divergence, both patients required an early, individualized rehabilitation plan directed at their specific functional deficits. The first program emphasized motor recovery, visual impairment, and independence in daily activities, whereas the second focused on gait, balance, coordination, and functional mobility. This convergence is clinically relevant because neurological recovery after stroke is mediated by neuroplasticity, functional reorganization, and task-specific training rather than by etiology alone [5,8].

The cases are also relevant because both strokes were mild at presentation (NIHSS 5 and NIHSS 4). Mild stroke should not be equated with negligible disability: visual-field impairment, upper-limb dysfunction, gait ataxia, and coordination deficits may substantially affect autonomy and quality of life. A structured rehabilitation pathway therefore remains appropriate even when the baseline NIHSS score is low.

Within a multimodal approach, both patients received adjunctive Cerebrolysin 30 ml/day. The EAN/EFNR guideline on pharmacological support for early motor rehabilitation after acute ischemic stroke includes Cerebrolysin as an add-on option, and the CARS randomized controlled trial provides supporting clinical evidence [9,10]. The present report is not designed to demonstrate treatment efficacy or to attribute the observed outcomes to any single component of care. Rather, it illustrates how guideline-informed pharmacological support may be integrated with etiological treatment and structured neurorehabilitation in routine clinical practice.

The interpretation of these cases is limited by their descriptive nature and by the absence of serial standardized outcome measures in the current report. Future documentation would be strengthened by predefined follow-up intervals and repeated measures such as NIHSS, modified Rankin Scale, and Barthel Index scores. Nevertheless, the cases provide a pragmatic reminder that recovery-oriented care should begin early, remain individualized, and extend to patients with mild as well as more severe stroke.

Conclusion

Although border zone and cardioembolic strokes differ substantially in pathophysiology and secondary prevention, both patients achieved favorable functional recovery following individualized, multidisciplinary neurorehabilitation. In line with contemporary European recommendations, post-stroke recovery is primarily driven by tailored, task-oriented rehabilitation adapted to patient-specific deficits.

These cases further support the concept that meaningful recovery may occur across different stroke mechanisms when evidence-based rehabilitation is implemented. Adjunctive pharmacological interventions, including Cerebrolysin, should be considered as part of a multimodal approach.

In line with European guideline recommendations, both patients received structured neurorehabilitation combined with adjunctive pharmacological support. The use of Cerebrolysin as an add-on therapy is supported by the EAN/EFNR guideline for early motor recovery after acute ischemic stroke, reinforcing its role within a multimodal rehabilitation strategy.

CASE SUMMARY	
 Patient	• 70 years • Border-zone ischemic stroke
 Challenge	• Hemiparesis and visual field deficit
 Treatment	• Cerebrolysin 30 mL/day IV x 10 days + rehabilitation
 Outcome	• Functional autonomy regained • Motor and visual improvement
 Take Home Message Despite divergent etiologies requiring distinct secondary prevention, early deficit-oriented neurorehabilitation combined with adjunctive Cerebrolysin was associated with functional recovery, highlighting the convergence of multimodal rehabilitation principles across different stroke mechanisms.	



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...in severe neurogenic dysphagia following severe TBI

Abstract

Background: Neurogenic dysphagia is a frequent and potentially life-threatening consequence of acquired brain injury, often resulting in aspiration, prolonged enteral feeding, tracheostomy dependence, and reduced quality of life. While Cerebrolysin has demonstrated neurorestorative and neuroplasticity-promoting properties in neurological disorders, its potential role in dysphagia rehabilitation remains poorly described. **Case Presentation:** We report the case of a 32-year-old male who sustained a severe traumatic brain injury on November 15, 2024, resulting in a minimally conscious state (MCS), decompressive craniectomy, severe neurogenic dysphagia, tracheostomy dependence, and jejunostomy feeding. Baseline swallowing assessment demonstrated absent functional oral intake and severe impairment across swallowing outcome measures (FOIS=1, GUSS=0, DOSS=1). The patient was enrolled in an intensive interdisciplinary neurorehabilitation program including speech-language pathology, physical therapy, occupational therapy, and rehabilitation medicine.

Intervention: Cerebrolysin was administered according to standard clinical protocols (Cerebrolysin 30 mL/day intravenously for 10 consecutive days, 3 repeated cycles) as an adjunct to intensive swallowing rehabilitation. Clinical swallowing assessments and functional outcomes were monitored longitudinally throughout treatment.

Outcomes: Over a 12-month period, the patient demonstrated progressive improvement in swallowing function, secretion management, airway protection, and feeding-related participation. Swallowing outcome measures improved to FOIS=4, GUSS=10, and DOSS=3. The patient was successfully decannulated on May 22, 2025, achieved safe oral intake of at least one consistency (IDDSI Level 4), and subsequently underwent jejunostomy removal on April 20, 2026, transitioning from complete enteral feeding dependence to functional oral feeding. No significant adverse events associated with Cerebrolysin administration were observed.

Conclusion: This case documents clinically meaningful recovery of swallowing function in a patient with severe neurogenic dysphagia following traumatic brain injury. Although causality cannot be established, the observed progression from tracheostomy and jejunostomy dependence to decannulation and oral feeding supports further investigation of Cerebrolysin as an adjunct to intensive neurorehabilitation and its potential role in facilitating neuroplasticity and functional recovery after severe acquired brain injury.

Keywords: Dysphagia; Cerebrolysin; Traumatic Brain Injury; Neurorehabilitation; Neuroplasticity; Swallowing Rehabilitation.

Introduction

Neurogenic dysphagia affects a substantial proportion of patients following acquired brain injury. According to the German S1 guideline for Neurogenic Dysphagia, dysphagia is a complex sensorimotor disorder affecting the safety and efficiency of swallowing and frequently occurs following acquired brain injury. Beyond its impact on nutrition and hydration, dysphagia is associated with aspiration pneumonia, prolonged hospitalization,

increased healthcare costs, and reduced quality of life. (1)

Recovery of swallowing function depends on the reorganization of distributed cortical and subcortical networks involved in sensorimotor control. Consequently, rehabilitation approaches increasingly aim not only to compensate for deficits but also to facilitate neuroplasticity and functional recovery.

Cerebrolysin is a peptide-based neurotrophic agent with demonstrated cerebroprotective and neurorestorative properties. Experimental and clinical evidence suggests that Cerebrolysin may promote neuronal survival, synaptic plasticity, neurogenesis, and functional recovery after neurological injury. Although it has been investigated in stroke (2) and traumatic brain injury, evidence regarding its potential role in dysphagia rehabilitation remains scarce.

This report describes the clinical course of a patient with severe neurogenic dysphagia treated with intensive interdisciplinary rehabilitation and adjunctive Cerebrolysin therapy. (1)

Case Presentation

We report the case of a previously healthy 32-year-old male who sustained a severe traumatic brain injury on November 15, 2024, resulting in a minimally conscious state (MCS), decompressive craniectomy, tracheostomy dependence, and jejunostomy feeding. Clinical and instrumental swallowing assessments demonstrated severe neurogenic dysphagia with absent functional oral intake, impaired airway protection, poor secretion management, and a high risk of aspiration. Baseline swallowing outcome measures confirmed profound impairment (FOIS=1, GUSS=0, DOSS=1). The patient was enrolled in an intensive interdisciplinary neurorehabilitation program including speech-language pathology, physical therapy, occupational therapy, and rehabilitation medicine.

Therapeutic Intervention

The patient participated in an intensive interdisciplinary neurorehabilitation program focused on restoring functional swallowing and promoting overall neurological recovery. Daily speech and language therapy (SLT) sessions were provided five days a week and included swallowing exercises targeting strength and coordination, neuromuscular electrical stimulation (NMES), sensory stimulation strategies, airway protection training, progressive oral intake trials and blue dye testing (BDT), compensatory and restorative swallowing techniques, and phonatory training using a speaking valve (SV).

In parallel, Cerebrolysin was administered according to institutional clinical protocols (Cerebrolysin 30 mL/day intravenously for 10 consecutive days, 3 repeated cycles) as a neurotrophic intervention intended to support neuroplasticity and neurological recovery. Treatment was delivered over several weeks with regular monitoring of swallowing performance and functional outcomes. Treatment adherence was complete, with no interruptions in Cerebrolysin administration and rehabilitation sessions was interrupted 3 weeks during march for holidays.

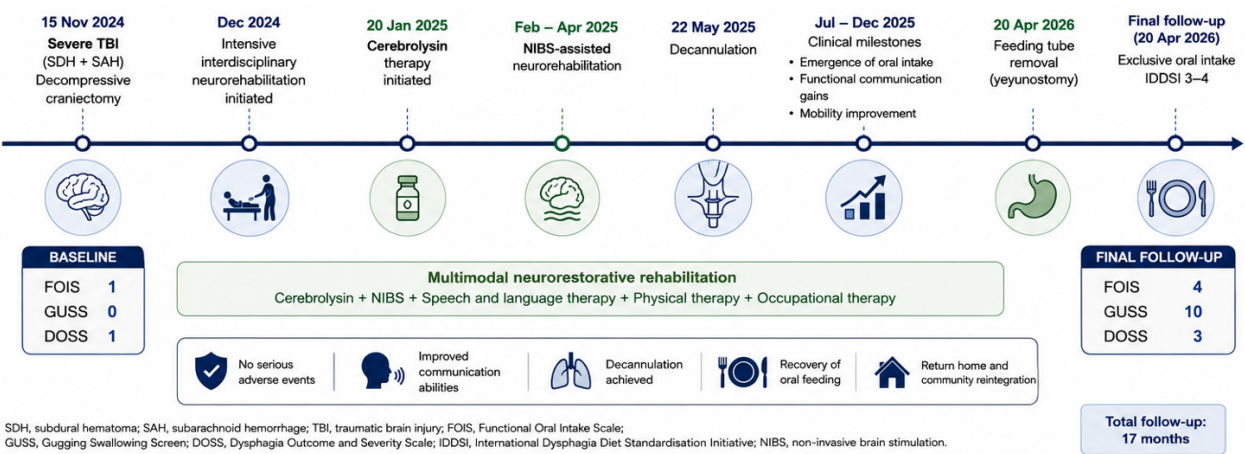


Figure 1: Clinical course and functional recovery

Outcomes

During follow-up, the patient demonstrated progressive recovery of swallowing function, reflected by improvements in functional swallowing scales (FOIS: 1→4, GUSS: 0→10, DOSS: 1→3). Clinical gains included improved secretion management, enhanced swallowing safety and efficiency, increased participation in feeding-related activities, and the emergence of vocalizations in response to verbal stimulation and repetition. Recovery was marked by successful decannulation on May 22, 2025, indicating improved airway protection and secretion control. Continued swallowing rehabilitation enabled the reintroduction and progression of oral intake, ultimately achieving safe oral feeding of at least one consistency (IDDSI Level 4). Following sustained nutritional and swallowing improvement, the jejunostomy tube was removed on April 20, 2026. These swallowing-related improvements occurred alongside ongoing neurological rehabilitation and were associated with meaningful gains in functional independence and quality of life. Treatment was well tolerated, with no significant adverse events associated with Cerebrolysin administration.

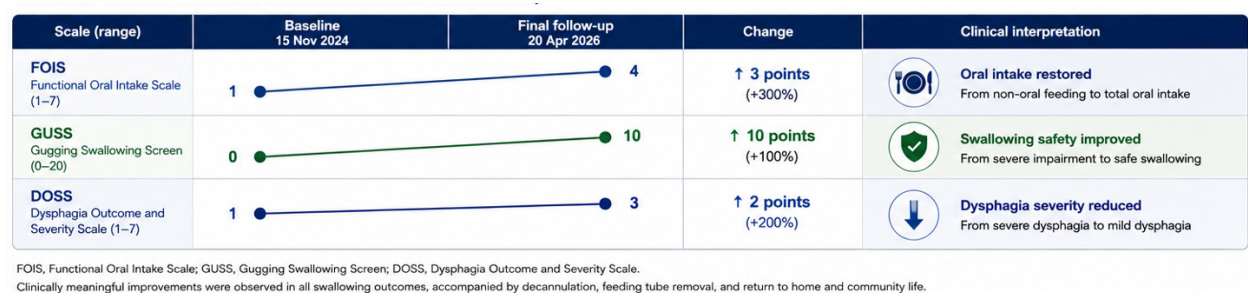


Figure 2: Functional outcomes from baseline to final follow-up

Discussion

This case highlights the potential role of Cerebrolysin as an adjunctive therapy within a comprehensive neurorehabilitation program for severe neurogenic dysphagia following traumatic brain injury. Over a 12-month period, the patient progressed from complete dependence on tracheostomy and jejunostomy, with absent functional oral intake, to successful decannulation, removal of enteral nutritional support, and safe oral feeding, accompanied by improvements across standardized swallowing outcome measures. Swallowing recovery is increasingly recognized as a neuroplastic process involving distributed sensorimotor, cognitive, and brainstem networks. (3) Accordingly, interventions capable of promoting neural repair and adaptive plasticity may complement conventional dysphagia rehabilitation. Cerebrolysin has been associated with improved functional outcomes in neurological populations through mechanisms including neuroprotection, neurotrophic activity, synaptic remodeling, and enhancement of neuronal recovery. In the present case, the temporal association between neurotrophic therapy and progressive restoration of swallowing function raises the possibility that Cerebrolysin may have contributed to recovery when combined with intensive interdisciplinary rehabilitation. (4) Importantly, recovery occurred despite the initial severity of neurological impairment, characterized by a minimally conscious state, tracheostomy dependence, jejunostomy feeding, and severe aspiration risk. The achievement of decannulation and subsequent removal of enteral nutritional support represent clinically meaningful milestones associated with reduced medical burden, improved participation, and enhanced quality of life. Nevertheless, the single-case design precludes any inference of causality, and spontaneous neurological recovery, rehabilitation intensity, and other concurrent interventions may have influenced outcomes. Further prospective studies, controlled trials, and mechanistic investigations are warranted to determine whether Cerebrolysin exerts clinically meaningful effects on swallowing recovery and to identify the patient populations most likely to benefit from neurotrophic therapy.

Conclusions

This case demonstrates substantial recovery of swallowing function in a patient with severe neurogenic dysphagia following traumatic brain injury who initially presented in a minimally conscious state with

tracheostomy dependence, jejunostomy feeding, and absent functional oral intake. Over 12 months, the patient achieved clinically meaningful outcomes, including decannulation, restoration of safe oral feeding, removal of enteral nutritional support, and improved swallowing-related functional scores. Although causality cannot be established from a single case, these findings support further investigation of Cerebrolysin as an adjunct to intensive interdisciplinary neurorehabilitation and its potential role in facilitating neuroplasticity and functional recovery after acquired brain injury.

Patient Perspective

The patient’s family described restoration of oral feeding as one of the most meaningful milestones in recovery, improving social participation and reducing caregiver burden.

CASE SUMMARY

 Patient

• 32 years • Severe TBI with neurogenic dysphagia

 Challenge

• Tracheostomy and jejunostomy dependence

 Treatment

• Cerebrolysin 30 mL/day IV x 10 days (3 cycles) + intensive neurorehabilitation

 Outcome

• FOIS 1 → 4 • GUSS 0 → 10 • DOSS 1 → 3

 Take Home Message

Severe post-traumatic dysphagia may remain responsive to intensive rehabilitation, with repeated Cerebrolysin cycles potentially improving swallowing safety, airway protection, and feeding-related participation.

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...as adjunct to rehabilitation medicine within the critical time window of a post-AIS patient

Abstract

Background: Severe ischemic stroke may result in persistent motor, language, swallowing, cognitive, and functional deficits despite acute management. Cerebrolysin has been successfully investigated as an adjunct to stroke rehabilitation because of its multimodal pharmacological and neurorestorative properties.

Case Presentation: A 65-year-old right-handed man presented with severe middle cerebral artery ischemic stroke (NIHSS 26), global aphasia, severe dysphagia, cognitive impairment, dense hemiplegia, and complete functional dependence. Cerebrolysin 30 mL/day intravenously for 21 consecutive days was initiated on day 4 after stroke onset as an adjunct to comprehensive multidisciplinary rehabilitation. At baseline, the Functional Independence Measure (FIM) was 18/126, Barthel Index 0/100, modified Rankin Scale (mRS) 5, and Montreal Cognitive Assessment (MoCA) 0/30. After one month, substantial improvement was observed across motor, functional, language, swallowing, and cognitive domains. A second Cerebrolysin cycle was administered at approximately three months post-stroke (30 mL/day, 5 days/week for 20 days) alongside continued rehabilitation.

Results: At the latest follow-up, approximately five months post-stroke, motor strength improved from 0/5 to 4/5, sensation normalized, and spasticity resolved. FIM increased to 110/126, Barthel Index to 100/100, and mRS improved from 5 to 2. Swallowing improved from severe impairment requiring nasogastric feeding to normal performance on swallowing assessment, while substantial recovery in language and cognition was observed, with MoCA increasing to 20/30.

Conclusion: This case documents substantial multidomain recovery following severe ischemic stroke during comprehensive multidisciplinary rehabilitation with Cerebrolysin administered as an adjunct treatment. Although causality cannot be established in a single case, the progressive improvements in motor function, independence, language, swallowing, and cognition support further investigation of Cerebrolysin as an adjunct to post-stroke rehabilitation.

Introduction

Stroke is characterized by the sudden onset of neurological deficits caused by cerebral ischemia or hemorrhage and remains a major cause of death and disability worldwide.^{1,2} Although reperfusion therapies have substantially improved the management of acute ischemic stroke, their benefit is limited by a narrow therapeutic window and by restricted eligibility. Consequently, many patients remain with significant neurological and functional deficits despite acute treatment.

An intervention that may address both the early phase of ischemic injury and subsequent recovery is Cerebrolysin, a neuropeptide preparation of porcine origin with multimodal pharmacological properties. Experimental and clinical studies suggest effects on excitotoxicity, oxidative stress, neuroinflammation, apoptosis, neuroplasticity, neurogenesis, synaptic repair, and vascular function.^{3–6} These properties may support recovery across multiple neurological domains when used as an adjunct to comprehensive rehabilitation.

The purpose of this case report is to present the early stroke management and progressive rehabilitation of a patient with severe ischemic stroke, global aphasia, dysphagia, cognitive impairment, and severe functional dependence who received Cerebrolysin as an adjunct to physical and rehabilitation medicine.

Case Report

This is a case of a 65-year-old, right-handed, retired businessman with hypertension, hypercholesterolemia, and diabetes mellitus who developed sudden hemiplegia, sensory loss, severe language impairment, dysphagia, and difficulty drinking. He was immediately brought to the emergency room, where cranial magnetic resonance imaging and angiography revealed a middle cerebral artery infarction involving the fronto-parietal region. He was admitted to the intensive care unit under the Neurology service.

The National Institutes of Health Stroke Scale score on admission was 26/42, consistent with severe stroke. A nasogastric tube was inserted because of dysphagia, and bladder and bowel dysfunction required catheterization and supportive management. After stabilization on the fourth hospital day, Cerebrolysin was initiated at 30 mL/day intravenously, diluted in normal saline, for 21 consecutive days. On the same day, the patient was referred to the Physical Medicine and Rehabilitation Department.

At initial physiatric assessment, the Glasgow Coma Scale score was 10/15. Muscle strength of the affected upper and lower limbs was 0/5, with severe facial weakness and absent sensation on the affected side. Mild spasticity was present. The Functional Independence Measure (FIM) score was 18/126, the Barthel Index was 0/100, and the modified Rankin Scale (mRS) score was 5, indicating severe disability and complete dependence. Language assessment using the Quick Aphasia Battery (QAB) demonstrated severe impairment across all assessed domains. The Gugging Swallowing Screen (GUSS) score was 3/6, and direct swallowing assessment could not be performed. The Montreal Cognitive Assessment (MoCA) score was 0/30.

A comprehensive rehabilitation program was initiated, including physical therapy, occupational therapy, speech and language therapy, swallowing rehabilitation, cognitive stimulation, prevention of complications, and nursing support. Physical therapy included range-of-motion exercises, progressive strengthening, electrical stimulation, anti-spasticity measures, trunk control, sensory re-education, and progressive mobility training. Occupational therapy focused on activities of daily living, socialization, and leisure participation. Speech and language therapy addressed global aphasia, dysphagia, and cognitive impairment.

After one month of rehabilitation and completion of the first 21-day Cerebrolysin cycle, substantial improvement was observed. The GCS improved from 10/15 to 14/15, while muscle strength of the affected limbs improved from 0/5 to 3-/5. Sensation improved, and spasticity decreased. The FIM increased from 18/126 to 72/126, the Barthel Index from 0/100 to 40/100, and the mRS improved from 5 to 4. Language performance also improved across all QAB domains. Although dysphagia persisted, the GUSS score improved from 3/6 to 5/6. Cognitive function improved from a MoCA score of 0/30 to 13/30. Rehabilitation was continued and progressively intensified over the following two months. The program included active and progressive resistance exercises, functional electrical stimulation, gait and balance training, transitional mobility, sensory re-education, activities of daily living training, intensified speech and language therapy, swallowing rehabilitation, and cognitive stimulation.

At approximately three months post-ictus, a second cycle of Cerebrolysin was prescribed at 30 mL/day intravenously, 5 days per week for 20 days, while multidisciplinary rehabilitation was continued. Following the second treatment cycle, further improvement was observed. Muscle strength of the affected upper and lower limbs improved to 4/5, facial muscle function became normal, sensation normalized, and no spasticity was observed. The FIM increased to 110/126, the Barthel Index reached 100/100, and the mRS improved to 2, indicating slight residual disability.

Language improved substantially across the QAB domains, including connected speech, comprehension, naming, repetition, reading aloud, and motor speech. The GUSS score reached 6/6, allowing direct swallowing assessment. The patient successfully passed tests with liquids, semisolids, solids, and mixed consistencies

without symptoms of dysphagia. Cognitive performance further improved, with the MoCA score increasing to 20/30. Improvements were observed in visuospatial and executive function, naming, attention, language, abstraction, delayed recall, and orientation. At the latest follow-up, approximately five months post-ictus, the patient maintained 4/5 muscle strength in the affected limbs, normal sensory function, and normal muscle tone. He was independent in activities of daily living, with a Barthel Index of 100/100, although reduced speed of performance and residual deficits in communication and cognition remained.

Timeline

Table 1: Clinical course and treatment timeline

Time Point	Clinical Events
Day 0 (Stroke onset)	MCA stroke; NIHSS 26; ICU admission
Day 4	GCS 10; MRC 0/5; FIM 18; BI 0; mRS 5; QAB severe aphasia; GUSS 3; MoCA 0; Cerebrolysin cycle 1 + rehabilitation started
1 month post-stroke	GCS 14; MRC 3-/5; FIM 72; BI 40; mRS 4; GUSS 5; MoCA 13
3 months post-stroke	Ongoing intensive rehabilitation; Cerebrolysin cycle 2 started
4 months post-stroke	MRC 4/5; FIM 110; BI 100; mRS 2; GUSS 6; MoCA 20
5 months post-stroke (follow-up)	Independent ADLs; BI 100; MRC 4/5; residual language and cognitive deficits

Discussion

Despite major advances in reperfusion therapy, many patients with ischemic stroke remain ineligible for thrombolysis or mechanical thrombectomy or continue to experience substantial disability. This has stimulated interest in therapeutic approaches targeting multiple components of the ischemic cascade and supporting subsequent brain recovery.

Cerebrolysin is a standardized neuropeptide preparation consisting of low-molecular-weight peptides and free amino acids. Experimental studies have demonstrated multimodal effects, including attenuation of excitotoxicity, oxidative stress, neuroinflammation, and apoptosis, together with neurotrophic and neuroplastic effects that may support neuronal survival, synaptic remodeling, and neurogenesis.^{3–6}

Experimental models of cerebral ischemia have demonstrated reductions in infarct volume and improvements in functional recovery.^{4–6} Importantly, recovery-promoting effects have also been observed when treatment was initiated after the hyperacute phase, supporting the concept that the therapeutic potential of Cerebrolysin may extend beyond acute brain protection and include mechanisms relevant to neuroplasticity and rehabilitation. Clinical studies have investigated Cerebrolysin in acute ischemic stroke, including the CASTA trial, which suggested potential benefits in patients with more severe stroke.⁷ A particularly relevant study for the present case is the Cerebrolysin and Recovery After Stroke (CARS) trial. In this randomized, double-blind, placebo-controlled study, patients received Cerebrolysin 30 mL/day for 21 days beginning 24–72 hours after stroke onset while participating in a standardized rehabilitation program. Cerebrolysin demonstrated superiority over placebo in upper-extremity motor function and global outcome and was safe and well tolerated.⁸

The present case showed progressive improvement across several clinically relevant domains. Functional recovery was reflected by improvement in the FIM from 18/126 to 110/126, the Barthel Index from 0/100 to 100/100, and the mRS from 5 to 2. Motor strength improved from complete paralysis to 4/5 in the affected limbs, sensation normalized, and spasticity resolved.

Language improved from profound impairment at baseline to substantial recovery across connected speech, comprehension, naming, repetition, reading, and motor speech. Swallowing improved from severe impairment requiring nasogastric feeding to normal performance on indirect and direct swallowing assessment. Cognitive performance also improved substantially, with the MoCA score increasing from 0/30 at baseline to 13/30 after the first treatment and rehabilitation phase and to 20/30 following continued rehabilitation and the second Cerebrolysin cycle.

The improvements observed in this patient occurred during intensive, multidisciplinary rehabilitation, and a causal relationship with Cerebrolysin cannot be established from a single case. Nevertheless, the temporal association between Cerebrolysin administration, continued rehabilitation, and progressive improvement across motor, functional, language, swallowing, and cognitive outcomes is clinically noteworthy.

The multimodal pharmacological properties of Cerebrolysin may provide a mechanistic rationale for its potential role as an adjunct to rehabilitation. By simultaneously influencing several components of ischemic injury and recovery, including neuronal survival, neuroinflammation, neuroplasticity, synaptic repair, neurogenesis, and vascular integrity, Cerebrolysin may support recovery across multiple neurological domains.^{3–6, 9}

Conclusion

This case demonstrates substantial and progressive recovery of a patient with severe ischemic stroke, global aphasia, dysphagia, cognitive impairment, profound sensorimotor deficits, and complete functional dependence who underwent comprehensive multidisciplinary rehabilitation with Cerebrolysin administered as an adjunct treatment during the early and subsequent phases of recovery.

Marked improvements were observed in sensorimotor function, activities of daily living, language, swallowing, and cognition. Functional outcomes improved from complete dependence to independence in activities of daily living, while dysphagia resolved and substantial recovery was observed in language and cognitive performance.

As a single case report, these findings cannot establish causality or separate the effects of spontaneous recovery, intensive rehabilitation, and pharmacological treatment. However, the progressive improvement observed across multiple neurological domains is consistent with the multimodal and neurorestorative properties attributed to Cerebrolysin and supports further investigation of its role as an adjunct to comprehensive post-stroke rehabilitation.

CASE SUMMARY



Patient

• 65 years • Severe MCA ischemic stroke



Challenge

• Global aphasia, dysphagia, and complete functional dependence



Treatment

• Cerebrolysin 30 mL/day IV x 21 days (2 cycles) + multidisciplinary rehabilitation



Outcome

• FIM 18 → 110 • mRS 5 → 2 • Barthel 0 → 100



Take Home Message

Despite initial complete functional dependence (FIM 18/126, Barthel Index 0/100, mRS 5) and complete paralysis of the affected limbs, this patient achieved marked recovery to near independence (FIM 110/126, Barthel Index 100/100, mRS 2), with restoration of motor strength, normalization of sensation, and resolution of spasticity.



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...as adjunct to outpatient neurorehabilitation for aphasia and dysphagia in multiterritorial stroke

Abstract

Background: Aphasia and dysphagia are disabling sequelae of stroke that impair communication, nutrition, independence, and participation. Cerebrolysin has been investigated as an adjunct to neurorehabilitation, but evidence regarding its use during subacute outpatient rehabilitation remains limited.

Case Presentation: A 49-year-old left-handed Filipino woman developed multiterritorial ischemic stroke involving the right middle and posterior cerebral artery territories, followed by bilateral cerebral and right cerebellar infarctions considered probably embolic in origin. Following neurological deterioration and medical complications, she developed severe aphasia, profound oropharyngeal dysphagia, dense left hemiparesis, and marked functional dependence. At discharge, her Modified Rankin Scale (mRS) score was 5, Quick Aphasia Battery (QAB) score was 4, and Gugging Swallowing Screen (GUSS) score was 14/20. Twenty-two days after discharge, Cerebrolysin 50 mL intravenously once daily was initiated for 21 treatment days as an adjunct to outpatient rehabilitation.

Results: By treatment day 11, QAB increased to 7, accompanied by improved verbal output and comprehension. By treatment day 19, GUSS improved to 18/20, allowing transition from nasogastric feeding toward oral intake. At 60 days after discharge, QAB increased to 9, GUSS reached 20/20, and mRS improved to 4. Spasticity progressed to MAS 4.

Conclusion: This case documents multidomain improvement during subacute outpatient rehabilitation incorporating Cerebrolysin. Although causality cannot be established, the temporal pattern and objective changes support further investigation of Cerebrolysin as an adjunct to rehabilitation.

Keywords: Cerebrolysin; ischemic stroke; aphasia; dysphagia; neurorehabilitation; subacute stroke rehabilitation

Introduction

Stroke is a major cause of long-term disability. Aphasia and dysphagia may impair communication, nutrition, independence, participation, and quality of life, while increasing the risk of complications such as aspiration pneumonia.^{1,2} Appropriately timed multidisciplinary rehabilitation is therefore fundamental to recovery.^{3,4} Access to rehabilitation remains uneven, particularly in resource-limited settings. In the Philippines, rehabilitation services and specialized professionals are concentrated in major urban centers, while geographic and financial barriers may limit continuity of care.^{5-7,10}

Cerebrolysin is a peptide-based preparation investigated for potential neuroprotective and neurorestorative effects following ischemic stroke.⁸ It should be considered an adjunct to, rather than a replacement for, rehabilitation. Previous studies have investigated Cerebrolysin in combination with structured rehabilitation, including CARS for motor recovery and ESCAS, in which Cerebrolysin combined with speech and language therapy was associated with improved language outcomes in patients with post-stroke aphasia.^{9,19}

Evidence regarding its use during subacute outpatient rehabilitation remains limited. We therefore report a patient with severe aphasia and dysphagia following multiterritorial ischemic stroke who received a 21-day course of Cerebrolysin as an adjunct to outpatient neurorehabilitation in a resource-limited setting.

Case Report

A 49-year-old left-handed Filipino woman with no previous history of stroke was admitted on February 24, 2026, with sudden impaired speech, facial asymmetry, and left-sided weakness. CT demonstrated acute ischemic infarction involving the right middle cerebral artery (MCA) and posterior cerebral artery (PCA) territories.

On hospital day (HD) 2, she was conscious and oriented, with slurred speech and left facial asymmetry. Her mRS was 2, QAB 10, and GUSS 20/20. Physical therapy was initiated.

On HD 5, she developed gastrointestinal distress, agitation, altered sensorium, tachypnea, and tachycardia, requiring ICU transfer. Acute pancreatitis and sepsis secondary to hospital-acquired pneumonia and skin and soft-tissue infection were diagnosed.

Following stabilization, physical therapy resumed. However, progressive neurological deficits developed. Repeat CT on HD 14 demonstrated new infarctions involving the left inferior frontal lobe, left lentiform nucleus, left capsulothalamic region, and right cerebellum, in addition to progression of the previous right-sided infarctions. The pattern was considered consistent with multiterritorial ischemic infarctions, probably embolic in origin.

Following neurological deterioration, mRS increased to 5 and QAB decreased to 3. The patient developed severe aphasia, profound oropharyngeal dysphagia, dense left hemiparesis, impaired mobility, and dependence in nearly all activities of daily living.

At reassessment on HD 35, mRS remained 5, QAB was 4, and GUSS was 14/20; nasogastric tube feeding continued. Cerebrolysin had been prescribed on HD 23 but could not initially be administered because of financial constraints. The patient was discharged on HD 36 with continued outpatient rehabilitation.

Subacute Outpatient Rehabilitation and Cerebrolysin

Cerebrolysin was initiated 22 days after discharge, approximately eight weeks after the index stroke. The patient received 50 mL intravenously, diluted with 50 mL of 0.9% sodium chloride, once daily for a planned 21-treatment-day course.

Treatment was generally well tolerated; mild itchiness was managed with an antihistamine. Rehabilitation was conducted twice weekly and included communication and swallowing exercises, motor and gait training, activities-of-daily-living training, caregiver education, and home exercises. Because of limited availability of speech-language pathologists and occupational therapists, rehabilitation was primarily delivered by the physical therapist, with regular physiatrist reassessment.

By treatment day 11, verbal output, comprehension, and functional communication had improved, with QAB increasing from 4 to 7. By treatment day 19, GUSS improved to 18/20, allowing discontinuation of nasogastric feeding and progression toward oral intake.

At 60 days after discharge, mRS had improved from 5 to 4, QAB to 9, and GUSS to 20/20. Spasticity progressed from MAS 2 to MAS 4, requiring escalation of baclofen.

Discussion

This case documents recovery of language and swallowing function during subacute outpatient rehabilitation following a severe multiterritorial ischemic stroke complicated by medical and neurological deterioration.

Cerebrolysin was administered as an adjunct to active rehabilitation. Its proposed neuroprotective and neurorestorative properties provide a rationale for investigating its potential role in supporting activity-dependent neurological recovery.⁸ The 50-mL/day, 21-day regimen used in this patient has precedent in the randomized study by Ladurner et al., although treatment in that study was initiated during the acute phase.¹⁷ Previous studies have similarly evaluated Cerebrolysin in combination with rehabilitation. CARS investigated its use alongside structured rehabilitation and reported exploratory benefits in upper-extremity motor recovery and global outcomes.¹⁹ More directly relevant, ESCAS evaluated Cerebrolysin combined with speech and language therapy and reported improved language outcomes in patients with nonfluent aphasia following acute left MCA stroke.⁹

The present patient differed substantially from ESCAS participants. She was left-handed and developed aphasia in association with a right MCA infarction within a broader multiterritorial stroke pattern. In the absence of formal language-lateralization testing, the condition should therefore not be definitively classified as crossed aphasia.²⁰

Table 1. Clinical Course and Major Events

Time point	Clinical status/intervention	Key findings
HD 2	Initial PM&R assessment	mRS 2; QAB 10; GUSS 20/20
HD 5–14	Medical and neurological deterioration	Pancreatitis, sepsis, new bilateral cerebral and right cerebellar infarctions
HD 35	PM&R reassessment	mRS 5; QAB 4; GUSS 14/20; NGT feeding
HD 36	Hospital discharge	Outpatient rehabilitation continued
22 days post-discharge	Cerebrolysin initiated	50 mL IV daily; planned 21 treatment days
Treatment day 11	Language improvement	QAB 7
Treatment day 19	Swallowing improvement	GUSS 18/20; NGT discontinued
60 days post-discharge	Follow-up	mRS 4; QAB 9; GUSS 20/20; MAS 4

Table 2. Changes in Clinical Outcome Measures

Outcome	Before Cerebrolysin	Follow-up	Clinical significance
QAB	4	7 on day 11; 9 at 60 days	Improved language and communication
GUSS	14/20	18/20 on day 19; 20/20 at 60 days	Progression from NGT to oral intake
mRS	5	4 at 60 days	Improved global disability
MAS	2	4 at 60 days	Progressive spasticity

A notable feature of this case is the delayed timing of Cerebrolysin administration. Treatment began approximately eight weeks after stroke, considerably later than in CARS or ESCAS. Nevertheless, progressive improvement was documented in language, swallowing, and global disability. QAB increased from 4 to 9, GUSS from 14/20 to 20/20, and mRS from 5 to 4. Improvements in standardized measures corresponded with clinically meaningful gains in verbal communication and restoration of oral feeding.

Recovery was not uniform. Despite improvement in language and swallowing, spasticity progressed from MAS 2 to 4. This illustrates the multidimensional nature of stroke recovery and emphasizes the value of assessing several functional domains.

The resource-limited rehabilitation setting is also relevant. Access to specialized speech-language and occupational therapy was limited, and rehabilitation relied heavily on available physical therapy, caregiver involvement, communication and swallowing exercises, and home-based activities. This reflects challenges encountered where multidisciplinary rehabilitation resources are geographically or financially constrained.^{5–7} Cerebrolysin cannot replace specialized rehabilitation. However, its integration into an existing rehabilitation program may warrant investigation where access to specialized services is limited. In this case, improvement occurred during concurrent rehabilitation, caregiver support, nutritional management, and ongoing medical recovery.

The temporal relationship between Cerebrolysin administration and improvement is clinically noteworthy but cannot establish causality. Spontaneous recovery, rehabilitation-related gains, nutritional improvement, and caregiver involvement may all have contributed. Nevertheless, the serial and concordant changes in QAB, GUSS, and mRS provide a clinically relevant, hypothesis-generating observation.

LIMITATIONS

This is a single-patient case report without a control group, and the independent contribution of Cerebrolysin cannot be separated from concurrent rehabilitation and spontaneous recovery. The complex multiterritorial stroke and medical complications may also have influenced the clinical trajectory.

Formal language-lateralization testing was not performed. In addition, the 50-mL regimen differs from the 30-mL regimens used in some rehabilitation studies.^{9,18,19} Limited access to specialized speech-language and occupational therapy may have influenced rehabilitation intensity.

CONCLUSION

This case documents clinically meaningful improvement in language, swallowing, and overall disability during subacute outpatient rehabilitation incorporating a 21-day course of Cerebrolysin initiated approximately eight weeks after multiterritorial ischemic stroke.

QAB improved from 4 to 9, GUSS from 14/20 to 20/20, and mRS from 5 to 4, accompanied by improved communication and restoration of oral feeding. Although the contribution of Cerebrolysin cannot be isolated, the temporal and multidomain improvement provides a clinically relevant, hypothesis-generating signal.

The observation supports further investigation of Cerebrolysin as an adjunct to task-specific rehabilitation during the subacute phase, particularly in patients with persistent aphasia and dysphagia and in settings with limited access to specialized rehabilitation services.

PATIENT PERSPECTIVE

Before the stroke, the patient was independent and professionally active. The loss of communication and oral feeding was distressing for both the patient and her family, while financial constraints affected continuity of care.

Improved communication and restoration of oral feeding substantially improved her mood, motivation, participation in family life, and the practical and emotional burden of care. Despite persistent motor deficits and spasticity, the patient and her family considered the improvement in communication and swallowing among the most meaningful aspects of her recovery.

CASE SUMMARY



Patient

• 49 years • Multiterritorial ischemic stroke



Challenge

• Severe aphasia, dysphagia, and dense hemiparesis



Treatment

• Cerebrolysin 50 mL/day IV x 21 days + outpatient rehabilitation



Outcome

• mRS 5 → 4 • QAB 4 → 9 • GUSS 14 → 20



Take Home Message

Meaningful recovery from severe post-stroke aphasia, dysphagia, and functional dependence may continue during the subacute outpatient rehabilitation phase as adjunctive Cerebrolysin treatment was temporally associated with objective improvements in language and swallowing.



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...in the management of chronic AIS

Abstract

Background: The criterion standard treatments for ischemic stroke patients, starting from systemic thrombolysis and/or undergoing endovascular recanalization therapy to intensive rehabilitation, are the best options available now-a-days, but still cannot achieve total recovery. Neuroprotective and neurotrophic agents seem to be promising therapeutic targets in stroke, even in ischemic and/or hemorrhagic stroke, either in the acute stage or to support neuro-recovery in subacute to chronic stages. Therefore, new therapies are needed as adjuvants in the re-habilitation phase for promoting the recovery and monitoring adverse effects of treatment.

Case Report: We describe a patient with an acute occlusion of the right middle cerebral artery who was treated with recombinant tissue-plasminogen activator (rtPA), underwent mechanical thrombectomy, and was then enrolled in a 1-month rehabilitation program. After the post-stroke recovery plateau, the patient received 10 days of 30 mL intravenous Cerebrolysin® to support further neuro-recovery, together with long-term rehabilitation. We utilized clinical standard assessment tools, including National Institutes of Health Stroke Scale (NIHSS), modified Rankin scale (mRS), modified Barthel Index (MBI), and function of ambulation, to evaluate the outcome of the patient, together with the adverse events monitoring. After Cerebrolysin® administration, the patient demonstrated improvement in all assessment scores at 1, 3, and 6 months.

Conclusions: Postoperative treatment with Cerebrolysin® in our patient with subacute ischemic stroke, after plateau recovery in the rehabilitation phase, together with the standard acute stroke regimen, improved the patient's recovery outcomes. No serious adverse effects were observed.

Keywords: Rehabilitation, Stroke, Mechanical Thrombolysis

Introduction

Intravenous administration of recombinant tissue-plasminogen activator (rtPA) within 4.5 hours of stroke onset together with other endovascular reperfusion strategies has been approved as a standard of care for acute ischemic stroke [1,2]. Furthermore, intensive rehabilitation programs have shown to reduce neurological and physical impairment, and improve function [3]. However, despite all therapeutic efforts, patients with stroke often remain with impaired motor functions, limiting their activities of daily living. Therefore, they have an unmet need for recovery treatment. Cerebrolysin® has anti-apoptotic, anti-oxidative, anti-inflammatory properties and stimulates neurogenesis and synaptic plasticity, which accelerates recovery of neurological functions after stroke [4-6]. Recent evidence from some clinical trials suggests that the neurotrophic agent Cerebrolysin® supports neuro-recovery in the acute to the very early subacute phases of stroke [7,8], but there is still a lack of evidence in the late subacute to chronic phases.

Case Report

A 71-year-old Thai man, with a history of hypertension and atrial fibrillation, treated with Warfarin (3 mg)

once at bedtime and Bisoprolol (2.5mg) once daily, was admitted to the hospital 1.5 hours after the onset of symptoms and presented with left hemiplegia, strabismus, severe dysarthria, left facial weakness, and left hemi-inattention with a baseline National Institutes of Health Stroke Scale (NIHSS) score of 15. His premorbid status was normal ambulation and independence in activities of daily living (modified Rankin scale=0).

The non-contrast computed tomography (CT) scan revealed right hyperdense middle cerebral artery (MCA) sign and hyperacute right MCA infarction with an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 7. The thrombolysis therapy was initiated according to the standard protocol by intravenous (i.v.) rtPA, total 66 mg (0.9 mg/kg). Computed tomography angiography (CTA) of the brain and neck after the rtPA treatment revealed right proximal MCA occlusion around the M2 segment, with an NIHSS score of 13. The patient was immediately referred to our institution for the mechanical thrombectomy. The thrombectomy was performed within 5 hours after stroke onset by using the stent retriever. An angiogram of the right internal carotid artery (ICA) revealed a complete occlusion of the whole posterior division of the right MCA (M2 segment), and distal occlusion of a few right ACA branches, including posterior internal frontal and paracentral sulcus branches. A post-thrombectomy angiogram showed recanalization of right proximal MCA and branches with a Thrombolysis in Cerebral Infarction (TICI) score of 3. No immediate complications were noted. The pre- and post-thrombectomy angiogram images of the right ICA are shown in Figures 1 and 2.

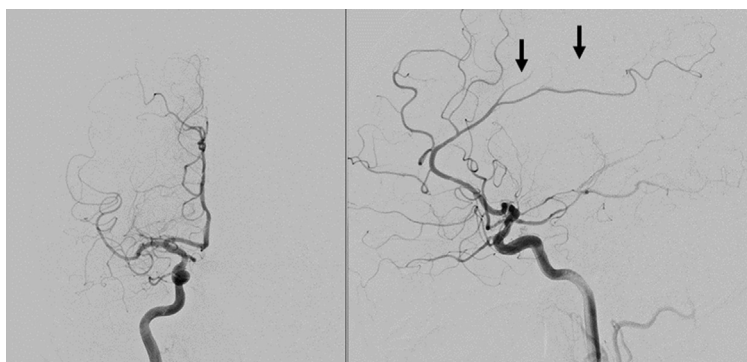


Figure 1: Angiographic images of the right internal carotid artery (ICA) on the anteroposterior and lateral views revealed segmental occlusion of the posterior division of the right middle cerebral artery (M2 segment). Distal occlusion of the few of cortical branches of the right anterior cerebral artery (ACA) was also observed (black arrows).

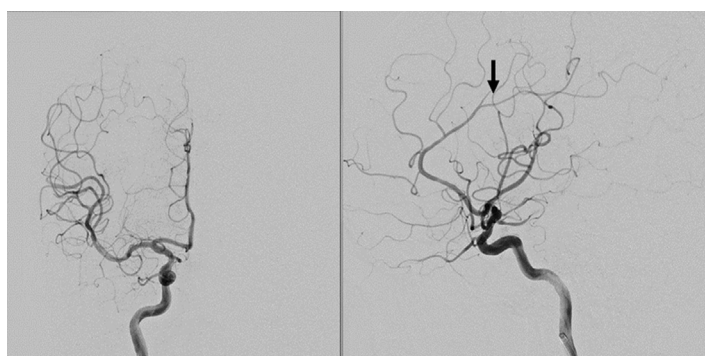


Figure 2: Angiographic images of the right ICA on AP and lateral views after endovascular thrombectomy, showing complete opacification of the posterior division of the right MCA (M2 segment), but distal occlusion of the right ACA cortical branches was still observed (black arrow).

An immediate post-thrombectomy CT brain showed a small hypodense hyperacute infarction at the right paracentral lobule, right pre- and post-central gyri, and right insular lobe. The patient still had hemiplegia, with a NIHSS score of 12. The 24-hour post-thrombectomy CT brain revealed intracerebral hemorrhage as a hyperdense lesion at the right pre- and postcentral gyri (Figure 3). Serial assessments of the NIHSS scores and modified Rankin scale (mRS) were obtained by vascular neurologists in the acute phase (Table 1) from baseline (pre-rtPA-bolus) until day 2 of admission to the rehabilitation program. The manual muscle testing was still grade 0 on the left upper and lower extremities. The functional outcome, assessed by modified Barthel Index (MBI) and ambulatory function, was evaluated on the day of enrollment for rehabilitation.

Table 1: Clinical Scores in the acute treatment phase

	NIHSS*	mRS**	MBI***	Ambulation
Admission (Day 0)	15	5	-	None
Post rtPA (2 h)	13	5	-	None
Post-thrombectomy (Day 0)	12	5	-	None
24 h post-thrombectomy (Day 1)	9	5	-	None
Before rehabilitation (Day 2)	9	5	10	None

*National Institutes of Health Stroke Scale; **Modified Rankin scale; ***Modified Barthel Index

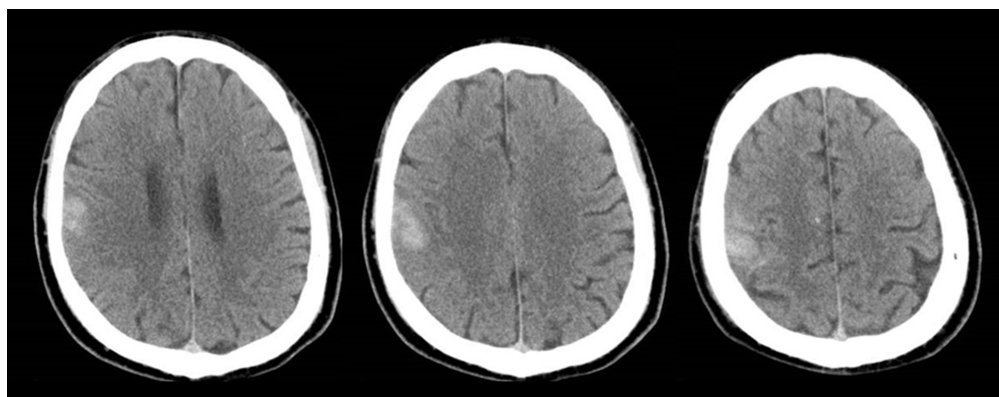


Figure 3: Computed tomography (CT) images of the brain 24 hours after thrombectomy, showing acute intracerebral hemorrhage at the right frontoparietal region, affecting the right pre- and postcentral gyri.

According to the guidelines for adult stroke rehabilitation and recovery, 2016 [9], the patient was then admitted to the rehabilitation unit on day 2 after admission and had participated in the rehabilitation program for 7 months post stroke. As soon as he became neurologically stable, an intensive re-habilitation therapy program started for 3 hours per day on every working day (5 days per week) consisting of 1 hour of physical therapy, 1 hour of occupational therapy, half an hour of speech therapy, and resting time of 30 minutes. Two weeks after starting the rehabilitation program, none of the assessment scores or muscle power tests showed any improvement. By the completion of the 4-week program, he seemed to have plateaued, but a follow-up CT scan 2 weeks after completion of the rehabilitation program showed interval changes of a sub-acute right MCA infarction with decreased density of hemorrhagic transformation at the right frontal lobe and postcentral gyrus, and a small subacute cortical infarction at the right inferior parietal lobe (Figure 4).

Cerebrolysin® was initiated once after 1 month of rehabilitation program by 30 mL Cerebrolysin® diluted in 70 mL normal saline intravenously for 10 consecutive days as an add-on to the conventional rehabilitation. Follow-up clinical assessments of impairment and disability were performed using the NIHSS, mRS, modified Barthel Index (MBI), and assessment of walking ability at baseline (before the initiation of Cerebrolysin® treatment) and at 1, 3, and 6 months after Cerebrolysin® administration. Oral medications were still taken: Dabigatran (150 mg) twice daily, Atorvastatin (40 mg) once daily, Bisoprolol (2.5 mg) once daily, Omeprazole (20 mg) once daily, and Lercanidipine (20 mg) once daily.

Initially, prior to the neurorehabilitation program, the patient had an NIHSS score of 9, scored 5 on the mRS, and 10 on the MBI. During the first 2 weeks of neurorehabilitation, the patient's functional and neurological status had improved to an NIHSS score of 7, a mRS of 4, and a MBI score of 50. The power of the left arm was graded 3 and the left leg was graded 0 by manual muscle testing. The patient was able to ambulate in a parallel bar with a left knee brace, plastic ankle-foot orthosis, and 1 personal assistant. After the second to fourth weeks, neither muscle power nor any function had changed. The patient was re-evaluated and asked to continue the rehabilitation program as an inpatient for another 6 months.

Further significant clinical improvement was evident at the follow-up visits at 1, 3, and 6 months after the initiation of Cerebrolysin® administration. Again, impairment and disability were assessed by the NIHSS, mRS, MBI, and walking ability (Table 2). While the initial improvement achieved with neurorehabilitation reached

a plateau with an NIHSS of 7, mRS of 4, and a MBI of 50, the patient experienced further significant and clinically relevant improvement after treatment with Cerebrolysin®. One month after Cerebrolysin® treatment, the patient's neurological and functional status improved to a NIHSS of 2, mRS of 3, and MBI of 75 and he was already able to walk independently with a single cane. He continued to further improve his functional capabilities until month 3, with a MBI of 95, while the neurological status remained the same (NIHSS of 2). At the final examination 6 months after treatment with Cerebrolysin®, the patient was able to walk in-dependently without gait aids. No serious adverse reactions to Cerebrolysin® occurred during or after the administration. He felt feverish and slightly uncomfortable during the i.v. administration. The patient was impressed with the standard of treatment, including the addition of the Cerebrolysin®, and has been able to return to work.

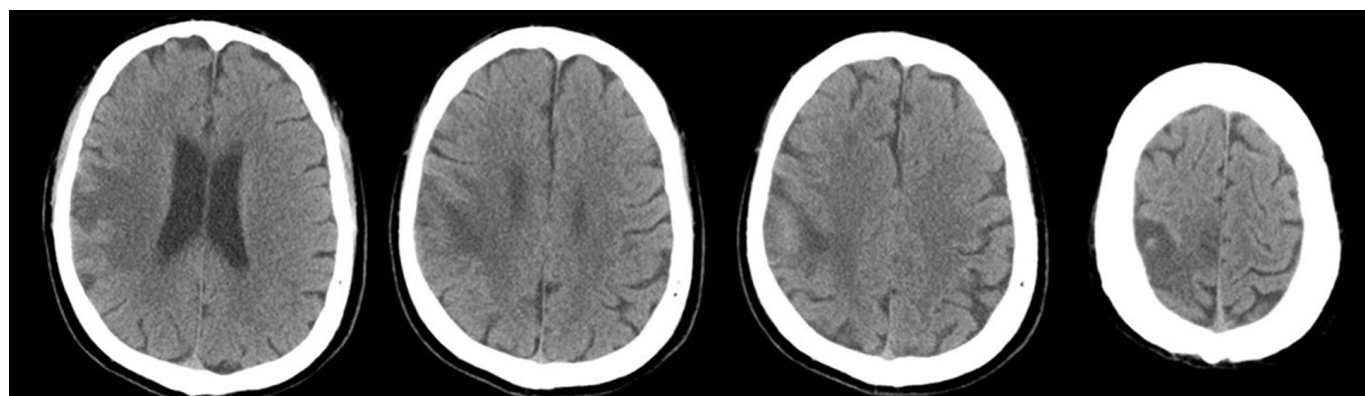


Figure 4: CT brain about 2 weeks after rehabilitation, showing late subacute right MCA's territorial infarction at the right paracentral lobule, right pre- and (particularly) postcentral gyri, with resolving hemorrhagic transformation.

Table 2: Clinical scores before and after treatment with Cerebrolysin®.

	NIHSS*	mRS**	MBI***	Ambulation
Before rehabilitation	9	5	10	None
After rehabilitation – before Cerebrolysin® treatment	7	4	50	Parallel bar with one person assisting
Month 1 after Cerebrolysin® treatment	2	3	75	Independent with a single cane walking
Month 3 after Cerebrolysin® treatment	2	3	95	Independent with a single cane walking
Month 6 after Cerebrolysin® treatment	2	2	95	Independent without gait aids

*National Institutes of Health Stroke Scale; **Modified Rankin scale; ***Modified Barthel Index

Discussion

There is still an ongoing controversy about the evidence of Cerebrolysin® in ischemic stroke patients. The findings in the Cochrane review in 2017 do not demonstrate clinical benefits of Cerebrolysin for treating acute ischemic stroke [10]. In contrast, a meta-analysis of 9 randomized clinical trials of Cerebrolysin® in 2018 demonstrated superiority of Cerebrolysin compared with placebo in different dosages from 30 to 50 mL for 10-21 days after stroke, with either an immediate onset of treatment or with a 7 day delay [7,11-15]. The clinical research on Cerebrolysin® in the late subacute to chronic phases is still ongoing, with only 1 published retrospective study on the reduction of spasticity, and 1 in patients with minimally conscious state after stroke [16,17]. Additionally, sufficient safety data in several neurological conditions, such as sub-arachnoid hemorrhage, traumatic brain injury, and mild cognitive impairment and dementia, have been published [18-20].

Generally, the published research clearly shows that patients with a baseline NIHSS of 15 only have a 23% chance of excellent recovery after 3 months [21]. We decided to treat such a patient with a 30 mL daily dosage for 10 days, which is the lowest dose, based on the established evidence and also based on the findings

from the Copenhagen Stroke Study of 1995, which showed that functional recovery was completed within 12.5 weeks (95% confidence interval (CI) 11.6 to 13.4) from stroke onset in 95% of patients [22]. Finally, this patient became independent in activities of daily living and ambulation. He also returned to work (at home). With an improved NIHSS score, modified Barthel index, modified Rankin scale, and walking ability, the short course of Cerebrolysin® has demonstrated effectiveness and safety in a subacute ischemic stroke patient who had reached a recovery plateau after 1 month of a neurorehabilitation program.

Cerebrolysin® together with rehabilitation dramatically improved the impairment and function in our patient, which had a great impact on his quality of life. The efficacy of Cerebrolysin® can be attributed to its neuroprotective and neurotrophic properties, similar to endogenous neurotrophic factors [23,24]. Further randomized controlled studies should be performed to compare the efficacy and safety of Cerebrolysin® at all stages of stroke recovery, especially the treatment window in late subacute to chronic phases of stroke. With increasing evidence from randomized clinical trials, the general public should benefit from Cerebrolysin treatment, as well as by reimbursed treatment costs.

Conclusion

The data suggest that Cerebrolysin® further enhances neurological recovery in late subacute stroke patients who previously underwent a standard acute stroke treatment regimen as well as a standard neurorehabilitation program. No serious adverse reaction was observed during and after the drug administration.

CASE SUMMARY



Patient

• 71 years • Right MCA ischemic stroke



Challenge

• Recovery plateau after thrombectomy and rehabilitation



Treatment

• Cerebrolysin 30 mL/day IV x 10 days + neurorehabilitation



Outcome

• NIHSS 7 → 2 • mRS 4 → 2 • MBI 50 → 95



Take Home Message

A recovery plateau does not necessarily mark the end of stroke recovery; late subacute rehabilitation with Cerebrolysin may enable further gains in neurological function, independence and walking ability.

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SINDI MITROVIC



Medicine Clinic for Rehabilitation “Dr. Miroslav Zotović”,
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...in upper- and lower-limb recovery following AIS

Abstract

Background: Severe ischemic stroke frequently results in substantial motor impairment and long-term disability. Pharmacological support combined with intensive neurorehabilitation has been proposed as a strategy to enhance post-stroke recovery. This case report describes the clinical course of a patient with severe ischemic stroke who received Cerebrolysin-supported intensive neurorehabilitation during the early subacute phase.

Case Presentation: A 55-year-old woman developed severe right-sided hemiparesis and dysarthria due to an ischemic stroke involving the posterior limb of the left internal capsule and posterior left lentiform nucleus. Intravenous thrombolysis was administered in the acute phase. Following stabilization, she entered a specialized inpatient neurorehabilitation program on day 12 post-stroke. Baseline assessments demonstrated severe motor impairment. Cerebrolysin 30 mL/day intravenously was administered for 21 consecutive days in combination with intensive multidisciplinary rehabilitation.

Outcomes: Over the 12-week observation period, upper-limb motor function improved substantially. Functional independence improved, while balance and gait recovered sufficiently to allow assisted ambulation. No treatment-related adverse events were observed.

Conclusion: This case illustrates meaningful recovery across upper-limb, lower-limb, balance, gait, and activities-of-daily-living domains during an early subacute rehabilitation program combining Cerebrolysin with intensive task-oriented neurorehabilitation. The findings are hypothesis-generating and support further investigation of pharmacologically supported neurorecovery strategies.

Keywords: Ischemic stroke; Cerebrolysin; neurorehabilitation; upper-limb recovery; gait recovery; intensive rehabilitation; motor recovery; case report

Introduction

Post-stroke motor impairment remains one of the leading causes of long-term disability after ischemic stroke. Recovery is influenced by spontaneous biological repair processes, neuroplasticity, lesion characteristics, corticospinal tract integrity, and rehabilitation intensity.^{1,2} Rehabilitation interventions based on task-specific practice, motor learning, and progressive functional training are central to maximizing recovery.

Pharmacological therapies that may support neurorecovery have attracted increasing interest, particularly when integrated into structured rehabilitation programs. Cerebrolysin is a standardized peptide preparation that has been investigated as an adjunct to rehabilitation after ischemic stroke. Experimental and clinical evidence suggests multimodal effects relevant to neuronal survival and recovery, including modulation of excitotoxicity, oxidative stress, inflammation, apoptosis, and neuroplastic processes.

Cerebrolysin has been evaluated in randomized clinical trials as an adjunct to standardized rehabilitation. In the CARS trial, patients receiving Cerebrolysin 30 mL/day for 21 days together with standardized rehabilitation demonstrated significantly greater improvement in upper-limb motor function, assessed by the Action Research Arm Test (ARAT), than placebo.³ The European Academy of Neurology (EAN) and European Federation of

NeuroRehabilitation Societies (EFNR) subsequently issued a weak recommendation for Cerebrolysin 30 mL/day intravenously for a minimum of 10 days as pharmacological support for early motor neurorehabilitation after moderate-to-severe ischemic stroke.⁴

Importantly, the EAN/EFNR guideline specifically addressed pharmacological interventions initiated within the first 7 days after stroke.⁴ Therefore, the treatment initiated on day 12 in the present case represents an early subacute rehabilitation application and should not be interpreted as a direct replication of the guideline-defined treatment window.

The present case describes recovery of upper- and lower-limb motor function, balance, gait, and activities of daily living in a patient with severe initial motor impairment who received Cerebrolysin as an adjunct to intensive multidisciplinary rehabilitation beginning on day 12 after ischemic stroke.

Patient Information

A 55-year-old woman was admitted to a specialized acute stroke hospital after the sudden onset of severe right-sided motor weakness and marked speech disturbance. The symptoms began during the night before admission, when she first noticed difficulty moving her right arm and leg. After waking up, the weakness and speech impairment became more pronounced, prompting emergency transport to the hospital by ambulance. On initial examination, she presented with right central facial palsy, severe right-sided motor deficit, and dysarthria/anarthria.

History obtained from her husband revealed no previously known chronic diseases, regular medication use, previous surgery, known drug allergies, smoking, or alcohol consumption. During hospitalization, arterial hypertension and hypercholesterolemia were identified as vascular risk factors, while thrombophilia was excluded during the diagnostic work-up.

Before the stroke, she had been fully independent in all activities of daily living and professionally active. She was an economist and company director living in Serbia and managing a family business operating in the United States, which required regular night-time work because of the time-zone difference.

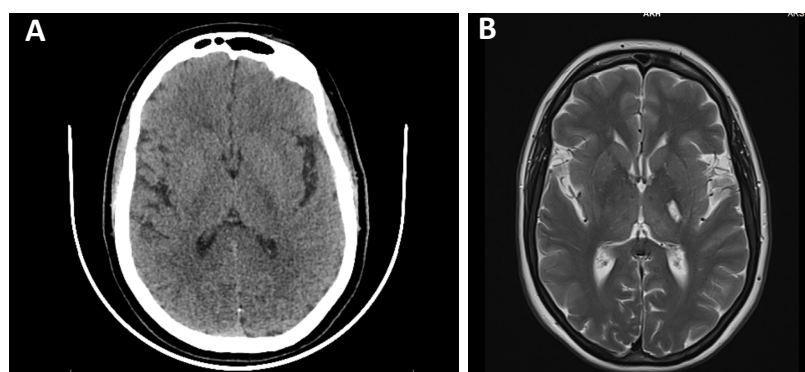


Figure 1: Neuroimaging findings during the acute phase and follow-up. (A) Initial non-contrast brain CT obtained during the acute diagnostic work-up, showing no evidence of intracranial hemorrhage or clearly visible acute ischemic changes. (B) Follow-up brain MRI demonstrating chronic ischemic sequelae in the posterior aspect of the left putamen, consistent with the previously documented subcortical ischemic lesion.

Diagnostic Assessment

Initial brain CT performed during the acute diagnostic work-up showed no evidence of intracranial hemorrhage or clearly visible acute ischemic changes. (Figure 1A) After exclusion of contraindications and stabilization of blood pressure, intravenous thrombolysis was administered according to standard protocol. Subsequent neuroimaging during the acute phase documented an ischemic lesion involving the posterior limb of the left internal capsule and the posterior part of the left lentiform nucleus. CT angiography showed no intracranial large-vessel occlusion. The lesion location was clinically consistent with the patient's severe right-sided motor deficit, given the involvement of subcortical motor pathways in the left internal capsule region.

During hospitalization, the diagnostic work-up included carotid and vertebral Doppler ultrasonography, transthoracic echocardiography, laboratory analyses, coagulation testing, and thrombophilia assessment. No cardioembolic source or thrombophilia was identified, while arterial hypertension and hypercholesterolemia were recognized as the main vascular risk factors.

A follow-up brain MRI demonstrated chronic ischemic sequelae in the posterior aspect of the left putamen, consistent with the previously documented subcortical ischemic lesion. (Figure 1B) The MRI also described a smaller ischemic sequela in the right occipital region and an incidental arachnoid cyst in the right pontocerebellar cistern. No signs of acute diffusion restriction were reported.

Table 1: Baseline neurological, motor, functional, and cognitive assessments at admission to inpatient rehabilitation (Day 12 post-stroke).

Measure	Baseline (day 12 post-stroke)
NIHSS	15
FMA-UE motor	3/36
ARAT	0/57
Barthel Index	30/100
MoCA	28/30
MAS	0 (hypotonia)

Therapeutic Intervention

The patient received intravenous thrombolytic therapy in the acute phase after exclusion of contraindications and stabilization of blood pressure. This was followed by standard post-stroke medical management, including antithrombotic, statin, antihypertensive, gastroprotective, antiedematous, antibiotic, and symptomatic therapy as clinically indicated.

After clinical stabilization, early rehabilitation was initiated during the acute hospital stay and focused on maintaining joint mobility, facilitating voluntary movement, gradual verticalization, prevention of secondary complications, and preparation for specialized inpatient neurorehabilitation. Due to persistent severe motor impairment and functional dependence, the patient was transferred to a specialized inpatient neurorehabilitation clinic on day 12 post-stroke, where she remained for approximately seven weeks.

At rehabilitation baseline, she presented with severe right upper-limb impairment and no functional use of the affected hand. She required assistance for sitting balance, was non-ambulatory, and depended on assistance for transfers and activities of daily living. Despite the severity of motor and functional impairment, cognition was preserved. As part of the early subacute stroke rehabilitation protocol, the patient received 30 mL of Cerebrolysin diluted in 70 mL of normal saline, administered intravenously over approximately 30 minutes once daily for 21 consecutive days.

The rehabilitation program consisted of individualized physiotherapy, occupational therapy, and speech therapy when clinically indicated, with treatment intensity gradually increased toward an intensive multidisciplinary program of up to approximately three hours of combined therapy per day. The program was designed as a multimodal, goal-oriented approach targeting postural control, balance, transfers, gait, upper-limb motor recovery, hand function, communication, and independence in activities of daily living.

Physiotherapy focused on verticalization, balance and gait training, strengthening, endurance training, and functional task practice. Occupational therapy emphasized recovery of the paretic upper limb through task-specific training, self-care activities, and reintegration of the affected hand into meaningful daily activities. High-intensity repetitive training and neuromuscular electrical stimulation were used to facilitate motor relearning and distal muscle recruitment. Following discharge from inpatient rehabilitation, the patient continued outpatient rehabilitation and a structured home exercise program until the 12-week follow-up.

Follow-up and Outcomes

Over the 12-week follow-up period, the patient demonstrated meaningful improvement across several functional domains, including upper-limb motor recovery, functional hand use, mobility, balance, and independence in activities of daily living.

Table 2: Longitudinal changes in motor and functional outcome measures from baseline to 12-week follow-up.

Outcome measure	Baseline	3 weeks	6 weeks	12 weeks
FMA-UE	3	14	23	34
ARAT	0	13	25	50
Barthel Index	30	45	50	75
MAS	0	1+	1	1
Berg Balance Scale	5	—	44	49
10-meter walking speed	0 m/s	—	0.37 m/s	0.46 m/s

Upper-limb recovery was clinically evident. FMA-UE increased from 3 at baseline to 34 at week 12, while ARAT improved from 0 to 50, reflecting a transition from absence of functional hand use to meaningful functional capacity of the affected upper limb. Barthel Index improved from 30 to 75, showing that motor gains were accompanied by a substantial increase in independence in daily activities. Muscle tone evolved from initial hypotonia to mild spasticity, without development of severe spasticity during the observed recovery period. Recovery was also observed in mobility-related domains. Berg Balance Scale improved from 5 at rehabilitation admission to 49 at inpatient rehabilitation discharge, and 10-meter walking speed increased from 0 m/s to 0.46 m/s. Clinically, this corresponded to a transition from non-ambulatory status at baseline to assisted short-distance walking with a quadripod cane at discharge from inpatient rehabilitation.

By the time of discharge from inpatient rehabilitation, the patient was independent in transfers and required only minimal assistance for basic daily activities and self-care. Active movements were present in all segments of the right upper limb, although coordination, dexterity, and movement speed remained impaired. No treatment-related adverse events were reported during the observed rehabilitation period.

Discussion

This case illustrates substantial recovery during the early subacute phase after severe ischemic stroke. On admission to rehabilitation (day 12), the patient had severe neurological and functional impairment (NIHSS 15, FMA-UE 3/36, ARAT 0/57), profound balance deficits, and was unable to walk independently. Over 12 weeks, marked improvements were observed across motor and functional domains, including FMA-UE (3→34), ARAT (0→50), balance, gait velocity, transfers, and activities of daily living.

The ARAT findings are particularly relevant in the context of Cerebrolysin-supported rehabilitation. In the randomized, placebo-controlled CARS trial, Cerebrolysin 30 mL/day for 21 days combined with standardized rehabilitation produced significantly greater improvements in upper-limb function than placebo, with ARAT improving by 30.7 versus 15.9 points at day 90.³ Similar to CARS, Cerebrolysin in this case was used alongside structured rehabilitation. However, the observed recovery represents an individual clinical observation and should not be interpreted as evidence of treatment efficacy.

Treatment timing warrants careful consideration. The EAN/EFNR guideline recommends Cerebrolysin 30 mL/day intravenously for at least 10 days as pharmacological support for early motor neurorehabilitation after moderate-to-severe ischemic stroke.⁴ Importantly, the supporting evidence is based on treatment initiation within the first 7 days after stroke.⁴ In the present case, Cerebrolysin was started on day 12 following acute stabilization and transfer to rehabilitation. Thus, the case should not be considered evidence for the guideline-defined acute treatment window, but rather an example of use during the early subacute rehabilitation phase.

Recovery likely reflected the combined effects of spontaneous biological recovery, lesion characteristics, residual neural integrity, motor learning, intensive task-specific rehabilitation, and rehabilitation-induced neuroplasticity.^{2,7} Improvements extended beyond the upper limb, with Berg Balance Scale increasing from 5 to 49, gait velocity from 0 to 0.46 m/s, and progression from non-ambulation to assisted walking.

No treatment-related adverse events were observed. As a single uncontrolled case, no causal conclusions regarding Cerebrolysin can be drawn, as recovery may have been influenced by multiple factors including thrombolysis, rehabilitation intensity, and the natural course of post-stroke recovery. Nevertheless, the consistent improvements across FMA-UE, ARAT, Barthel Index, Berg Balance Scale, and walking velocity provide a clear description of clinically meaningful recovery and support further investigation of pharmacologically supported rehabilitation in patients with moderate-to-severe stroke and severe early motor impairment.

Patient Perspective

Looking back, I believe that the work-centered lifestyle I had followed for many years, often putting everyone else before myself, may have contributed to the stroke I suffered in May 2024. The night of the stroke is something I will never forget. Despite having my husband and daughter by my side, I felt helpless and initially hoped that the weakness would pass and that I would regain feeling on my right side. It was only when I could no longer get myself into bed that I realized the seriousness of what was happening.

When I arrived at the rehabilitation clinic, I could not imagine ever standing or using my right arm and hand again. After discussing with Dr. Sindi Mitrović, I agreed to receive Cerebrolysin therapy as part of my rehabilitation program. I was initially skeptical, but throughout the three-week treatment period I experienced no side effects other than occasional difficulties with venous access.

After the first week of Cerebrolysin and daily therapy, I began to feel stronger and more confident. The encouragement of my therapists motivated me to work harder, and I was surprised by how quickly I progressed. As my strength improved, I increasingly took the initiative to perform exercises on my own and gradually regained independence in everyday activities, from transferring in and out of bed to dressing myself and later performing household tasks at home.

Continuing rehabilitation after discharge was challenging, and even simple daily activities initially required much more time and effort than before. However, I remained persistent and continued the exercises I had learned. As I learned more about stroke recovery from other patients, I became aware of how serious my condition had been and how fortunate I was with the recovery I achieved.

In my personal opinion, my recovery was supported by a combination of faith, determination, intensive rehabilitation, the dedication of my therapists and nurses, the support of my family, and the care I received from Dr. Mitrović. I now believe that Cerebrolysin played an important role in strengthening and accelerating my recovery. The greatest achievement for me was regaining independence and returning to activities that once seemed impossible.

CASE SUMMARY



Patient

• 55 years • Severe subcortical ischemic stroke



Challenge

• Severe hemiparesis and loss of hand function



Treatment

• Cerebrolysin 30 mL/day IV x 21 days + intensive multidisciplinary rehabilitation



Outcome

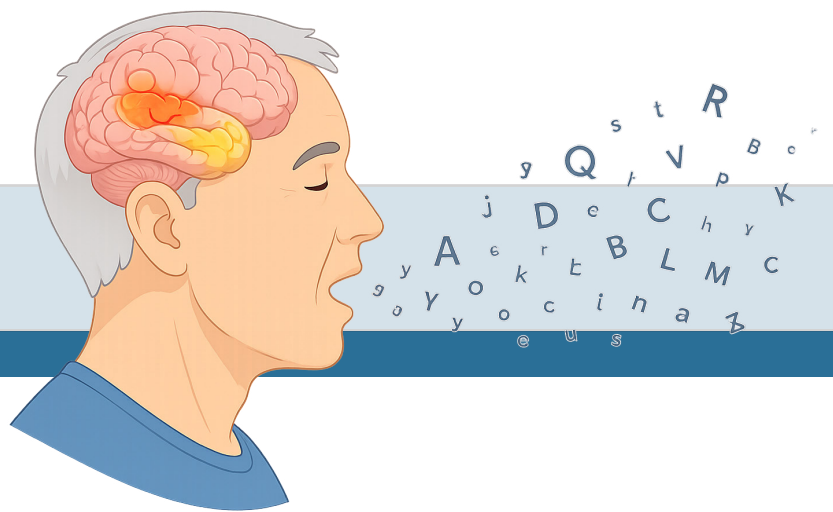
• FMA-UE 3 → 34 • ARAT 0 → 50 • BI 30 → 75



Take Home Message

Cerebrolysin should be viewed as a pharmacological enhancer of active rehabilitation, providing complementary synergies that may help maximize neurorecovery.

Aphasia





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Aphasia is one of the most common and disabling consequences of stroke. Language production and comprehension can also be a prominent sign after moderate- and severe traumatic brain injury (TBI). Following damage to the language-dominant brain networks, individuals may experience difficulties with speech production, language comprehension, reading and writing, often resulting in significant limitations in communication, independence and social participation. In both conditions, rehabilitation aims to maximise functional communication and support meaningful participation in daily life.

Speech and language therapy remains the cornerstone of aphasia rehabilitation, with strong evidence supporting its effectiveness across different stages of recovery. In recent years, advances in neuroscience have expanded our understanding of neuroplasticity and the brain's capacity for reorganisation following injury. This has encouraged the development of complementary therapeutic strategies designed to enhance the effects of conventional rehabilitation and provide additional opportunities for recovery, particularly in individuals with persistent language impairment.

Among those, non-invasive brain stimulation such as repetitive transcranial magnetic stimulation (rTMS) has gained increasing attention as potential adjunct to intensive speech and language therapy. In parallel, pharmacological treatment strategies utilizing the polypeptide preparation Cerebrolysin have recently shown promising results. The ESCAS study, published in *Stroke* and subsequently recognised as an Editor's Pick, provides strong evidence that personalised rehabilitation strategies incorporating pharmacological support may improve language outcomes in individuals with chronic post-stroke aphasia.

Although most available evidence and clinical experience relate to post-stroke aphasia, interest in applying similar therapeutic principles to TBI-related aphasia is increasing. Given the complexity and heterogeneity of traumatic brain injury, further research is needed to define optimal treatment strategies and identify patients most likely to benefit.

The cases presented in this chapter highlight the impact of aphasia following both stroke and TBI and demonstrate the importance of individualised, multidisciplinary rehabilitation. They reflect the evolving landscape of aphasia care, in which established therapeutic approaches are increasingly complemented by advances in neurorehabilitation and emerging evidence-based interventions aimed at improving communication and quality of life.



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...in the management of aphasia after traumatic intracranial hemorrhage

Abstract

Aphasia is a common and disabling consequence of dominant-hemisphere brain injury, and the pharmacological options after traumatic intracranial hemorrhage are limited. A 69-year-old man developed severe aphasia after traumatic intracranial hemorrhage. On day 7 after traumatic brain injury (TBI), he was transferred for inpatient rehabilitation, where the Korean version of the Western Aphasia Battery (K-WAB) showed marked language impairment, with an Aphasia Quotient (AQ) of 66.2 (scale 0–100; higher scores indicate better language function). He received intravenous Cerebrolysin, 30 mL/day infused over 60 minutes, for 21 consecutive days, together with daily speech-language therapy. By day 28, the AQ had risen to 97.1, with gains in both expressive and receptive language, and no adverse events were recorded. Spontaneous subacute recovery and the concurrent speech-language therapy may account for the change, and a single patient cannot establish an effect; the time course and the size of the change nonetheless raise the possibility of an adjunctive neurorestorative contribution from Cerebrolysin in post-traumatic hemorrhagic aphasia. Controlled studies in TBI populations are needed.

Keywords: traumatic intracranial hemorrhage; aphasia; Cerebrolysin; speech-language therapy; case report

Introduction

Aphasia is a common and disabling consequence of dominant-hemisphere brain injury, including hemorrhagic contusion [1]. Compared with ischemic and hemorrhagic events, pharmacologic strategies to enhance neurorecovery after traumatic intracranial hemorrhage remain relatively limited [2]. Currently, there are no universally accepted therapeutic strategies for acute TBI neurorecovery; however, interventions such as amantadine and methylphenidate are occasionally utilized off-label in clinical practice to promote arousal and cognitive processing, albeit with mixed efficacy [3]. Cerebrolysin, a neuropeptide preparation with neurotrophic properties, has shown benefits in neuroprotection, synaptic plasticity, and functional recovery, particularly in ischemic events and certain types of spontaneous intracerebral hemorrhage (ICH) [4,5]. A recent randomized controlled trial reported a therapeutic effect of Cerebrolysin in post-ischemic aphasia [6], but clinical evidence in post-traumatic aphasia remains scarce. We report a case of substantial language recovery after a 21-day course of Cerebrolysin combined with conventional speech-language therapy (SLT) in a patient with left traumatic frontal-temporal ICH and subarachnoid hemorrhage (SAH). To ensure transparency and completeness, this manuscript was prepared in accordance with the CARE guidelines [7].

Patient Information

A 69-year-old male with no significant prior medical history was found collapsed at his workplace around lunchtime, having reported to work as usual that morning. Heteroanamnesis obtained from coworkers and

emergency responders indicated a presumed mechanical fall resulting in head trauma. He first presented to the emergency department of another hospital, where brain CT showed hemorrhagic contusion of the left frontal and temporal lobes with a small volume of acute subarachnoid hemorrhage (Figure 1). He was admitted for observation, but during his short stay, he developed symptoms of acute delirium. At the request of the patient and his caregivers, he was subsequently transferred to our institution for further management. The anatomical distribution of these traumatic lesions directly corresponded with the structural networks governing language and cognition, providing a clear etiology for the patient's acute delirium and subsequent cognitive-linguistic deficits.

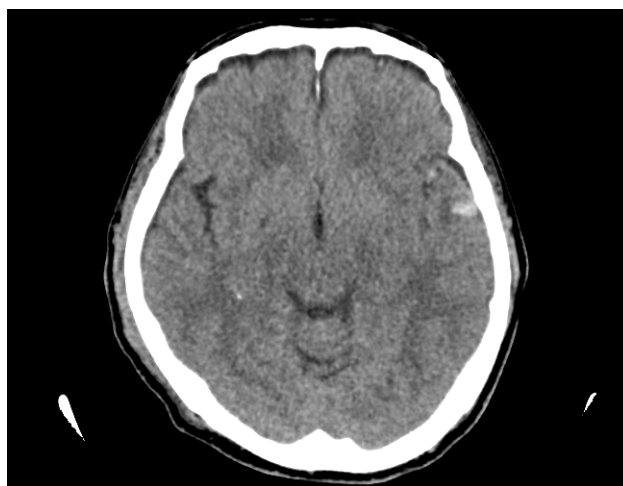


Figure 1: Brain computed tomography (CT) on admission showing multifocal hemorrhagic contusion

Clinical Findings and Timeline

Initial comprehensive neurological and psychiatric examinations upon transfer to our institution revealed severe global aphasia and acute delirium. Furthermore, the detailed neurological examination demonstrated mild quadriparesis, with motor strength decreased to Medical Research Council (MRC) grade 4/5 in all four extremities. He was admitted to the neurosurgery department through the emergency department and received ICU care for 3 days. He was managed conservatively to control intracranial pressure and prevent hemorrhage expansion, achieving sufficient clinical stability. On day 7 after injury, he was transferred to the Department of Rehabilitation Medicine for neurorehabilitation. Bedside language examination at that time showed severe global aphasia. The clinical course and the interventions are summarized in Table 1.

Table 1: Timeline of clinical events and interventions

Time point	Clinical, imaging and laboratory findings	Therapeutic strategy
Day-1	Reported to work as usual; found collapsed at workplace around lunchtime (heteroanamnesis). CT at outside hospital showed hemorrhagic contusion in the left frontal and temporal lobes with a small amount of acute subarachnoid hemorrhage.	Admission to outside hospital for observation
Day 0	Development of acute delirium; Transferred to our institution at patient and caregiver request. Neurological exam revealed severe aphasia, delirium, and quadriparesis (MRC grade 4).	Admission to our NICU; Conservative ICP management
Day 7	K-WAB AQ 66.2 (global aphasia); Clinical stability achieved	Transferred to rehabilitation medicine
Days 7-27	Resolving hemorrhagic contusions confirmed on follow-up imaging	Cerebrolysin 30 mL/day IV + daily speech-language therapy
Day 28	Repeat K-WAB AQ 97.1; near-complete functional language recovery	Continuation of standard neurorehabilitation

Diagnostic Assessment

Formal language testing on day 7 using the Korean version of the Western Aphasia Battery (K-WAB) gave an Aphasia Quotient (AQ) of 66.2 (scale 0–100; higher scores indicate better language function), consistent with severe global aphasia. Follow-up CT demonstrated resolving hemorrhagic contusions in the left frontal and temporal regions without new lesions or complications. The anatomical distribution corresponded well with the patient's expressive and receptive language deficits.

Therapeutic Intervention

From day 7 after injury, the patient received intravenous Cerebrolysin (EVER Neuro Pharma GmbH, Unterach, Austria) 30 mL/day, diluted in 100 mL of 0.9% sodium chloride and infused over 60 minutes, for 21 consecutive days. Treatment was combined with daily speech-language therapy targeting comprehension, naming, repetition, spontaneous speech, and functional communication. Acute TBI intrinsically carries a higher risk of epileptic seizures due to direct cortical injury and perilesional edema. While there are theoretical concerns about the seizure-threshold-lowering effects of certain neurostimulating agents, Cerebrolysin was administered under close observation. The patient tolerated the treatment exceptionally well, and no clinical seizure activity, infusion reactions, neurological worsening, or other adverse events were observed during the treatment period.

Follow-Up and Outcomes

On day 28 after TBI onset, repeat K-WAB assessment showed dramatic improvement, with the AQ increasing from 66.2 to 97.1. The patient demonstrated near-complete restoration of expressive and receptive language abilities, with fluent functional communication in daily interactions. Although spontaneous biological recovery and the effects of intensive SLT must be considered, the degree of language recovery far exceeded what is commonly expected over a short subacute interval in patients with initially severe aphasia after traumatic hemorrhagic injury. Follow-up brain CT showed decreased attenuation of the hemorrhagic contusions in the left frontal and temporal lobes (Figure 2).

Discussion

This case demonstrates remarkable short-term recovery from post-traumatic hemorrhagic aphasia following combined Cerebrolysin and speech-language therapy. The temporal association between treatment initiation and substantial improvement in K-WAB scores suggests that Cerebrolysin may have contributed to accelerated language recovery.

Several mechanisms could underlie such an association. Treatment with Cerebrolysin has been reported to promote neuroplasticity through synaptogenesis, dendritic sprouting, and neuronal survival, and to modulate neurotrophic signaling pathways [8]. In hemorrhagic injury, such effects may be particularly relevant in perihematoma and diaschitic cortical regions, where viable but functionally suppressed networks can potentially be re-engaged during rehabilitation.

Clinical evidence for Cerebrolysin is strongest in ischemic stroke, including randomized trials showing improved motor and cognitive outcomes when combined with rehabilitation [9,10]. Emerging preclinical and translational studies also suggest benefits in hemorrhagic injury and traumatic hemorrhage models, including enhanced neuroplasticity and functional restoration [4,5]. Initial RCTs based on these findings have shown evidence for positive clinical effects of Cerebrolysin on cognitive parameters after TBI [11]. The present case raises the possibility that these benefits may extend to language-domain recovery.

The main limitation is the single-patient design, which precludes causal inference. The concurrent use of daily SLT is an important confounder, as speech-language intervention remains the standard of care and likely contributed substantially to recovery. In addition, spontaneous neurological improvement during the subacute phase is expected. Nevertheless, the magnitude of AQ improvement from 66.2 to 97.1 over 21 days is notable and well beyond what is typically expected in an early rehabilitation timeframe, supporting further prospective investigation.

Conclusion

This case suggests that Cerebrolysin may provide additive benefit when used alongside conventional speech-language therapy in aphasia rehabilitation after traumatic intracranial and subarachnoid hemorrhage. Given the limited pharmacologic options available for traumatic hemorrhage recovery, larger controlled studies are warranted to evaluate efficacy, optimal timing, and safety in language rehabilitation.

Patient Perspective

The patient's family reported profound relief following the rapid recovery of language. Initially, the severe aphasia and acute delirium caused immense distress and communication barriers. However, the visible daily improvement during the 21-day Cerebrolysin infusion and concurrent speech therapy provided great reassurance. The patient expressed satisfaction at regaining the ability to communicate effectively with his family and medical staff, noting no specific discomfort or adverse effects during inpatient rehabilitation.

CASE SUMMARY



Patient

- 69 years
- Post-traumatic aphasia after intracranial hemorrhage



Challenge

- Severe global aphasia



Treatment

- Cerebrolysin 30 mL/day IV x 21 days + daily SLT



Outcome

- K-WAB AQ 66.2 → 97.1
- Near-complete speech recovery
- Restored functional communication



Take Home Message

In severe post-traumatic aphasia, Cerebrolysin combined with intensive speech-language therapy was associated with rapid, near-complete language recovery.



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...in the management of speech and motor functions after AIS

Abstract

Ischemic stroke remains a leading cause of mortality and long-term disability despite advances in reperfusion therapy. Secondary ischemic injury and limited endogenous neuroplasticity often result in persistent motor, cognitive, and speech deficits. Multimodal treatment strategies that combine reperfusion, systemic stabilization, early rehabilitation, and neuroprotective interventions may improve outcomes.

We present two clinical cases illustrating the use of neuropeptide therapy (Cerebrolysin) within a multimodal framework: (1) acute large vessel occlusion (LVO) stroke with severe neurological deficit, and (2) subacute recurrent stroke with prominent cognitive impairment and retrograde amnesia. In both cases, Cerebrolysin was administered alongside standard care and early rehabilitation.

Both patients demonstrated marked improvement in neurological, functional, and cognitive outcomes without adverse effects. These observations support the potential role of multimodal neurorecovery strategies incorporating neurotrophic therapy in ischemic stroke.

Keywords: ischemic stroke; Cerebrolysin; cerebroprotection; reperfusion therapy; aphasia; neurorehabilitation

Introduction

Acute Ischemic stroke continues to impose a major global health burden, in Kazakhstan the incidence rates for AIS are amongst the world's highest more than 40000 (reported in 2024) new strokes per annum accompanied with high rates of mortality and long-term disability (4). Even with timely reperfusion through thrombolysis or mechanical thrombectomy, many patients experience persistent deficits due to secondary ischemic injury and insufficient neuroplastic recovery.

Large vessel occlusion strokes are particularly associated with severe outcomes, including motor deficits and aphasia. Cognitive impairment is also common and significantly affects independence and quality of life. (5,6,7) Current stroke care emphasizes a multimodal approach, combining reperfusion, physiological stabilization, and early rehabilitation. Increasing attention is being given to neuroprotective and neurotrophic agents that may enhance recovery by supporting neuronal survival and plasticity.

Cerebrolysin, a peptide-based neurotrophic preparation, has been investigated for its pleiotropic effects, including cerebroprotection, modulation of neurotrophic factors, and support of synaptic remodeling. (1,2) This report presents two clinically distinct cases to illustrate its potential role across different stages of ischemic stroke.

Case Presentation

Case 1: Acute LVO stroke with severe neurological deficit

A 45-year-old male presented within one hour of symptom onset with sudden left-sided hemiplegia and speech disturbance. On admission, neurological examination revealed severe stroke (NIHSS 26), impaired

consciousness (GCS 11–12), hemiplegia, dysarthria, and hemineglect. CT imaging demonstrated occlusion of the M1 segment of the right middle cerebral artery (ASPECTS 9) (Figure 1A).

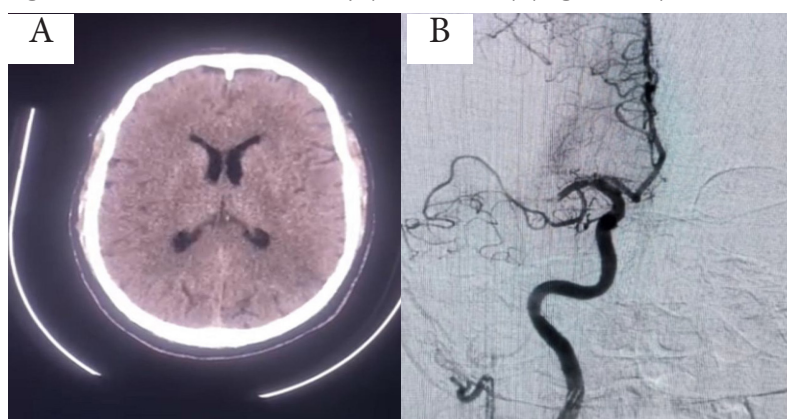


Figure 1. **(A)** Computed tomography of the brain on admission revealing ischemic lesion of the M1 segment of the right middle cerebral artery (ASPECTS - 9 points). **(B)** Angiographic images of the right internal carotid artery: segmental occlusion of the M1 segment of the right MCA (black arrow).

An additionally performed angiography showed segmental occlusion of the M1 segment of the right middle cerebral artery (black arrows) (Figure 1B). Urgent mechanical thrombectomy was performed with a door-to-puncture time of 40 minutes, achieving complete reperfusion (TICI 3).

Following intervention, the patient received **multimodal therapy**, including hemodynamic stabilization, metabolic modulation (correction of water-electrolyte and metabolic disorders, including maintenance of normoglycemia and acid-base balance), early rehabilitation, and Cerebrolysin 30 ml intravenously for 10 days. By day 10, there was marked clinical improvement: NIHSS decreased from 26 to 2, modified Rankin Scale (mRS) improved to 1, and Barthel Index reached 90. Motor function was fully restored, speech significantly improved, and neglect resolved.

Case 2: Subacute recurrent stroke with cognitive impairment

A 54-year-old female with hypertension and prior left MCA stroke presented with progressive neurological symptoms over 7–8 days, including headache, gait instability, and cognitive decline. Family members reported retrograde amnesia and impaired recall of recent events.

On admission, she was conscious (GCS 15) with NIHSS 8–9 and mRS 3. Neurological examination revealed significant cognitive impairment without major motor deficits.

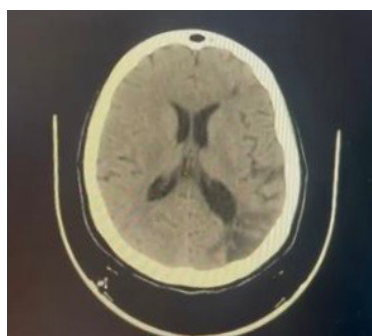


Figure 2. Native CT scan of the brain of patient D. upon admission.

CT imaging showed subacute ischemic changes in the left frontal and parietal lobes (Figure 2). A rehabilitation-focused multimodal strategy was initiated, including blood pressure control, metabolic optimization, individualized rehabilitation and Cerebrolysin 30 ml intravenously for 10 days.

By day 14, substantial recovery was observed: NIHSS improved to 1, mRS to 0, and Barthel Index to 100. Cognitive performance improved significantly (MMSE +5, MoCA +7), with regression of retrograde amnesia and restoration of daily functioning (Table 1 and 2).

Table 1: Dynamics of cognitive impairment according to the Mini-Mental State Examination (MMSE) scale in patient D.: 18 → 20 → 23 points, demonstrating a positive recovery trend.

Mini-Mental State Examination (MMSE)						
Date	10/10/2025		13/10/2025		21/10/2025	
Paragraph	Score	Grade	Score	Grade	Score	Grade
Final assessment	30	18	30	20	30	23

Table 2: Dynamics of cognitive impairment according to the Montreal Cognitive Assessment (MoCA) scale in patient D.: 15 → 16 → 22 points, which corresponds to the restorative positive dynamics of cognitive functions

Montreal Cognitive Assessment (MoCA)						
Education	Higher education					
Gender	Female					
Date	10/10/2025		13/10/2025		21/10/2025	
Final assessment	30	15	30	16	30	22

Discussion

These cases illustrate the successful administration of a multimodal therapeutic strategy in both acute and subacute ischemic stroke. While reperfusion remains the cornerstone of acute management, it does not fully prevent secondary injury processes, including inflammation, oxidative stress, and apoptosis. These mechanisms contribute to ongoing neuronal damage and limit recovery.

Cerebroprotective therapy may complement standard care by targeting these processes. Cerebrolysin has been shown to exert pleiotropic effects, including modulation of neurotrophic factors (e.g., BDNF, NGF), stabilization of the blood–brain barrier, and promotion of synaptic plasticity and neurogenesis.(1)

In the first case, early administration following successful thrombectomy was associated with rapid neurological recovery, including resolution of severe deficits such as hemiplegia and neglect. Importantly, no safety concerns were observed in the early post-reperfusion period.

In the second case, the predominant deficits were cognitive, including memory impairment and retrograde amnesia, reflecting disruption of distributed neural networks. The observed improvement suggests that combining pharmacological neurotrophic support with structured cognitive rehabilitation may enhance functional recovery in such patients.

Available clinical evidence supports the safety of Cerebrolysin in acute stroke settings, including after thrombolysis and thrombectomy, without increased risk of hemorrhagic transformation. Clinical trials and meta-analyses also suggest potential benefits in neurological and functional recovery, particularly when integrated into comprehensive rehabilitation strategies.(2)

Speech recovery, particularly in post-stroke aphasia, may also benefit from combined pharmacological and rehabilitative approaches. Previous studies have demonstrated improved outcomes when Cerebrolysin is used alongside targeted speech therapy.(3)

Overall, these observations align with contemporary concepts of stroke care, emphasizing not only reperfusion but also protection of the ischemic penumbra and enhancement of neuroplasticity.

Conclusion

The presented cases support the feasibility and potential benefit of a multimodal approach to ischemic stroke management that integrates reperfusion, systemic stabilization, early rehabilitation, and cerebroprotective therapy.

Cerebrolysin administration in both acute and subacute settings was well tolerated and associated with meaningful improvements in motor, cognitive, and speech functions.

However, these findings are based on descriptive observations and should be interpreted cautiously. Controlled studies are required to confirm efficacy and define optimal treatment protocols.

Limitations

This report is limited by its descriptive design, lack of control group, and short follow-up. Improvements may reflect spontaneous recovery, effects of reperfusion, or rehabilitation. Larger randomized studies are needed to establish causal relationships and long-term outcomes.

CASE SUMMARY	
 Patient • 45 years • Acute LVO stroke (M1 MCA occlusion)	 Patient • 54 years • Recurrent ischemic stroke
 Challenge • Severe stroke with hemiplegia and neglect	 Challenge • Retrograde amnesia and cognitive decline
 Treatment • Cerebrolysin 30 mL/day IV x 10 days + mechanical thrombectomy	 Treatment • Cerebrolysin 30 mL/day IV x 10 days + rehabilitation
 Outcome • NIHSS 26 → 2 • mRS → 1 • BI → 90	 Outcome • NIHSS 8-9 → 1 • mRS 3 → 0 • BI → 100 • MMSE 18 → 23 • MoCA 15 → 22
 Take Home Message Cerebrolysin integrated with reperfusion therapy, standard care, and individualized neurorehabilitation was associated with substantial recovery after acute large-vessel occlusion stroke and with improvements in neurological, functional, and cognitive outcomes after recurrent stroke.	

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...in the management of Wernicke's aphasia after AIS

Abstract

Post-stroke aphasia is a debilitating condition affecting approximately one-third of stroke survivors, profoundly impairing communication, social participation, and quality of life. While speech-language therapy (SLT) remains the standard of care, pharmacological agents such as Cerebrolysin may enhance recovery through neuroprotection and neuroplasticity. We report the case of a 38-year-old female lawyer who developed acute Wernicke's aphasia and right-sided hemiparesis following an ischemic stroke. Despite timely thrombolysis and mechanical thrombectomy, she experienced significant neurological deficits. Early multidisciplinary rehabilitation, combined with a 10-day course of Cerebrolysin, memantine, and sertraline, was associated with substantial improvements in language, motor function, and independence over three months. This case highlights the potential synergistic effect of Cerebrolysin, in a young patient, with early reperfusion, intensive rehabilitation including pharmacotherapy and SLT, especially in settings where optimal post-stroke rehabilitation resources may be limited.

Keywords: stroke, rehabilitation, treatment

Introduction

Aphasia is one of the most disabling consequences of stroke, affecting roughly one-third of survivors [1]. Clinical presentations vary widely, from difficulty retrieving words to complete loss of speech, comprehension, reading, or writing abilities. These deficits profoundly impact daily functioning, social interaction, employment, and psychological well-being [2]. Recovery is most rapid within the first three to six months, yet many patients continue to experience residual deficits despite standard care [3].

Speech-language therapy remains the cornerstone of aphasia rehabilitation. However, pharmacological agents such as memantine [4] and donepezil [5] have demonstrated limited efficacy [6]. Cerebrolysin, a neurotrophic peptide preparation, has been shown to promote neurogenesis and synaptogenesis, facilitating rewiring of language networks after ischemic injury. Evidence suggests that combining Cerebrolysin with speech-language therapy (SLT) may enhance functional recovery, as demonstrated in the Efficacy and Safety of Cerebrolysin in the Treatment of Aphasia After Acute Ischemic Stroke (ESCAS) trial [3].

Diagnosing and managing aphasia is particularly challenging in low- and middle-income countries (LMICs). Limited access to trained speech-language pathologists, delayed presentation to hospital, lack of standardized assessment tools, and insufficient rehabilitation infrastructure can impede timely intervention, reducing the potential for optimal recovery. Pharmacological adjuncts that enhance neuroplasticity may therefore be particularly valuable in such contexts [6]. Only 1 to 5 % of Buenos Aires population have real access to all reperfusion therapies [7].

Case Presentation

A 38-year-old female lawyer with no significant past medical history presented with sudden-onset Wernicke's aphasia and severe right-sided hemiparesis while moving houses. She arrived at the hospital two hours after symptom onset. Initial assessment revealed a score of 21 on the National Institutes of Health Stroke Scale (NIHSS), and fluent Wernicke's aphasia was diagnosed. Her pre-stroke modified Rankin Scale (mRS) score was 0, indicating full functional independence.

Diagnostic Assessment

Brain MRI (Figure 1) revealed restricted diffusion in the left basal ganglia and ipsilateral parietal cortex (Wernicke area), consistent with acute ischemic lesions. Intracranial imaging showed absent flow in the left internal carotid artery and middle cerebral artery, confirming large-vessel occlusion. Prompt imaging and diagnosis allowed initiation of reperfusion therapy within the recommended window, which is often a challenge in LMICs due to delays in access and diagnostic limitations [7].

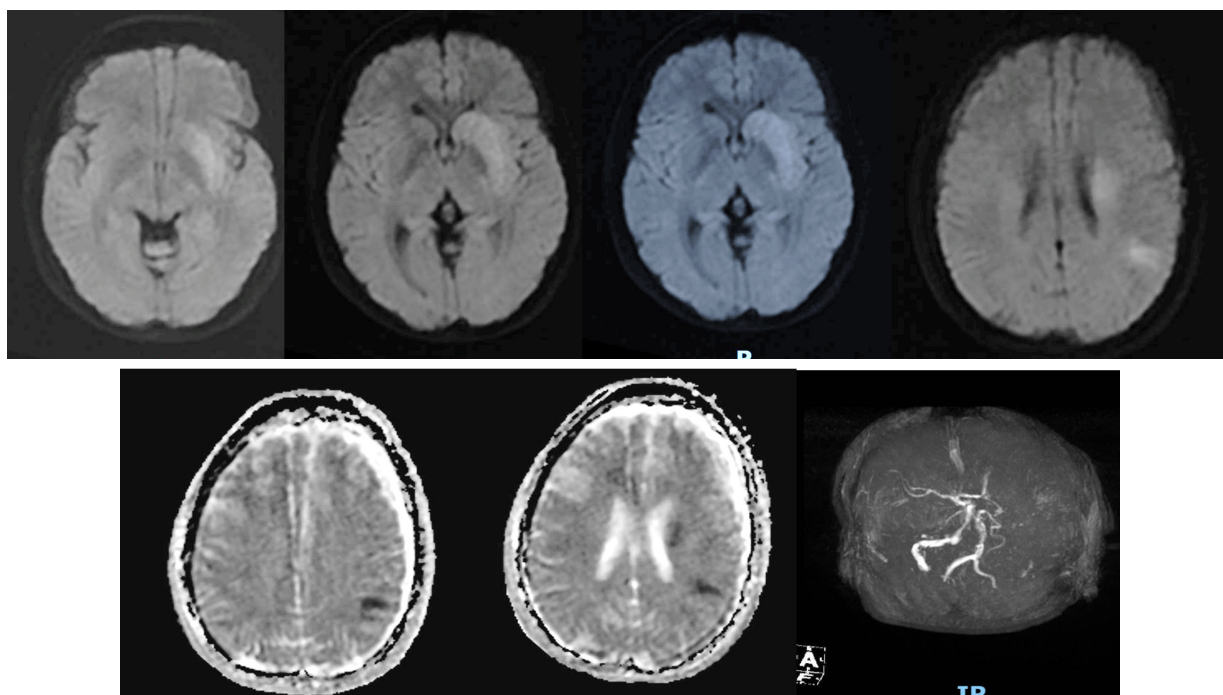


Figure 1: Brain MRI on Admission

Therapeutic Intervention

The patient received intravenous alteplase (recombinant tissue plasminogen activator [rt-PA]) followed by emergency mechanical thrombectomy. Two stents were successfully placed in the left internal carotid artery, achieving Thrombolysis in Cerebral Infarction (TICI) grade IIc reperfusion. Antiplatelet therapy included tirofiban and clopidogrel. During hospitalization, she developed decreased consciousness due to hemorrhagic transformation; tirofiban was discontinued, and no neurosurgical intervention was required. She remained on mechanical ventilation for five days, after which she was successfully extubated.

At extubation, she was alert and oriented, with moderate residual hemiparesis, dysphagia, and mild aphasia. Clinical assessments demonstrated a NIHSS score of 17, a mRS score of 3, a Western Aphasia Battery (WAB) score of 37, and a Barthel Index (BI) score of 35, indicating substantial neurological impairment and severe functional dependency (see Supplementary File S1 for details regarding these assessment scales) (Figure 2).

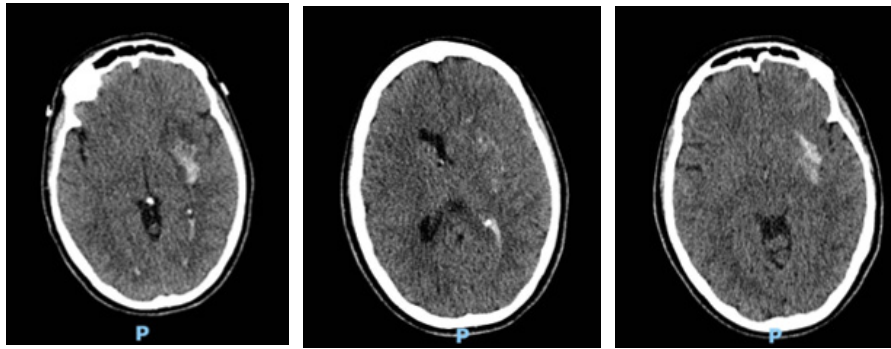


Figure 2: CT scan after extubation on day 5 with hemorrhagic transformation

Rehabilitation and Pharmacological Intervention

The patient was transferred to a neurological rehabilitation facility with a nasogastric tube, aphasia, hemiparesis and mild post stroke depression. She participated in a multidisciplinary rehabilitation program including physical therapy, occupational therapy, SLT, and psychological support.

The rehabilitation program, which is often difficult to access in low- and middle-income countries (LMICs), consisted of physical therapy sessions twice a day, occupational therapy three times a week, SLT for one hour four times a week, and psychological support once a week.

Pharmacological therapy included a 10-day course of Cerebrolysin (30 mL/day), sertraline 50 mg/day, and memantine 20 mg/day [3].

After 30 days, her aphasia had significantly improved (the patient was able to understand one step orders), the nasogastric tube was removed following a successful swallowing assessment, and she began ambulating with assistance. Clinical assessments showed a NIHSS score of 14, mRS score of 3, WAB score of 45, and BI score of 52. The NIHSS score was 14, although this value was disproportionately elevated due to high subscores in the visual and sensory deficits domains.

At three-month follow-up, the patient achieved independent ambulation and near-complete resolution of dysphagia. Residual deficits included minimal aphasia and mild hypophonia. Clinical assessments showed a NIHSS score of 6, mRS score of 1, WAB score of 69, and BI score of 79, reflecting substantial functional recovery (Table 1 and Figure 2).

Table 1: Clinical and functional outcomes over time (NIHSS, mRS, WAB, BI)

Time Point	NIHSS	mRS	WAB	BI
Admission	21	0	37	35
30 days	14	3	45	52
3 months	6	1	69	79

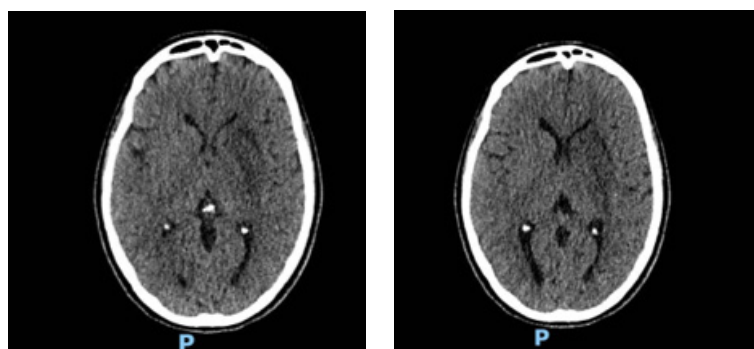


Figure 3: Brain CT scan at three-month follow-up

Discussion

This case illustrates that even with optimal acute stroke care, including thrombolysis, thrombectomy, and stenting, severe aphasia may persist, necessitating intensive rehabilitation. Aphasia profoundly impacts communication, social engagement, and the ability to return to work.

In LMICs, challenges in aphasia care are magnified. Many patients experience delays in clinical presentation, limited access to diagnostic imaging, acute treatment [7] and scarce availability of trained speech-language pathologists. Rehabilitation facilities are often under-resourced, and standardized assessments may be unavailable, making it difficult to monitor progress or tailor interventions. Pharmacological agents that enhance neuroplasticity, such as Cerebrolysin, may help bridge these gaps when combined with available SLT, improving functional outcomes [3].

Clinical recovery of speech fluency and understanding in this patient might be likely to be compensated for by the right hemisphere's homologous language regions following severe degradation of the left temporal network. There are some case reports that reinforce the critical role of right-hemisphere plasticity in recovery and suggest that future clinical approaches could focus on targeted therapeutic stimulation, such as repetitive transcranial magnetic stimulation (rTMS), of right-hemisphere pathways to optimize language rehabilitation. It is also important to highlight the value of advanced functional perfusion imaging, such as brain single-photon emission computed tomography (SPECT), especially when standard structural imaging modalities like magnetic resonance imaging (MRI) or computed tomography (CT) appear negative. Such functional techniques may help identify underlying metabolic or perfusion abnormalities that are not visible on structural scans, thereby enabling more targeted neurorehabilitation strategies. It would have been very interesting in our case to perform functional imaging to help us understand more the complex rehabilitation process [11-13].

In patients presenting with severe acute ischemic stroke (typically defined by a high NIHSS score and large vessel occlusion), mechanical thrombectomy (MT) has become the gold standard of care. According to high-quality clinical evidence, the percentage of patients achieving a functional independent outcome, defined as a mRS score of 0–2 at 90 days, is approximately 45% to 50%.

The landmark HERMES meta-analysis, which pooled data from pivotal trials such as MR CLEAN, ESCAPE, and REVASCAT, demonstrated that 46% of patients treated with MT achieved functional independence, compared to only 26.5% in the control group receiving best medical management alone [6].

Cerebrolysin is believed to facilitate cerebroprotection [6], neurogenesis and synaptogenesis, supporting the rewiring of language networks after ischemic injury. In this patient, its addition to early multidisciplinary rehabilitation appeared to accelerate recovery, resulting in significant improvements in language, motor function and independence. These findings align with previous studies, including the ESCAS trial, which reported enhanced outcomes when Cerebrolysin was combined with SLT [3].

Conclusion

This case highlights the tailored multidisciplinary treatment (including early reperfusion thrombolysis plus thrombectomy, intensive rehabilitation, concomitant pharmacotherapy memantine, sertraline) and the potential of Cerebrolysin as an adjunct to early neurorehabilitation in severe post-stroke aphasia. In combination with structured SLT, it can enhance significant recovery in language, motor function, and independence, especially in young patients. The case also underscores the need for tailored strategies in countries and regions where limited access to rehabilitation resources may hinder optimal recovery. Early, intensive, and multidisciplinary intervention remains critical to achieving the best functional outcomes and improving quality of life for stroke survivors.

CASE SUMMARY



Patient

- 38 years
- Acute ischemic stroke



Challenge

- Severe post-stroke aphasia



Treatment

- Cerebrolysin 30 mL/day IV × 10 days + SLT



Outcome

- NIHSS 21 → 6
- WAB 37 → 69
- mRS 3 → 1
- BI 35 → 79



Take Home Message

Following successful thrombolysis and mechanical thrombectomy, adjunctive Cerebrolysin combined with intensive speech-language and multidisciplinary rehabilitation was associated with substantial three-month improvements in aphasia, neurological function, and independence.

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...in the management of aphasia and motor deficits after AIS

Abstract

Recovery of motor and speech functions after ischemic stroke remains challenging. We report a 39-year-old male in the late recovery phase following a left middle cerebral artery infarction, presenting with severe right-sided hemiparesis and complex motor aphasia. He underwent a multidisciplinary rehabilitation program including physical therapy, speech therapy, neuropsychological support, and repeated intravenous courses of Cerebrolysin (20 ml, 10 infusions every 3 months). Over one year, he demonstrated improved muscle strength, reduced spasticity, enhanced shoulder and elbow range of motion, faster walking speed, and increased independence in daily activities. Speech function improved with enhanced comprehension, grammar, and fewer paraphasias, reflected in a reduction of the Wasserman Aphasia Scale score from 48 to 40 points. Course-based Cerebrolysin therapy combined with comprehensive rehabilitation was safe and contributed to meaningful functional recovery, supporting its role in multidisciplinary neurorehabilitation to enhance neuroplasticity.

Keywords: ischemic stroke, neurorehabilitation, Cerebrolysin, hemiparesis, motor aphasia, neuroplasticity

Introduction

Stroke is a leading cause of mortality and long-term disability, imposing substantial social and economic burdens. Despite advances in acute-phase interventions, including reperfusion therapy, many survivors develop persistent motor deficits and cognitive impairments, such as aphasia. Motor deficits affect 70–90% of patients acutely, with more than half remaining impaired at one year. (1) Aphasia occurs in 15–38% of patients and significantly diminishes quality of life. (2)

Modern rehabilitation emphasizes early initiation, continuity, and a multidisciplinary approach. Pharmacological support with neurotrophic agents can enhance outcomes. Cerebrolysin, a mixture of low-molecular-weight peptides and amino acids, mimics endogenous neurotrophic factors such as BDNF. Its mechanisms include stimulation of neurogenesis and synaptogenesis, neuroprotection during ischemia, and antioxidative effects. Clinical trials demonstrate that Cerebrolysin improves motor, cognitive, and speech recovery when it is combined with rehabilitation. (3,4,5)

Patient Information

A 39-year-old male presented in the late recovery phase after a left middle cerebral artery ischemic stroke on March 23, 2024. Initial symptoms included right-sided weakness and speech impairment. Comorbidities included stage III hypertension, dyslipidemia, and high cardiovascular risk.

Clinical Findings at Admission (March 3, 2025)

Neurological examination revealed right facial paresis, severe right-sided spastic hemiparesis (MAS 3), a positive Babinski reflex, reduced pain and tactile sensitivity, impaired balance, and a spastic gait requiring a cane. Functional assessment is summarized in Table 1.

Table 1: The table summarizes the patient's level of disability, mobility, balance, gait, and upper-limb motor function

Scale	Score
Modified Rankin Scale (mRS)	4
Barthel Index	75
Rivermead Mobility Index	9
Berg Balance Scale	41
Hauser Ambulation Index	4
Walking speed (10 m test)	0.6 m/s
Shoulder flexion/extension	3/3
Shoulder adduction/abduction	3/3
Elbow flexion/extension	3/3
Elbow pronation/supination	3/3
Wrist flexion/extension	1/2
Wrist adduction/abduction	2/2

Rehabilitation Program

The patient underwent a 1-year multidisciplinary program combining physical therapy, speech therapy, neuropsychological therapy, and pharmacological support. Physical therapy included therapeutic exercises, occupational therapy, treadmill training, biofeedback, robotic therapy (Armeo, Amadeo, Diego, MJS), massage, electrical stimulation, and virtual reality therapy. Speech therapy focused on speech production, phrase formation, attention and perseveration control, and writing skills. Neuropsychological therapy targeted praxis, memory, and complex aphasia.

Pharmacological therapy included baseline medications (losartan, amlodipine, aspirin, atorvastatin, escitalopram, baclofen, omeprazole), with specific interventions including Cerebrolysin (20 ml IV, 10 infusions every 3 months) and botulinum toxin (Xeomin, 800 units) for focal spasticity. Goals were independent ambulation, functional hand use, improved balance and strength, and resumption of social activities such as singing.

Follow-up and Outcomes

Motor Recovery

After 12 months of intensive multidisciplinary rehabilitation, the patient demonstrated clinically meaningful improvements in motor function and independence. Muscle strength increased on the Medical Research Council (MRC) scale, indicating a substantial improvement in voluntary motor control and the ability to perform functional movements against gravity and, depending on the muscle group, increasing resistance. Muscle tone improved by one point on the Modified Ashworth Scale (MAS), which was associated with reduced spasticity and facilitated more effective use of the affected limb during rehabilitation and activities of daily living.

Marked gains were also observed in shoulder mobility, with flexion increasing from 10° to 60° and abduction from 20° to 80°. These changes substantially expanded the patient's functional range of movement and potentially contributed to improved reaching ability, positioning, and use of the upper limb in everyday activities. Enhanced walking speed and greater independence in daily activities further indicate that the observed neurological improvements translated into meaningful functional gains, moving beyond impairment-based outcomes towards improved mobility and autonomy.

Speech and Cognitive Function

Relevant improvements were also observed in communication and cognitive function. Speech comprehension and grammatical abilities improved, accompanied by fewer paraphasias and perseverations, suggesting more effective language processing and greater control of verbal output. The improvement in the Wasserman Aphasia Scale from 48 to 40 points reflected a clinically relevant reduction in aphasia severity and was associated with improved functional communication. Auditory-verbal memory improved markedly, with the

number of recalled words increasing from 2 to 6, representing a threefold increase in immediate memory performance. Improvements in praxis may have further supported the patient's ability to plan and perform purposeful actions, while better mood and motivation were particularly relevant for sustained participation in the demanding, long-term rehabilitation program.

Safety

No adverse events related to Cerebrolysin were observed.

Discussion

This case illustrates the potential for substantial and sustained functional recovery after ischemic stroke when long-term, intensive, multidisciplinary rehabilitation is combined with pharmacological support aimed at facilitating neuroplasticity. (1,6,7) The patient underwent a comprehensive 1-year rehabilitation program integrating physical, occupational, speech, and neuropsychological therapies with technologically assisted interventions, including robotic therapy, treadmill training, biofeedback, electrical stimulation, and virtual reality. This approach provided repeated, task-specific stimulation across multiple functional domains and created favourable conditions for activity-dependent neural reorganization. (6,7)

A distinctive feature of this case was the integration of repeated Cerebrolysin treatment courses into the rehabilitation program. Cerebrolysin was administered at a dose of 20 mL intravenously for 10 consecutive infusions every 3 months, resulting in four treatment courses during the year. The rationale for this approach lies in the prolonged and dynamic nature of post-stroke recovery. Although recovery is generally most rapid during the early post-stroke period, meaningful functional improvement may continue for months or even longer, particularly when patients remain exposed to intensive, individualized, and progressively challenging rehabilitation. (1,6,7)

Recovery is also not necessarily linear. Different neurological functions may improve at different rates, while apparent recovery plateaus do not inevitably represent the end of the rehabilitation potential. Instead, they may indicate a need for renewed therapeutic stimulation or modification of rehabilitation goals. (1,6,7) Repeated pharmacological support may therefore be of particular interest during prolonged rehabilitation, accompanying successive phases of functional recovery and supporting patients as new therapeutic challenges and opportunities emerge. (3-5)

Pre-clinical and clinical evidence suggests that Cerebrolysin exerts multimodal effects relevant to post-stroke recovery, including neurotrophic activity and effects associated with neuronal survival, synaptic plasticity, and functional reorganization of neuronal networks. (3,4,8) These mechanisms may be complementary to intensive rehabilitation, in which repeated motor, cognitive, and behavioural training provides the activity-dependent stimulation necessary to promote and consolidate functional recovery. (4,6,7) Cerebrolysin should therefore not be considered a replacement for rehabilitation, but rather a potential pharmacological adjunct supporting the biological processes underlying rehabilitation-induced neuroplasticity. (3-5)

The improvements observed in this patient extended beyond a single neurological domain and included strength, spasticity, ambulation, hand function, balance, speech, and participation in meaningful social activities, including singing. This multidimensional recovery reflects the importance of a comprehensive rehabilitation strategy addressing impairment, activity, and participation. (6,7) In addition to intensive therapy, focal spasticity management with botulinum toxin may have facilitated motor training and contributed to improved functional performance. (9,10)

Naturally, the specific contribution of Cerebrolysin cannot be isolated in a single-patient case. The favourable outcome was likely influenced by several interacting factors, including the intensity and duration of rehabilitation, the combination of therapeutic modalities, spasticity management, patient motivation and adherence, and the individual's intrinsic recovery potential. (1,3,6)

Overall, the case supports the concept that long-term recovery after stroke should be regarded as a dynamic

process requiring continued reassessment and adaptation of therapeutic interventions. (1,6,7) Repeated Cerebrolysin courses may represent one pharmacological approach to supporting this extended period of recovery, in combination with intensive, activity-dependent rehabilitation. (3-5) Although controlled studies are needed to define the optimal frequency and duration of repeated treatment, the present case provides a practical example of sustained, multidimensional functional improvement during a prolonged rehabilitation program.

Conclusion

Treatment-course-based Cerebrolysin therapy combined with physical, speech, and neuropsychological rehabilitation was safe and led to significant improvements in motor, cognitive, and speech functions. Its inclusion in multidisciplinary rehabilitation programs may enhance neuroplasticity and optimize functional recovery after ischemic stroke.

CASE SUMMARY

**Patient**

- 39 years
- Left MCA ischemic stroke with aphasia

**Challenge**

- Severe spastic hemiparesis and motor aphasia

**Treatment**

- Cerebrolysin 20 mL/day IV x 10 days (every 3 months) + multidisciplinary rehabilitation

**Outcome**

- MAS 3 → 2
- Wasserman Aphasia Scale 48 → 40
- Improved independence

**Take Home Message**

Multidisciplinary rehabilitation incorporating Cerebrolysin was associated with meaningful improvements in motor and speech function, functional independence, and walking performance after ischemic stroke, supporting its potential role as a well-tolerated adjunct to neurorehabilitation in patients with combined motor and language impairments.

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...in the management of aphasia after AIS

Abstract

Post-stroke aphasia is among the most disabling consequences of ischemic stroke, affecting approximately one-third of survivors and significantly impairing communication and quality of life. We report the case of a 44-year-old man who developed severe post-stroke aphasia after an ischemic infarction in the territory of the left middle cerebral artery. The patient underwent a comprehensive rehabilitation program combining pharmacological therapy with Cerebrolysin, structured speech and language therapy, and physiotherapy. Over three rehabilitation courses, progressive improvement in language function and neurological status was observed. The Western Aphasia Battery score increased from 44 to 51 points, corresponding to a transition from severe to moderate aphasia. This case illustrates the potential benefit of a multidisciplinary rehabilitation strategy and supports the use of Cerebrolysin as an adjunctive treatment in post-stroke aphasia.

Keywords: cystic-gliotic lesion, post-stroke aphasia, speech and language therapy, rehabilitation

Introduction

Post-stroke aphasia is an acquired disorder of language affecting comprehension, speech production, reading, and writing. (3) Approximately one-third of stroke survivors develop aphasia, and a considerable proportion continue to experience chronic language impairment despite standard rehabilitation. (2,4) Speech and language therapy is regarded as the mainstay of aphasia treatment; however, recovery outcomes vary widely. (1,5,7) This variability has stimulated interest in pharmacological agents capable of enhancing neuroplasticity and supporting functional recovery. Cerebrolysin, a neuropeptide preparation with multimodal cerebroprotective and neurotrophic effects, has been investigated as an adjunctive therapy in post-stroke rehabilitation. (6,8) We present a case of severe post-stroke aphasia treated with a comprehensive rehabilitation program including Cerebrolysin and structured speech therapy. (8)

Patient Information

A 44-year-old man was admitted with sudden onset of speech disturbance and right-sided weakness. More than four hours had elapsed from symptom onset to hospital admission. His medical history was notable for arterial hypertension (stage III, grade 3, high additional risk), cerebral atherosclerosis (stage III), and bronchial asthma. Family history revealed that his mother had suffered two previous strokes. Prior to the index event, the patient was independent in daily activities and professionally active.

Clinical Findings

During the acute phase of hospitalization, the patient exhibited pronounced right-sided hemiparesis and severe impairment of verbal communication. On transfer to the inpatient rehabilitation department for day 14, his general condition was moderately severe. He was conscious but unable to communicate effectively because of

aphasia. Physical examination showed stable cardiovascular and respiratory parameters, with no abnormalities of abdominal organs or pelvic functions. Neurological examination revealed complex sensory-motor aphasia with marked limitation of spontaneous speech and comprehension. Muscle strength was markedly reduced on the right side, particularly in the upper limb and hand. A right-sided Babinski sign was present, along with moderate hypertonia in the right arm and hemihypesthesia. Coordination was unstable in the Romberg position. On standardized scales, the National Institutes of Health Stroke Scale score was 16 points and the modified Rankin Scale score was 3 points. Language assessment using the Western Aphasia Battery yielded a score of 44 points, corresponding to global aphasia with severe impairment of comprehension, repetition, naming, and writing.

Diagnostic Assessment

Computed tomography of the brain with angiography confirmed an ischemic atherothrombotic stroke in the territory of the left middle cerebral artery. Based on clinical and neuropsychological assessment, the diagnosis of post-stroke global aphasia was established. No alternative etiologies for language impairment were identified. (Figure 1)

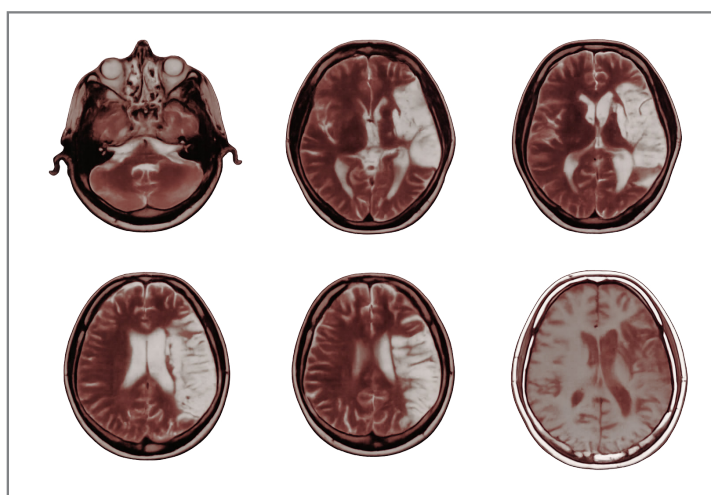


Figure 1. MRI brain (09.01.2023); MRI reveals a large post-ischemic cystic-gliotic lesion in the left frontal, temporal, and parietal lobes (left MCA territory) measuring approximately 109 × 45 × 98 mm, with cystic transformation of the left basal ganglia and secondary Wallerian degeneration of the corticospinal tract.

Therapeutic Intervention

After stabilization of the acute condition, the patient entered a structured rehabilitation program. He completed three rehabilitation courses, each lasting two weeks and repeated at three-month intervals. The program included intravenous administration of Cerebrolysin at a dose of 30 mL diluted in 200 mL of saline for 14 infusions per course, in addition to standard secondary prevention therapy with antihypertensive agents, antithrombotics, and statins. Daily one-hour speech and language therapy sessions were conducted throughout each course. Physiotherapeutic procedures included electrophoresis with proserin, magnetotherapy, and electrical stimulation of the affected limbs. The therapeutic strategy aimed to combine neurobiological support of recovery with intensive functional training.

Follow-Up and Outcomes

After the first rehabilitation course, the patient demonstrated modest improvement in neurological status, with a reduction of NIHSS score to 12–13 points and an increase of the WAB score to 46 points. After completion of three rehabilitation courses, further improvement in language function was observed. (Figure 2 and 3) The WAB score reached 51 points, indicating a transition from severe to moderate aphasia. Clinically, the patient showed expansion of spontaneous speech, improved comprehension of moderately complex verbal instructions, better performance in repetition and naming tasks, and reduced frequency of paraphasias. His communicative activity increased, and he developed greater motivation for verbal interaction.

Motor function also improved. Muscle strength in the right upper and lower limbs increased, allowing partial restoration of independent mobility and functional use of the affected extremities. No adverse reactions related to Cerebrolysin were recorded during treatment. For secondary prevention, continued blood pressure monitoring, long-term antihypertensive and antithrombotic therapy, statins, and regular neurological follow-up were recommended.

Timeline

Table 1: Clinical course and treatment timeline

Time point	Clinical events and interventions
Day 0	Sudden onset of aphasia and right-sided weakness
>4 hours	Hospital admission
Acute phase	Diagnosis of ischemic stroke in left middle cerebral artery territory
Early rehabilitation	Transfer to rehabilitation department; WAB 44, NIHSS 16, mRS 3
Course 1 (2 weeks)	Cerebrolysin, speech therapy, physiotherapy
After course 1	WAB 46, NIHSS 12–13, MRS 3
Courses 2–3	Repeated comprehensive rehabilitation at 3-month intervals
After course 2	WAB 46, NIHSS 13, MRS 3
After course 3	WAB 51, moderate aphasia, NIHSS 10, MRS 2.

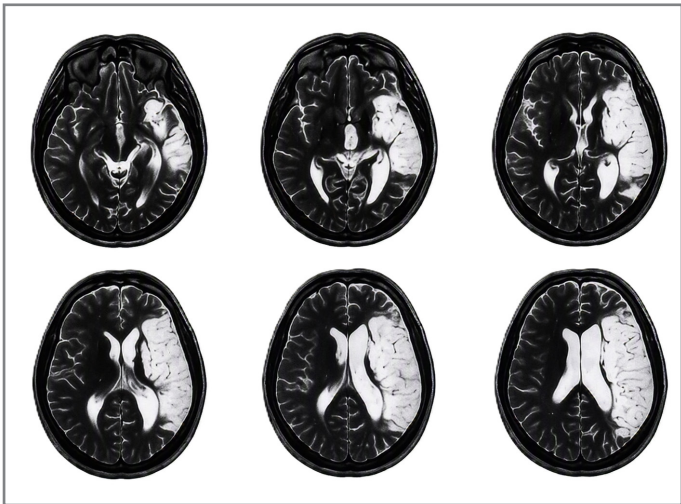


Figure 2. MRI brain (23.09.2024); MRI demonstrates chronic post-ischemic cystic-gliotic changes in the left cerebral hemisphere with a lesion measuring approximately 112 × 47 × 96 mm, associated with Wallerian degeneration of the corticospinal tract and signs of chronic cerebrovascular disease.

Discussion

This case illustrates the potential benefits of a comprehensive rehabilitation approach in severe post-stroke aphasia. The combination of intensive speech and language therapy with pharmacological support may enhance recovery by acting on both functional and neurobiological levels. (1,5,7) Cerebrolysin exerts multimodal effects that are relevant for post-stroke recovery, including modulation of neurotrophic factors such as brain-derived neurotrophic factor, reduction of neuroinflammation, activation of anti-apoptotic signaling pathways, and attenuation of oxidative stress and glutamate-mediated excitotoxicity. These mechanisms may promote neuroplastic reorganization of language networks damaged by ischemia. (8)

The improvement in Western Aphasia Battery score from 44 to 51 points in this patient parallels observations from clinical trials in which Cerebrolysin combined with rehabilitation produced greater functional gains than rehabilitation alone. Although spontaneous recovery cannot be excluded, the progressive nature of improvement across three structured treatment courses suggests a treatment-associated effect. The favorable safety profile observed in this case is consistent with previously published data. (8)

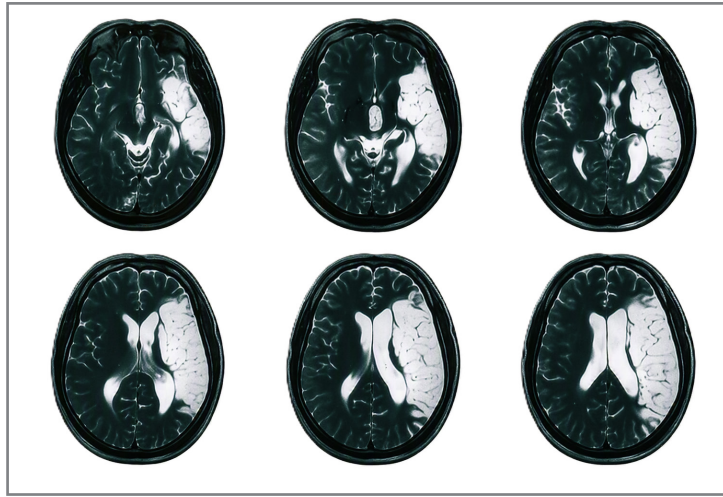


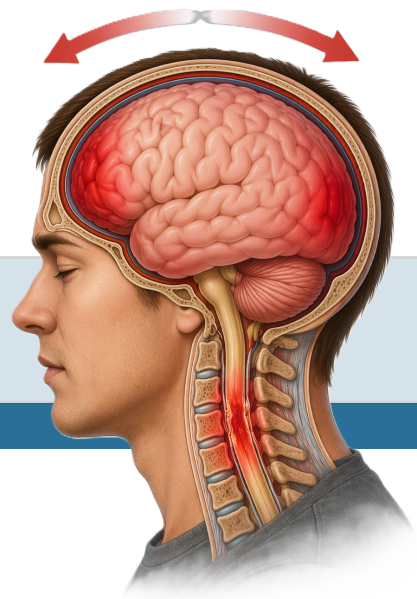
Figure 3. MRI brain (02.11.2025); MRI demonstrates chronic post-ischemic cystic-gliotic changes in the left cerebral hemisphere with a lesion measuring approximately 112 × 47 × 96 mm, associated with secondary Wallerian degeneration of the left corticospinal tract and atrophic changes of the corpus callosum and left cerebral peduncle. Ventricular asymmetry and moderate enlargement of the cisterna magna are also noted, along with MRI signs of chronic cerebrovascular disease (Fazekas grade 2)

Conclusion

This case demonstrates that a multidisciplinary rehabilitation strategy combining speech and language therapy with Cerebrolysin may contribute to meaningful recovery in patients with severe post-stroke aphasia. The observed improvement in language and neurological function supports the potential role of Cerebrolysin as an adjunctive therapy during the early and subacute stages of stroke recovery. Notably, our findings are consistent with the results of the ESCAS study (8), which demonstrated that Cerebrolysin administered in combination with intensive speech and language therapy was associated with significant improvements in language outcomes and neurological recovery in patients with post-stroke aphasia. Further controlled clinical studies are warranted to clarify its efficacy and optimal use in post-stroke language rehabilitation.

CASE SUMMARY	
 Patient	• 44 years • Left MCA ischemic stroke with severe aphasia
 Challenge	• Severe post-stroke global aphasia
 Treatment	• Cerebrolysin 30 mL/day IV x 14 days + 3 rehabilitation courses + speech therapy
 Outcome	• NIHSS 16 → 10 • WAB 44 → 51 • mRS 3 → 2
 Take Home Message Repeated intensive rehabilitation courses combined with Cerebrolysin were associated with progressive improvements in language, communication, motor function, and overall neurological recovery, highlighting the potential for meaningful gains even in patients with initially severe aphasia.	

Acute Traumatic Brain and Spinal Cord Injury





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Traumatic brain injury (TBI) remains one of the most complex challenges in critical care, neurosurgery and neurorehabilitation. While the initial management of acute neurotrauma focuses on stabilisation, surgical intervention when required, and prevention of secondary injury, the long-term consequences of TBI are increasingly recognised as major determinant of patient outcome. Recovery does not end at hospital discharge; rather, many patients continue to experience persistent cognitive, emotional, behavioural and functional impairments that may significantly affect their quality of life, independence and social reintegration.

From a neurosurgical perspective, long-term follow-up after TBI is essential to identify and address these evolving challenges. The consequences of brain injury can emerge or become more apparent months or even years after the initial event, highlighting the need for structured assessment and coordinated multidisciplinary care. Special attention should be directed towards cognitive impairment, attention deficits, mood disturbances and neuropsychiatric complications, which often remain underrecognised despite having a substantial impact on recovery.

Recent clinical research has strengthened the evidence base for targeted interventions in the subacute phase after TBI. The CAPTAIN trial represents an important milestone in this field, demonstrating the potential of structured rehabilitation to improve outcomes in patients with persistent post-traumatic impairments. Notably, the study reported encouraging results in neuropsychiatric outcomes, addressing these frequent and disabling complications following brain injury. These findings reinforce the importance of recognising emotional and behavioural sequelae as integral components of TBI management rather than as secondary considerations.

In parallel, pharmacological strategies to support recovery after TBI are gaining increasing scientific attention. Cerebrolysin represents the first compound to develop a dedicated clinical evidence base in TBI, contributing to a broader understanding of pharmacological strategies aimed at supporting neurological recovery. Importantly, emerging evidence has also contributed to its inclusion in clinical guidelines addressing specific post-TBI impairments, including attention deficits, further supporting the need for evidence-based therapeutic strategies in long-term rehabilitation.

The cases presented in this chapter reflect the evolving understanding of TBI as a chronic neurological condition that requires continued care beyond the acute phase. They emphasise the importance of comprehensive follow-up, early recognition of persistent symptoms and personalised rehabilitation strategies. Through collaboration among neurosurgeons, neurologists, rehabilitation specialists, and allied healthcare professionals, the goal extends beyond survival after injury towards achieving meaningful recovery, functional independence and improved long-term quality of life for individuals affected by traumatic brain injury.



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...in the management of persistent tetraplegia after moderate TBI

Abstract

Background: Persistent severe motor deficits after traumatic brain injury (TBI) require careful reassessment when the clinical presentation is not fully explained by initial cranial computed tomography (CT) findings. Serial imaging and multidisciplinary evaluation are particularly important in older patients with intracranial hemorrhage and relevant comorbidities.

Case presentation: An 82-year-old woman receiving chronic anticoagulation was admitted after a traumatic injury caused by a falling advertising panel. She presented with altered consciousness, motor aphasia, and flaccid tetraplegia. Initial CT revealed multicompartiment intracranial hemorrhage, including subdural hematoma and subarachnoid hemorrhage. As the severity of the motor deficit remained unexplained by cranial CT findings, magnetic resonance imaging (MRI) was performed and demonstrated bilateral abnormalities affecting the descending motor pathways, extending from the brainstem into the upper cervical spinal cord, as well as a small acute ischemic lesion. The patient received multidisciplinary supportive management, including intensive care, rehabilitation measures, and adjunctive Cerebrolysin. Consciousness and speech improved, whereas the motor deficit persisted at discharge.

Conclusion: This case highlights the importance of serial neuroimaging and expanded MRI evaluation when severe neurological deficits appear disproportionate to initial CT findings after TBI. It also demonstrates the complexity of recovery-oriented care in older patients with combined traumatic, hemorrhagic, ischemic, and systemic complications. As a single descriptive case, it does not allow causal attribution of outcome to any individual therapeutic intervention.

Keywords: traumatic brain injury; tetraplegia; subdural hematoma; subarachnoid hemorrhage; corticospinal tract; cervical spinal cord; Cerebrolysin; case report

Introduction

Traumatic brain injury (TBI) is a heterogeneous condition caused by an external force and may range from mild injury to life-threatening neurological damage. Its clinical course reflects both the primary injury and secondary processes that may evolve over time, including intracranial hemorrhage, cerebral edema, ischemic complications, and systemic insults. Integrated, individualized management is therefore essential, particularly in older patients and in those receiving chronic anticoagulant treatment [1,2].

When a severe motor deficit persists or progresses despite apparently insufficient explanatory findings on cranial CT, the diagnostic assessment should be broadened. Serial CT is important for tracking evolving hemorrhagic lesions, while MRI may provide additional information regarding brainstem, corticospinal tract, and cervical spinal cord involvement. This case report describes an older woman with moderate TBI, multicompartiment intracranial hemorrhage, persistent tetraplegia, and MRI abnormalities involving bilateral descending motor pathways. The report is structured in accordance with the CARE reporting recommendations [3].

Case presentation

Patient Information and Initial Clinical Findings

On 29 March 2024, an 82-year-old woman (patient initials: C.M.) was brought by ambulance after being struck by a falling advertising panel. Her medical history included arterial hypertension, thyroid nodules, and chronic anticoagulant treatment. On admission, she had confusional syndrome, somnolence (GCS 10/15: E4, V2, M4), motor aphasia, and flaccid tetraplegia. Bilateral pupillary light reflexes were present, cranial nerve examination was otherwise reported as normal, deep tendon reflexes were symmetrical, plantar responses were flexor bilaterally, and an occipital contused wound was documented.

Timeline

Table 1: Clinical course and treatment timeline

Day	Clinical course and investigations
Day 0	Admission after head trauma. GCS 10/15, motor aphasia, flaccid tetraplegia. CT: left fronto-temporo-parietal subdural hematoma, temporal subarachnoid hemorrhage, 4 mm midline shift.
Day 1	CT: increased frontal contusion; persistent hemorrhages. Aphasia and tetraplegia persist.
Day 7	Improved consciousness; persistent tetraplegia.
Day 8	CT: enlarged frontal hemorrhage with vasogenic edema; later respiratory failure and pulmonary sepsis.
Day 10	MRI: bilateral corticospinal tract abnormalities from brainstem to cervical cord; small right thalamic infarct.
Day 11	Conscious, dysarthric, spastic tetraplegia.
Day 39	Stable consciousness; persistent motor deficits.
Day 39+	Improved consciousness and speech; ongoing motor impairment.

Diagnostic Assessment and Clinical Course

The admission cranial CT showed an acute left fronto-temporo-parietal subdural hematoma measuring approximately 10 mm, with extension along the falx cerebri, associated left temporal subarachnoid hemorrhage, and a rightward deviation of the midline structures of approximately 4 mm. Neurosurgical intervention was not indicated at that time (Figure 1).

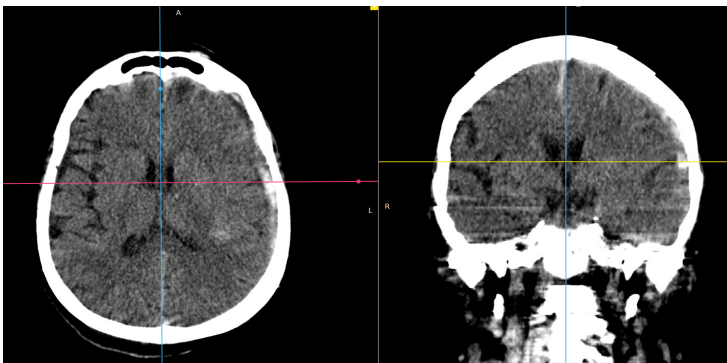


Figure 1. Admission cranial CT . Axial and coronal images demonstrate a left hemispheric extra-axial hemorrhagic collection consistent with acute subdural hematoma, associated mass effect, and rightward deviation of the midline structures.

A follow-up CT performed on 30 March documented progression of the left paramedian frontal contusion. On 6 April, CT showed a left frontal intraparenchymal hemorrhagic focus that had increased from 32 mm to 37 mm, with marked perilesional vasogenic edema, together with residual multicompartiment subdural and subarachnoid hemorrhage. Midline structures were no longer deviated (Figure 2).

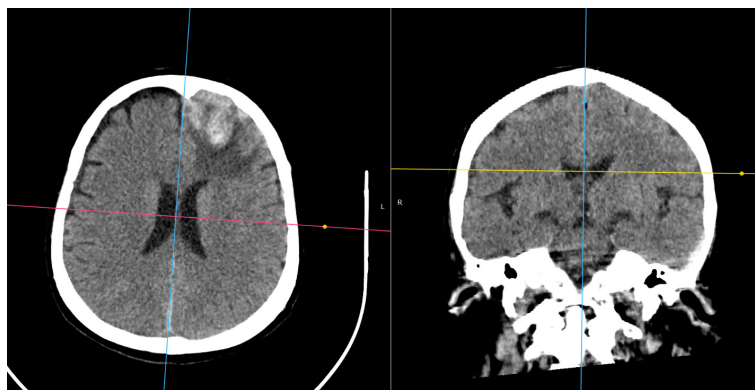


Figure 2. Follow-up cranial CT . Axial and coronal images demonstrate the left frontal intraparenchymal hemorrhagic focus with surrounding vasogenic edema. Serial CT assessment documented evolution of the hemorrhagic contusion and residual multicompartiment extra-axial hemorrhage.

Because the persistent tetraplegia was not adequately explained by the cranial CT findings, repeat cranial CT and MRI were obtained on 8 April. MRI demonstrated T2 and FLAIR hyperintensity with a degree of diffusion restriction along the corticospinal tracts bilaterally and symmetrically at the pontine level and subsequently at the medullary pyramids. The abnormalities extended into the upper cervical spinal cord, involving anterior and lateral columns; more caudally, T2 hyperintensity was also reported in the posterior columns (Figure 3).

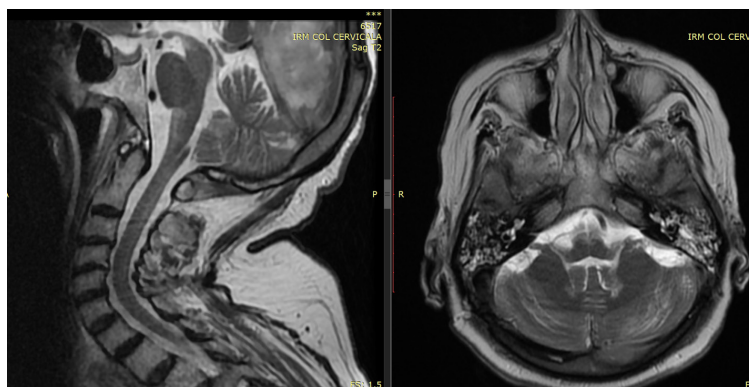


Figure 3. MRI showing. sagittal T2-weighted cervical image and axial posterior-fossa image illustrate abnormalities extending through the bulbo-ponto-medullo-cervical region.

MRI also identified a small acute ischemic lesion in the right anteromedial thalamus and a small chronic lacunar ischemic lesion in the right medial thalamus (Figure 4). The acute thalamic lesion was clinically relevant but did not, in isolation, explain the bilateral motor deficit.

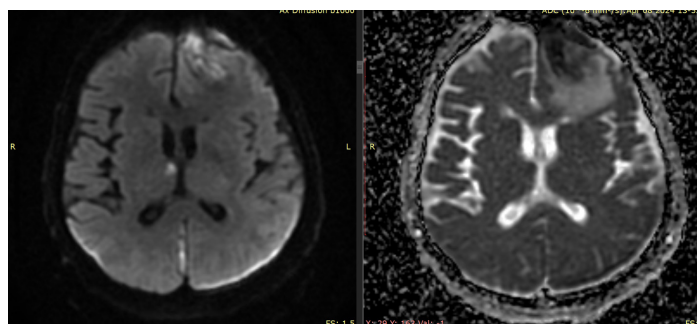


Figure 4. Diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) map . The images support the presence of a small acute ischemic lesion in the right anteromedial thalamus.

Therapeutic interventions

The patient was managed conservatively from a neurosurgical perspective and was monitored in intensive care. The documented treatment included analgesics, hemostatics, antihypertensive therapy, anti-edema medication, enteral nutrition, and later antibiotic treatment for pulmonary sepsis. Anticoagulant therapy was

also documented during the subsequent clinical course. Adjunctive Cerebrolysin was administered as follows: 40 mL at treatment initiation on the day of the admission (one 100ml slow perfusion), 20 mL/day during the early follow-up period, and 40 mL/day after readmission to intensive care. The discharge plan included Cerebrolysin 10 mL/day for 10 days/month, monthly for 1 year, together with anticoagulant therapy and physiotherapy.

Follow-up and Outcomes

During hospitalization, the patient showed favorable evolution in consciousness and speech. The initial flaccid tetraplegia evolved into spastic tetraplegia. At neurological reassessment, she was conscious and dysarthric, with preserved oculomotricity, symmetrical reactive pupils, brisk deep tendon reflexes bilaterally, and lower-limb muscle strength graded 1/5. The motor deficit persisted at discharge, and the patient remained dependent on nasogastric feeding. The available source document does not provide standardized serial functional scores or long-term follow-up data.

Discussion

This case highlights several clinically important aspects of TBI care. First, the initial presentation combined a moderate impairment of consciousness (GCS 10/15) with focal and diffuse neurological deficits, including motor aphasia and tetraplegia. The admission CT confirmed multicompartment traumatic intracranial hemorrhage. The subsequent enlargement of the left frontal hemorrhagic contusion and the persistence of extra-axial blood collections illustrate why serial imaging is important when the neurological deficit is severe or the clinical course is evolving. TBI is dynamic, and secondary injury mechanisms may alter both imaging findings and functional outcome over time [1,2].

Second, the persistent tetraplegia was disproportionate to the supratentorial CT findings. This prompted MRI assessment, which showed bilateral symmetrical signal abnormalities along the corticospinal tracts at the pontine and medullary levels, extending into the upper cervical spinal cord. These findings provide an anatomical correlate for the motor syndrome and demonstrate the value of expanded neuraxis imaging when cranial CT alone does not explain the clinical picture. The exact pathophysiological mechanism of the tract abnormalities should remain a neuroradiological and clinical interpretation rather than an over-specified conclusion from the available data.

Third, the clinical course was complicated by pulmonary sepsis and respiratory failure, both of which are relevant systemic stressors in an older patient with acute brain injury. The small acute right anteromedial thalamic ischemic lesion added further complexity but was insufficient by itself to account for the bilateral motor deficit.

The patient received multimodal supportive treatment, complication management, physiotherapy, and adjunctive Cerebrolysin. Randomized controlled studies in moderate-to-severe TBI have evaluated Cerebrolysin as an adjunct intervention to standard care, including the CAPTAIN I and CAPTAIN II trials [4,5]. A prospective meta-analysis of the CAPTAIN trial series has also been published [6].

This report describes a single clinical case and does not allow conclusions regarding treatment efficacy or the contribution of individual therapeutic interventions. Limitations include the absence of standardized serial outcome assessments and long-term follow-up data. Future reports would benefit from structured documentation of functional recovery using validated measures, including neurological status, motor function, activities of daily living, and swallowing ability.

Conclusion

Persistent tetraplegia after TBI requires a structured diagnostic reassessment when the initial cranial CT findings do not fully explain the motor deficit. In this older patient with multicompartment intracranial hemorrhage, serial CT documented evolving traumatic lesions, while MRI identified bilateral corticospinal tract and upper cervical spinal cord abnormalities and a small acute thalamic ischemic lesion. The case underscores the importance of serial imaging, multidisciplinary care, and cautious interpretation of outcomes within a multimodal treatment strategy.

CASE SUMMARY



Patient

- 82 years
- TBI with multicompartiment hemorrhage



Challenge

- Persistent tetraplegia despite moderate TBI



Treatment

- Cerebrolysin 40 mL/day IV on admission, 10 mL/day IV x 10 days/month for 1 year + intensive care + rehabilitation



Outcome

- Improvement of consciousness and speech
- tetraplegia persisted



Take Home Message

In complex TBI with multifactorial secondary brain injury, adjunctive Cerebrolysin integrated with intensive care and rehabilitation was associated with recovery of consciousness and communication, highlighting the potential for domain-specific neurorecovery despite persistent severe motor deficits.



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...in management of moderate TBI

Abstract

Moderate traumatic brain injury (TBI) often leads to impairments in cognitive, speech, and motor functions, which significantly diminish daily activity levels and overall quality of life¹. We present a clinical case of an 18-year-old female patient who suffered a brain contusion, subdural haemorrhage, fractures of the left ribs (II–V), and contusion of the left kidney following a road traffic accident. After being transferred to a medical rehabilitation unit, the patient underwent a multidisciplinary approach that included physical therapy, occupational therapy, speech-language therapy, psychological support, and a course of Cerebrolysin. In the first 10 days of rehabilitation, we observed improvements in gait and coordination, enhanced memory, and a reduction in vestibulo-atactic and cephalalgic symptoms. This case underscores the effectiveness of comprehensive early rehabilitation following moderate TBI, especially with the use of neurotrophic pharmacotherapy.

Keywords: traumatic brain injury, rehabilitation, brain contusion, Cerebrolysin, cognitive impairment.

Introduction

Traumatic brain injury (TBI) is one of the leading causes of long-term disability among young individuals. According to WHO data, over 69 million cases of TBI are reported annually², with about 10% occurring in individuals under 25 years of age³. Moderate TBIs, which include brain contusions and intracranial haemorrhages, can result in impairments in motor function, coordination, balance, speech, cognition, and emotional well-being. Effective rehabilitation necessitates a multidisciplinary approach, and pharmacological support for neuroplasticity — particularly using Cerebrolysin — has demonstrated effectiveness in restoring cognitive and neurological functions after TBI⁴.

Patient Information

An 18-year-old female patient was injured in a road traffic accident on 30 November 2024 while traveling as a passenger in a vehicle. She sustained a closed moderate TBI with brain contusion and subdural hemorrhage in the temporal region and cerebellar tentorium, accompanied by fractures of the left ribs II–V and contusion of the left kidney. At admission her Glasgow Coma Scale (GCS) score was 11 points. She was transferred to the rehabilitation unit on 9 January 2025 because of persistent neurological and functional deficits. The patient presented with general weakness, gait disturbances, upper-limb tremor, impaired coordination, memory impairment, headache, dizziness, episodic dysfunction of pelvic organs, emotional exhaustion, and anxiety. Neurological Examination: Facial asymmetry noted, particularly in the nasolabial triangle. Palpebral fissures are symmetric, but there is a limitation of lateral eye movements. Arm reflexes are more pronounced on the right side (D>S), while lower-limb reflexes are brisk and symmetric. The patient demonstrated intention tremor during coordination tests, and the Romberg test revealed an unstable position. Speech exhibited elements of dysarthria. Memory impairment is evident. Physiological functions are not under control.

Clinical Findings

Functionally, the patient required assistance for turning in bed, sitting, standing, and transfers. Walking and stair negotiation were not possible. Joint range of motion was preserved, while muscle strength was reduced to 2–4/5 across major muscle groups. Initial outcome measures showed severe disability: Barthel Index 25/100, Berg Balance Scale 15/56, modified Rankin Scale 4, and Rancho Los Amigos cognitive level IV. Montreal Cognitive Assessment (MoCA) was not feasible at admission because of limited cognitive participation.

Diagnostic Assessment

The working diagnosis was status after moderate closed TBI with cerebral contusion and subdural hemorrhage, complicated by vestibulo-atactic syndrome, gait abnormality, dysarthria, cognitive impairment, and functional dependence. Associated extracranial injuries included fractures of left ribs II–V and left kidney contusion. ICD-10 coding included S06.31, S37.00, R42, and R26.8. The patient was evaluated by a multidisciplinary team, which included a physical therapist, occupational therapist, speech-language therapist, and psychologist. An individualized rehabilitation plan was formulated, incorporating three hours of active rehabilitation divided into short 30-minute sessions. Rehabilitation Goals Included: Verticalization and restoration of gait, Restoration of self-care skills, Improvement of coordination and balance, Control of body position in space, Enhancement of speech, Improvement of psychological status and socialization

Therapeutic Intervention

The rehabilitation program was delivered as three hours of active therapy daily, divided into shorter 30-minute sessions to optimize tolerance and attention.

Physical therapy focused on progressive verticalization, bed mobility, transfer practice, trunk control, balance retraining, strength recovery, flexibility, endurance, gait re-education, and coordination tasks. Occupational therapy targeted self-care retraining, transfer independence, kitchen-related activities, visuospatial tasks, upper-limb coordination, and memory-oriented cognitive exercises relevant to daily routines. Speech-language therapy addressed dysarthric speech, verbal processing, comprehension of multi-step commands, and cognitive-communication recovery. Psychological and psychiatric support focused on anxiety reduction, emotional stabilization, motivation, and social reintegration. Medical treatment included Cerebrolysin 30 mL intravenously diluted in 50 mL sodium chloride for 14 days, alongside ibuprofen 400 mg once daily and omeprazole 20 mg once daily.

Timeline

Table 1: Clinical course and treatment timeline.

Week	Clinical recovery dynamics
Week 1	Moderate neurological deficits at admission, including gait disturbance, impaired coordination, and memory dysfunction. Pharmacological treatment and intensive multidisciplinary rehabilitation were initiated.
Week 2	Progressive improvement in general condition, pelvic organ control, psycho-emotional status, gait, and coordination. Neurological deficits decreased, although memory impairment persisted. Continuous medical monitoring was no longer required.
Week 3	Further gains in gait, balance, endurance, and cognitive function. The patient was able to follow complex instructions and perform balance training, indicating improved functional independence.
Week 4	Continued neurological recovery with stable functional improvement during ongoing rehabilitation.
Week 5	Memory continued to improve. The patient was fully oriented in time and place, although responses remained slightly delayed.
Week 6	Coordination, endurance, and emotional status improved further. Gait and coordination recovered completely, while mild short-term memory impairment persisted. Rehabilitation goals were achieved, and the patient was discharged with follow-up by the primary care physician.

Follow-Up and Outcomes

At discharge, the patient achieved independent bed mobility, sit-to-stand transitions, transfers, level walking, and stair negotiation. Muscle strength improved to 4–5/5 in all major groups with preserved range of motion. Outcome measures confirmed substantial recovery. Barthel Index improved from 25/100 to 90/100, Berg Balance Scale from 15/56 to 53/56, modified Rankin Scale from 4 to 2, Rancho Los Amigos level from IV to IX, and MoCA reached 24/30. She was fully oriented in time and place, able to execute complex instructions, and demonstrated restored continence, independent ambulation, and self-care performance. Mild residual short-term memory slowing remained, and outpatient neurological follow-up was arranged.

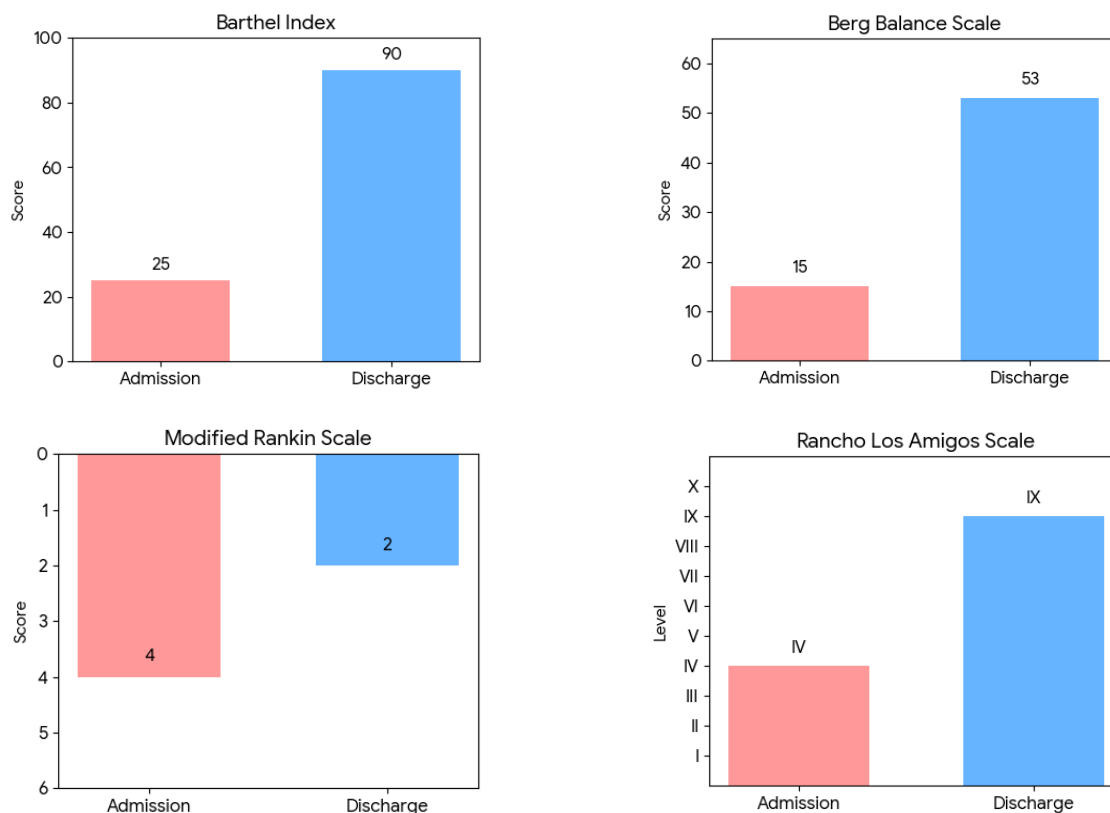


Figure 1: Main clinical assessments at admission and discharge.

Discussion

Compared with published evidence from the literature, the pace of recovery in this case of a patient with moderate TBI appears particularly favorable for the degree of initial motor, balance, continence and cognitive impairment. In many reports involving adolescents and young adults with cerebral contusion and subdural hemorrhagic lesions, restoration of independent gait and higher-level cognitive task execution often extends over several months rather than weeks, especially when vestibulo-atactic features and dysarthria are present. The relatively rapid transition from Rancho level IV to IX, together with the marked Barthel and Berg gains over approximately five weeks, supports the potential benefit of early high-intensity interdisciplinary intervention during the critical neuroplastic phase after injury. While direct comparison is limited by differences in lesion burden, acute neurosurgical management, and rehabilitation dose across studies, this trajectory aligns with literature suggesting that younger age, preserved musculoskeletal range, and early task-specific therapy are positive prognostic factors.

This case illustrates the importance of early, structured, multidisciplinary neurorehabilitation in severe TBI recovery. The patient presented with a combination of vestibulo-atactic dysfunction, cognitive impairment, dysarthria, impaired continence, and severe dependence in mobility and self-care. Such multidomain deficits are typical after cerebral contusion with subdural bleeding and require simultaneous rather than sequential rehabilitation interventions. Several aspects make this case notable. Despite severe early functional limitations, the patient showed rapid and clinically meaningful gains within the first 10 days, particularly in gait, balance,

continence, and task engagement. The integration of physical, occupational, speech, and psychological therapies likely produced synergistic benefits, with adjunctive Cerebrolysin® supporting neuroplasticity and cognitive recovery.

Conclusions

Comprehensive rehabilitation incorporating neurotrophic therapy (Cerebrolysin) significantly improved motor, cognitive, and speech functions following moderate TBI.

The patient regained the ability to walk independently, follow complex instructions, and perform self-care skills. Early rehabilitation is critical for achieving a stable functional outcome.

CASE SUMMARY	
 Patient	• 18 years • Moderate TBI with subdural hemorrhage
 Challenge	• Severe functional dependence and cognitive impairment
 Treatment	• Cerebrolysin 30 mL/day IV x 14 days + multidisciplinary rehabilitation
 Outcome	• mRS 4 → 2 • Berg Balance 15 → 53 • Barthel 25 → 90
 Take Home Message	An intensive multidisciplinary rehabilitation program combined with Cerebrolysin was associated with rapid, clinically meaningful recovery across motor, cognitive, communicative, emotional, and functional domains, enabling independent walking, self-care, and near-normal cognition within six weeks.



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...in management of severe TBI

Abstract

Severe traumatic brain injury (sTBI) is a major cause of death and disability worldwide, resulting in a significant individual and socioeconomic burden. Current treatment guidelines do not include any recommendations for neuroprotective or neuroregenerative drugs. Here, we present a combined treatment with Cerebrolysin and Citicoline in two cases. Both drugs are experimentally better than clinically proven in their own effectiveness, but there is almost no clinical data on the combination of the two. Our case study hints at a promising approach that may improve neurological outcome after sTBI. The first patient was a 29 years male motorcyclist suffered polytrauma in a high-speed accident. He had severe bilateral chest trauma and fractures in both thighs and an sTBI. In addition to surgical and standard neurocritical care according to the evidence-based guidelines, he was given neuroprotective therapy with Cerebrolysin (50ml/day) and Citicoline (3 g/day), by continuous intravenous infusion (IV), for 21 days. The second patient was a 30 years male ski mountaineer who had suffered a fall over 300m in open terrain. In addition to the sTBI, he had fractures in the cervical spine, ribs, pelvis, and lower extremities, as well as lung contusions and massive soft tissue trauma. After initial treatment in a local hospital, he was transferred to our department and received the same neuroprotective drugs, like all of our patients with sTBI. Considering the severity of the injuries (Injury Severity Score [ISS]: 43/50, Revised Trauma Score [RTS: 5.0304, 2.7794]) and the unfavorable outcome probability (Hukkelhoven Score) of 93.1% and 82.6%, the outcomes of both patients are surprisingly encouraging 1 year after the accident. They achieved a Glasgow Outcome Score of 6 and 5 and grades 2 and 4 on the modified Rankin Scale, respectively. Currently, both are able to take care of themselves in activities of daily life to a large extent. Neuroprotective drugs may improve the regeneration of cell membranes, improve blood brain barrier integrity, and reduce neuroinflammation leading to secondary damage to the injured brain. Our clinical experience and data suggest that the combined administration of Citicoline and Cerebrolysin may contribute to better recovery, without relevant side effects. However, it would be important to validate these results by means of a controlled, prospective study.

Keywords: Cerebrolysin, multi-modal therapy, neuroprotection, secondary brain damage, severe TBI

BACKGROUND

Severe traumatic brain injury (sTBI) is a leading cause of death and disability, especially among young male adults in low- and middle-income countries, shifting to elderly patients in developed countries. This so called “hidden pandemic” affects more than 13 million patients annually in Europe and the US alone.[1] sTBI causes the death of about 11.8/105 people in Austria, which is comparable with data from other European countries.[2,3] In survivors, sTBI often has life-changing sequelae such as motor and cognitive deficits, leading to a life of dependency; consequently, sTBI has a significant socio-economic burden and the individual burden. The mechanisms of injury and underlying physiological and cellular processes accompanying the primary and secondary brain injuries are complex and require multimodal treatment.

Nevertheless, current guide-lines, for example, from the Brain Trauma Foundation (BTF), aim to provide evidence- based recommendations for the various manifestations of sTBI.[4,5] Outcomes may be improved by adequate early care on scene, in the emer-gency department (ED),[6] and in the intensive care unit (ICU). In addition, sTBI should not be understood as purely acute or static, but as a complex, acute to chronic neurodegenerative disease. It no longer seems so clear that sTBI-induced damage can only be treated within a few hours after the trauma, and the possibility of a longer therapeutic window of time for pharmacological interven-tion is in discussion.[7] For reduction of secondary damage, anti-oxidants, branched-chain amino acids, and ω -3 poly-unsaturated fatty acids have shown promising pre-clinical results.[8]

However, pharmacological research has not yet identified a “gold standard” to prevent secondary brain damage. Although there are promising data from animal studies, the only positive findings in retrospective [9,10] and prospective “real life” clinical trials [11,12] were achieved with Citicoline and Cerebrolysin. These were hints of reduced mortality and better functional outcome as measured by enhanced Glasgow Outcome Score (GOSE) and modified Rankin Scale (mRS).[13] However, these agents—whether administered orally or intravenously— have not produced significant clinical improvements when administered as single drugs and are discussed critically in large, random-ized prospective trials.[13–15]

CASE 1

A 29-year-old Caucasian male patient collided as motorcy-clist head-on with a car at about 65 mph. His helmet was broken on impact with the frame of the car’s windscreen. Table 1 shows the patient’s status on arrival of emergency medical service (EMS), the pattern of injuries as well as the emergency care measures administered. Whole- body CT scan in the ED revealed punctiform cerebral hemor-rhages (especially in the left temporal lobe), bilateral serial rib fractures, a left scapular fracture, prehospital-drained pneumothorax on the left, laceration, and atelectasis of the left lower lobe, ventrocranial edge detachment on the 11th and 12th thoracic vertebrae, wedge shaped compression fractures of the 1st and 4th lumbar vertebrae, and multi-ple fractures in both hip joints. After placement of a probe to measure the intracranial pressure (ICP) in the ED, the patient was admitted to ICU with stable ventilation and hemodynamic parameters (norepinephrine 0.2 μ g/kg/ min). Citicoline (3 g/day) was added to the usual stand-ard care. ICP increased repeatedly up to 19 mmHg during the first days, responding to deepening of analgosedation and osmotherapy.

Table 2 shows laboratory findings and hemodynamic support in the first 24 h. The further course was relatively stable with regard to the ICP and receding brain edema; weaning from ventila-tion was initiated from Day 10. Subsequently, the patient exhibited an extreme vegetative imbalance, so that in ad-dition to the established antisymphathetic (carvedilol) and antipsychotic medication (quetiapine, tiapride, and oxaz-epam), continuous administration of propofol had to be re-established repeatedly.

Three weeks after the accident, magnetic resonance tomography (MRT) revealed signs of intracranial axonal injuries and microbleeds (Figure 1), seen as spotted susceptibility artifacts on the anterior tem-poral lobe and in the frontobasal region (left > right), in the basal ganglia on both sides, as well as in the left posterior border zone and in the white matter on both sides, in the high frontal to occipital regions.

In summary, this indicates multilocular small shear hemorrhages as well as left fron-tobasal and temporal contusion zones, compatible with a diffuse axonal trauma stage 1. On Day 21, the patient finally underwent stabilization of both femoral necks with inter-locking nails. A dilatative tracheostomy was also performed. Somatosensory evoked potentials (SSEPs) on Day 23 revealed a missing central answer on the right-brain side; on the left a central answer was derived with limited accessibility. During the following days, the patient appeared stressed, showed repeated periods of restlessness with sweating and tremors, and moved his extremities in a completely uncon-trolled, stretching manner. Electroencephalogram (EEG) on Day 28 showed signs of general diffuse brain dysfunction (moderate to severe) and reduced reactivity to photogenic stimuli, but no typical epileptic potentials.

Table 1: Status and measures on scene

Item	Case 1	Case 2
GCS on scene	4	3
Pupils	Both narrow, no reaction to light	Both wide, minimal reaction to light
BP	90/60	88/60
HR	80	64
SpO ₂	92	93
RF	16	8
Injuries	TBI III°; Left serial rib fractures and pneumothorax, femoral neck fracture both sides; Fract. Vert. TH XI–L II	TBI III°; Multiple fractures of upper and lower extremities; Serial rib fractures; Fract. Vert. C IV + spinal cord injury
Airway	ETI	ETI
Breathing	CMV	CMV
Circulation	500 mL HES; 1000 mL crystalloid	1000 mL HES; 1000 mL crystalloid

Abbreviations: BP, blood pressure; CMV, controlled mechanical ventilation; ETI, endotracheal intubation; fract.vert.TH (C, L), fracture of thoracic (cervical, lumbar) vertebra; GCS, Glasgow Coma Score; HES, hydroxy ethyl starch; HR, heart rate; RF, respiratory frequency; SpO₂ measured at the finger tip; TVI, traumatic brain injury.

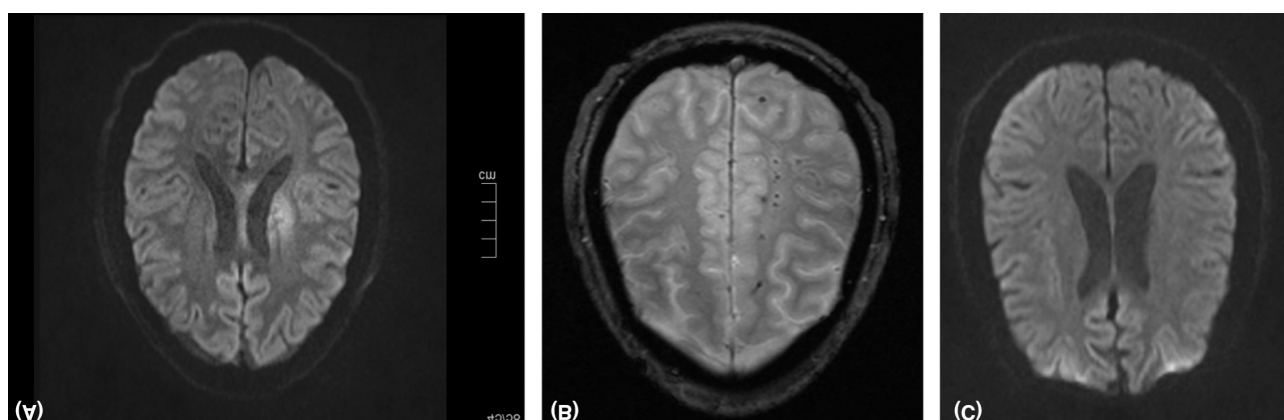


Figure 1: (A-C) Magnetic resonance tomography (MRT), Case 1: (left) MRT of the 29-year-old male patient, 3 weeks after the accident. Diffusion-weighted (DWI) sequences ($b = 1000$) demonstrated multifocal areas of abnormal bright signal along the corpus callosum and within the left corona radiata and body of caudate nucleus corresponding to axonal injuries after the trauma. (Middle) On T2*-sequences multifocal areas of punctiform susceptibility artifacts at the gray-white matter junction, more pronounced at the left parietal region, in the corpus callosum and the temporal lobe (not shown) were visible, indicating small foci of posttraumatic bleeding. (Right) Follow-up MR 18 months later showed that the edematous areas on DWI-sequences and the microbleeds had been resolved. The size of the ventricles and the sulci seems to be a bit wider than right after the accident.

On Day 31, more or less with very limited hope for recovery, a supportive therapy with Cerebrolysin was initiated—a novel therapeutic approach for us at that time. 10 days later, the patient began to react to verbal stimulation in a targeted manner for the first time. Further improvement followed rapidly; the neurological examination before transfer to open ward on Day 45 states that the patient was now awake and kept eye contact, gaze tracking was easier to the right than to the left, and muscular tone was generally increased. No co-operation was achieved while examining facial muscles, but he showed indicated movement, when prompted, with fingers and forearm. There was a tendency for spontaneous but uncontrolled stretching spasm of the left leg, but no active movement of the lower extremities when requested.

One month later, at the time of discharge from hospital (Day 73), the patient presented awake and mobile in the armchair. He was able to clearly follow simple prompts; questions were adequately answered with a nod of the head. He showed signs of a tetraparesis, pronounced on the left, and a grasping reflex on the right.

One year after the accident, and after a series of botulinum toxin treatments in the rehabilitation center, the dis-abling spastic increase in muscular tone of the right leg had significantly regressed. The patient was safely mo-bile, using a three-wheeled bicycle. Six months after this, the patient was mobile on his own by public transporta-tion and regular bicycle, and visiting friends and cafes.

Table 2: Laboratory parameters at 24 h after admission in ICU

Item	Case 1	Case 2
ICP (mmHg, mean $\pm$ SD)	17.4 $\pm$ 5.9	11.4 $\pm$ 3.7
S-100B	6.44	1.73
NSE	52.9	46.8
IL-6	676	154
CRP	<0.1	16
PCT	0.7	1.1
Leukocytes	13.1	10.9
Erythrocytes	3.3	2.8
Hemoglobin	10.5	8.6
Thrombocytes	161	120
Norepinephrine (mcg/kg/min, mean dose)	0.25 $\pm$ 0.1	0.12 $\pm$ 0.07
Fluid balance (mL/24 h)	+4100	+800

Abbreviations: CRP, C-reactive protein; ICP, intracranial pressure; IL- micrograms/kilogram/minute; mls, milliliters; NSE, neuron specific enolase; PCT, Procalcitonin; S-serum protein S-100B; SD, standard deviation.

Outcome and follow-up

GOSE/mRS at discharge: 4/4, 1 year after the accident: 5/3, and after 18 months: 6/2.

The final MRT examination 18 months after the acci-dent (Figure 2) shows a gliotic scar cicatricial high parietal remaining as sequelae of the axonal trauma, and a small defect on the left temporal lobe in the area of the previ-ously identified contusion. Overall, the patient had sub-stantially improved; in particular, the frontal contusion zone on the left had receded.

CASE 2

A 30-year-old sportsman fell from a great height (approx. 300 m, Figure 2) during a ski mountaineering trip. Rescue was delayed due to a lack of cell- phone coverage in this remote area, as well as poor weather conditions. The heli-copter emergency service (HEMS) arrived approximately 2 h after the accident. Table 1 shows the patient's status on arrival of HEMS, his pattern of injuries and the emergency care measures administered. The patient was admitted at the nearest trauma center (level II) 4 h after the accident.

The CT scan revealed cerebral contusions, traumatic sub-arachnoid (SAH), and subdural hemorrhage (SDH), an unstable fracture of the 4th cervical vertebra with spinal cord injury, a pneumothorax with rib fractures and multi-ple fractures of the upper and lower extremities. An exter-nal fixator was placed on both lower extremities, followed by plating and screwing of the cervical spine and the left hip on the next day. A postoperative CT scan found ex-tensive brain edema and a new ischemic zone in the area of the posterior circulation, compressing the 4th ventricle.

After being rejected by the nearest neurosurgical uni-versity hospital because of the evidently hopeless situation, the patient was transferred to our institution (for labora-tory findings and hemodynamic support on admission (see Table 2). A CT scan (Figure 2) on arrival shows edema-tous swelling of both cerebellar hemispheres and the right occipital lobe with space-occupying effect in the posterior cranial fossa, and a persistent dislocation fracture of the 4th cervical vertebra.

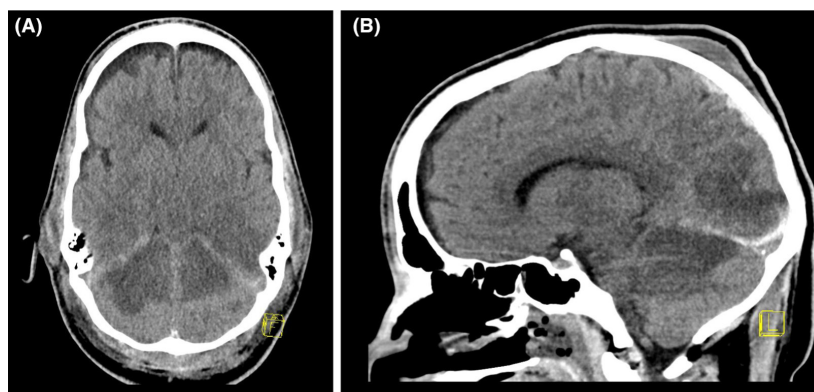


Figure 2: (A, B) Cranial computer tomography (CCT) scan, Case 2: CCT of a 30-year-old male patient, 1 day after the accident (left image) demonstrates extensive edematous swelling within the anterior cerebellar lobes as well as in both posterior temporal and occipital lobes due to extensive hypoperfusion of the posterior circulation. The cerebellar tentorium (right image) is slightly bowed upward and a slight compression of the basal cistern and the IV ventricle is shown; however, liquor flow was patent.

An external ventricular drainage (EVD) was placed, followed by suboccipital decompressive craniotomy with dural expansion surgery on the next day, after interdisciplinary discussion of prognosis, supported by deducible SSEPs over both hemispheres. In addition to standard medical care (comprising “optimal handling,” deep analgo-sedation, hemodynamic, and re-spiratory optimization) the patient received Cerebrolysin and Citicoline. After prolonged weaning, characterized by vegetative disbalances and delayed recovery from analgo-sedation, EEG yielded severe abnormal EEG curves with general slowing, no distinct focus, nor typical epilep-tic potentials.

On Day 33 after the trauma, the consulting neurologist stated: Contact via blink of an eye possible, the patient can follow this request. During the examina-tion, the evaluation of pain was possible. The patient was able to keep eye contact only for a short time and was able to raise the right corner of the mouth a little if requested. He was not able to stick out his tongue. Upper extremities (UE): left distal increased tone in the sense of spasticity, right rather flaccid. Lower extremities (LE): both legs im-mobilized, no examination possible. After 50 more days in the acute rehabilitation process in ICU including replacing the EVD with a ventriculo-peritoneal shunt, the patient was transferred to a specialized clinic for neurorehabilitation. At that time, the report of the neurologist reads as follows: The patient was awake, followed simple prompts, speech comprehension appeared to be well preserved, simple linguistic utterances were possible. Mimic muscles appeared bilaterally symmetrical. He was able to lift and hold UE on the same side against gravity on request, degree of strenght 3-4, increase in tone right > left. LE: Tone spastically increased on both sides, right > left. Left leg painful when moving the hip, right leg could be lifted on request.

Outcome and Follow-up

One year after the accident, the patient was finally dis-charged from the rehabilitation center, able to move by himself with a rollator, and was able to independently manage the transfer from bed to wheelchair and vice versa. He shows pronounced deficits in short-term memory; long-term memory is well preserved. He was usually in a euthymic mood and was looking forward to further development steps.

GOSE/mRS at discharge from hospital: 3/4, 1 year after the accident: 5/4, and after 18 months: 6/4.

Treatment Concept

Immediately after admission to the ICU of our level 1 trauma center (Wiener Neustadt General Hospital, Austria), all patients with sTBI (Glasgow Coma Score [GCS] 3–8, intubated on scene), who are assessed as hav-ing a significant chance of survival, receive Cerebrolysin (50 ml/day) and Citicoline (3 g/day), both given intra-venously for 21 days, continuously via motor syringe, in addition to all the standard measures according to BTF guidelines. We hypothesize that the combined effects of these two pleiotropic agents due to their anti- inflammatory properties, reconstitution of the blood–brain-barrier, and stimulation of membrane and

axonal regeneration can optimize the neurocognitive outcome. Cerebrolysin is a standardized, lipid-free, low-molecular weight neuropeptide preparation, which passes the blood–brain-barrier and mimics the actions of endogenous neurotrophic factors. Proteins present in soluble tissue extracts and in the extra-cellular matrix have been shown to influence the survival and development of cultured neurons.[16]

The tissue-extract-derived neuropeptides contained in Cerebrolysin promote neurotrophic stimulation (survival and maintaining the phenotype of highly differentiated neuronal cells), neuro-modulation (changes in neuronal and synaptic plasticity synapses),[17] and metabolic regulation such as preventing lactic acidosis and increasing the resilience against hypoxic conditions.[9,12] In addition, Cerebrolysin significantly reduces tissue Plasminogen Activator (tPA)- and fibrin-damaged endothelial cell permeability, which is associated with a significant reduction in proinflammatory and procoagulatory activity.[18] Citicoline (Cytidine 5'-diphosphocholine) is chemically identical to the essential endogenous intermediate in the biosynthetic pathway of phosphatidylcholine. It is hydrolyzed to choline and cytidine triphosphate and crosses the blood–brain barrier to be reassembled to Citicoline inside the brain. It mediates neuronal membrane integrity and repair, and it accelerates the reabsorption of cerebral oedema and the restoration of the blood–brain barrier integrity after TBI.[15,19] Citicoline also increases cerebral dopamine and norepinephrine levels, which causes improved hypoxia tolerance.[20]

DISCUSSION

In these case reports, we describe the clinical development of two patients with sTBI, presenting with GCS 3–4 on site. After surgical intervention both required long-term care at the ICU, followed by intensive rehabilitation measures. Motor vehicle accidents and falls from heights resulting from sports activities are typical causes of sTBI in this age group and of high individual and socio-economic impact. It is of enormous importance to give especially young patients every chance for a life that is as free of disabilities as possible and to reintegrate them into their social environment and work process. Recovery of motor functions and cognitive abilities leads to a significant improvement of activities of daily living.

The optimal care for sTBI patients must be started at the emergency site and continued through the emergency department (ED) and the early surgical phase, with ICU treatment closely following the BTF guidelines.[4,5] Starting at the earliest possible time, at the latest when the patient is admitted to the ICU, the described supplementary therapeutic concept should complement the standard treatment of sTBI patients. To the best of our knowledge, these are the first cases reporting this specific pharmacological combination in sTBI, resulting in unexpectedly favorable outcomes (Table 3). In the recent literature, we found only one paper reporting a combined administration of Citicoline and Cerebrolysin in moderate TBI, a RCT, with remarkable positive results.[21]

There are two aspects that we attribute to the continuous and high-dose administration of neuroregenerative drugs, among all other attempts to optimize the individual recovery of our patients. Firstly, we did not observe the development of critical brain oedema in these patients, neither in the early nor in the later stages, despite the extremely massive trauma in both cases. Stabilization of damaged cell membranes, reduction and/or acceleration of the absorption of brain oedema are well described effects of Citicoline.[22,23] The need for analgesication and vasopressors was accordingly moderate. This naturally has a positive effect on gastrointestinal motility, which reduces the risk of translocation and bacteremia. Overall, this results in better stability during the most critical phase of the first 10 days after the trauma.

Secondly, we observed a relatively good neurocognitive long-term outcome in these patients in terms of GOSE and mRS, despite the diffuse axonal trauma, typical for massive acceleration or deceleration trauma. After a phase of “vegetative storm,” typically a sign of diffuse axonal trauma, the patients developed positive cognitive abilities over the next few weeks.

Despite the prolonged rehabilitation (especially in case 2), the patients recovered much better than expected in terms of cognitive competence and mood stability. The latter may be due in particular to the positive effects of Cerebrolysin, as was shown in the meta-analysis by Ghaffarpasand et al.[24] and the recently published “CAPTAIN” trial.[12] Cerebrolysin may stimulate neurotrophic activity and improve neuromodulation and

metabolic regulation.[25] Cerebrolysin and Citicoline were safe in toxicological tests, showing no significant systemic side effects.[23] In rare cases (<1/1000) agitation, loss of appetite, dizziness, or pruritus were observed in awake (stroke) patients receiving Cerebrolysin. In a retrospective cohort study among 7769 adult patients, Muresanu et al. did not find any difference in adverse effects between Cerebrolysin and placebo controls.[9] Side effects of Citicoline are also very rare and of mild intensity; single cases suffering from headache, diarrhea, elevated liver enzymes, and weight loss were reported.

Table 3: Injury severity and prognosis scores

Score	Case 1	Case 2
Hukkelhoven (27)		
Mortality	77.0%	77.0%
Poor outcome	93.1%	82.6%
ISS (28)	43	50
RTS (29)	5.0304	2.7794
TRISS (30)- probability of survival	50.67%	8.49%

Abbreviations: ISS, injury severity score; RTS, revised trauma score; TRISS, trauma and injury severity score.

LIMITATIONS

Despite our experience of more than a decade with Citicoline, and about 4 years with Cerebrolysin, we are well aware of the limitations of these exemplary observations and the ongoing discussion about the effectivity of both drugs. Nevertheless, our data can be understood as a hint that neuroprotective and neuroregenerative mechanisms may be supported by these two externally supplied pharmacologic substances. The effects of our multimodal treatment concept may be worth testing in larger, ideally prospective, and randomized clinical trials.

CASE SUMMARY			
 Patient	• 29 years • Severe TBI with polytrauma	 Patient	• 30 years • Severe TBI after 300m fall
 Challenge	• Diffuse axonal injury and prolonged disorder of consciousness	 Challenge	• Brain edema, SAH/SDH and cervical spinal injury
 Treatment	• Cerebrolysin 50 mL/day IV + Citicoline 3 g/day x 21 days + neurocritical care	 Treatment	• Cerebrolysin 50 mL/day IV + Citicoline 3 g/day x 21 days + decompressive neurosurgery
 Outcome	• GOSE 4 → 6 • mRS 4 → 2 • Independent mobility regained	 Outcome	• GOSE 3 → 6 • mRS 4 → 4 • Independent transfers and rollator assisted mobility
 Take Home Message By potentially limiting secondary brain injury and cerebral oedema during the acute phase of severe TBI, Cerebrolysin may help preserve brain integrity and contribute to unexpectedly favorable long-term neurocognitive outcomes.			

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...in the management of severe traumatic axonal injury

Abstract

Severe traumatic axonal injury (TAI) is a devastating form of traumatic brain injury characterized by diffuse white matter disruption and prolonged disorders of consciousness. We report the case of an 18-year-old male who sustained severe TBI following a pedestrian-versus-vehicle collision. Initial Glasgow Coma Scale (GCS) was 10 at the scene, deteriorating to 7 on admission and progressing to prolonged coma. Initial CT demonstrated diffuse cerebral edema and punctate hemorrhagic lesions suggestive of TAI. The patient was managed with structured neurocritical care according to the institutional CREVICE protocol and received early Cerebrolysin for 10 days. Advanced MRI with susceptibility-weighted imaging and diffusion tensor tractography confirmed severe axonal injury involving deep and interhemispheric white matter tracts. Despite initial severity and prolonged coma, the patient demonstrated progressive neurological recovery. Functional outcome improved from GOSE 5 at discharge to GOSE 6 at 3 months and GOSE 8 at 6 months, with near-normalization of neuropsychological performance.

Keywords: Traumatic axonal injury, diffuse axonal injury, neurocritical care, neurorecovery

Introduction

Traumatic axonal injury (TAI), historically referred to as diffuse axonal injury (DAI), represents one of the most devastating forms of traumatic brain injury (TBI). It is caused by rapid acceleration-deceleration and rotational forces that generate shearing stress within the brain, resulting in widespread disruption of axonal fibers, particularly at the gray-white matter junction, corpus callosum and brainstem. TAI is frequently associated with prolonged loss of consciousness, severe neurological impairment, and unfavorable long-term cognitive outcomes.^{1–3}

Computed tomography (CT) remains the first-line imaging modality in severe TBI but may substantially underestimate the burden of axonal injury. Advanced magnetic resonance imaging (MRI), particularly susceptibility-weighted imaging (SWI), diffusion-weighted imaging (DWI), and diffusion tensor imaging (DTI) with tractography, has significantly improved the detection and characterization of hemorrhagic and non-hemorrhagic axonal lesions and may better correlate with neurological and cognitive outcomes.^{2,7–10} Despite advances in neurocritical care, no specific pharmacological therapy has consistently demonstrated efficacy in traumatic axonal injury. The ongoing CeLATA initiative was designed to further explore the potential role of Cerebrolysin in patients with traumatic axonal injury in a real-world multicenter setting.^{11–14}

We present the case of a young patient with severe traumatic axonal injury confirmed by MRI and tractography who experienced complete functional and cognitive recovery following early administration of Cerebrolysin and structured neurocritical care management based on the institutional Consensus REvised Imaging and Clinical Examination (CREVICE) protocol.

Patient Information

An 18-year-old previously healthy male was admitted after a high-velocity pedestrian-versus-vehicle collision. Prehospital emergency services found the patient with a Glasgow Coma Scale (GCS) score of 10. Due to psychomotor agitation, 5 mg of intravenous diazepam was administered during transport.

Clinical Findings

On arrival at the emergency department, neurological status had deteriorated to a GCS score of 7, requiring rapid sequence intubation and mechanical ventilation. Initial examination revealed severe traumatic brain injury without major extracranial trauma. Pupils were symmetric and reactive. Hemodynamic status was stable (blood pressure 175/102 mmHg, heart rate 83 beats/min, oxygen saturation 99% on 100% oxygen). The patient subsequently developed deep and prolonged impairment of consciousness, remaining with a GCS score of 3 for several days, disproportionate to sedative exposure and suggestive of severe traumatic axonal injury.

Timeline

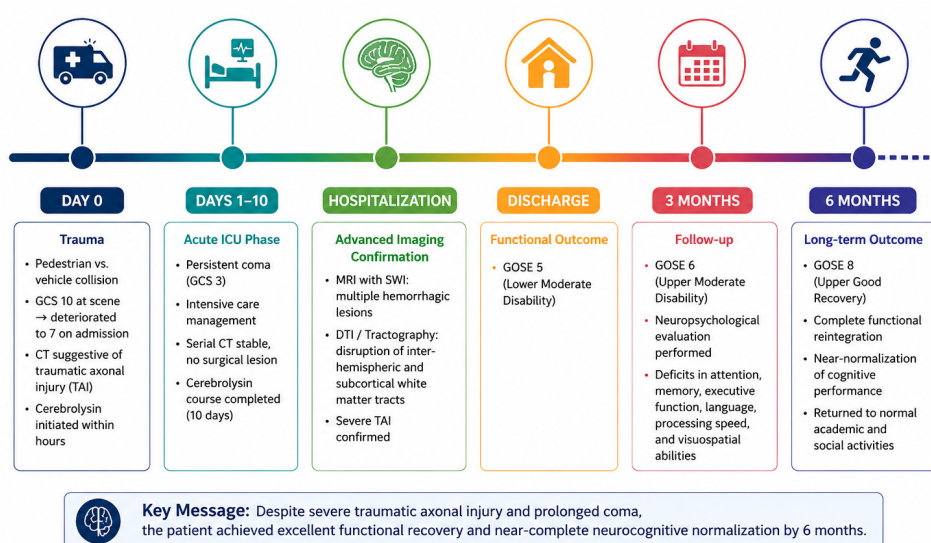


Figure 1: Clinical Timeline

Diagnostic Assessment

Initial CT showed diffuse cerebral edema with partial loss of gray-white matter differentiation and multiple punctate hemorrhagic lesions suggestive of traumatic axonal injury. (Figure 1) No large mass lesion or surgical intracranial hematoma was identified. Follow-up CT demonstrated preserved basal cisterns, no midline shift and persistent punctate hemorrhages. Brain MRI revealed multiple hemorrhagic lesions on SWI involving cortical-subcortical junction and deep white matter. (Figure 2) Diffusion tensor imaging and tractography confirmed disruption of interhemispheric and subcortical white matter tracts, consistent with severe traumatic axonal injury. (Figure 3)

Therapeutic Intervention

The patient was managed in the intensive care unit according to the institutional CREVICE protocol, including structured neurocritical care, serial neurological examinations, ventilatory optimization, and hemodynamic stabilization. Mechanical ventilation was maintained with midazolam and fentanyl sedation. Intracranial pressure monitoring was not available. Based on the early suspicion of traumatic axonal injury, the patient was enrolled in the CeLATA protocol and received Cerebrolysin within hours of admission. Treatment was initiated within 8 hours of trauma and consisted of 30 mL/day administered as an intravenous infusion diluted in 0.9% saline to a total volume of 100 mL for 10 consecutive days. The timing of the first infusion (time-to-needle) was recorded according to protocol. The treatment was well tolerated, with no adverse effects observed. Patients

without good recovery (GOS-E <7) at Day 30 were eligible for two additional recovery-phase treatment cycles (10 mL/day intravenously on Days 31–40 and Days 61–70); however, these were not required in the present case.

Follow-up and Outcomes

The patient gradually recovered consciousness and neurological function during hospitalization without seizures or autonomic complications like episodes of paroxysmal sympathetic hyperactivity. At discharge, functional outcome was GOSE 5 (lower moderate disability). At 3-month follow-up, he improved to GOSE 6, and at 6 months achieved GOSE 8 with complete functional reintegration and no significant neurological or cognitive sequelae.

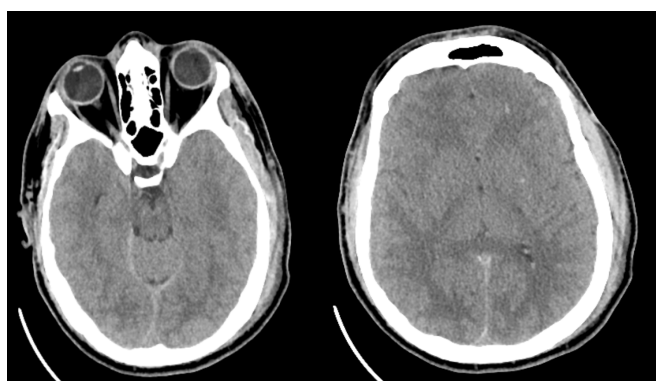


Figure 2: Initial head CT demonstrating diffuse cerebral edema with partial loss of gray-white matter differentiation and punctate hemorrhagic lesions suggestive of traumatic axonal injury.

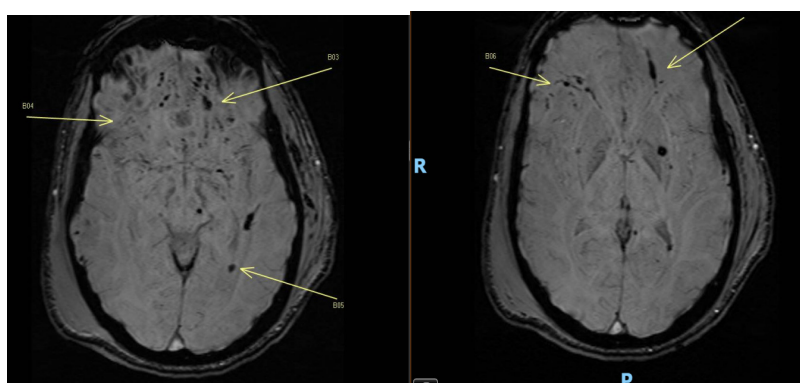


Figure 3: MRI susceptibility-weighted imaging (SWI) demonstrating multiple hemorrhagic foci involving the cortical-subcortical junction and deep white matter, consistent with hemorrhagic traumatic axonal injury.

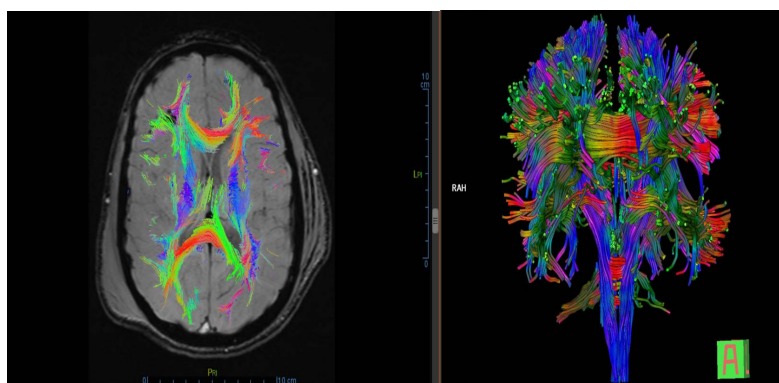


Figure 4: Diffusion tensor imaging and tractography showing disruption and decreased integrity of interhemispheric and subcortical white matter tracts.

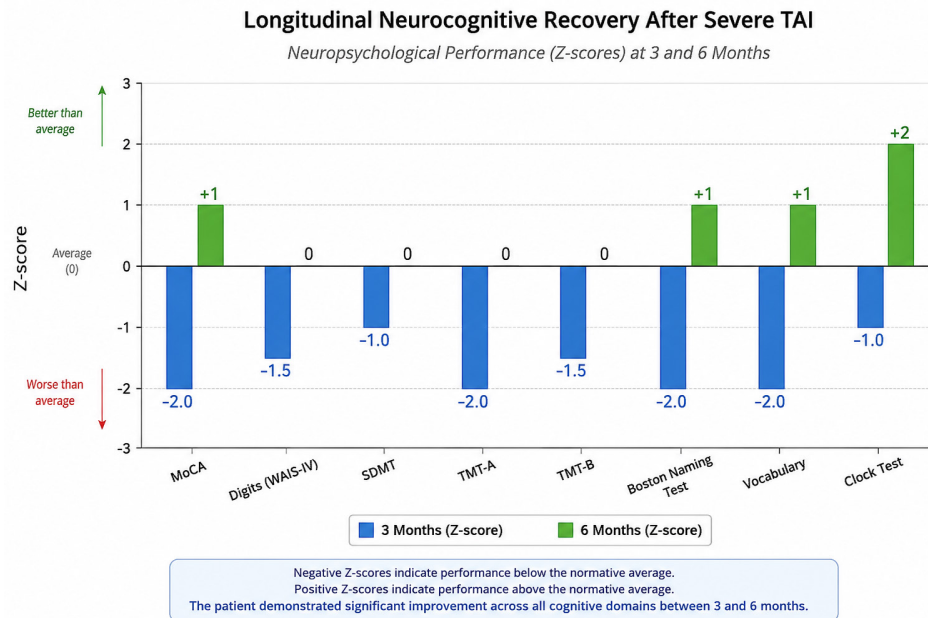


Figure 5: Neuropsychological evolution.

Discussion

Traumatic axonal injury (TAI) remains one of the most challenging forms of traumatic brain injury due to its diffuse pathology, limited therapeutic options, and frequently poor neurological and cognitive outcomes.^{1–3} The present case highlights key aspects of contemporary TAI management, including early clinical suspicion, limitations of conventional neuroimaging, the value of advanced MRI techniques, and the potential role of neurorestorative therapy such as Cerebrolysin.

A notable feature in this case was the discrepancy between the initial neurological status and subsequent deterioration. The patient initially presented with a GCS score of 10 at the scene, progressing to deep coma despite the absence of major intracranial mass lesions on CT. This pattern resembles the “talk and deteriorate” phenomenon traditionally associated with evolving hematomas. However, in TAI, neurological decline may occur without surgically treatable lesions, reflecting secondary axonal injury mechanisms such as cytoskeletal disruption, mitochondrial dysfunction, calcium-mediated proteolysis, neuroinflammation, and impaired axonal transport.^{2,6} Accordingly, prolonged coma disproportionate to CT findings should raise suspicion for severe TAI. Initial CT demonstrated diffuse cerebral edema and subtle punctate hemorrhagic lesions suggestive of TAI; however, the full extent of injury was only identified on MRI. This reinforces the limitations of CT in diffuse axonal injury and underscores the diagnostic value of advanced MRI modalities.^{2,7–10} MRI findings provided definitive radiological confirmation and correlated more closely with the patient’s prolonged impaired consciousness than CT alone.

Despite severe initial presentation and extensive imaging abnormalities, the patient achieved a favorable long-term outcome, culminating in GOSE 8 at 6 months. The observed recovery suggests preserved neuroplastic potential in young patients when secondary injury is minimized and structured neurocritical care is provided. Management followed the institutional CREVICE protocol, which emphasizes serial neurological assessment, repeat imaging, ventilatory and hemodynamic optimization, metabolic stabilization, and prevention of secondary brain injury in settings without invasive multimodal neuromonitoring. Although advanced tools such as intracranial pressure monitoring were unavailable, structured protocolized care may have contributed to outcome optimization, particularly relevant in resource-limited environments.

Early administration of Cerebrolysin was another key aspect. Its use is supported by the concept of a therapeutic window in secondary axonal injury. The favorable recovery observed aligns with findings from the CAPTAIN II study and subsequent meta-analyses.^{11,12} This case also reflects the rationale of the ongoing CeLATA initiative focusing on TAI as a model for neurorestorative interventions.

Finally, emerging multimodal ultrasound-based approaches such as ReCCUs-TTECCUs may further enhance bedside assessment of intracranial dynamics and cerebral physiology where invasive monitoring is unavailable. Integration of such tools with structured protocols may improve individualized care in the future.

Conclusion

This case illustrates the potential for complete functional and cognitive recovery in severe TAI despite prolonged coma, advanced MRI and tractographic abnormalities, and the absence of invasive multimodal neuromonitoring. Early clinical suspicion, advanced neuroimaging confirmation, structured neurocritical care based on the CREVICE protocol, and timely administration of Cerebrolysin may have contributed to the favorable outcome observed in this patient.

CASE SUMMARY



Patient

- 18 years
- Severe traumatic axonal injury



Challenge

- Prolonged coma after severe TBI



Treatment

- Cerebrolysin 30 mL/day IV × 10 days + neurocritical care



Outcome

- GOSE 5 → 8
- Complete functional recovery



Take Home Message

Even after severe TAI with prolonged coma and extensive MRI abnormalities, complete cognitive and functional recovery may be achieved, if the combination of early diagnosis, advanced neuroimaging and timely Cerebrolysin administration are provided.



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...in the management of anterior spinal artery syndrome

Abstract

Background: Anterior spinal artery syndrome is a rare ischemic myelopathy with limited evidence for disease-specific pharmacological treatment, and its prognosis is often variable and may be unfavorable. Cerebrolysin has been investigated as a neurorecovery agent after cerebral ischemic stroke, but its role in spinal cord ischemia remains uncertain. We report this case because neurological and radiological improvement was observed after multimodal management that included adjunctive Cerebrolysin and structured neurological rehabilitation.

Case presentation: A 78-year-old man with no known chronic diseases was admitted with tetraparesis and sensory disturbance involving the trunk and lower limbs. Symptoms first occurred 3 days before hospitalization, lasted approximately 30 minutes, and relapsed 2 days later with persistence. Neurological examination showed severe upper-limb paresis, marked bilateral lower-limb paresis, loss of pain and temperature sensation from the C7 dermatome downward, preserved symmetric upper-limb deep tendon reflexes, and absent lower-limb reflexes. Cervical MRI demonstrated elevated STIR signal in the anterior spinal cord with an “owl-eyes” appearance, consistent with anterior spinal cord involvement at the C7 level. A compression fracture of the C7 vertebral body and C6/C7 disc protrusion causing minor spinal cord compression were also identified. Anterior spinal artery syndrome attributed to local cervical structural pathology was diagnosed. Surgical treatment was not undertaken. The patient received intravenous steroids, Cerebrolysin infusions at 30 mL/day for 21 days, antiplatelet and lipid-lowering therapy, venous thromboembolism prophylaxis, and neurological rehabilitation. After approximately 40 days of rehabilitation, paresis and sensory deficits decreased; the patient could stand independently and walk with a walker. At 6 months, neurological examination showed further reduction of lower-limb paresis, and follow-up MRI showed a less intense spinal cord lesion without edema.

Conclusion: This case illustrates neurological and radiological improvement after combined conservative treatment, adjunctive Cerebrolysin, and structured rehabilitation in anterior spinal artery syndrome. A biologically plausible but unproven mechanism is that Cerebrolysin may help stabilize the blood–spinal cord barrier, by analogy with experimental evidence suggesting protection of blood–brain barrier integrity through reduced endothelial permeability and preservation of tight-junction proteins. However, causality cannot be established from a single case. Recovery may have reflected acute supportive therapy, rehabilitation, spontaneous neurological improvement, neurorestorative treatment, blood–spinal cord barrier stabilization, or a combination of these factors. Prospective data are needed before routine Cerebrolysin use can be recommended for spinal cord ischemia.

Keywords: Anterior spinal artery syndrome; spinal cord infarction; Cerebrolysin; neurorehabilitation; case report.

Introduction

Anterior spinal artery syndrome is an uncommon cause of acute myelopathy caused by ischemia in the territory supplying the anterior two-thirds of the spinal cord. The typical clinical pattern combines motor weakness below the lesion with loss of pain and temperature sensation, with relative sparing of posterior column modalities. Etiologies overlap with cerebral stroke mechanisms but also include aortic disease or procedures, hypotension, embolic disease, degenerative or traumatic spinal pathology, vertebral fracture, and disc-related vascular compromise [1-4].

Magnetic resonance imaging is central to diagnosis. T2/STIR hyperintensity in the anterior cord, frequently described as the owl-eyes or snake-eyes sign on axial images, supports anterior horn and anterior cord involvement, although the sign is not entirely specific and must be interpreted with the clinical context and differential diagnosis [1,5]. Evidence for acute pharmacological treatment is limited; care generally emphasizes urgent recognition, exclusion of compressive lesions, individualized antithrombotic or vascular-risk management, prevention of complications, and early rehabilitation [2-4,6].

Cerebrolysin is a porcine brain-derived peptide preparation investigated primarily in cerebral ischemic stroke and neurorehabilitation. In the CARS randomized trial, Cerebrolysin 30 mL/day for 21 days beginning 24-72 hours after stroke onset plus standardized rehabilitation was associated with improved upper-limb motor recovery compared with placebo, but extrapolation to spinal cord ischemia is uncertain [7]. Recent prospective and propensity-matched stroke cohorts also reported favorable functional and safety signals when Cerebrolysin was used as an adjunct to successful endovascular reperfusion, although these findings remain exploratory and require randomized confirmation [12,13].

This case describes a patient with cervical anterior spinal artery syndrome who improved clinically and radiologically after multimodal treatment including Cerebrolysin. The exact mechanism of the recovery remains uncertain. The blood-spinal cord barrier (BSCB) is the spinal cord functional counterpart of the blood-brain barrier, formed by specialized endothelial cells with tight junctions, pericytes, basement membrane, and astrocytic end-feet. BSCB disruption can permit inflammatory cells and blood-derived mediators to enter spinal cord parenchyma, potentially amplifying edema and secondary injury after traumatic or ischemic spinal insults [9,10]. Because Cerebrolysin has been shown experimentally to reduce impaired cerebral endothelial permeability and preserve tight-junction proteins in a blood-brain barrier model, a similar BSCB-stabilizing effect in spinal cord ischemia is biologically plausible but unproven [11].

Patient Information

A 78-year-old man was admitted to the Neurology Department with tetraparesis and sensory disorders of the trunk and lower extremities. He had no known chronic diseases. Available family, psychosocial, medication, and vascular risk-factor histories were unremarkable in the source documentation. The first neurological episode occurred 3 days before hospitalization and lasted approximately 30 minutes. Symptoms relapsed 2 days later and then persisted, prompting hospital admission.

Clinical Findings

On admission, neurological examination revealed severe upper-limb paresis and marked bilateral lower-limb paresis. Pain and temperature sensation were reduced from the C7 dermatome downward. Deep tendon reflexes in the upper limbs were present and symmetric, whereas lower-limb reflexes were absent. Pyramidal signs and bladder dysfunction were not present.

Timeline

Table 1: Clinical course and treatment timeline

Time Point	Clinical events and management
3 days before admission	Transient tetraparesis and sensory symptoms lasting approximately 30 minutes.
1 day before admission	Relapse of symptoms with persistence, prompting neurological admission.
Admission	Neurological examination showed tetraparesis, dissociated sensory loss from C7 downward, preserved upper-limb reflexes, and absent lower-limb reflexes. Cervical MRI showed anterior cord STIR hyperintensity with an owl-eyes appearance plus C7 compression fracture and C6/C7 disc protrusion.
Hospital day 5	Because neurological status remained unchanged, Cerebrolysin 30 mL/day IV was started for 21 days as an adjunct to conservative treatment.
Approximately 40 days of rehabilitation	Paresis and sensory deficits decreased; the patient could stand independently and walk with a walker.
6-month follow-up	Further reduction of lower-limb paresis; control MRI showed a less intense spinal cord lesion without edema.

Diagnostic Assessment

Cervical spine MRI performed on admission showed elevated STIR signal in the anterior spinal cord, described as the owl-eyes sign. MRI also showed a compression fracture of the C7 vertebral body and protrusion of the C6/C7 intervertebral disc causing minor spinal cord compression. CSF analysis, aortic/spinal vascular imaging, laboratory tests, and cardiac/embolic work-up were reported as normal in the source documentation. The final diagnosis was anterior spinal artery syndrome, considered secondary to cervical structural pathology with presumed compromise of the anterior spinal artery or its local supply.

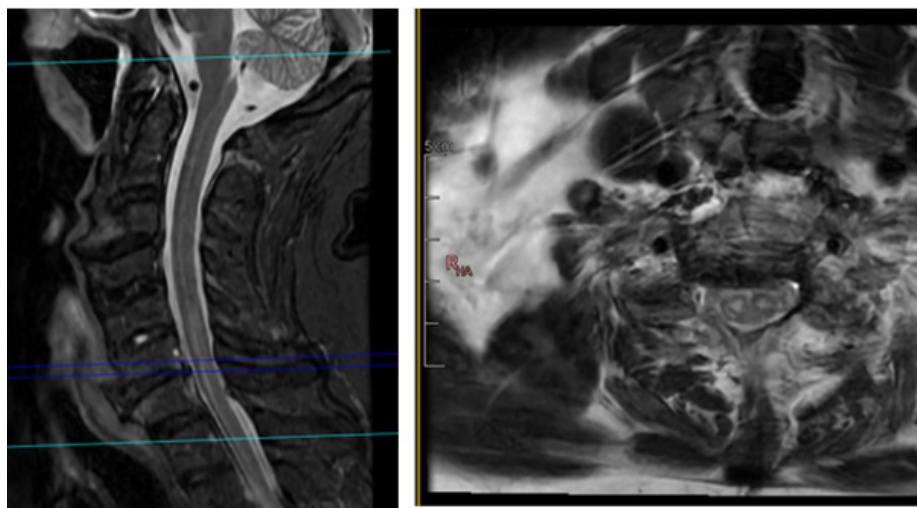


Figure 1: Cervical MRI on admission. Sagittal and axial images from the supplied poster show anterior cord involvement with an owl-eyes appearance on axial imaging, together with cervical structural pathology.

Therapeutic Intervention

The patient was assessed as not suitable for surgical treatment. Acute and secondary-prevention management consisted of intravenous dexamethasone 8 mg three times daily, antiplatelet therapy, lipid-lowering therapy, and venous thromboembolism prophylaxis. Because the neurological status remained unchanged by hospital day 5, adjunctive Cerebrolysin was initiated at 30 mL/day intravenously for 21 days. The patient subsequently underwent structured neurological rehabilitation.

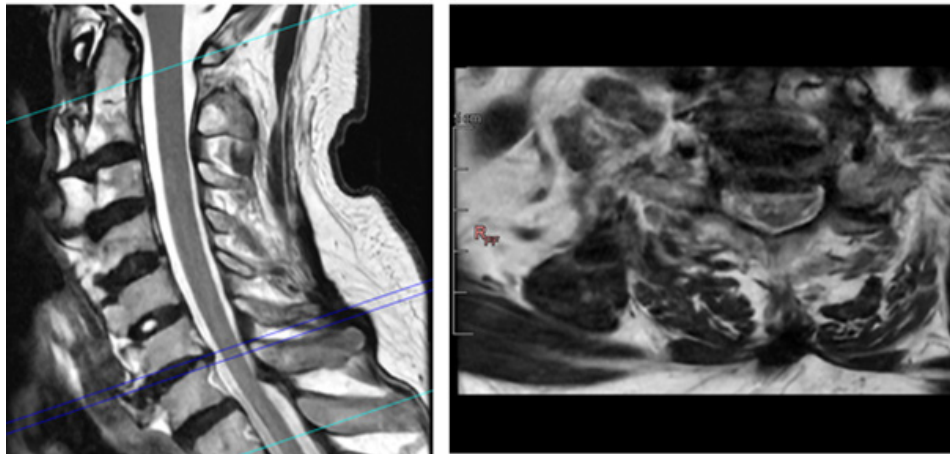


Figure 2: Cervical MRI after 6 months. Follow-up sagittal and axial images from the supplied poster show less intense cord signal abnormality and no edema compared with baseline imaging.

Follow-up and Outcomes

After approximately 40 days of rehabilitation, the neurological examination showed significant symptom reduction. The patient had only slight global lower-limb muscle weakness and distal upper-limb weakness. He could stand independently and ambulate with the help of a walker. Pain and temperature sensory disorders in the trunk and lower extremities had decreased.

At 6 months, neurological follow-up showed further improvement with reduction of lower-limb paresis. Control MRI showed a less intense signal from the lesion and no edema. No adverse or unanticipated events were reported by the patient.

Discussion

Interpretation and relevance

This case is clinically relevant because it documents neurological and radiological improvement in an older patient with cervical anterior spinal artery syndrome after multimodal treatment including adjunctive Cerebrolysin. To our knowledge, this is the first reported case of Cerebrolysin administration in anterior spinal artery syndrome.

The clinical syndrome was compatible with anterior spinal cord involvement: tetraparesis, loss of pain and temperature sensation below C7, and MRI evidence of anterior cord signal abnormality. The presence of C7 compression fracture and C6/C7 disc protrusion provides a plausible local mechanism, as vertebral fracture and degenerative or disc-related cervical pathology have been reported as less common causes of anterior spinal artery syndrome [1,2].

Cerebrolysin was used as an adjunct to standard medical and rehabilitation measures. In cerebral ischemic stroke, randomized and meta-analytic evidence has suggested possible neurorecovery benefits, especially when combined with rehabilitation, but evidence quality, heterogeneity, and generalizability remain important limitations [7,8]. In addition, Cerebrolysin has been evaluated as an add-on therapy after mechanical thrombectomy in acute ischemic stroke cohorts, including different studies, with exploratory signals toward improved functional outcomes and reduced hemorrhagic complications in selected patients [12,13]. There are no robust prospective data demonstrating efficacy in spinal cord ischemia. Consequently, improvement in this case should be interpreted as hypothesis-generating rather than proof of treatment effect.

Mechanistic considerations: blood-spinal cord barrier and Cerebrolysin

The BSCB is not simply a passive anatomical boundary. Like the BBB, it contributes to central nervous system homeostasis by limiting paracellular flux through endothelial tight junctions and by regulating exchange between the systemic circulation and spinal cord tissue. Disruption of this barrier after spinal cord injury or ischemia-reperfusion may expose the cord to inflammatory mediators, plasma proteins, and immune-cell trafficking, thereby promoting vasogenic edema, secondary inflammatory injury, and delayed neurological deterioration [9,10].

This provides a mechanistic hypothesis for the present observation. Cerebrolysin has experimental evidence of endothelial barrier protection in BBB-related models: it reduced tPA- and fibrin-impaired cerebral endothelial permeability, downregulated proinflammatory and procoagulant proteins, and increased tight-junction proteins including zonula occludens-1, occludin, and claudin [11]. By analogy, Cerebrolysin could hypothetically mitigate secondary spinal cord injury through BSCB stabilization, although no direct clinical evidence currently proves this mechanism in anterior spinal artery syndrome.

Strengths and limitations

Strengths of this case report include a clear temporal sequence, characteristic clinical and MRI findings, use of follow-up MRI, and functional follow-up showing clinically meaningful recovery. The report also highlights an uncommon therapeutic approach that may inform future case aggregation or registry design.

Limitations are substantial. This is a single case without a control, recovery after spinal cord infarction can occur gradually with rehabilitation, and the contribution of Cerebrolysin cannot be separated from spontaneous recovery, steroids, secondary-prevention therapy, thromboprophylaxis, and rehabilitation.

Take-away lessons

Anterior spinal artery syndrome should be considered in acute or recurrent cervical myelopathy with motor weakness and dissociated sensory loss. MRI evidence of anterior cord involvement, especially an owl-eyes pattern, supports the diagnosis but should be interpreted with competing diagnoses in mind. In this case, multimodal therapy including adjunctive Cerebrolysin and rehabilitation was followed by functional and MRI improvement. A biologically plausible but unproven mechanism is blood-spinal cord barrier stabilization, by analogy with experimental evidence for Cerebrolysin-related protection of cerebral endothelial barrier function. The observation warrants careful reporting and further study, not routine therapeutic adoption.

CASE SUMMARY



Patient

• 78 years • Anterior spinal artery syndrome



Challenge

• Tetraparesis and sensory loss



Treatment

• Cerebrolysin 30 mL/day IV x 21 days + rehabilitation



Outcome

• Independent standing • Assisted walking • MRI improvement at 6 months



Take Home Message

In anterior spinal artery syndrome, stabilization of the blood–spinal cord barrier represents a promising cerebroprotective target, with Cerebrolysin as a potential adjunct to support neurorecovery, although clinical efficacy remains to be established.



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...after surgical excision of cerebral glioma

Abstract

Multimodal treatment of patients with a brain tumor primarily involves microsurgical excision, ideally radical, or at least subtotal resection. Tumors in deep or inaccessible locations may require biopsy followed by adjuvant therapy with chemotherapy, radiotherapy, or radiosurgery. Beyond controlling tumor growth, preserving neurological function and promoting brain plasticity are essential goals. Persistent inflammation and intracranial hypertension can trigger secondary injury through edema, excitotoxicity, and ischemia, potentially resulting in irreversible neuronal damage. Multimodal strategies, including neuroprotective measures such as Cerebrolysin administration, may help prevent or mitigate these secondary processes, supporting recovery and functional outcomes. Clinically, patients may present with headache, nausea, vomiting, seizures, or subtle cognitive and motor deficits, progressing in severe cases to deterioration of consciousness. Incorporating cerebroprotective interventions in perioperative management represents a promising approach to enhance recovery, functional independence, and quality of life in neurosurgical oncology patients.

Keywords: cerebral glioma, Cerebrolysin, brain protection, multimodal neurooncological treatment

Introduction

Gliomas represent one of the most challenging tumors in neuro-surgery due to their infiltrative growth pattern, high recurrence rate, and the difficulty of achieving complete surgical excision without causing significant neurological deficits. Despite advances in microsurgical techniques, intraoperative navigation, and perioperative multimodal management, the prognosis of patients with high-grade gliomas remains poor, with survival and quality of life significantly affected by the balance between aggressive tumor resection and preservation of neurological function [1].

Tumor resection, whether subtotal or radical, is often accompanied by peri-tumoral edema, ischemia, and secondary inflammatory cascades that compromise the viability of adjacent tissue. This so-called 'penumbra zone' represents an area of vulnerable but potentially salvageable brain parenchyma [2,3]. Protecting this zone and enhancing functional recovery are therefore crucial objectives in glioma surgery.

In recent years, the concept of cerebroprotection has gained increasing relevance, not only in acute stroke and traumatic brain injury but also in the context of planned neurosurgical interventions [4-9]. While cranial surgery for tumor resection is a controlled procedure, it invariably produces mechanical and biochemical stress comparable to brain trauma. Surgical manipulation, vascular compromise, ischemia-reperfusion injury, and postoperative edema all contribute to neuronal dysfunction and the risk of long-term disability [10,11]. Thus, the application of cerebroprotective agents during and after glioma surgery offers a rational therapeutic strategy to minimize iatrogenic damage, facilitate neuroplasticity, and improve clinical outcomes [5,7,9,12]. Cerebrolysin, a neuropeptide preparation with documented neuroprotective and neurorestorative properties, has shown promise in conditions such as traumatic brain injury, stroke, and neurodegenerative diseases [4-

9,13,14]. Its mechanisms include the modulation of neurotrophic signaling, anti-apoptotic effects, reduction of excitotoxicity, and promotion of synaptic remodeling and neurogenesis [1]. Translating these benefits into the multimodal management of glioma patients represents a novel but logical extension of its therapeutic use.

We present a case in which multimodal treatment, including Cerebrolysin, was employed as an adjuvant treatment following surgical resection of an anaplastic astrocytoma. This report highlights the potential role of cerebroprotection in planned neurosurgical oncology, aiming to optimize patient recovery and quality of life beyond the oncological control of the disease.

Patient Information

A 50-year-old woman with no significant medical history presented with severe, disabling headaches unresponsive to analgesics. Neurological assessment and MRI revealed a temporal lobe intracranial tumor. In October 2019, a biopsy confirmed an anaplastic astrocytoma, Grade III. The patient subsequently underwent subtotal tumor resection, followed by adjuvant chemotherapy with Temozolomide (200 mg/m² daily for 42 days) and holocranial radiotherapy (3 Gy/day for 10 days) at another hospital.

The patient came for a second opinion, with imaging findings consistent with a left temporal lesion suggestive of residual or recurrent glioma, resistant to previous radio- and chemotherapy.

Follow-up imaging, PET-CT, documented a left fronto-temporal residual lesion with extensive cerebral hypoperfusion and ischemia secondary to the tumor, as well as hypermetabolic areas corresponding to residual-recurrent tumor (Figure 1). Neurological evaluation revealed intact cranial nerves and cerebellar function, but right hemiparesis (3/5 on the Daniels scale) with preserved muscle stretch reflexes.

The second surgical procedure was performed without intra-operative complications (Figure 2). Two weeks after the second glioma resection, the patient developed cerebral edema that was unresponsive to conservative management, including conventional doses of dexamethasone. Consequently, a decompressive craniectomy with duroplasty was performed (Figure 3). Following this procedure, antibiotic and analgesic therapy were included in the postoperative treatment plan.

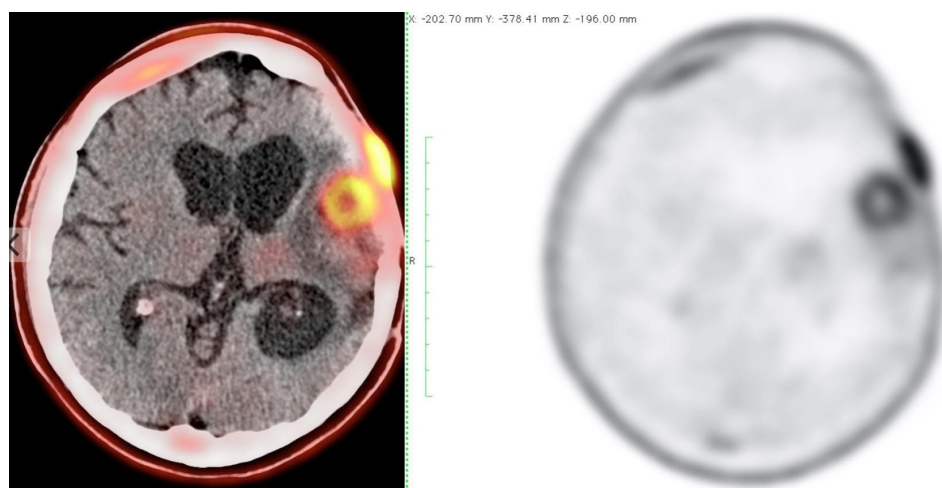


Figure 1: Pet CT scan FDG. Hypermetabolic temporal lesion compatible with residual or recurrent lesion.

After a multidisciplinary discussion involving the oncology, internal medicine, and neurosurgery teams, it was decided to initiate Cerebrolysin therapy immediately after surgery. Before administering the treatment, informed consent was obtained from the patient's family. The patient received Cerebrolysin according to the treatment schedule shown in Table 1.

At home, 3 days after surgery, the patient began a physical rehabilitation program as outlined below.

She attended sessions three times per week in the afternoons. During the initial assessment, she presented with right-sided hemiplegia—the right upper limb was in the flaccid stage, while the right lower limb exhibited hypotonia with no activity in the anterior tibial muscle. Her emotional state was characterized by reluctance and poor cooperation with treatment.

Rehabilitation was initiated using proprioceptive neuromuscular facilitation (PNF) techniques, functional exercises, Russian current electrostimulation, stretching of muscle chains, and both passive and active joint

mobility exercises. The main objectives were to restore trunk control, mobility, and strength in the right lower limb to improve gait and facilitate transfers (e.g., from bed to wheelchair and from wheelchair to dining area), while also addressing recovery of the right upper limb.

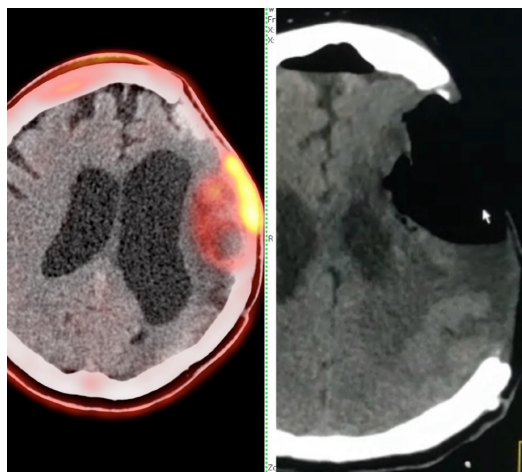


Figure 2: Pre- and postoperative cranial tomography

Over the following 4 weeks, the patient showed positive progress. In the right lower limb, active mobility was achieved with limited hip range of motion, knee hyperextension, and a plan-tar-pointed foot position, but with improved mobility in all five toes, indicating the onset of an extensor synergy. The right upper limb also demonstrated improvement, with activation of the deltoid and biceps muscles, leading to a flexor synergy pattern that enabled active elbow flexion and finger flexion with thumb opposition.

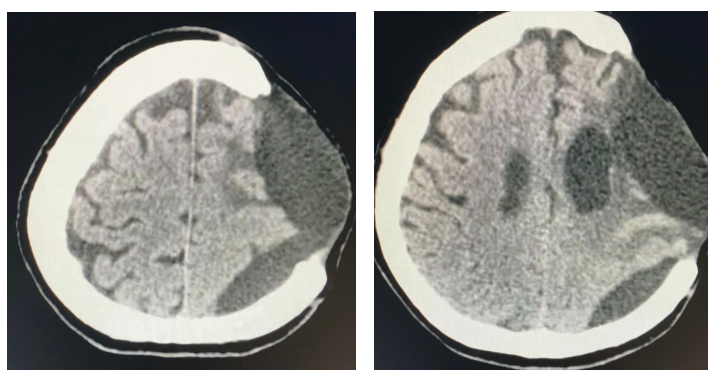


Figure 3: Simple cranial tomography after decompressive craniotomy

A few months later, with continued rehabilitation, the patient was able to walk with the assistance of a four-point cane and an ankle-foot orthosis (AFO), which helped prevent tripping. Due to knee hyperextension, a knee brace with adjustable side bars was used, enabling the patient to ambulate approximately 20 meters. In the right upper limb, improvements were also noted: shoulder flexion reached 30°, shoulder extension 15°, shoulder abduction 20°, and elbow flexion 90°. Recovery of finger extension and hand opening progressed more slowly compared to the lower limb. However, rehabilitation was temporarily suspended due to the COVID-19 pandemic.

Finally, a cranioplasty using a PEEK mesh was performed, with a favorable outcome during the late postoperative period (Figure 4). Clinical observations revealed a significant improvement in motor function, particularly in manual force, as assessed by the Daniels scale (improved from 3 to 4.5 points), and in independent standing and walking, as reflected in Barthel Index scores before and after Cerebrolysin treatment (Table 2).

The patient's neurological state improved considerably, as evidenced by the clinical assessment, leading to a notable improvement in her quality of life and that of her caregivers. Preoperative and postoperative MRI follow-up was conducted, with an 8-month interval between the first and second postoperative scans following multimodal treatment. The follow-up MRI revealed no evidence of residual tumor or recurrence, showing only postsurgical changes (Figures 5–7).

The patient demonstrated favorable clinical progress compared with her preoperative condition, achieving independence in daily activities and self-feeding. However, during subsequent clinical and radiological follow-up, the patient contracted COVID-19 and unfortunately passed away due to complications related to the

infection.

Table 1: Cerebrolysin schedule

Renacenz (Cerebrolysin) Injectable Solution 10 ml				
	1st Week	2nd Week	3rd Week	4th Week
Monday	5 vials plus 50 ml of saline solution to be infused over 1.5 hours	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour
Tuesday	5 vials plus 50 ml of saline solution to be infused over 1.5 hours	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour
Wednesday	5 vials plus 50 ml of saline solution to be infused over 1.5 hours	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour
Thursday	5 vials plus 50 ml of saline solution to be infused over 1.5 hours	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour
Friday	5 vials plus 50 ml of saline solution to be infused over 1.5 hours	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour	3 vials plus 70 ml of saline solution to be infused over 1 hour



Figure 4: Cranioplasty with Peek's mesh

Table 2: Barthel Index before and after Cerebrolysin multimodal adjuvant treatment

Barthel Scale	Feeding	Grooming Aseo personal	Dressing	Bladder and Bowel Control	Mobility	Ambulation	Total Index
T0. Pre-Cerebrolysin	0	0	0	10	5	5	20
T1-2 weeks	5	5	5	10	5	5	35
T2- End Cerebrolysin Treatment	5	5	5	10	5	10	40
T3-3-month Follow- up	10	5	10	10	10	10	55

Discussion

The conventional management of cerebral edema and ischemia following tumor resection relies on corticosteroids, osmotic agents, and in severe cases, decompressive craniectomy [8]. These strategies, while

effective in reducing acute intracranial hypertension, do not address the long-term mechanisms of neuronal injury, including excitotoxicity, oxidative stress, and apoptosis [15]. More-over, they do not actively promote brain repair or neuroplasticity. In this regard, cerebroprotective and neurorestorative therapies offer a valuable adjunct to standard care [5,7,9,12].

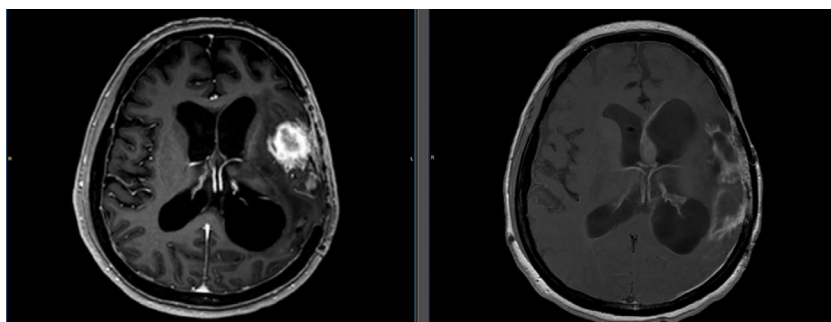


Figure 5: Axial preoperative and postoperative MRI scans obtained 8 months after multimodal treatment

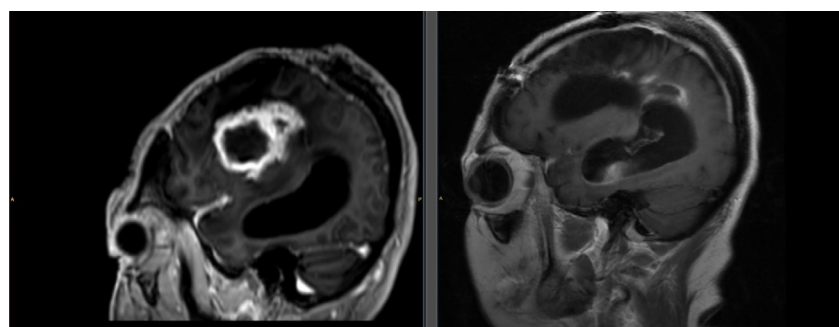


Figure 6: Sagittal MRI images before and after multimodal treatment

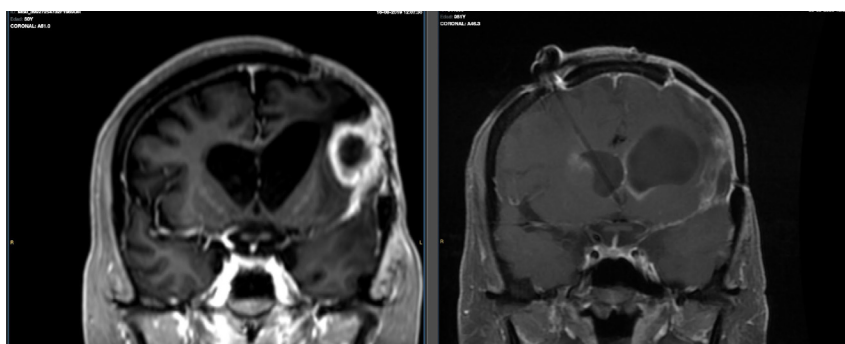


Figure 7: Coronal MRI images before and after multimodal treatment

Cerebrolysin has been extensively studied in the setting of traumatic brain injury and ischemic stroke, where its administration has been associated with improved functional recovery, reduced lesion expansion, and enhanced cognitive outcomes [4-9]. The underlying rationale is that acute brain injury—whether traumatic, vascular, or surgical—triggers a similar cascade of secondary damage, involving glutamate excitotoxicity, mitochondrial dysfunction, free radical production, and activation of pro-inflammatory pathways [16,17]. Glioma surgery, though elective, shares many of these pathophysiological features due to tumor-induced mass effect, peri-tumoral ischemia, and surgical manipulation [1].

In the present case, the administration of Cerebrolysin as a multimodal strategy following tumor resection and decompressive surgery could be related to functional improvement in motor strength and independence, despite the unfavorable baseline prognosis of a high-grade glioma. While this outcome cannot be attributed solely to pharmacological intervention, it suggests that the cerebroprotective therapy may have contributed to the rescue of peri-lesional tissue and to the enhancement of neuroplasticity during recovery [5,7,9,12]. The relevance of cerebroprotection and multimodal treatment in planned neurosurgery lies not only in minimizing immediate postoperative deficits but also in improving long-term quality of life. With advances in oncological therapies extending survival, functional preservation has become an equally

important goal of care. Patients surviving with profound neurological deficits face significant limitations, caregiver burden, and reduced quality of life. Therefore, multimodal treatment and the incorporation of neuroprotective strategies in perioperative protocols may help shift outcomes from mere survival to meaningful recovery [1].

Importantly, the field lacks randomized controlled trials evaluating the role of Cerebrolysin or similar agents in brain tumor surgery. Most evidence is derived from stroke and traumatic brain injury literature, and extrapolation to glioma surgery remains hypothetical [4-7]. Nonetheless, the overlapping mechanisms of injury provide a strong rationale for such investigations. Furthermore, as surgery-induced brain trauma is predictable and temporally controlled, it represents an ideal setting to test prophylactic and perioperative cerebroprotective interventions [1].

Future research should focus on establishing standardized multimodal treatment protocols and exploring the role of neuroprotective and neurorestorative agents, such as Cerebrolysin, within integrated strategies that include surgery, rehabilitation, and neurorehabilitation. Until then, individual cases such as the one presented here may help generate hypotheses and encourage the design of controlled clinical studies.

Conclusion

The multimodal treatment, including surgical resection, rehabilitation, and neurorestorative therapy, demonstrates that, beyond tumor resection and standard oncological therapies, the use of cerebroprotective agents may support functional recovery in patients undergoing complex neurosurgical procedures.

While the role of cerebroprotection in planned neurosurgery is not yet established, our early experience suggests that it could represent an important adjunct to multimodal care.

Future controlled studies in brain tumor patients are warranted to determine the efficacy, safety, and optimal integration of Cerebrolysin into perioperative treatment protocols.

Consent to publish

Consent was obtained from the patient and her family for the publication of this clinical case report and any accompanying images.

CASE SUMMARY



Patient

• 50 years • Recurrent anaplastic astrocytoma (Grade III)



Challenge

• Postoperative hemiparesis and refractory cerebral edema



Treatment

• Cerebrolysin 30-50 mL/day IV x 28 days + rehabilitation



Outcome

• Daniels Scale 3 → 4.5 • BI 20 → 55 • Independent standing and assisted walking regained



Take Home Message

Following glioma resection, Cerebrolysin may support peri-lesional tissue preservation and neuroplasticity, potentially promoting functional recovery and quality of life beyond survival.

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...after intramedullary spinal cord tumor surgery

Abstract

Postoperative neurological deterioration remains a feared complication of intramedullary spinal cord tumor surgery, even with modern microsurgical and electrophysiological techniques. Evidence for pharmacologic neurorecovery strategies beyond corticosteroids is limited. We report a 35-year-old man who underwent microsurgical resection of a presumed cervical intramedullary ependymoma under full neuromonitoring. Despite stable intraoperative somatosensory evoked potentials, motor evoked potentials, and D-wave signals, he awoke with profound quadriparesis, including complete loss of lower-limb motor power. Standard intensive care management with high-dose corticosteroids and early physiotherapy was initiated. In addition, off-label Cerebrolysin was started on postoperative day 0 at 30 mL intravenously daily for 14 days, followed by 5 mL daily for 60 days. Histopathology unexpectedly revealed malignant lymphoma. The patient showed progressive neurological recovery: supported standing by 2 weeks, walker-assisted ambulation by 1 month, and cane-assisted ambulation by 2 months. Follow-up magnetic resonance imaging demonstrated complete lesion resolution and marked edema subsidence.

Keywords: Cerebrolysin, intramedullary spinal cord tumor, postoperative spinal cord injury, neurorecovery, case report

Introduction

Intramedullary spinal cord tumors are uncommon and surgically challenging lesions. Even with advances in microsurgical techniques and intraoperative neuromonitoring, postoperative weakness may occur because of unavoidable manipulation of eloquent spinal cord tissue, edema, ischemia, and inflammatory secondary injury. (4,5) Corticosteroids remain the conventional perioperative strategy, but neurological recovery is often incomplete or delayed. (1-3, 6-8)

Cerebrolysin, a peptide preparation with neurotrophic and neuroprotective properties, has been studied extensively in ischemic stroke and traumatic brain injury. (1-3, 6-8) However, its use in postoperative spinal cord injury after intramedullary tumor surgery has not been well documented. (4,5) This case is presented in CARE format to highlight a possible role for early Cerebrolysin administration in enhancing postoperative motor recovery. (6-8)

Patient Information

A 35-year-old man presented with severe right brachialgia of 6 months' duration, poorly responsive to medical therapy and worsening after physiotherapy. Initial cervical magnetic resonance imaging (MRI) showed only mild multilevel disc bulges that did not explain symptom severity, although a faint intramedullary hyperintense cord signal was retrospectively appreciable (Figure 1).

Over the following 2 months, the patient deteriorated rapidly, developing heaviness of the right lower limb and wasting of the intrinsic muscles of the right hand, while the brachialgia persisted.



Figure 1: MRI cervical spine T2 WI sagittal view showing multiple mild cervical disc bulge that do not explain the patient severe symptoms. Note the faint hyperintense signal within the cord.

Clinical Findings

Neurological examination before surgery demonstrated progressive myelopathic features with right-sided upper-limb muscle wasting and lower-limb heaviness, raising suspicion of an intramedullary cervical cord lesion.

Timeline

Table 1: Clinical course and treatment timeline

Time point	Clinical course
Initial presentation	Severe right brachialgia, nondiagnostic MRI
2 months later	Rapid deterioration with right leg heaviness and hand wasting
Preoperative workup	Contrast MRI, spectroscopy, perfusion, tractography suggest ependymoma
Surgery day	Microsurgical gross total resection under SSEP/MEP/D-wave monitoring
Postoperative day 0	Profound quadriparesis; Cerebrolysin 30 mL/day started
2 weeks	Able to stand with physiotherapist support
1 month	Ambulating with walker
2 months	Walking with cane; MRI shows lesion and edema resolution

Diagnostic Assessment

Repeat contrast-enhanced cervical MRI revealed an oblong intramedullary enhancing mass with extensive cord edema above and below the lesion (Figure 2). Advanced imaging, including MR spectroscopy, perfusion, and tractography, strongly favored ependymoma. Based on the radiological appearance and the patient's rapid progression, surgical resection with curative intent was planned. The principal diagnostic challenge was the misleading radiological phenotype. All preoperative studies suggested a benign intramedullary ependymoma, whereas final pathology demonstrated primary malignant lymphoma in an extremely rare intramedullary location (Figure 3).

Therapeutic Intervention

The patient underwent microsurgical excision through a posterior cervical approach. Gross total resection was the operative goal because the lesion was presumed benign. Intraoperative neuromonitoring with somatosensory evoked potentials, motor evoked potentials, and D-wave remained satisfactory throughout

the procedure. A 2 g infusion of methylprednisolone was administered during tumor dissection. Central myelotomy was performed with the aid of a nerve stimulator to accurately identify the midline, followed by microsurgical excision under high magnification.

Despite stable monitoring, the patient emerged with severe postoperative neurological deterioration: 0/5 motor power in both lower limbs and only gravity-assisted movements in both upper limbs. He was transferred immediately to the intensive care unit.

Postoperative management included continuation of methylprednisolone for 3 days followed by dexamethasone, intensive early physiotherapy, and off-label Cerebrolysin initiated on postoperative day 0. The Cerebrolysin regimen consisted of 30 mL intravenous infusion daily for 14 days, followed by 5 mL daily for 60 days.

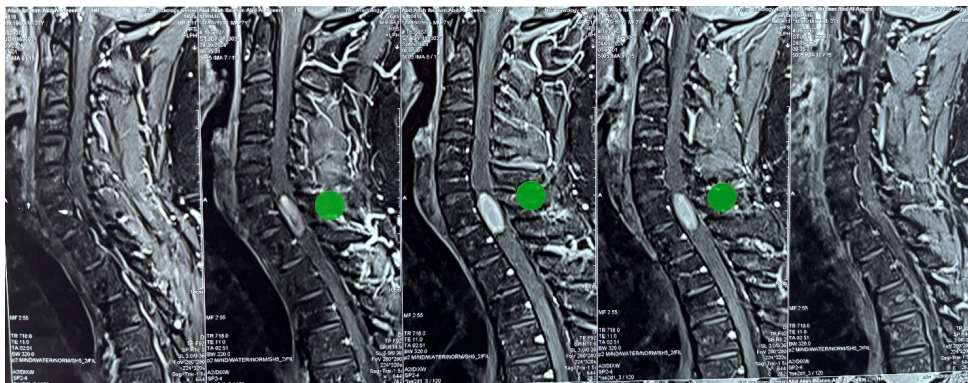


Figure 2: MRI cervical spine T1WI with contrast showing oblong shaped hyperintense intramedullary mass with extensive cord edema above and below the lesion.

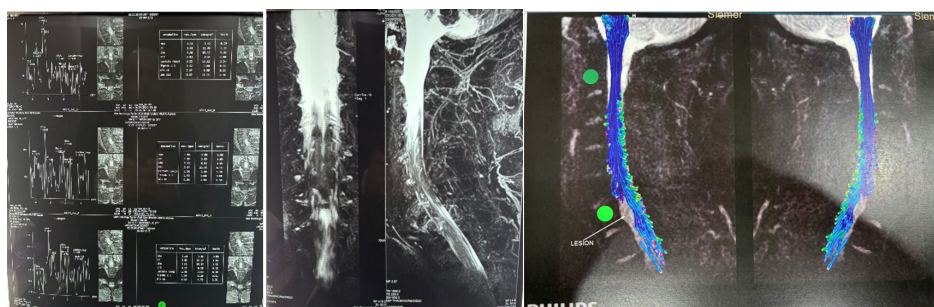


Figure 3: MRI spectroscopy, perfusion and tractography for the lesion all aimed at ependymoma.

Follow-Up and Outcomes

Neurological recovery was progressive and clinically meaningful. By the end of the second postoperative week, the patient was able to stand with physiotherapist assistance. At 1 month, he was walking with a walker. By the end of the second month, he was independently ambulatory with mild cane support.

Histopathology unexpectedly confirmed malignant lymphoma, prompting referral to oncology 1 month after surgery for staging and adjuvant chemoradiotherapy planning after positron emission tomography.

Follow-up cervical MRI at 2 months demonstrated complete resolution of the intramedullary lesion with marked subsidence of surrounding cord edema (Figure 4). No adverse effects attributable to Cerebrolysin were observed during the treatment period.

Discussion

This case illustrates three important clinical lessons. First, rare intramedullary lymphoma may radiologically mimic ependymoma, even when advanced imaging techniques are used. Second, profound postoperative deficits may occur despite stable intraoperative neuromonitoring, likely reflecting secondary injury mechanisms rather than immediate tract interruption alone. Third, early neurorecovery therapy may be valuable in selected cases.(6-8)

The patient's severe postoperative weakness was disproportionate to the intraoperative monitoring findings. A plausible explanation is secondary neuronal injury from edema, inflammatory cascades, oxidative stress, and free-radical-mediated cellular dysfunction after manipulation of an infiltrative malignant lesion. The extensive

preoperative edema likely increased susceptibility to this phenomenon. (4, 5)
The degree and speed of recovery in this case were notable given the immediate postoperative status. Conventional contributors such as corticosteroids, decompression, edema resolution, and intensive rehabilitation undoubtedly played an important role. However, the addition of early Cerebrolysin may have augmented recovery through several biologically plausible mechanisms.(1-3, 8)

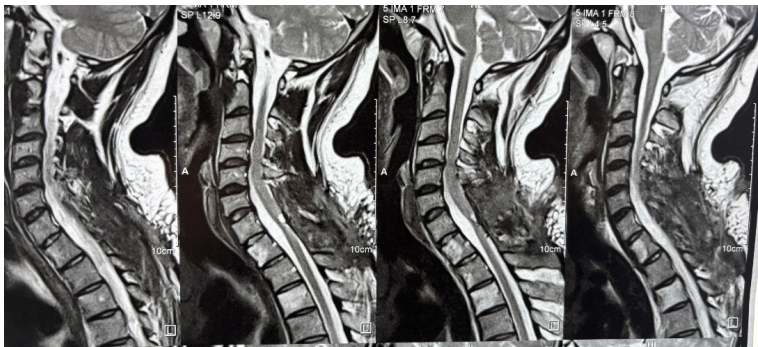


Figure 4: MRI cervical spine T2 sagittal view showing complete subsidence of the intramedullary lesion with resolution of the edema.

Cerebrolysin contains low-molecular-weight neuropeptides and amino acids that mimic endogenous neurotrophic factors, including brain-derived neurotrophic factor, nerve growth factor, glial-derived neurotrophic factor, and ciliary neurotrophic factor. These pathways support neuronal survival, axonal sprouting, synaptogenesis, and functional reorganization.(1, 3, 8) Experimental literature also suggests anti-inflammatory effects through reduction of pro-inflammatory cytokines, attenuation of oxidative injury, and promotion of neurovascular remodeling and neurogenesis.(1-5)
In the context of postoperative spinal cord injury, these actions may translate into reduced secondary damage, improved synaptic reconnection, and enhanced neuroplasticity within preserved descending tracts. The patient’s recovery trajectory—from complete paraplegia to cane-assisted walking within 8 weeks—supports the hypothesis that these mechanisms may be clinically relevant.
The main limitation is that this is a single observational case without controls, preventing attribution of causality. Recovery may have resulted from decompression, steroid therapy, natural resolution of edema, rehabilitation, or the lymphoma biology itself. Nevertheless, the striking temporal association justifies further study.

Conclusion

This case suggests that early postoperative Cerebrolysin administration may be a useful adjunct in severe neurological deterioration after intramedullary spinal cord tumor surgery. Although definitive conclusions cannot be drawn from a single case, the favorable neurological recovery observed here supports further prospective investigation in postoperative spinal cord neurorecovery.

CASE SUMMARY	
 Patient	• 35 years • Postoperative spinal cord injury
 Challenge	• Profound postoperative quadriparesis
 Treatment	• Cerebrolysin 30 mL/day IV x 14 days + 5 mL/day x 60 days
 Outcome	• Standing at 2 weeks, walker-assisted ambulation at 1 month, Cane-assisted ambulation at 2 months
 Take Home Message	
Early multimodal neurorecovery incorporating Cerebrolysin and intensive rehabilitation was associated with substantial functional recovery after severe postoperative spinal cord injury, supporting prospective evaluation while acknowledging that causality cannot be established from a single case.	



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...in a patient suffering from two pathologies: TBI and AIS

Abstract

We report a 62-year-old man with poorly controlled hypertension and a recent ischemic stroke who sustained an acute traumatic brain injury (TBI) after a motor vehicle accident. Cranial imaging demonstrated a right frontal hemorrhagic contusion together with chronic left parietotemporal post-ischemic changes. After initial anti-edema treatment, Cerebrolysin 30 mL/day was administered intravenously for 7 days, beginning on day 3 after injury, together with supportive care and early mobilization. The patient showed progressive neurological recovery: Glasgow Coma Scale score improved from 12 to 14 and National Institutes of Health Stroke Scale score decreased from 7 to 3 within 14 days, with return to the pre-injury functional baseline (modified Rankin Scale 2). Follow-up neuroimaging showed regression of the traumatic lesion and surrounding edema. This case illustrates the diagnostic and therapeutic complexity of acute TBI superimposed on recent cerebrovascular disease and describes favorable short-term recovery temporally associated with multimodal management including Cerebrolysin. Because this is a single case, no causal treatment effect can be inferred.

Keywords: traumatic brain injury; Cerebrolysin; ischemic stroke; neurorecovery; hemorrhagic contusion; case report

Introduction

Traumatic brain injury (TBI) is a heterogeneous condition in which primary mechanical injury is followed by secondary processes that may include cerebral edema, altered perfusion, excitotoxicity, inflammation, oxidative stress, and metabolic dysfunction. Acute management is therefore directed primarily at preventing secondary brain injury through stabilization of oxygenation and circulation, monitoring and treatment of intracranial hypertension when indicated, appropriate neurosurgical management of mass lesions, seizure-risk assessment, and early multidisciplinary rehabilitation once the patient is clinically stable [1,2]. Despite advances in neurocritical care, no single pharmacological neurorecovery strategy is universally accepted for acute TBI, and functional recovery remains highly variable.

The clinical situation becomes more complex when TBI occurs in a patient with recent cerebrovascular disease. Residual focal deficits and chronic structural abnormalities after ischemic stroke may complicate neurological examination and interpretation of acute neuroimaging. Stroke recovery itself depends on organized multidisciplinary rehabilitation and activity-based training, while pharmacological approaches intended to enhance neuroplasticity and neurorecovery continue to be investigated [3,4].

Cerebrolysin is a parenteral neuropeptide preparation with neurotrophic and neuroprotective properties that has been studied as an adjunct to standard care in both TBI and ischemic stroke. In moderate-to-severe TBI, randomized CAPTAIN trials and their prospective meta-analysis reported favorable multidimensional functional and neuropsychological outcomes with Cerebrolysin added to usual care, with safety and tolerability

comparable to placebo [5-7]. A randomized pilot study in mild TBI with intracranial contusion hemorrhage also reported improved cognitive recovery after 30 mL/day Cerebrolysin [8]. In ischemic stroke rehabilitation, randomized studies have evaluated Cerebrolysin together with standardized rehabilitation, including 30 mL/day regimens initiated during the early recovery period [9,10]. However, evidence specifically addressing acute TBI in patients with recent stroke sequelae is scarce.

We present a patient with a recent ischemic stroke and residual neurological deficits who developed an acute right frontal hemorrhagic contusion after a motor vehicle accident. The case emphasizes diagnostic differentiation of new traumatic injury from pre-existing post-ischemic changes and describes the clinical course after multimodal treatment including early Cerebrolysin administration.

Case Presentation

A 62-year-old man was admitted 40 minutes after a motor vehicle accident with altered consciousness and disorientation. His medical history was significant for ischemic stroke 3 months earlier, resulting in mild residual right-sided weakness, and poorly controlled hypertension. Before the accident, his functional status was stable, with a modified Rankin Scale (mRS) score of 2, indicating slight disability but preserved independence in daily activities.

On admission, the patient was stuporous but responsive, with a Glasgow Coma Scale (GCS) score of 12/15 (E3V4M5). Blood pressure was 150/100 mmHg, heart rate 92 beats/min, and oxygen saturation remained above 95%. Neurological examination showed spatial disorientation with preserved orientation in time, anisoreflexia more pronounced on the right, pathological reflexes in the right wrist, and increased tone in the right upper and lower limbs, findings consistent with residual deficits from the previous stroke. Local examination identified a 3 × 2 cm superficial abrasion over the right frontal scalp.

Diagnostic Assessment

Initial cranial CT demonstrated an acute right frontal hemorrhagic contusion measuring approximately 2 × 2 cm, with mild ventricular deformation but no midline shift or skull fracture. Chronic left parietotemporal cystic-atrophic changes consistent with the previous ischemic stroke were also present. The principal diagnostic challenge was to distinguish new traumatic pathology from pre-existing post-stroke abnormalities. Correlation of the trauma history, neurological examination, and serial neuroimaging supported the diagnosis of acute TBI superimposed on chronic post-ischemic brain changes.

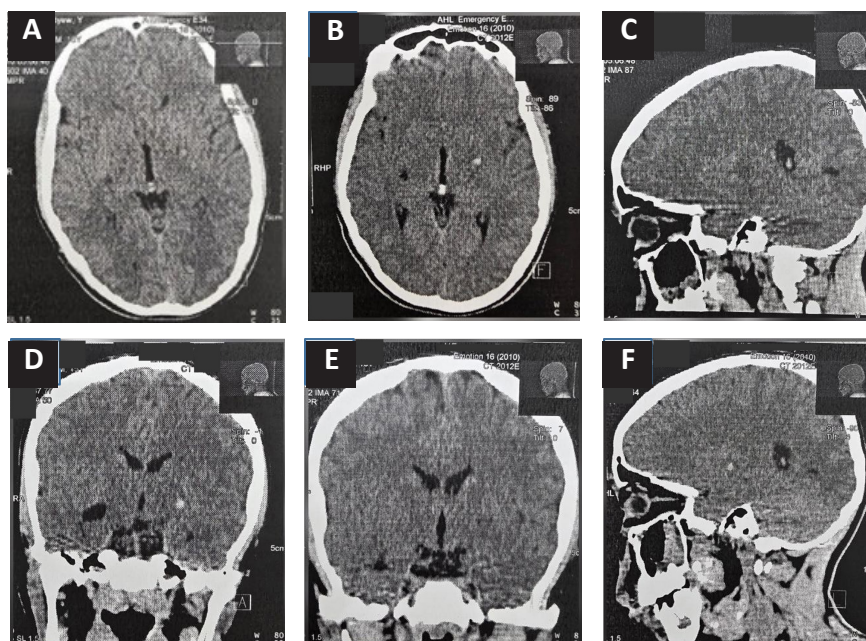


Figure 1. Multiview cranial CT panel. (A) Baseline axial CT demonstrating the acute right frontal hemorrhagic contusion; (B) follow-up axial CT 7 days later showing interval regression of the traumatic hemorrhagic lesion; (C) baseline coronal CT; (D) follow-up coronal CT 7 days later; (E) baseline sagittal CT; and (F) follow-up sagittal CT 7 days later. Image contrast has been optimized to improve visualization of the traumatic lesion. Chronic left parietotemporal post-ischemic changes are distinct from the acute right-sided traumatic lesion.

Therapeutic Intervention

The patient initially received anti-edema therapy with intravenous 20% mannitol, 250 mL every 8 hours for 3 days, together with supportive monitoring. On day 3, Cerebrolysin 30 mL/day was initiated by intravenous infusion and continued for 7 consecutive days. No neurosurgical intervention was required. Physiotherapy was introduced on day 5, focusing on early mobilization and prevention of deconditioning.

Timeline of Clinical Course

Table 1: Clinical timeline and key outcomes

Day	Clinical event	Key outcomes
0	Motor vehicle accident; CT diagnosis	GCS 12; NIHSS 7; pre-injury mRS 2
1-3	Mannitol and supportive care	GCS improved to 13
3	Cerebrolysin started (30 mL/day IV)	-
5	Physiotherapy/early mobilization introduced	-
7	Clinical reassessment	GCS 14; NIHSS 4
10	Cerebrolysin course completed	-
14	Follow-up assessment/neuroimaging	NIHSS 3; mRS 2

Follow-Up and Outcomes

The patient demonstrated progressive neurological improvement throughout hospitalization. By day 7, GCS improved to 14, while NIHSS decreased from 7 to 4, reflecting improvement in orientation, responsiveness, and focal neurological deficits. By day 14, NIHSS further improved to 3 and the patient had returned to his pre-trauma functional baseline (mRS 2). Follow-up neuroimaging demonstrated regression of the right frontal traumatic lesion and surrounding edema, while chronic post-stroke changes remained stable. Functionally, the patient regained his pre-injury level of independence and remained mildly disabled because of residual deficits related to the previous stroke. The family perceived the cognitive and motor recovery after the traumatic event as faster than during the earlier stroke rehabilitation, particularly with respect to orientation and responsiveness. Cerebrolysin was well tolerated during the 7-day treatment course, and no clinical seizures or other treatment-related adverse events were observed.

Discussion

This case illustrates several clinically relevant issues in the management of TBI in a patient with recent ischemic stroke sequelae. First, pre-existing neurological deficits and chronic post-ischemic structural changes can obscure the clinical and radiological distinction between recurrent cerebrovascular disease and new traumatic pathology. In the present patient, the trauma mechanism, right frontal scalp injury, acute right frontal hemorrhagic contusion, and stable chronic left parietotemporal post-ischemic changes supported the diagnosis of acute TBI superimposed on prior stroke-related brain injury.

Second, the patient improved during a multimodal treatment course that included anti-edema therapy, supportive monitoring, Cerebrolysin beginning on day 3, and early physiotherapy. GCS increased from 12 to 14, NIHSS decreased from 7 to 3, and the patient returned to his pre-injury mRS of 2 within 14 days. These changes were temporally associated with treatment but cannot be attributed to Cerebrolysin alone because spontaneous recovery, edema regression, supportive care, and mobilization were concurrent contributors.

The observed course is consistent with, but does not prove, findings reported in controlled studies of Cerebrolysin after TBI. CAPTAIN II evaluated Cerebrolysin as an adjunct to standard care in moderate-to-severe TBI and used 50 mL/day for the first 10 days followed by later 10 mL treatment cycles; the multidimensional primary outcome favored Cerebrolysin at day 90, with safety and tolerability comparable to placebo [5]. CAPTAIN I used a similar regimen and reported signals of benefit in several cognitive and functional measures, although the primary intention-to-treat multivariate endpoint did not reach conventional statistical significance [6].

A prospective meta-analysis of the CAPTAIN trial series (185 patients) found a small-to-medium overall effect favoring Cerebrolysin at days 30 and 90 [7]. In a separate randomized pilot study of mild TBI with intracranial contusion hemorrhage, 30 mL/day for 5 days was associated with greater improvement in cognitive measures at 12 weeks than placebo [8]. The 30 mL/day dose used in our patient therefore falls within a dose range previously studied in TBI, although the treatment duration and clinical context were different.

Evidence from ischemic stroke provides additional context because this patient was still within the recovery period after a stroke 3 months earlier. In the CARS trial, Cerebrolysin 30 mL/day for 21 days, initiated 24-72 hours after ischemic stroke and combined with standardized rehabilitation, was associated with improved upper-limb motor recovery and global outcome at day 90 [9]. Other randomized studies have also examined early Cerebrolysin combined with rehabilitation after ischemic stroke [10]. Nevertheless, stroke studies cannot be directly extrapolated to acute TBI, and the coexistence of recent stroke and traumatic hemorrhagic contusion makes the present case clinically distinct.

Post-traumatic seizures are an important safety consideration in patients with cerebral contusions and intracranial hemorrhage. Current severe-TBI guidance recognizes cortical contusion and intracerebral hematoma among risk factors for early post-traumatic seizures and supports antiseizure prophylaxis in selected patients when the anticipated benefit outweighs treatment-related risks [2]. In addition, the Cerebrolysin product information lists epilepsy as a contraindication [11]. In the present patient, no clinical seizures occurred during hospitalization, and Cerebrolysin was well tolerated. No additional electrophysiological investigations, such as electroencephalography (EEG) or quantitative EEG, were performed; therefore, this case cannot determine whether Cerebrolysin altered cerebral electrical activity or cortical excitability. This distinction is important because previous research has used quantitative EEG to investigate Cerebrolysin-associated changes in brain electrical activity after TBI [11]. Accordingly, the present report is limited to clinical tolerability and the absence of clinically observed seizures and should not be interpreted as evidence regarding electrophysiological effects or seizure threshold.

The principal limitations are the single-patient design, short follow-up, absence of a comparator, and the inability to separate spontaneous recovery and edema resolution from the effects of individual treatment components. NIHSS is primarily a stroke scale and is not a comprehensive TBI outcome measure; future reports would benefit from TBI-specific functional and neuropsychological assessments and longer follow-up. The favorable temporal course observed here should therefore be interpreted as hypothesis-generating rather than evidence of efficacy.

Conclusion

This case describes favorable short-term neurological and functional recovery after an acute right frontal hemorrhagic contusion in a patient with recent ischemic stroke sequelae who received multimodal treatment including Cerebrolysin. The patient returned to his pre-injury functional status within 14 days. The temporal association is clinically noteworthy and is consistent with prior research evaluating Cerebrolysin as an adjunct to standard care in TBI; however, causality cannot be inferred from a single case. Further controlled studies are required to clarify the role, optimal timing, dosing, and safety considerations of adjunctive neurorecovery therapies in patients with TBI and cerebrovascular comorbidity.

CASE SUMMARY



Patient

• 62 years • TBI with recent ischemic stroke sequelae



Challenge

• Acute TBI superimposed on prior stroke



Treatment

• Cerebrolysin 30 mL/day IV x 7 days + anti-edema therapy



Outcome

• GCS 12 → 14 • NIHSS 7 → 3 • mRS → 2



Take Home Message

Despite pre-existing ischemic stroke sequelae and a new hemorrhagic brain contusion, early multimodal treatment including Cerebrolysin was associated with rapid recovery to pre-trauma functional status.

PUBLISHED

Scan the QR Code to access PubMed and search with author's name, Cerebrolysin and 2026.





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...in the management of severe TBI with acute subdural hematoma

Abstract

Background: Severe traumatic brain injury (TBI) may evolve dynamically after emergency surgery, particularly when intracranial hemorrhage, seizures, systemic complications, and secondary ischemic lesions coexist. We report the multidisciplinary management and short-term evolution of an older patient with severe TBI.

Case presentation: A 71-year-old man was admitted comatose (Glasgow Coma Scale score 3) after a presumed fall. Initial computed tomography (CT) showed an acute left convexity subdural hematoma measuring up to 18 mm, a 13-mm midline shift with subfalcine and uncal herniation signs, multifocal subarachnoid and intraventricular hemorrhage, cerebral contusions, and a non-displaced left parieto-frontal fracture. Emergency left fronto-temporo-parietal craniotomy and hematoma evacuation were performed. The subsequent course included seizures, respiratory and infectious complications, recurrent right-sided motor deficits, delirium, and a recent right capsulo-lenticular ischemic lesion on magnetic resonance imaging (MRI). Management included neurosurgery, intensive care, anticonvulsant therapy, rehabilitation, and adjunctive Cerebrolysin with dose adjustments during the clinical course. At discharge, the patient was conscious and cooperative, partially oriented, and had improved right-sided muscle strength to 4/5.

Conclusion: This case illustrates the dynamic evolution of severe TBI and the importance of serial imaging, repeated neurological assessment, seizure management, systemic complication control, and coordinated neurorehabilitation. As an individual case report, it cannot establish the efficacy or causality of any single therapeutic intervention.

Keywords: severe traumatic brain injury; acute subdural hematoma; post-traumatic seizures; neurorehabilitation; case report

Introduction

Severe TBI is a heterogeneous condition in which primary mechanical injury may be followed by evolving intracranial hemorrhage, cerebral edema, seizures, systemic complications, and secondary ischemic injury. Management therefore requires rapid neurosurgical decision-making, intensive monitoring, repeated neurological assessment, and individualized rehabilitation [1,2].

This case is clinically relevant because emergency evacuation of a large acute subdural hematoma was followed by a complex but favorable short-term trajectory involving recurrent seizures, suspected secondary cerebral ischemia, delirium, and gradual motor improvement. The report also documents the use of adjunctive Cerebrolysin within a multimodal treatment plan; this intervention has been investigated as add-on therapy in moderate-to-severe TBI, but the present case cannot determine its independent effect [3-5].

Patient Information and Clinical Findings

A 71-year-old man was brought to the emergency department on 23 February 2026 in a comatose state

(GCS 3). He had been found collapsed at home by relatives after a presumed traumatic fall; the discharge documentation described a fall down stairs. Relevant medical history included previous left carotid-territory ischemic stroke, cerebral small-vessel disease, hypertension, dyslipidemia, ascending aortic aneurysm, and chronic neurological and musculoskeletal comorbidities.

On admission, the patient was intubated and mechanically ventilated. Examination showed anisocoria with left mydriasis and weak light reactivity, right central facial paresis, flaccid right hemiparesis, reduced right-sided deep tendon reflexes, a right Babinski sign, and a left parieto-occipital contused wound.

Diagnostic Assessment and Therapeutic Intervention

Emergency non-contrast head CT showed an acute left convexity subdural hematoma up to 18 mm thick with mass effect, associated falcine and tentorial subdural blood, bilateral traumatic subarachnoid hemorrhage, intraventricular hemorrhage, multifocal contusions, a non-displaced left parieto-frontal fracture, and a 13-mm rightward midline shift with subfalcine and left uncus herniation signs (Figure 1).

Emergency left fronto-temporo-parietal craniotomy and evacuation of the acute subdural hematoma were performed. Early postoperative CT demonstrated reduction of the residual subdural collection and improvement of the midline shift, with postoperative pneumocephalus and diffuse left hemispheric edema (Figure 2).

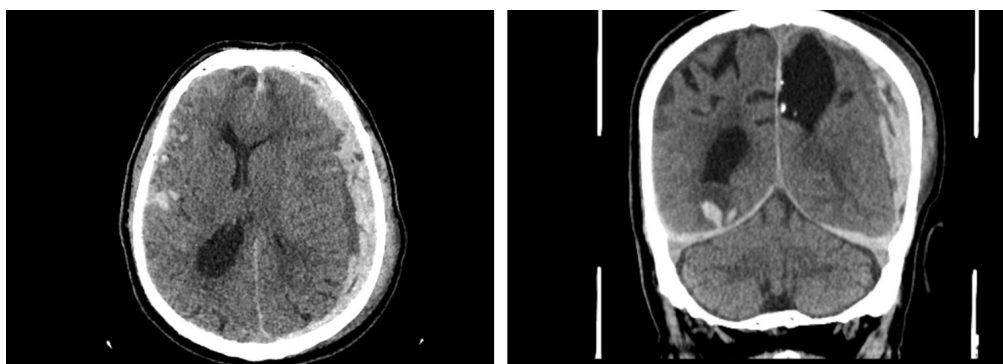


Figure 1. Admission non-contrast head CT. Axial and coronal images show the acute left convexity subdural hematoma with mass effect and marked rightward midline shift.

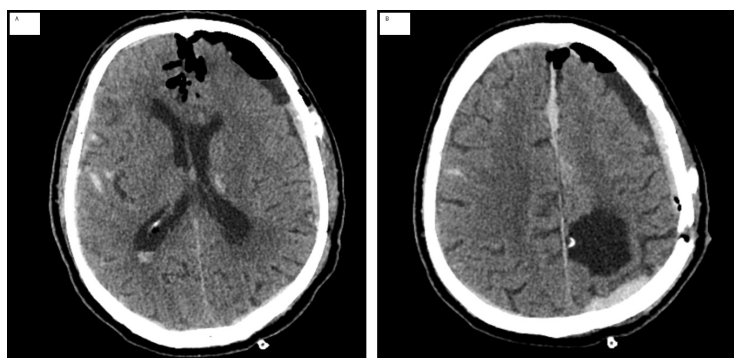


Figure 2. Early postoperative head CT. Axial images show postoperative changes after evacuation of the acute left subdural hematoma, residual collections, pneumocephalus, and improved midline alignment.

Clinical course, follow-up, and outcomes

Postoperatively, the patient was managed in intensive care. He was extubated safely on the day of surgery but developed a generalized tonic-clonic seizure controlled with diazepam. A second generalized seizure occurred on 24 February during removal of the subgaleal drain. Anticonvulsant therapy was intensified. Cerebrolysin, initiated as adjunctive therapy at 50 mL/day, was reduced to 20 mL/day after the first seizure, temporarily interrupted after the second seizure, and reintroduced at 50 mL/day on 26 February after clinical reassessment. On 28 February, the patient developed severe hypertension, hypoxemia, fever, psychomotor agitation, mixed aphasia, and recurrent right hemiparesis. Chest CT angiography showed segmental partially obstructive pulmonary filling defects and bilateral pulmonary consolidation. Head CT showed metabolizing traumatic lesions and a new right caudate/internal-capsule hypodensity suspicious for ischemic injury (Figure 3). Antibiotic treatment and continued monitoring were provided.

After stabilization, the patient was transferred to Neurology on 6 March. Active and passive physiotherapy, bedside and standing mobilization, anticonvulsant treatment, vascular prevention, and supportive care were continued. During the Neurology admission, delirium with confabulation, false recognition, impaired attention and memory, behavioral disturbance, anxiety, and depression required psychiatric assessment and symptomatic treatment.

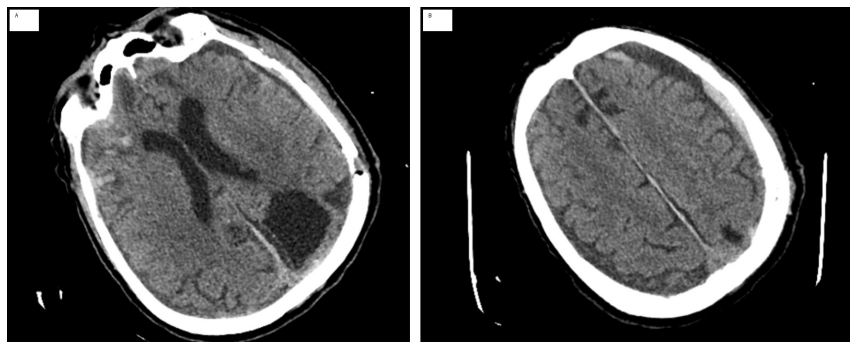


Figure 3. Follow-up non-contrast head CT during neurological deterioration. Axial images demonstrate evolving post-traumatic changes and the right caudate/internal-capsule hypodensity suspicious for secondary ischemic injury.

Brain MRI on 27 March documented residual post-traumatic hemorrhagic lesions, a right parieto-occipital intraparenchymal hematoma with vasogenic edema, a recent right capsulo-lenticular ischemic lesion with diffusion restriction, and ventricular enlargement with imaging features suggestive of altered transependymal resorption (Figure 4). On 13 April, focal motor seizures affecting the left side with secondary generalization were controlled with anticonvulsant medication. Continued adjunctive Cerebrolysin 50 mL/day was documented within the multimodal treatment plan.

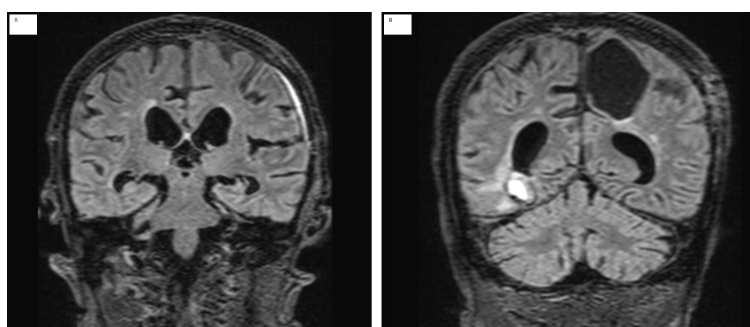


Figure 4. Brain MRI performed on 27 March 2026. Coronal FLAIR images document residual post-traumatic lesions, ventricular enlargement, and the right capsulo-lenticular lesion described as recent ischemic injury.

At discharge on 21 April 2026, the patient was conscious, cooperative, and partially oriented in time and space. He had symmetric reactive pupils, residual right central facial paresis, right-sided spastic hemiparesis with muscle strength improved to 4/5, bradylalia, bradypsychia, and a mild post-traumatic anxiety-depressive disorder. Active and passive physiotherapy and anticonvulsant therapy were continued after discharge. The discharge plan also included Cerebrolysin 10 mL/day for 10 days per month.

Discussion

This case illustrates the need to treat severe TBI as a dynamic process rather than a single acute event. The large acute subdural hematoma, marked midline shift, and herniation signs required emergency evacuation. Serial CT and MRI were clinically useful because the subsequent course included evolving hemorrhagic lesions, edema, seizures, systemic complications, and a secondary ischemic lesion. Current severe TBI guidance emphasizes structured monitoring and prevention of secondary injury [1,2].

The relationship between the seizures and individual treatment components cannot be inferred from this report. Post-traumatic seizures are recognized complications of severe TBI, particularly in the context of intracranial hemorrhage and contusions. The dose adjustments and temporary interruption of Cerebrolysin are therefore reported transparently as part of the chronology, without assigning causality. Cerebrolysin has been investigated as add-on therapy to standard care in randomized studies and a prospective meta-analysis

of the CAPTAIN trial series [3-5]. However, a single descriptive case cannot demonstrate efficacy, safety beyond the observed patient course, or the contribution of one intervention within a complex multimodal pathway. The report’s strengths are the detailed clinical chronology, serial neuroimaging, and documentation across Neurosurgery, Intensive Care, Neurology, Psychiatry, and rehabilitation. Its limitations include the absence of standardized serial functional scales beyond GCS and muscle strength, uncertainty regarding the exact injury mechanism, and the lack of long-term follow-up. Future documentation would be strengthened by serial Glasgow Outcome Scale-Extended, modified Rankin Scale, Barthel Index, and cognitive assessments.

Timeline

Table 1: Clinical course and treatment timeline

Date	Key clinical event
23 Feb 2026	Admission with GCS 3; CT showed a large acute left subdural hematoma with herniation signs. Emergency craniotomy and evacuation. ICU transfer; extubation; generalized seizure.
24-26 Feb 2026	Second generalized seizure; anticonvulsant therapy intensified; adjunctive Cerebrolysin temporarily interrupted and subsequently reintroduced after reassessment.
28 Feb 2026	Hypoxemia, fever, and neurological deterioration. Chest CT angiography and repeat head CT; secondary ischemic injury suspected.
6 Mar 2026	Transfer to Neurology; active and passive rehabilitation continued.
27 Mar 2026	Brain MRI documented residual traumatic lesions, recent right capsulo-lenticular ischemic injury, and ventricular enlargement.
13 Apr 2026	Focal motor seizures with secondary generalization; controlled with anticonvulsant medication.
21 Apr 2026	Discharge: conscious, cooperative, partially oriented; residual right spastic hemiparesis with strength improved to 4/5.

Conclusion

In severe TBI, emergency surgery may be only the first step in a prolonged multidisciplinary pathway. Serial imaging, repeated neurological examination, seizure control, management of systemic complications, and early rehabilitation were central to this patient’s short-term improvement. The case supports careful documentation of evolving complications and treatment decisions while avoiding causal conclusions that cannot be established from an individual observation.

CASE SUMMARY

 Patient

• 71 years • Severe TBI with acute subdural hematoma

 Challenge

• Coma, seizures and secondary ischemic injury

 Treatment

• Cerebrolysin 50 mL/day IV, 10mL/day x 10 days/month + surgery + ICU case + rehabilitation

 Outcome

• Muscle strength improved to 4 • Discharged cooperative, partially oriented

 Take Home Message

In severe TBI, early integration of Cerebrolysin into multimodal acute care followed by individualized neurorehabilitation was associated with meaningful neurological and motor recovery despite an initial GCS of 3 and a complex clinical course.



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...in severe TBI complicated by cranioplasty infection and repeated cranial reconstruction

Abstract

Background: Severe traumatic brain injury (TBI) requiring decompressive craniectomy carries substantial risks of death, persistent cognitive and language disability, post-craniectomy complications, and prolonged dependence. Recovery may be further disrupted by cranioplasty infection and the need for repeated cranial reconstruction.

Case presentation: A 53-year-old man sustained severe TBI in a work-related accident, with a left frontoparietal acute subdural hematoma causing cerebral compression, skull-base and mandibular fractures, and right-sided otorrhagia. Emergency decompressive craniectomy and hematoma evacuation were followed by tracheostomy, temporary gastrostomy, and early cranioplasty. During neurorehabilitation, cognitive impairment, mixed aphasia, imbalance, incoordination, and generalized weakness persisted. Surgical-site fistulization and *Staphylococcus aureus* infection subsequently required debridement and removal of the infected bone flap. During later rehabilitation, fluctuating alertness, agitation, somnolence, disorientation, and worsening postural instability prompted urgent CT and neurosurgical review. No acute surgically remediable lesion was found, and prolonged carbamazepine prophylaxis was discontinued because of a suspected medication-related contribution. After definitive reconstruction of the large left frontotemporoparietal defect, the patient showed substantial neurological recovery. At the latest assessment, he was fully conscious and oriented, with normal limb strength, although mixed predominantly motor aphasia, memory impairment, emotional lability, sensory deficits, and ataxic gait persisted. Cerebrolysin was administered twice during rehabilitation at 10 ml/day for 10 consecutive days.

Conclusion: This case demonstrates meaningful neurological recovery despite severe TBI, repeated neurosurgical procedures, cranioplasty infection, and prolonged neurobehavioral deficits. It emphasizes longitudinal multidisciplinary reassessment, prompt evaluation of new deterioration, surgical source control, medication review, and continued neurorehabilitation. The repeated use of Cerebrolysin was temporally associated with improvement in neurological function.

Keywords: severe traumatic brain injury; acute subdural hematoma; decompressive craniectomy; cranioplasty; surgical-site infection; neurorehabilitation; Cerebrolysin; case report

Introduction

Severe traumatic brain injury remains a major cause of death and long-term neurological disability. In patients with mass effect or refractory intracranial hypertension, decompressive craniectomy may be lifesaving, although survival can be accompanied by cognitive, language, behavioral, motor, and gait impairment [1–3]. Functional outcome depends on injury characteristics, prevention of secondary injury, systemic complications, surgical timing, rehabilitation, and patient-specific factors.

Cranioplasty restores cranial protection and contour and may also influence cerebrospinal fluid dynamics,

cerebral perfusion, and rehabilitation potential. Infection is among its most consequential complications because it may require debridement, implant removal, antimicrobial therapy, and delayed reconstruction [4–6]. We report a patient with severe TBI and acute subdural hematoma who demonstrated substantial neurological recovery despite cranioplasty infection, removal of the infected flap, transient neurobehavioral deterioration, and repeated cranial reconstruction.

Patient Information

A 53-year-old man with no documented pre-injury neurological disability sustained a severe work-related head injury on 29 June 2025. Acute diagnoses included a left frontoparietal subdural hematoma with cerebral compression, skull-base fracture, left mandibular fracture, and right-sided otorrhagia. Emergency left decompressive craniectomy with evacuation of the subdural hematoma was performed.

A tracheostomy was undertaken on 7 July 2025 and subsequently decannulated. A gastrostomy was placed on 15 July and removed on 28 July, indicating sufficient recovery of airway and swallowing-related functions. Cranioplasty was performed on 1 August 2025.

Early Rehabilitation

The patient entered inpatient neurorehabilitation on 4 September 2025 with impaired memory and attention, speech difficulty, generalized weakness, dynamic imbalance, and incoordination. CT on 10 September, although affected by motion artefacts, demonstrated a left frontoparietal hygroma of approximately 10 mm, ventricular compression, and approximately 3 mm rightward midline shift.

Multidisciplinary neurorehabilitation was initiated, and Cerebrolysin was administered at 10 ml/day for 10 consecutive days.

Cranioplasty infection and bone-flap removal

Persistent fistulous drainage subsequently developed in the left frontoparietal and parieto-occipital operative region. On 18 November 2025, the patient underwent excision of the fistulous tracts, debridement of necrotic tissue, and removal of the infected bone flap. Culture of wound discharge grew *Staphylococcus aureus*. The postoperative course was satisfactory, and no recurrent drainage was reported.

CT on 19 November demonstrated postoperative changes, a small left hemispheric subdural hygroma, left frontal subarachnoid cystic dilatation, and approximately 7 mm rightward midline shift. Doxycycline 100 mg twice daily for 10 days was prescribed after discharge.

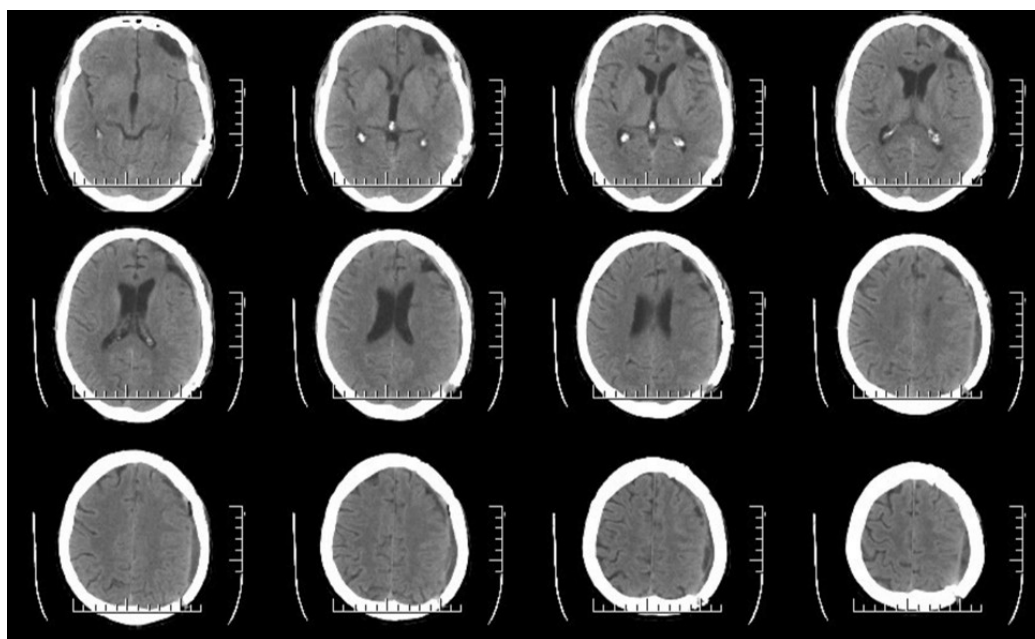


Figure 1: Cranial CT performed on 12 November 2025, demonstrating late postoperative changes following evacuation of a left hemispheric subdural hematoma, including a small left hemispheric subdural hygroma, postoperative gliotic changes, and mild rightward midline shift (~2 mm).

Transient neurobehavioral deterioration

The patient was readmitted for planned neurorehabilitation on 15 January 2026. Compared with the previous admission, orientation and writing had improved, although clinically important memory impairment and mixed aphasia persisted.

During 22–23 January, he developed reduced alertness, nocturnal agitation, daytime somnolence, disorientation, behavioral change, and worsening postural instability. Given the history of severe TBI, multiple operations, and recent wound infection, urgent CT and neurosurgical assessment were performed to exclude recurrent structural or infectious pathology.

Laboratory testing showed no major acute abnormality. CT demonstrated a large left frontotemporoparietal bone defect, chronic postoperative gliotic and cystic changes, mild ventricular enlargement, and only approximately 2 mm rightward midline shift. Neurosurgical assessment identified no acute lesion requiring operative treatment.

The family reported a similar episode during previous exposure to a higher carbamazepine dose. In the absence of documented seizures, carbamazepine, which had been continued as prophylaxis, was discontinued and clinical reassessment planned. Other centrally acting agents with sedative potential, including clonazepam, alprazolam, and zopiclone, represented additional confounders. Because serum drug levels, sodium, EEG, and formal adverse-drug-reaction assessment were unavailable, medication-related encephalopathy remained a clinical suspicion rather than a confirmed diagnosis. A further 10-day course of Cerebrolysin at 10 ml/day was administered during this rehabilitation period.

Definitive cranial reconstruction

Preoperative CT on 13 May 2026 demonstrated a large left frontotemporoparietal defect measuring approximately 133 × 104 mm, a small left basal frontal encephalomalacic focus, and chronic vascular changes. Definitive cranioplasty was performed during the 13–18 May 2026 neurosurgical admission.

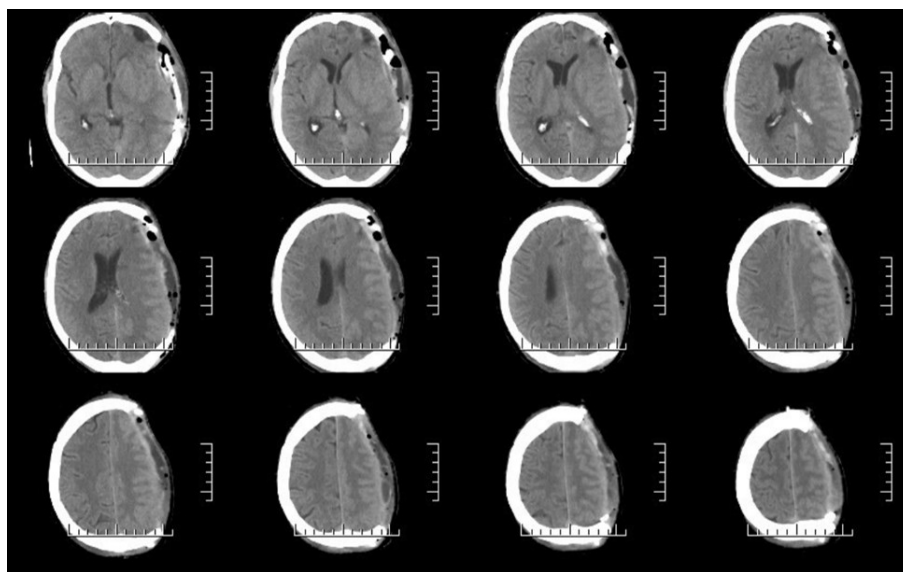


Figure 2: Cranial CT performed on 19 November 2025, demonstrating postoperative changes following removal of the bone flap, placement of an external drain within the postoperative cavity, and evacuation of a left hemispheric subdural hematoma. Postoperative gliotic changes, a small left hemispheric subdural hygroma, and left frontal subarachnoid cystic dilatation are also present, with rightward displacement of the midline structures by approximately 7 mm.

Follow-up and Outcomes

Across approximately 12 months, the clinical trajectory was characterized by survival after a life-threatening mass lesion, successful liberation from tracheostomy and gastrostomy, control of the *S. aureus* surgical-site infection after removal of the infected bone flap, repeated neurorehabilitation, and definitive cranial reconstruction.

At the latest documented assessment in June 2026, the patient was fully conscious with a Glasgow Coma Scale score of 15 and oriented to time, place, and person. Limb strength had recovered to Medical Research Council

grade 5/5 with normal muscle tone. Bulbar function, articulation, and phonation were normal, and sphincter function was preserved.

Nevertheless, recovery remained incomplete. Residual mixed aphasia with predominantly motor features, memory impairment, emotional lability, left hemihypoesthesia, ataxic gait, mild left-sided dysmetria, brisker left-sided reflexes, bilateral extensor plantar responses, and bilateral palmomental reflexes persisted.

Overall, the outcome can therefore be characterized as meaningful and substantial neurological recovery rather than complete recovery. Improvement occurred during a complex longitudinal course involving repeated neurosurgical procedures, infection control, medication reassessment, two courses of Cerebrolysin, and continued multidisciplinary neurorehabilitation. Consequently, the contribution of any individual intervention cannot be quantified.

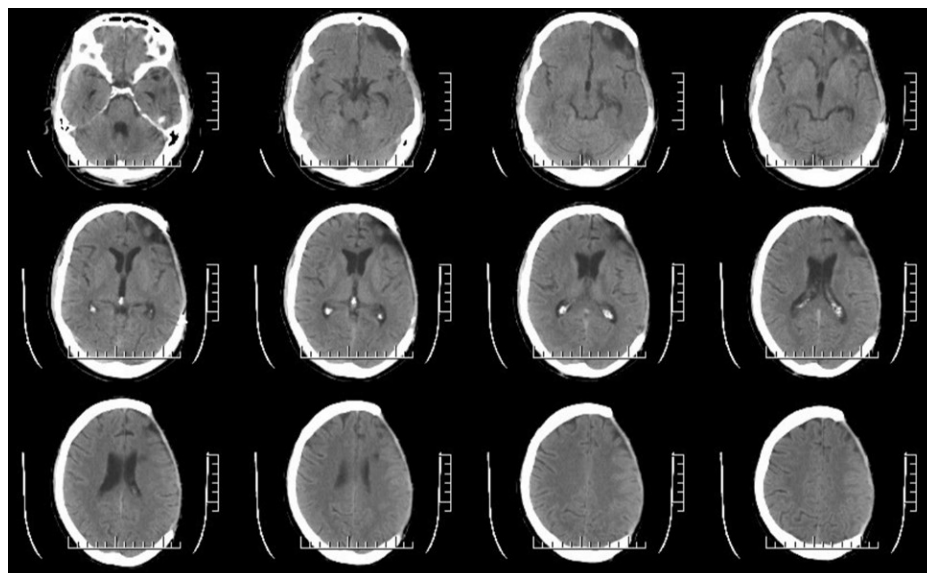


Figure 3: Cranial CT on 13 May 2026 showing a left frontotemporoparietal bone defect (~133 × 104 mm) with a small left basal frontal area of encephalomalacia.

Discussion

This case is clinically instructive because favorable recovery occurred despite cumulative biological and treatment burdens: severe mass-lesion TBI, decompressive craniectomy, repeated cranial reconstruction, *S. aureus* surgical-site infection, removal of the infected flap, and transient neurobehavioral deterioration. It also illustrates why prognosis after severe TBI should be reassessed longitudinally. Initial injury severity informs prognosis but does not fully determine the extent of recovery achievable through prevention of secondary injury, complication control, neuroplasticity, rehabilitation, and family support [7,8].

Decompressive craniectomy can reduce intracranial pressure and mortality in selected patients with refractory intracranial hypertension, although favorable functional outcome is not guaranteed [1–3]. Following craniectomy, a large skull defect may alter intracranial compliance, cerebrospinal fluid circulation, venous return, cerebral blood flow, and metabolism. The clinical spectrum of syndrome of the trephined may include motor, cognitive, language, behavioral, and gait manifestations that improve after cranioplasty [4,5]. In this patient, the large persistent defect coincided with cognitive-language and gait impairment. However, the absence of documented positional symptoms, perfusion abnormalities, or a quantified immediate response to cranioplasty prevents a formal diagnosis.

Cranioplasty infection can interrupt rehabilitation and require further anesthesia, debridement, implant removal, antimicrobial treatment, and delayed reconstruction. In this case, fistula formation, necrotic tissue, positive *S. aureus* culture, and bone-flap removal confirm a clinically significant surgical-site infection. Source control appeared successful according to the available clinical record, allowing subsequent definitive reconstruction. The documented antimicrobial regimen, however, should not be generalized because detailed susceptibility data and other infectious-disease information were unavailable.

The episode of somnolence, agitation, disorientation, and worsening balance highlights the importance of systematic reassessment when new deterioration occurs after severe TBI. Structural, infectious, metabolic, epileptic, and medication-related causes must be considered. Repeat CT and neurosurgical review excluded an acute surgically remediable lesion. The subsequent discontinuation of prolonged carbamazepine prophylaxis also illustrates the importance of medication reconciliation. However, concurrent benzodiazepines and zopiclone were important confounders, and the absence of serum carbamazepine levels, sodium measurements, EEG, and a documented post-withdrawal time course prevents causal attribution.

Contemporary guidance supports short-duration antiseizure prophylaxis when indicated and does not support prolonged exposure without an appropriate clinical indication [9]. The present case therefore underlines the need to reassess both the indication and duration of centrally acting medication during prolonged neurorehabilitation. Cerebrolysin was administered twice during the rehabilitation course, each time at 10 ml/day for 10 consecutive days. Its multimodal neurotrophic and neurorestorative properties may be relevant to recovery following severe brain injury. In this patient, the repeated courses were temporally associated with further neurological improvement; however, because of the complex clinical course, concomitant rehabilitation, surgical interventions, medication changes, and natural recovery, the contribution of any single intervention cannot be quantified.

Limitations

Important limitations include the absence of complete acute injury severity metrics, detailed operative reports, comprehensive rehabilitation-dose information, standardized neuropsychological and aphasia assessments, and functional independence measures. Serum carbamazepine concentrations, sodium values, and EEG were unavailable during the episode of transient deterioration. CT findings were derived from clinical reports rather than central image review.

Conclusion

Meaningful neurological recovery is possible after severe TBI even when the course is complicated by cranioplasty infection, removal of an infected flap, prolonged cognitive-language impairment, transient neurobehavioral deterioration, and repeated cranial reconstruction. This case emphasizes the importance of longitudinal multidisciplinary follow-up, systematic investigation of every new deterioration, effective surgical source control, reassessment of potentially cognition-impairing medication, and continued goal-directed neurorehabilitation.

The repeated administration of Cerebrolysin was temporally associated with further improvement in neurological function and may have supported the overall neurorestorative process. Nevertheless, its contribution cannot be separated from the effects of rehabilitation, repeated neurosurgical interventions, medication changes, and natural recovery. The case therefore supports cautious longitudinal prognostic reassessment rather than attribution of recovery to a single intervention.

CASE SUMMARY



Patient

• 53 years • Severe TBI with acute subdural hematoma



Challenge

• Cranioplasty infection and repeated cranial reconstruction



Treatment

• Cerebrolysin 10 mL/day IV x 10 days (2 cycles) + neurosurgery + multidisciplinary rehabilitation



Outcome

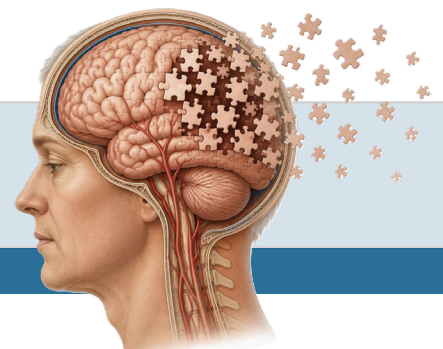
• GCS → 15 • Muscle strength recovered to 5/5 • Neurological recovery achieved



Take Home Message

Even after severe traumatic brain injury complicated by multiple neurosurgical procedures, cranioplasty infection, and prolonged neurobehavioral deficits, substantial neurological recovery may still occur when potentially reversible factors are identified and addressed.

Functional and Cognitive Recovery in Neurological Disorders





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INTRODUCTION

The role of Cerebrolysin as stand-alone or combination therapy...

Recovery after neurological injury is a multidimensional process, but after stroke, cognitive recovery is often a critical prerequisite for meaningful functional recovery. Motor recovery alone does not guarantee independence. A patient may regain the ability to walk, for example, but remain dependent because impaired attention, slowed information processing, memory, or executive function limits safe mobility, communication, decision-making, and participation in rehabilitation. Conversely, improving cognition can increase a patient's ability to engage with therapy, learn new strategies, and translate neurological recovery into everyday function. Functional and cognitive recovery are therefore closely linked, with cognitive recovery often providing the foundation for broader functional gains.

This relationship is particularly important after stroke. Cognitive impairment may result from the location and severity of the acute lesion, but also be fortified by pre-existing or covert cerebrovascular disease, white matter damage, or neurodegenerative processes. Recovery is therefore influenced by the condition of the wider brain network and its innate ability to reorganize and compensate after injury. Beside already established capacity for spontaneous improvement, there is unmet need to further promote neuroplasticity and restore both cognitive and functional abilities.

Within this context, the multimodal mechanism of action of Cerebrolysin provides a biologically plausible rationale for its use as an adjunct to neurological rehabilitation. Pre-clinical and clinical evidence suggest that its pleiotropic effects may support neuronal survival, neuroplasticity, synaptic remodeling and network reorganization, while also beneficially influencing mechanisms involved in secondary brain injury.

The ultimate goal of neurorestorative treatment is to help patients regain cognitive competence and translate recovery into meaningful functional independence. The clinical cases presented in this chapter illustrate different patterns of cognitive and functional recovery and highlight the potential for continued improvement beyond the acute phase.



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...in a case of Guillain-Barré Syndrome with tetraparesis

Abstract

Guillain–Barré Syndrome (GBS) is a rare immune-mediated neuropathy commonly triggered by preceding infections. While pathogens such as *Campylobacter jejuni*, cytomegalovirus, and Zika virus have established associations with GBS, emerging evidence suggests that SARS-CoV-2 infection may also act as a potential trigger through immune dysregulation, including pro-inflammatory cytokine activation and neuroinflammatory pathways. (1,2,3,4) However, the relationship between COVID-19 and GBS remains incompletely understood.

We report the case of a patient who developed acute inflammatory demyelinating polyneuropathy (AIDP), a GBS variant, following COVID-19 infection, presenting with tetraparesis and hoarseness of voice, resulting in significant functional impairment and dependence on caregivers. Considering the potential neurotropism of SARS-CoV-2 and inflammatory mechanisms contributing to neural injury, Cerebrolysin was administered as part of a multimodal treatment approach. Its neurotrophic and neurorestorative effects, including modulation of neuroinflammation, support of neuroplasticity, and promotion of neuronal survival pathways, provided the rationale for its use.

Treatment included plasmapheresis, cholinesterase inhibitors, vitamins, vasodilating agents, and Cerebrolysin. Clinical assessment, electroneuromyography (ENMG) monitoring, and functional scales (5) demonstrated progressive motor recovery. The treatment was well tolerated, with no adverse events reported.

This case suggests that Cerebrolysin may represent a potential neurorestorative therapeutic option in patients with post-COVID GBS. Further studies are required to evaluate its efficacy and underlying mechanisms.

Keywords: Guillain-Barré Syndrome, tetraparesis, neurorestorative treatment, SARS-CoV-2

Introduction

Guillain–Barré Syndrome (GBS) is an acute immune-mediated polyradiculoneuropathy characterized by progressive weakness, sensory disturbances, and, in severe cases, respiratory or autonomic dysfunction. It is commonly triggered by infections such as *Campylobacter jejuni*, cytomegalovirus, Epstein–Barr virus, and Zika virus. The underlying pathophysiology involves immune-mediated damage to peripheral nerves through molecular mimicry, autoantibody production, complement activation, and inflammatory mechanisms.

Since the COVID-19 pandemic, increasing numbers of cases have described GBS following SARS-CoV-2 infection, suggesting a potential post-infectious association. Proposed mechanisms include immune dysregulation, excessive cytokine production, and neuroinflammatory responses that may contribute to peripheral nerve injury. Although a temporal relationship has been observed, the exact causal mechanisms remain incompletely understood.

Recovery from severe GBS often requires prolonged rehabilitation, particularly in patients with extensive

motor impairment. Therefore, therapeutic approaches that not only halt immune-mediated nerve damage but also support neural recovery are of clinical interest. Cerebrolysin is a neuropeptide preparation with neuroprotective and neurotrophic properties that has been widely investigated in stroke rehabilitation. Proposed mechanisms include modulation of neuroinflammation, reduction of excitotoxicity, promotion of neuroplasticity, and stimulation of neuronal survival and repair.

This report describes the clinical course and functional recovery of a patient with severe post-COVID GBS treated with standard therapy followed by two courses of Cerebrolysin as part of a multimodal neurorehabilitation program.

Patient Information

A male patient developed severe COVID-19 infection confirmed by PCR on Day 0. Chest computed tomography demonstrated bilateral polysegmental pneumonia involving approximately 72% of lung tissue, requiring hospitalization and treatment according to institutional protocols.

Approximately three weeks after the acute infection, the patient developed progressive weakness affecting both upper and lower extremities. Additional symptoms included impaired fine motor function, hoarseness of voice, dysphagia, and choking episodes. The neurological deficits resulted in significant functional dependence and inability to walk independently.

The patient had no relevant family history. The major antecedent medical event was severe SARS-CoV-2 infection.

Clinical Findings

Neurological evaluation on Day 21 demonstrated severe tetraparesis. Muscle strength was reduced to 3.0–3.5/5 in the upper extremities and 2.0–2.5/5 in the lower extremities. Neurological examination also revealed impaired fine motor function, dysphonia, and dysphagia accompanied by choking episodes. As a result of these deficits, the patient was unable to ambulate independently and required substantial assistance with daily activities. According to the Guillain–Barré Disability Scale, the severity of lower-limb impairment corresponded to a level requiring wheelchair assistance.

Timeline

Table 1. Clinical Course and Treatment Timeline

Time Point	Clinical Course and Therapeutic Interventions
Day 0	Severe COVID-19 infection confirmed by PCR. Chest CT demonstrated bilateral polysegmental pneumonia with approximately 72% lung involvement. The patient was hospitalized and treated according to institutional COVID-19 protocols.
Day 21	Following resolution of the acute infection, progressive neurological symptoms developed, including weakness of the upper and lower extremities, dysphonia, dysphagia, choking episodes, and impaired fine motor function.
Day 21	Admitted to the neurology department. Neurological examination revealed tetraparesis with muscle strength of 3.0–3.5/5 in the upper extremities and 2.0–2.5/5 in the lower extremities. Diagnosis: acute inflammatory demyelinating polyneuropathy (AIDP), Guillain–Barré Syndrome variant.
Days 21–51	Standard treatment was administered, including seven plasmapheresis sessions, Proserin, Nukleo 2.0, pentoxifylline, and vitamin B6. Disease progression stabilized; however, significant motor deficits and functional dependence persisted.
Day 51	Follow-up ENMG demonstrated moderate-to-severe sensorimotor demyelinating polyneuropathy with absent sensory responses. The first neurorestorative treatment course was initiated, consisting of Cerebrolysin 30 mL/day intravenously for 10 days followed by 5 mL/day intramuscularly for 20 days, together with supportive neurorehabilitation therapy.

Day 81	Clinically meaningful improvement was observed. Upper-extremity strength improved to approximately 4/5 and lower-extremity strength to approximately 3.5/5. ENMG demonstrated improved motor nerve conduction, and the patient regained independent ambulation.
Day 84	A second Cerebrolysin treatment course was initiated using the same dosing regimen (30 mL/day intravenously for 10 days followed by 5 mL/day intramuscularly for 20 days).
Day 127	Further neurological recovery was documented. Upper-extremity strength reached 5/5 and lower-extremity strength improved to 4.5/5. Follow-up ENMG showed continued restoration of motor nerve conduction and the reappearance of sensory nerve responses. The patient regained independence in activities of daily living, including dressing and self-care, and was able to walk without assistance.
Throughout Follow-up	No adverse events or treatment-related complications associated with Cerebrolysin therapy were reported.

Diagnostic Assessment

Brain CT revealed no acute intracranial abnormalities. Lumbar spine MRI showed degenerative changes, including L3–L4 and L4–L5 disc protrusions and an L5–S1 disc herniation. Duplex ultrasonography of the lower extremities excluded venous thrombosis.

Cerebrospinal fluid examination was unremarkable. Routine laboratory investigations were within normal limits except for mildly elevated blood glucose levels (7.4 mmol/L). Serological testing showed IgG antibodies against cytomegalovirus, Epstein–Barr virus, and herpes simplex virus types 1 and 2, indicating prior exposure. HIV testing was negative.

Electroneuromyography (ENMG) revealed a sensorimotor polyneuropathy of mixed axonal–demyelinating type with predominant demyelinating features. The examination demonstrated fragmented M-responses of the tibial nerve, reduced nerve conduction velocity, and decreased amplitudes in motor fibers, findings consistent with acute inflammatory demyelinating polyneuropathy accompanied by secondary axonal involvement. These findings supported the diagnosis of acute inflammatory demyelinating polyneuropathy (AIDP), the most common variant of Guillain–Barré Syndrome.

Therapeutic Intervention

Following admission, the patient received standard therapy for Guillain–Barré Syndrome. Treatment included seven sessions of plasmapheresis, Proserin 500 µg administered intramuscularly once daily for seven days, Nukleo 2.0 administered intramuscularly once daily for eight days, pentoxifylline 100 mg intramuscularly once daily for five days, and vitamin B6 administered intramuscularly once daily for fifteen days. This treatment successfully stabilized disease progression; however, significant neurological deficits persisted and functional recovery remained limited.

Given the persistent impairment, neurorestorative treatment was initiated. The first Cerebrolysin course consisted of 30 mL/day administered intravenously for 10 consecutive days, followed by 5 mL/day administered intramuscularly for 20 days. Concomitant therapy included intravenous tiotic acid, Neuromidin 20 mg orally twice daily, Keltican twice daily, and vitamin B-complex supplementation. Following clinical improvement, a second Cerebrolysin course was administered using the same dosing schedule.

Treatment was well tolerated, and no adverse events or treatment-related complications were reported during the observation period.

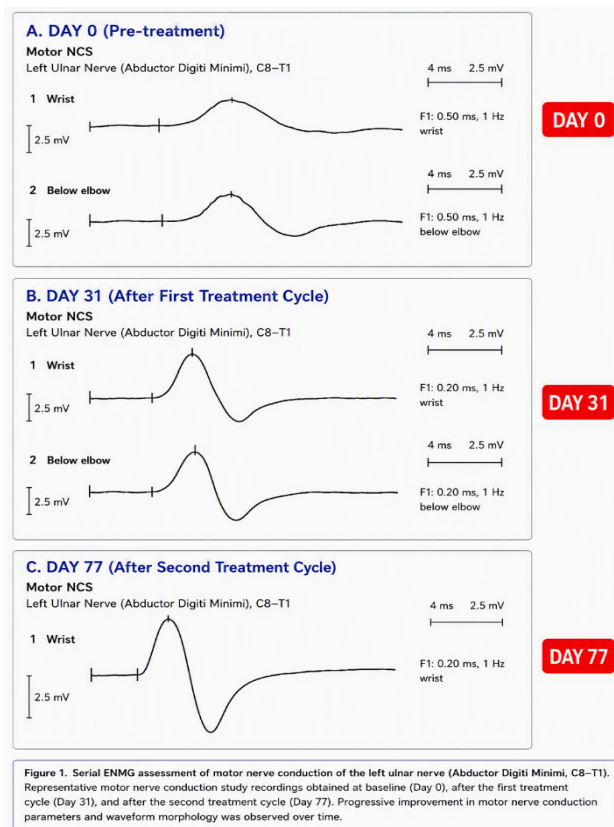


Figure 1: Dynamics of upper limbs signal of nerve-muscular motor conduction. ENMG from day 0: signs of moderate damage of nerves of upper extremities by demyelinating type – reduction of the speed of propagation of excitation (SPE) along the nerves, increase in the latency of responses. ENMG on day 31: positive dynamics in the form of restoration of the motor function of the nerves of the upper extremities. ENMG on day 77: positive dynamics was recorded in the form of restoration of the motor function of the nerves of the upper extremities

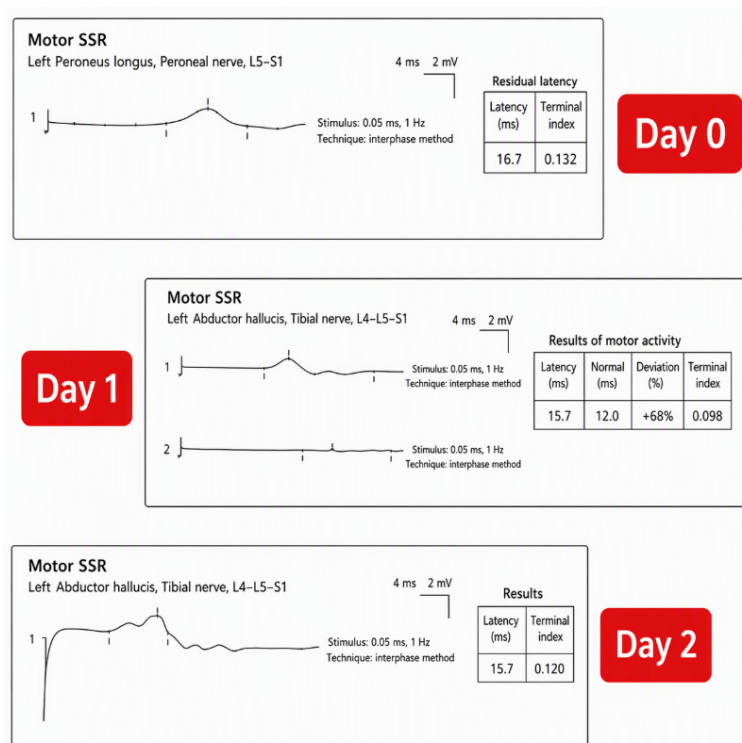


Figure 2: Dynamics of lower limbs signal of nerve-muscular motor conduction. ENMG from day 0: signs of moderate to severe damage of motor nerves of the low extremities by demyelinating type – reduction of the speed of propagation of excitation (SPE) along the nerves. ENMG on day 31: positive dynamics in form of restoration of motor function of the nerves of the lower extremities. ENMG on day 77: positive dynamics was recorded in the form of restoration of the motor function of the nerves of the lower extremities.

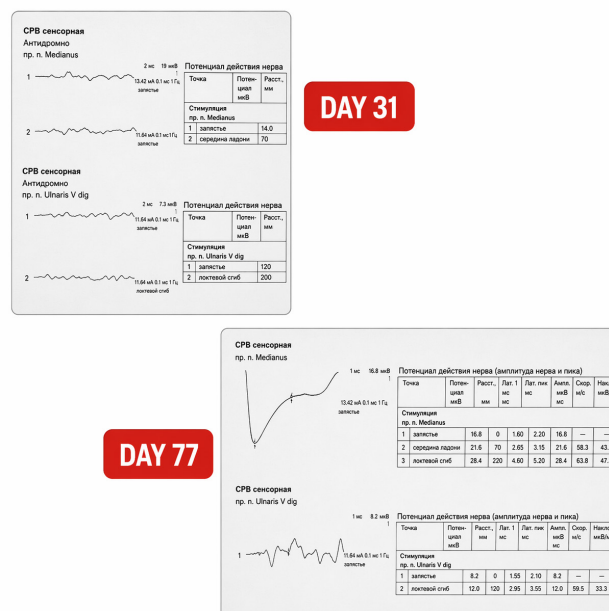


Figure 3: Dynamics of upper limbs signal of nerve-muscular sensory conduction. ENMG dated 17.10.2020: sensory polyneuropathy. Sensory nerve responses was absent at the time of this investigation. ENMG dated 02.12.2020: responses on sensory nerves with minimal positive dynamics.

Follow-Up and Outcomes

Following the first course of Cerebrolysin, clinically meaningful improvement became evident. Muscle strength increased to approximately 4/5 in the upper extremities and 3.5/5 in the lower extremities. The patient regained the ability to walk independently without caregiver assistance, and ENMG demonstrated improvement in nerve conduction parameters.

After completion of the second treatment course, neurological recovery continued. Upper-extremity strength improved to 5/5, while lower-extremity strength reached 4.5/5. The patient regained independence in activities of daily living, including dressing and self-care, attended follow-up visits without assistance, and was able to walk long distances without support. Serial ENMG assessments demonstrated progressive restoration of motor nerve function and reappearance of sensory nerve responses that had previously been absent. Electrophysiological improvement was particularly evident in nerve conduction velocity, which increased from 23.8 m/s to 63.9 m/s in the lower extremities and from 48.1 m/s to 53.7 m/s in the upper extremities. At the final follow-up visit, the patient attended independently, reflecting substantial recovery of mobility and functional status. Serial evaluations using the Hughes Disability Scale and the Global Guillain–Barré Functional Recovery Scale demonstrated progressive functional improvement throughout the observation period, with recovery of both upper- and lower-extremity motor function and restoration of independent mobility.

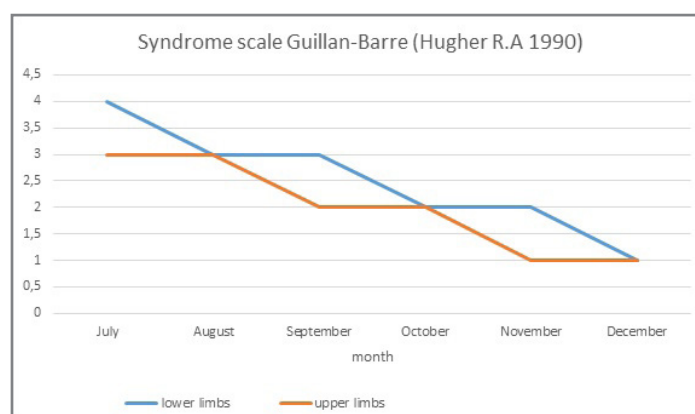


Figure 4: GBS separate dynamics of upper and lower limbs motor activity. At the moment of the disease onset since acute signs of tetraparesis development lower extremities were damaged more pronouncedly, resulted with the score 4.0 – (confined to a wheelchair or bed), function of upper extremities was evaluated with the score 3.0 (some movements saved, but is not able to perform neither of the actions from the first 2 points).

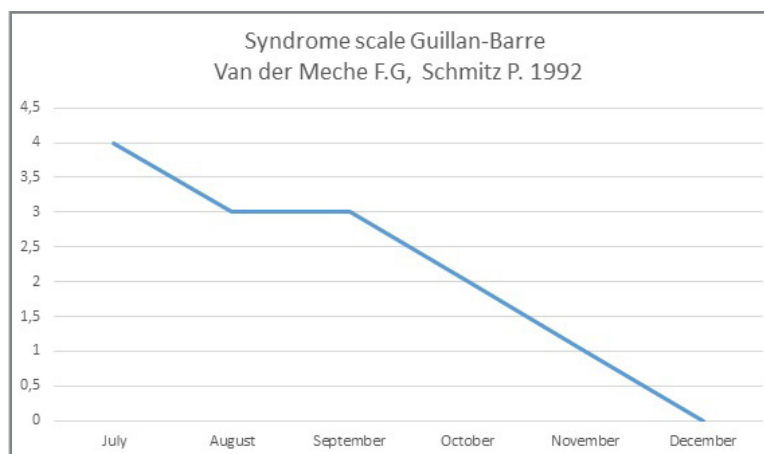


Figure 5: GBS common dynamics of upper and lower limbs motor activity. In the second scale of Guillain Barre Syndrome evaluation the general movement activity of upper and lower extremities is evaluated. July, August – evaluation score 4,3 without neurorestorative therapy is corresponding to the absent of movement ability more than 10 meters with walker. Following 3 months on the background of two courses of neurorestorative therapy patients achieves symptoms regress, possibility to walk without walker support on himself, ability to hand work.

Discussion

This case describes substantial neurological recovery in a patient with severe post-COVID Guillain–Barré Syndrome treated with standard therapy followed by two courses of Cerebrolysin as part of a multimodal rehabilitation strategy.

The temporal relationship between severe SARS-CoV-2 infection and the subsequent development of acute inflammatory demyelinating polyneuropathy is consistent with previously reported cases of post-COVID GBS. The patient developed progressive tetraparesis, dysphagia, and dysphonia approximately three weeks after the acute infection, a timeframe compatible with an immune-mediated neurological complication.

Although plasmapheresis halted disease progression, motor recovery remained limited during the initial phase of treatment. More pronounced clinical and electrophysiological improvements became evident after initiation of neurorestorative therapy. These improvements included gains in muscle strength, restoration of independent ambulation, recovery of activities of daily living, increased nerve conduction velocities, and reappearance of sensory responses on electrophysiological testing.

Cerebrolysin has demonstrated neuroprotective and neurorestorative effects in several neurological disorders, particularly ischemic stroke. Proposed mechanisms include modulation of neuroinflammatory pathways, enhancement of neuroplasticity, support of neuronal survival, and stimulation of repair processes. These biological effects may also be relevant in post-infectious peripheral nerve injury, where inflammation and secondary neuronal dysfunction contribute to disability.

However, interpretations should remain cautious. Guillain–Barré Syndrome may undergo spontaneous recovery, and the contributions of concomitant rehabilitation measures and supportive pharmacological therapies cannot be excluded. Consequently, a causal relationship between Cerebrolysin treatment and the observed recovery cannot be established based on a single case report.

Nevertheless, the parallel improvements observed in clinical status and electrophysiological parameters highlight the potential value of further research investigating neurorestorative therapies in severe post-infectious peripheral neuropathies.

Patient Perspective

During follow-up visits, the patient described his recovery as follows:

“I feel the strength returning to my legs and arms. I really want to run and shake hands with everyone I meet. I enjoy every movement that I had previously taken for granted.”

CASE SUMMARY



Patient

- 70 years
- Post-COVID Guillain-Barré syndrome (AIDP variant)



Challenge

- Severe tetraparesis, dysphagia and loss of independent ambulation



Treatment

- Cerebrolysin 30 mL/day IV x 10 days, Cerebrolysin 5 mL/day IV x 20 days + plasmapheresis + rehabilitation



Outcome

- Upper limb strength: 3-3.5/5 → 5/5
- Lower limb strength: 2-2.5/5 → 4.5/5
- Independent walking



Take Home Message

Cerebrolysin supported rapid and clinically meaningful motor recovery in a severe case of post-COVID Guillain-Barré syndrome and can be associated with restoration of motor nerve function and regained ability to walk independently.

PUBLISHED

Scan the QR Code to access PubMed and search with author's name, Cerebrolysin and 2026.





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...in the treatment of hypertension-associated moderate VCI

Abstract

Background: Arterial hypertension is an important risk factor for cerebrovascular disease and vascular cognitive impairment. Chronic hypertension may contribute to cerebral small-vessel disease and progressive neurological and cognitive dysfunction despite antihypertensive treatment. A comprehensive therapeutic approach addressing both vascular risk factors and neurological consequences may therefore be clinically relevant.

Case presentation: We present the case of a 63-year-old man with a six-year history of arterial hypertension, class I obesity, dyslipidemia, and hypertensive encephalopathy accompanied by moderate cognitive impairment and high trait anxiety. At presentation, blood pressure was 160/100 mmHg, brain MRI demonstrated Fazekas grade II small-vessel disease, and cognitive assessment showed an MMSE score of 27 and a Clock Drawing Test score of 6. The patient received standard antihypertensive therapy together with Cerebrolysin 30 mL intravenously once daily for 21 days, excluding weekends. Blood pressure subsequently stabilized at 130/80 mmHg. Cognitive performance improved progressively, with MMSE scores increasing to 28 at Day 30 and 29 at Day 90, while Clock Drawing Test scores increased to 7 and 9, respectively. Trait anxiety decreased from a high to a low level and remained low throughout follow-up. Headache and dizziness also improved.

Conclusion: Comprehensive treatment including blood-pressure control and a course of Cerebrolysin was associated with sustained improvement in cognitive and psycho-emotional measures over 90 days. The observation is consistent with previous evidence suggesting potential cognitive benefits of Cerebrolysin in vascular dementia and with recent C-REGS2 data showing improved 90-day cognitive outcomes, particularly among patients with pre-existing cognitive impairment. However, causal conclusions cannot be drawn from this single case.

Keywords: hypertensive encephalopathy; arterial hypertension; vascular cognitive impairment; anxiety; cerebrovascular insufficiency; Cerebrolysin; MMSE; Clock Drawing Test.

Introduction

Chronic arterial hypertension is a major risk factor for cerebrovascular disease and vascular cognitive impairment. Sustained blood-pressure elevation contributes to cerebral small-vessel disease and structural brain injury, which may manifest clinically as cognitive impairment before the development of overt dementia. Effective blood-pressure control is fundamental to preventing further vascular brain injury. However, stabilization of blood pressure does not necessarily reverse established neurological or cognitive consequences of chronic cerebrovascular disease. This provides a rationale for comprehensive approaches combining vascular risk-factor management with interventions aimed at supporting neurological function and recovery.

Cerebrolysin has been investigated in vascular cognitive disorders, including vascular dementia. In a randomized, double-blind, placebo-controlled multicenter trial involving 242 patients with vascular dementia, Cerebrolysin added to basic treatment was associated with improvements in cognitive and global clinical outcomes over

24 weeks. A subsequent Cochrane review found possible benefits in cognition and general function, although the certainty of evidence was considered very low because of methodological limitations and heterogeneity among the available studies.

More recently, the C-REGS2 comparative-effectiveness study provided evidence regarding cognitive outcomes after moderate acute ischemic stroke. Among 1,769 patients, 1,021 received Cerebrolysin and 748 received standard treatment. At 90 days, ordinal MoCA outcomes favored Cerebrolysin, with a more pronounced effect in patients with pre-existing cognitive impairment. A dedicated 2026 analysis reported a MoCA effect of +3.24 points in favor of Cerebrolysin among patients with pre-stroke cognitive impairment, compared with +0.8 points among those without previous impairment.

Against this background, we describe a patient with hypertensive encephalopathy and moderate cognitive impairment who demonstrated progressive cognitive and psycho-emotional improvement during 90 days of comprehensive treatment.

Patient Information

A 63-year-old man with a six-year history of arterial hypertension presented for medical evaluation. Before seeking medical attention, he had experienced recurrent headaches and dizziness but had not undergone regular medical follow-up and had self-medicated with analgesics.

Clinical assessment established essential arterial hypertension, grade 2, with high cardiovascular risk. The patient had class I obesity (BMI 32.01 kg/m²), a positive family history, and marked dyslipidemia. The neurological diagnosis was hypertensive encephalopathy (ICD-10 I67.4) accompanied by moderate cognitive impairment and anxiety symptoms.

Clinical Findings

Baseline blood pressure was 160/100 mmHg. Laboratory investigations demonstrated total cholesterol 245 mg/dL, triglycerides 251 mg/dL, LDL cholesterol 160 mg/dL, VLDL cholesterol 50 mg/dL, HDL cholesterol 35 mg/dL, and an atherogenicity coefficient of 6.0. Echocardiography demonstrated left ventricular hypertrophy. Ultrasound examination of the brachiocephalic arteries revealed an atherosclerotic plaque in the distal right common carotid artery causing approximately 25% stenosis, without hemodynamically significant impairment of blood flow.

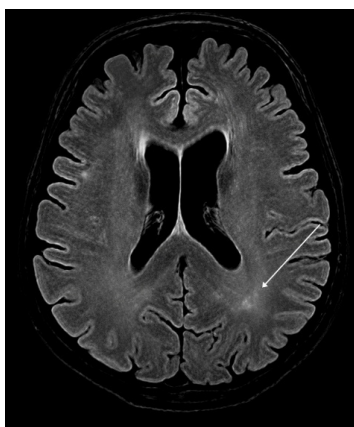


Figure 1. Brain MRI demonstrating findings consistent with vascular encephalopathy and Fazekas grade II small-vessel disease.

Baseline cognitive assessment showed an MMSE score of 27 and a Clock Drawing Test score of 6. The Spielberger–Khanin Anxiety Inventory demonstrated low state anxiety but high trait anxiety. No signs of depression were identified using the Zung Self-Rating Depression Scale.

Diagnostic Assessment

The diagnosis was based on the medical history, clinical examination, blood-pressure measurements, laboratory investigations, cardiovascular and cerebrovascular imaging, and standardized cognitive and psycho-emotional assessments.

The overall findings indicated arterial hypertension with multiple vascular risk factors, including obesity, marked dyslipidemia, left ventricular hypertrophy, carotid atherosclerosis, and MRI evidence of cerebral small-vessel disease. Cognitive impairment was identified in the context of vascular encephalopathy, accompanied by high trait anxiety without clinically relevant depression.

The final diagnosis was hypertensive encephalopathy (I67.4) associated with moderate cognitive impairment and anxiety symptoms.

Timeline

Table 1: Clinical course and treatment timeline

Time/Day	Clinical course and intervention
Baseline	Headache, dizziness, elevated blood pressure (160/100 mmHg), mild cognitive impairment and high trait anxiety. Initiated standard antihypertensive therapy plus Cerebrolysin 30 mL IV.
Days 1–21	Continued Cerebrolysin 30 mL IV once daily (weekdays only).
Discharge	Improvement in headache and dizziness; blood pressure reduced to approximately 130/80 mmHg. Continued outpatient pharmacological treatment.
Day 30	Further cognitive and psycho-emotional improvement with reduced anxiety.
Day 90	Sustained psycho-emotional benefits and continued cognitive improvement.

Therapeutic Intervention

The patient received standard antihypertensive therapy together with Cerebrolysin 30 mL intravenously once daily for 21 days, excluding weekends.

After completion of the treatment course, continued pharmacological management, blood-pressure and heart-rate monitoring, lifestyle modification, and follow-up by the general practitioner, cardiologist, and neurologist were recommended. Thus, treatment addressed both the underlying vascular risk factors and the neurological manifestations of the disease.

Follow-up and Outcomes

The patient demonstrated progressive improvement in cognitive and psycho-emotional status.

At Day 30, the MMSE increased from 27 to 28 and the Clock Drawing Test from 6 to 7. Trait anxiety decreased from a high to a low level, while state anxiety remained low.

At Day 90, the MMSE reached 29 and the Clock Drawing Test 9 points. The low level of trait anxiety was maintained. Blood pressure stabilized at approximately 130/80 mmHg, while headache and dizziness significantly improved. No negative neurological changes were documented.

Importantly, cognitive improvement continued after completion of the 21-day Cerebrolysin course. However, because anti-hypertensive therapy and other components of comprehensive management continued during follow-up, the observed improvement cannot be attributed to Cerebrolysin alone.

Discussion

This case describes a patient with hypertensive encephalopathy, cerebral small-vessel disease, and cognitive impairment who demonstrated progressive improvement in cognitive performance during 90 days of comprehensive treatment. MMSE improved from 27 to 29 points and Clock Drawing Test performance from 6 to 9 points, while high trait anxiety decreased to a low level.

The findings are clinically relevant because cognitive impairment associated with hypertension and cerebral small-vessel disease may reflect persistent consequences of vascular brain injury. Blood-pressure control is essential to limit further vascular damage, but established cognitive dysfunction may not necessarily normalize following stabilization of blood pressure alone. A comprehensive approach addressing both vascular risk and neurological manifestations may therefore be of interest.

Previous clinical evidence provides relevant context. In the randomized, double-blind, placebo-controlled multicenter trial by Guekht et al., 242 patients with vascular dementia received Cerebrolysin or placebo

in addition to basic treatment. After 24 weeks, Cerebrolysin was associated with greater improvement in cognitive and global clinical outcomes. A subsequent Cochrane review of six trials also suggested possible benefits in cognition and general function. These findings support clinical interest in Cerebrolysin for vascular cognitive disorders but do not establish its efficacy in hypertensive encephalopathy.

The recent C-REGS2 findings provide additional, although indirect, support for an effect on cognitive outcomes after cerebrovascular injury. In 1,769 patients with moderate acute ischemic stroke, ordinal MoCA outcomes at 90 days favored Cerebrolysin. The effect was particularly pronounced in patients with pre-existing cognitive impairment. A dedicated analysis reported a +3.24-point MoCA effect in patients with pre-stroke cognitive impairment compared with +0.8 points in those without previous impairment. Although C-REGS2 investigated acute ischemic stroke rather than hypertensive encephalopathy, these findings are noteworthy because they suggest that patients with pre-existing cognitive vulnerability may be particularly relevant when evaluating cognitive outcomes.

Cerebrolysin has been investigated as a multimodal peptide preparation with neurotrophic, anti-inflammatory, anti-apoptotic, antioxidant, and neuroplastic effects. Such properties could theoretically complement vascular risk-factor control by supporting neuronal function and adaptive plasticity in patients with established vascular brain injury. The continued cognitive improvement after completion of the 21-day treatment course is compatible with this hypothesis, but the present case cannot establish a mechanistic relationship.

The improvement in anxiety should also be interpreted cautiously. It occurred together with improved blood-pressure control and relief of headache and dizziness, and therefore may reflect the overall therapeutic response rather than a specific effect of Cerebrolysin.

This case should be regarded as hypothesis-generating rather than evidence of treatment efficacy. Nevertheless, the sustained cognitive improvement observed in this patient, together with previous evidence in vascular dementia and recent C-REGS2 cognitive findings after ischemic stroke, supports further investigation of strategies aimed at cognitive preservation and recovery in patients with vascular brain injury.

Conclusion

In this patient with hypertensive encephalopathy, cerebral small-vessel disease, and moderate cognitive impairment, comprehensive treatment with antihypertensive therapy and a 21-day course of Cerebrolysin was associated with progressive improvement in cognitive performance and sustained reduction in trait anxiety over 90 days.

The observation is compatible with previous evidence suggesting potential cognitive benefits of Cerebrolysin in vascular dementia and with C-REGS2 findings indicating improved cognitive outcomes after acute ischemic stroke, particularly among patients with pre-existing cognitive impairment. However, the different clinical populations and study designs preclude direct extrapolation, and causality cannot be established from this case.

CASE SUMMARY



Patient

• 63 years • Hypertensive encephalopathy with moderate cognitive impairment



Challenge

• Cerebral small-vessel disease, cognitive decline and high anxiety



Treatment

• Cerebrolysin 30 mL/day IV x 21 days + antihypertensive therapy



Outcome

• MMSE 27 → 29 • Clock drawing test 6 → 9



Take Home Message

In a patient with hypertensive encephalopathy, small-vessel disease, and cognitive impairment, multimodal treatment including Cerebrolysin was associated with sustained cognitive and emotional improvement over 90 days.



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...in functional and cognitive post-stroke recovery

Abstract

A male patient born in 1954 presented with acute ischemic stroke involving the left middle cerebral artery territory, manifesting as sensory aphasia and right hemiparesis. Initial neurological severity was substantial, with a National Institutes of Health Stroke Scale (NIHSS) score of 16. Brain MRI confirmed acute infarction of the left temporal and parietal lobes. Standard acute stroke management was initiated, including Cerebrolysin 10 mL intravenously once daily. At 2 weeks, speech recovered completely and motor deficits improved partially. During 1-year follow-up, moderate cognitive impairment emerged and was managed with donepezil, escitalopram, repeated Cerebrolysin courses, and comprehensive rehabilitation. After 1 year, NIHSS improved to 6 and Mini-Mental State Examination (MMSE) improved from 22 to 24. This case highlights the potential safety and supportive role of repeated Cerebrolysin use across different rehabilitation stages after ischemic stroke.

Keywords: Acute ischemic stroke, Aphasia, Neurorehabilitation, Long-term follow-up

Introduction

Recovery after ischemic stroke evolves across acute, subacute, and chronic phases, often involving persistent motor, language, and cognitive deficits and remains a major contributor to global disability (3). Pharmacologic strategies that may enhance neuroplasticity and support long-term recovery are of particular interest when integrated with multidisciplinary rehabilitation, especially in the context of ongoing ischemia/reperfusion-related secondary injury mechanisms (1, 4). Cerebrolysin has been studied as a neuropeptide preparation with possible neurotrophic and neurorestorative effects in stroke recovery and is considered a potential adjunct to standard care (2). Post-stroke recovery processes, including angiogenesis and neuronal remodeling mediated by immune cells, further support the biological plausibility of enhanced functional improvement over time (5). This report describes an extraordinary case of early language recovery followed by longitudinal cognitive and motor improvement over 1 year in a patient treated with repeated Cerebrolysin courses alongside structured rehabilitation.

Patient Information

A male patient born in 1954 was hospitalized in acute condition after awakening with impaired speech and weakness of the right arm and leg. According to his wife, symptoms were first noted in the morning upon waking. His past medical history was notable for a previous ischemic stroke in 2015, from which he had completely recovered. Vascular risk factors included hypertension, with blood pressure on admission measuring 150/90 mmHg.

Clinical Findings and Timeline

Neurological examination on admission demonstrated sensory aphasia and right-sided hemiparesis with Medical Research Council strength graded 3/5. Stroke severity was reflected by an NIHSS score of 16.

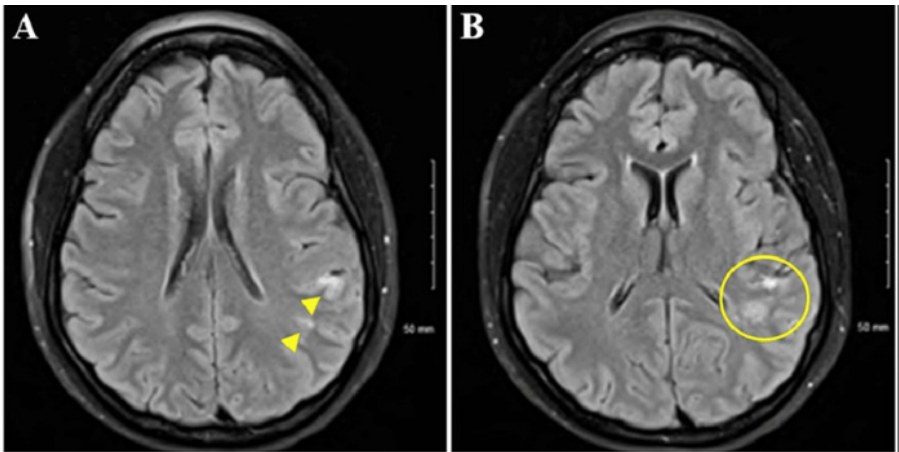


Figure 1: MRI on admission.

Timeline

Table 1: Clinical course and treatment timeline

Time point	Clinical event
Day 0	Acute ischemic stroke; NIHSS 16; sensory aphasia; right hemiparesis 3/5
First 2 weeks	Complete speech recovery; motor improvement to 4/5
90 Days	NIHSS 9
Month 4	MMSE 22; moderate cognitive impairment identified
Months 4–12	Repeated 10-day Cerebrolysin courses every 3 months + rehabilitation
Year 1	NIHSS 6; MMSE 24

Diagnostic Assessment

Brain MRI showed acute infarction in the territory of the left middle cerebral artery involving the left temporal and parietal lobes, anatomically consistent with the observed aphasia and contralateral motor deficits. At 90-day follow-up, the patient had an NIHSS score of 9. Four months after stroke, neurocognitive reassessment revealed moderate cognitive impairment, with an MMSE score of 22.

Therapeutic Intervention

In the acute stroke phase, the patient received mannitol, acetylsalicylic acid, enalapril, atorvastatin and Cerebrolysin. Cerebrolysin was initially prescribed intravenously once daily. Following the identification of post-stroke cognitive impairment at 4 months, treatment was expanded to include donepezil 5 mg once daily and escitalopram 5 mg once daily. Cerebrolysin was continued as a longitudinal neurorecovery strategy, administered every 3 months for 1 year as a 10-day course of 30 mL intravenously once daily. In parallel, the patient underwent comprehensive rehabilitation including occupational therapy and neuropsychological training.

Follow-Up and Outcomes

Two weeks after stroke onset, the patient showed complete recovery of speech and partial motor recovery, with right-sided weakness improving from 3/5 to 4/5. At 4 months, despite strong language recovery, moderate cognitive impairment was identified. With continued

pharmacological treatment and rehabilitation, further gradual improvement was observed. At 1 year, the NIHSS score improved from 16 to 6, indicating substantial neurological recovery. Cognitive performance also improved, with MMSE increasing from 22 to 24. Cerebrolysin was well tolerated across all treatment periods, and no safety concerns were reported.

Discussion

This case illustrates meaningful multidomain recovery after left middle cerebral artery ischemic stroke, including rapid restoration of speech, progressive motor improvement, and partial cognitive recovery over 1 year.

The particularly striking feature is the complete recovery of speech within 2 weeks despite an initially severe presentation with sensory aphasia and temporal-parietal infarction. While spontaneous recovery and early reperfusion-independent neurobiological restitution may explain part of this trajectory, the concurrent use of Cerebrolysin may have supported early neuroplastic adaptation. (1,2,4)

The later emergence of vascular cognitive impairment is clinically relevant and reflects a common yet often underrecognized challenge in stroke survivors. Repeated Cerebrolysin cycles, combined with donepezil, escitalopram, occupational therapy, and neuropsychological training, were associated with stabilization and mild improvement in MMSE over the following months. (2)

The principal limitation is the single-case design, which prevents attribution of causality to Cerebrolysin alone. The patient received multimodal treatment; natural recovery, secondary prevention and rehabilitation interventions likely all contributed to the favorable outcome. (1,4) Nevertheless, the safe use of Cerebrolysin in both early and later recovery phases and the sustained functional gains make this an instructive case for extraordinary neurorecovery.

Conclusion

This case demonstrates that repeated Cerebrolysin administration across acute and chronic recovery stages was safe and associated with favorable language, motor, and cognitive outcomes after ischemic stroke. Although the contribution of multimodal rehabilitation must be acknowledged, this extraordinary recovery course supports further controlled studies examining the role of Cerebrolysin in different phases of stroke rehabilitation.

Patient Perspective

According to the family, the most meaningful improvement was the rapid restoration of communication in the first weeks, followed by gradual recovery of independence in daily activities during the first year.

CASE SUMMARY	
 Patient	• 70 years • MCA ischemic stroke
 Challenge	• Sensory aphasia and hemiparesis
 Treatment	• Cerebrolysin 30 mL/day IV x 10 days + rehabilitation
 Outcome	• NIHSS 16 → 6 • MMSE 22 → 24 • Complete speech recovery
 Take Home Message Long-term monitoring and repeated Cerebrolysin administration integrated with structured rehabilitation may support sustained recovery and help address emerging post-stroke cognitive impairment.	



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...of post-herpes simplex encephalitis with neuropsychiatric symptoms

Abstract

Herpes simplex encephalitis (HSE) is a severe central nervous system (CNS) infection associated with cognitive decline, psychotic symptoms, and epilepsy. Despite aggressive antiviral and corticosteroid treatments, post-HSE complications remain challenging to manage. We report a case of a 33-year-old female patient with post-HSE neuropsychiatric symptoms who showed significant improvement following Cerebrolysin treatment. The patient was treated with acyclovir and dexamethasone in the acute phase, followed by Cerebrolysin administration in the post-acute phase. This case highlights the potential therapeutic role of Cerebrolysin in managing post-encephalitic cognitive dysfunction, underscoring the need for further studies.

Keywords: herpes simplex encephalitis, neuropsychiatric symptoms, Cerebrolysin, case report

Introduction

Herpes simplex encephalitis (HSE) is a common cause of viral encephalitis that can lead to severe neurological and neuropsychiatric sequelae, including cognitive impairment, epilepsy, and behavioral abnormalities [1,2]. Standard treatment with intravenous acyclovir and corticosteroids mitigates acute infection but does not prevent long-term complications [3,4]. Currently, no established treatments exist for managing post-HSE complications. Cerebrolysin is a neuropeptide preparation with potential neurorestorative effects [5]. Cerebrolysin has shown promise in experimental models of neuroregeneration [6]. However, clinical evidence in post-encephalitic patients remains limited. This report describes a case that demonstrated a clinically meaningful benefit from Cerebrolysin administration.

Case Presentation

A 33-year-old female with no prior medical history presented to the emergency department with fever (38.4°C), headache, and anterograde amnesia. The patient reported upper respiratory symptoms for 5 days prior to admission. Initially, she presented with fever and voiding difficulty, leading to a misdiagnosis of cystitis at another hospital. However, despite receiving treatment for a urinary tract infection, the patient's symptoms progressed, and on day 5 of symptom onset, she was transferred to our hospital due to altered consciousness. Upon arrival at the emergency department, routine blood tests and urine analysis were performed; however, no significant abnormalities were found to explain the fever and impaired consciousness. Consequently, a lumbar puncture was performed to investigate the possibility of a central nervous system (CNS) infection or other neurological disorders.

Cerebrospinal fluid (CSF) analysis revealed an elevated white blood cell (WBC) count (65 cells/ μ L; lymphocytes 80%, monocytes 14%, neutrophils 5%, atypical cells 1%), red blood cells (RBCs) 15 cells/ μ L, protein 97.8 mg/dL, and glucose 65 mg/dL (with corresponding serum glucose of 130 mg/dL). Herpes simplex virus type 1 (HSV-1) DNA was detected in the CSF, confirming the diagnosis of herpes simplex encephalitis (HSE). The

clinical course is summarized in Table 1. Brain magnetic resonance imaging (MRI) demonstrated a diffuse cortical diffusion restriction lesion centered on the insular region (Figure 1A-F). Electroencephalography (EEG) showed continuous periodic lateralized epileptiform discharges (PLEDs) at 0.3 Hz in the right temporal region, first appearing one minute after the second period of eye closure (Figure 2A-C).

Table 1: Timeline of the patient's clinical course, diagnostic findings, and therapeutic interventions during hospitalization and follow-up

Timeline	Clinical Course & Interventions
Day 0	First Admission - Fever, Urinary symptoms, Confusion, Anterograde Amnesia - Acyclovir 10mg/kg three times daily (14 days) - Dexamethasone 2mg four times daily (4 days) - MMSE 18/30
Day 7	HSV-1 Confirmed in CSF - CSF: WBC 65(Lymphocyte 80%, monocyte 14%), - Protein 97.8 - MRI: Right temporal involvement - EEG: Periodic epileptiform discharges in the right temporal region
Day 30	Discharged - Cognitive impairment persists (MMSE 22/30) - New symptoms: Agitation, Behavioral changes
Day 45	Second Admission - Worsening neuropsychiatric symptoms - Dysphagia present
Day 50	Cerebrolysin Treatment 10 mL BID for 1 week, then 10 mL TID for 3 weeks - Initial response minimal
Week 14	Gradual Improvement - MMSE increased 26/30 - Behavioral symptoms improved
Month 6	Full Recovery - MMSE 30/30 - Return to work (Bakery) - MRI: Residual right temporal atrophy - EEG: Normalized rhythm

Abbreviations: BID, twice daily; TID, three times daily

The patient received intravenous acyclovir (10 mg/kg every 8 hours) for two weeks, which led to an improvement in urinary frequency and urgency. Cognitive function also showed partial improvement, with the Mini-Mental State Examination (MMSE) score increasing from 18 to 22. However, persistent amnesia and new-onset dysphagia were observed one month after discharge. The patient was subsequently readmitted due to worsening neuropsychiatric symptoms and progressive swallowing dysfunction, characterized by food retention in the mouth without swallowing. Despite the initial improvement following treatment for herpes simplex encephalitis, neurological and psychiatric manifestations gradually worsened after discharge. The patient developed disinhibited sexual behavior and exhibited episodes of irritability, verbal aggression, and physical aggression. The patient's family reported increasing agitation, confusion, and behavioral changes, which significantly impaired daily functioning.

Given the worsening neuropsychiatric symptoms and swallowing difficulties, further evaluation and management were deemed necessary. A psychiatric consultation was performed, and considering the temporal

association of symptom onset, the findings strongly suggested that the neuropsychiatric manifestations were attributable to herpes simplex encephalitis.

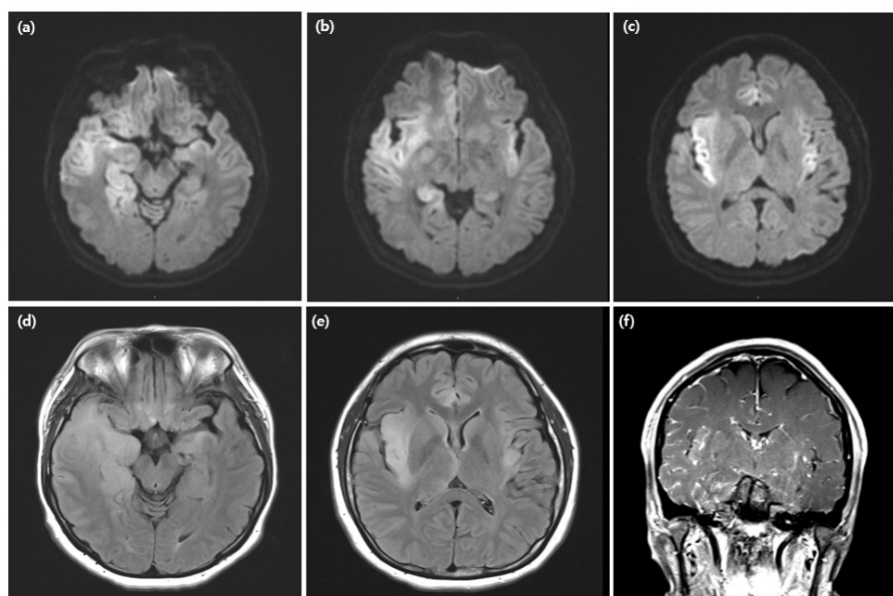


Figure 1: Brain MRI diffusion-weighted images. A–C indicated a diffuse cortical diffusion restriction lesion centered on the insular region. Brain MRI FLAIR images; D–E also demonstrated this finding. Additionally, brain MRI with gadolinium enhancement (F) suggested focal cerebral edema and a diffuse inflammatory lesion in the right temporal and left insular regions.

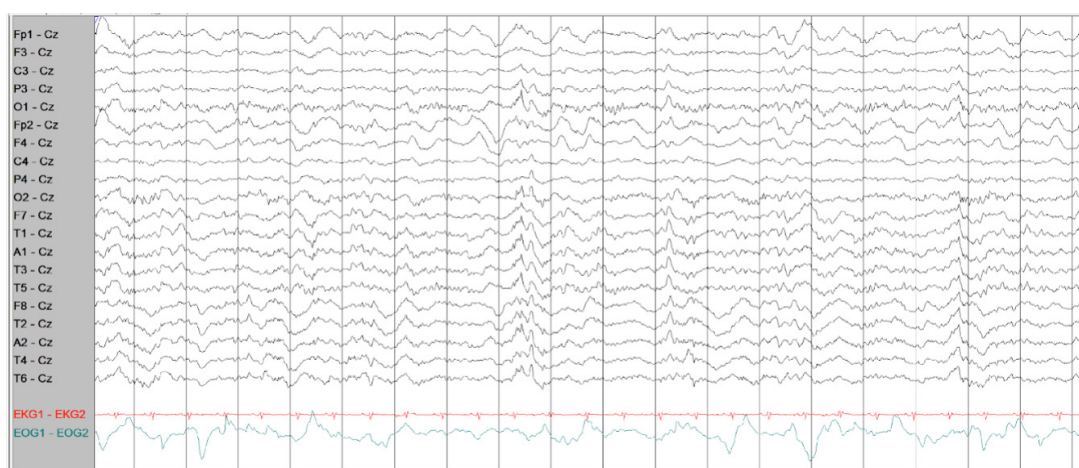


Figure 2: The initial EEG showed continuous periodic lateralized epileptiform discharges at 0.3 Hz in the right temporal region, first appearing one minute after the second period of closed eyes. This EEG was obtained five minutes after the second period of eyes closed with awake.

The patient received intravenous Cerebrolysin infusion [7]. The treatment regimen consisted of 10 mL of Cerebrolysin di-luted in 100 mL of saline solution, administered intravenously twice daily during the first week and subsequently increased to three times daily, with a total daily dose of 30 mL. No adverse effects or complications were observed during the treatment period. Initial clinical improvements were minimal. However, after 4 weeks of Cerebrolysin therapy, the patient exhibited gradual improvement in both cognitive and behavioral symptoms. Throughout the 4-week course of Cerebrolysin treatment, the patient underwent only basic motor rehabilitation and did not receive any additional specialized physical or speech therapy. Over time, cognitive function, neuropsychiatric symptoms, and motor abilities steadily improved. At 6 months post-treatment, the patient's MMSE score recovered to 30, indicating a return to normal cognitive function. The patient was able to return to work as a baker and successfully resumed operating her own bakery. The patient reported that before treatment, she had significant difficulties managing her daily life and felt hopeless about returning to work. After undergoing Cerebrolysin therapy, she gradually regained confidence and cognitive function. Follow-up brain MRI (6 months post-treatment) showed residual cerebromalacia in the right anterior temporal region with a dilated right ventricular horn (Figure 3). Follow-up EEG demonstrated a normalized background rhythm without epileptiform discharges (Figure 4).

The patient reported: ‘At first, I was afraid I would never be able to bake again,’ reflecting her initial distress and later satisfaction with the treatment outcome. She expressed great satisfaction with the treatment and was relieved to regain independence in her personal and professional life.

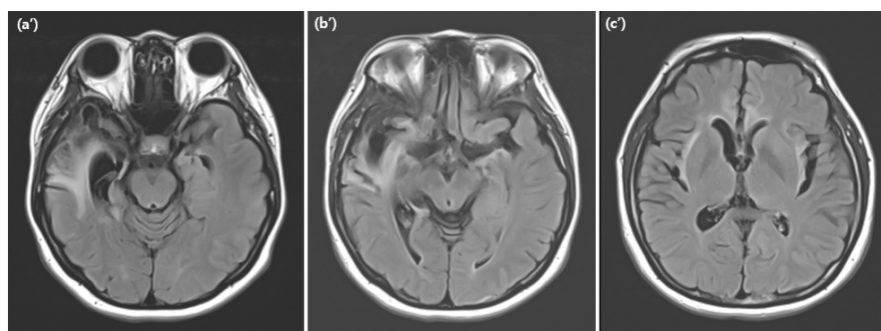


Figure 3: Second Brain MRI (FLAIR) after 6 months showed cerebromalacia in the right anterior temporal region combined with a dilated right ventricle horn (A-C).

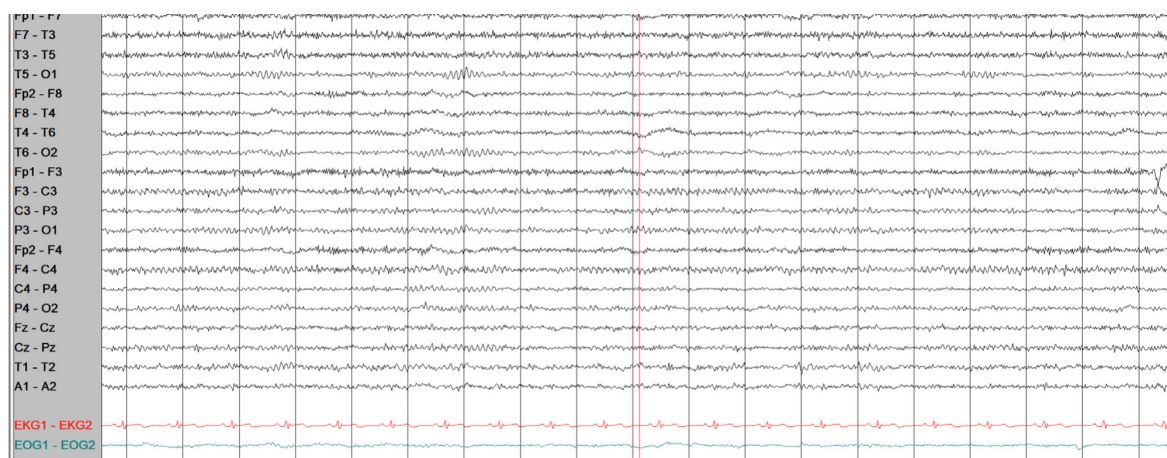


Figure 4: Follow-up EEG revealed normal background activity without definitive epileptiform discharges. This EEG was obtained three minutes after the second period of eyes closed with awake.

Discussion

This case suggests that Cerebrolysin may contribute to long-term neurological recovery in patients with neuropsychiatric and functional impairments following herpes simplex encephalitis (HSE). Current therapeutic approaches for HSE-related neuroinflammation primarily include corticosteroids such as dexamethasone, hydrocortisone, and methylprednisolone, while experimental studies have investigated toll-like receptor agonists, interferon- α , and intravenous immunoglobulin as immunomodulatory strategies [4]. Although no clinical studies have yet demonstrated the efficacy of Cerebrolysin in viral encephalitis, its beneficial effects in other CNS disorders provide a rationale for exploring its use in this setting [8-11].

The potential role of Cerebrolysin in HSE may be explained by three complementary mechanisms. First, it exerts anti-inflammatory effects, which may be relevant given the central role of neuroinflammation in the development of neurological, cognitive, and psychiatric sequelae after viral encephalitis [12]. Experimental studies have shown that Cerebrolysin reduces inflammatory cytokines, including IL-1 β , TNF- α , and IL-6, and suppresses microglial activation, effects that may help attenuate secondary brain injury [6].

Second, Cerebrolysin has neuroprotective properties through the enhancement of neurotrophic factors, including BDNF, NGF, and GDNF [5]. These effects may promote neuronal survival, preserve synaptic connectivity, and reduce apoptosis, potentially limiting the progressive neurodegeneration observed after HSE and other viral encephalitides. Third, Cerebrolysin promotes neuroplasticity and neuroregeneration, mechanisms that have been associated with improved neurological recovery in stroke, traumatic brain injury, and subarachnoid hemorrhage [8-10]. In patients with more severe stroke (NIHSS ≥ 12), Cerebrolysin has been

associated with enhanced functional recovery, likely through stimulation of synaptic formation and dendritic growth [8]. It is generally well tolerated, although caution is advised in patients with renal impairment [9].

Given these anti-inflammatory, neuroprotective, and neurorestorative effects, Cerebrolysin may facilitate recovery of motor, cognitive, and psychiatric deficits following HSE. However, evidence remains limited to case observations, and the clinical improvement observed in this patient cannot establish efficacy. Nevertheless, this case highlights the potential of Cerebrolysin as a therapeutic adjunct for post-HSE neuropsychiatric sequelae and supports the need for larger studies to define its efficacy and optimal treatment regimen.

Conclusion

This case highlights the potential benefit of Cerebrolysin in treating cognitive and neuropsychiatric dysfunction following HSE. Given its strong safety profile and neuroprotective properties, Cerebrolysin could be considered an adjunctive therapy for HSE, particularly in preventing long-term neurological sequelae. Given the lack of established treatments for post-HSE complications, further research is warranted to explore the neuroprotective and regenerative effects of Cerebrolysin in this patient population.

CASE SUMMARY

**Patient**

- 33 years
- Post-herpes simplex encephalitis

**Challenge**

- Severe cognitive, behavioral and swallowing impairment

**Treatment**

- Cerebrolysin 30 mL/day IV x 28 days

**Outcome**

- MMSE 18 → 30
- Behavioral symptoms resolved, returned to work

**Take Home Message**

Cerebrolysin treatment was associated with marked and sustained cognitive and functional recovery after herpes simplex encephalitis, supporting its potential as a neurorestorative treatment option for post-encephalitic deficits.

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...on the brain's functional state in dementia of Alzheimer's type

Abstract

Due to the increasing incidence and prevalence of Alzheimer's disease worldwide, improving treatment methods is important for modern society. Clinical trial and evaluation of the efficacy and safety of the drug Cerebrolysin in the complex treatment of dementia in Alzheimer's disease are conducted at the clinical base of the Republican Scientific and Practical Center for Mental Health (Minsk, Belarus). The effectiveness of the drug is illustrated by a clinical case: patient K., 82 years old, suffering from moderate dementia, received Cerebrolysin 20.0 in the form of intravenous infusions for 20 days. As a result, a positive effect on the cognitive status and functional state of the central nervous system was noted according to pathopsychological and neurophysiological studies. There was no negative dynamics in MMSE. Achieved a 2.7 points reduction in ADAS-cog scores. Self-care skills and concentration improved: the patient held the topic of conversation longer and felt more confident. The effect obtained in the presented clinical case indicates that Cerebrolysin helps slow down the process of neuron degeneration in Alzheimer's type dementia.

Keywords: Dementia, Alzheimer's Disease, Cerebrolysin

Introduction

Deficiency of neurotrophic growth factors plays a significant role in the pathogenesis of primary neurodegenerative diseases. This fact is the basis for the neurotrophic strategy of Alzheimer's disease therapy [1, 2]. Due to the ability of Cerebrolysin to reduce the process of abnormal amyloidogenesis, inhibit the process of neuroapoptosis, and hinder the implementation of various pathogenetic mechanisms leading to neurodegeneration and neuronal death, studies of its effectiveness in Alzheimer's disease have been undertaken. Clinical trials have been conducted in several countries around the world to study the therapeutic efficacy of Cerebrolysin in Alzheimer's disease. The results of these studies have shown statistically and clinically significant therapeutic effects of Cerebrolysin on cognitive, general, and functional parameters in the stages of mild and moderate dementia [2-4]. Cerebrolysin has been added to the range of pharmacological drugs as an alternative. In addition to essential medicines: NMDA antagonists, cholinesterase inhibitors, and Cerebrolysin are included in modern protocols for the diagnosis and treatment of Alzheimer's disease in Belarus and the Russian Federation [5,6]. At the initiative of the manufacturing company EVER Neuro Pharma GmbH, clinical trials and evaluation of the effectiveness of Cerebrolysin in the treatment of Alzheimer's disease are being conducted at the clinical base of the State Institution Republican Scientific and Practical Center for Mental Health. Its clinical effectiveness and the dynamics of the neurodegenerative process are illustrated by a clinical example. A clinical case. Patient K., 82 years old. Heredity is not psychopathologically burdened. Early development without special features. Higher education, graduated from the University of Economics, majoring in economics. She worked as a specialist, then as a director of a department store. Currently retired, group 2 disabled person. She is married and has two children. She lives with her husband. It is observed by an

ophthalmologist for initial cataracts, retinal angiopathy, moderate hypermetropia of both eyes. According to her husband, the first manifestations of the disease were noted against the background of COVID-19 infection in 2021, at first there was slight forgetfulness, then she began to feel confused in unfamiliar places. Fully serviced by her husband. She doesn't navigate her own apartment, she doesn't leave the house (gets lost), doesn't cook, can't count money, doesn't remember her date of birth, age, and doesn't know the current date. She currently has disability group 2, and is diagnosed with dementia with Alzheimer's disease (F00).

Receives memantine 20 mg daily. When seeking medical help, complaints about progressive memory loss, loss of household skills. The patient's general condition is satisfactory. Temperature 36.6 °C. Height 160 cm. Weight 63kg. The body mass index is 24.61. The physique is correct. She's well-fed. The skin is of ordinary color. Visible mucous membranes are unchanged. The lymph nodes are not enlarged and are painless on palpation. Musculoskeletal system without deviations from the norm. Blood pressure: 130/80 mmHg, rhythmic pulse rate, 76/minute. The boundaries of the heart are not expanded. The heart tones are dull, rhythmic. The number of breaths per minute is 16. Breathing is vesicular, on both sides, there is no wheezing. No pathology was detected on the part of the digestive and excretory organs. Examination of the Neurological Status Revealed No Focal Symptoms.

Outwardly neat (her husband helps to carry out hygiene procedures, prepares clothes, helps to get dressed). She is disoriented in place, time, and approximately oriented in her own personality. Correctly calls the last name, first name, patronymic. She doesn't remember her date of birth, doesn't know how old she is, or what month it is. She doesn't remember where she worked. She knows who brought her, correctly calls her husband's name and patronymic, and with outside help, she gave him her home address. Household skills such as cleaning, washing, cooking, and putting on clothes for the occasion have largely been lost. Her handwriting has become illegible, she does not understand what she is writing at dictation. Not critical to the condition. In an even mood. She is calm and submissive in her behavior. Beyond hallucinatory-delusional disorders. There are no aggressive, suicidal tendencies. The result of filling in the Khachinsky scale is 2 points.

Neuropsychologist's consultation. Patient K., 82 years old. She lives in a city apartment with her husband, who takes care of her. Has a second disability group. She is partially oriented in place, but not oriented in time. He cannot name the date, time of the year, or his own address. He correctly designates the country and city of residence. Self-orientation is incomplete: he correctly calls his last name, first name, patronymic, does not remember his date of birth, age, profession. Questions are often not answered to the point, because it is difficult to understand oral speech at the decoding stage. Reduced concentration of attention. The emotional background is smooth, emotional manifestations are monotonous, and when it is difficult to complete a task, he shows anxiety. Criticism of the current mental state is reduced. The pace of speech and mental activity is slow. Partially assimilates the instructions. The purpose of the pathopsychological examination was to diagnose intellectual disability.

A. Methods: Mini-mental state examination (MMSE), Alzheimer's disease assessment scale – cognitive subscale (ADAS-cog+). The results of the survey. MMSE: 11 points – moderate level of dementia. Impaired: memory function, incomplete orientation in place, time, and self. Reading skills are preserved, writing and counting skills are lost. ADAS-cog+: 61.3 points.

B. Conclusion:

- intellectual disability corresponding to a moderate level of dementia was revealed. Orientation in place, time, self, short-term and long-term memory are impaired;
- needs care and supervision. The MMSE (11 points) and ADAS-cog+ (61.3 points) test results are presented in (Tables 1, 2).

Pronounced diffuse disturbances of cortical rhythmicity are recorded on the background EEG in a state of passive wakefulness. The peak frequency is less than the maximum allowable value of 6.1 Hz. The alpha rhythm is practically absent (index 15%), while the maximum values of its frequency are shifted to the frontal region (Figure 1 and 2). Low-amplitude slow activity of the delta and theta ranges with an index of 35% is recorded in all leads without zonal differences. The computer-generated pathological patterns revealed during

the compilation of the electroencephalogram map indicate a decrease in the functional state of the brain. The MRI Report. Diffuse cortical atrophy, more pronounced in the temporal lobes. The size of the ventricles, the grooves of the convection, and the Sylvian fissure are increased. Signs of hippo-campal atrophy. The quantitative content of amyloid proteins A β 40, A β 42, and phosphorylated tau protein in the blood was determined by en-zyme immunoassay. The patient's relatives refused to perform a lumbar puncture and cerebrospinal fluid examination. There was a deviation in the blood concentration of A β 42 (38 pg/ml, norm 8-10 pg/ml), A β 40 (59,8 pg/ml, norm 30-40 pg/ml), phosphorylated tau protein (21 pg/ml, norm 8-10 pg/ml), (Table 3). In general and biochemical blood tests any deviation was not revealed.

Taking into account complaints, medical history, clinical and laboratory examination data and in accordance with the ICD-10 criteria, the diagnosis was established: F00. Dementia in Alzheimer's disease (G30). Patient K. included in the "Post-marketing observational prospective study evaluating clinical outcomes and tolerability of the drug Cerebrolysin, solution for injection, ampoules of 5 ml, 10 ml and 20 ml, manufactured by EVER Neuro Pharma GmbH, Austria, in patients with vascular dementia and dementia in Alzheimer's disease." The patient and her accompanying spouse signed a voluntary informed consent to participate in the study. In the hospital of the Republic Research Center for Mental Health in the day care department, a course of treatment with Cerebrolysin was performed by slow intravenous infusions of 20 ml in 0.9% sodium chloride solution (9 mg NaCl/ml). The procedures were performed daily, with the exception of weekends, 20 in total. The duration of the infusion was 20-40 minutes. The tolerability of the treatment is good, no adverse reactions were noted. At the end of treatment, the patient was examined again: examination by a psychiatrist, consultation with a psychologist, EEG registration, determination of biomarkers of CNS damage. In neurological status – without dynamics. At the psychiatrist's appointment, there was an improvement in self-service skills and concentration: the patient held the topic of conversation longer and felt more confident. Consultation with a neuropsychologist. The result of the MMSE test did not differ from the initial one – 11 points, while the result of the ADAS-cog+ test showed a difference of 2.7 points (Tables 1, 2).

A detailed comparative analysis of the results obtained using the MMSE technique revealed: a slight improvement in orientation in time and place; preservation of perception, concentration, and short-term memory.

Table 1: Data from a psychological examination using the MMSE of patient K. in dynamics: before and after the course of treatment with Cerebrolysin.

Cognitive sphere	Examination before the start of therapy	Post-therapy examination
Orientation in Time	1	0
Orientation in a Place	2	2
Perception	3	3
Attention and Calculation	1	1
Memory	0	0
Speech, Reading, Writing	4	5
Total Score	11	11

A comparison of the results of the study using the ADAS-cog+ technique revealed:

deterioration of short-term verbal memory (word recognition); slight improvement in constructive and ideational practice; improved understanding of instructions; slight improvement in concentration.

Overall, the dynamics showed a stable state of cognitive functions: moderate degree of dementia (with severe cognitive impairment). As a result of qualitative data analysis, we can talk about the improvement of speech functions (writing, speech), the ability to follow instructions, the ability to execute commands, the ability to express their thoughts and perceive information. The patient's emotional state is stable: she has an even, calm mood.

On the background EEG, diffuse disturbances of cortical rhythms with a predominance of low activity in the theta and delta ranges, alternating with alpha waves without zonal differences (Figure 3). When compared with the data of the previous examination, significant positive dynamics was noted: the delta activity index

decreased from 35.5 to 28.6%, theta activity – from 60.4 to 40.4%, and the alpha activity index in the occipital regions increased from 11.4% to 17.5% (Figure 4). There was a pronounced effect of reducing the level of A β 42 to 16,2 pg/ml, the others studied markers of CNS damage in the blood did not have sharp fluctuations. At the same time, there was a tendency to increase the concentration of A β 40 to 61 pg/ml and to decrease phosphorylated tau protein to 18 pg/ml (Table 1). The assessment of the dynamics of these indicators is important as prognostic signs of the severity, aggressiveness of the course of the disease and the effectiveness of therapy. [7-8]. According to current data, amyloid proteins can independently induce hyperphosphorylation of tau protein and its deposition in CNS neurons. At the same time, tauopathy in patients with a clinical diagnosis of Alzheimer's disease can be considered as a secondary pathological process mediated by the toxic effect of amyloid proteins.

Table 2: Psychological examination data using the ADAS cog+ scale.

Task	Examination before strating therapy	Post-therapy examination
Word recall	7,3	7,3
Naming Objects and Fingers	1	1
Commands	4	3
Constructional Praxis	4	3
Ideatorial Praxis	5	4
Orientation	6	6
Word Recognition	5	7,3
Remembering Test Instructions	5	5
Comprehension of Spoken Language	4	3
Word Finding Difficulty	4	4
Understanding	3	3
Concentration and Distraction	3	3
Crossing Out Numbers	5	5
Passing the Maze	5	4
Total Score	61,3	58,6

Upon completion of the course of treatment in accordance with the current protocol for providing medical care to patients with organic, including symptomatic, mental disorders [5], recommendations are given: memantine, tablets for oral administration immediately after meals, 20 mg, the maximum daily dose is 20 mg; neurocognitive rehabilitation; supervision of a psychiatrist–narcologist at the place of residence. Working with the patient's immediate environment included determining the need for constant monitoring. Recommendations on maintaining physical status are given: compliance with the diet, hygiene procedures, daily walks. The issues of safety and the risks of incidents in everyday life when the patient is left unattended were discussed. For example, she may leave home and get lost, turn on the gas, or take medication several times due to a memory disorder. In accordance with the recommendations of the World Health Organization, special attention should be paid to the safety measures of both the patient and his immediate environment [10].

Discussion

The pathogenesis of Alzheimer's disease is multicomponent. Accordingly, the treatment of the disease includes a wide range of pharmacological agents that differ in their mechanism of action. Substitution therapy aimed at overcoming neurotransmitter deficiency in various neural systems has been universally approved and included in guidelines, clinical recommendations, and treatment protocols for Alzheimer's disease and Alzheimer's dementia. Acetylcholinesterase inhibitors rivastigmine, donepezil and galantamine are mainly used to overcome cholinergic insufficiency, the effectiveness and safety of which for Alzheimer's sufferers

have been convincingly demonstrated in numerous domestic and foreign clinical studies. The main drug of the glutamatergic strategy for the treatment of Alzheimer's disease is memantine, which can cause neuroprotective and positive symptomatic effects at the level of still preserved glutamatergic synapses [11, 12]. However, these drugs provide a symptomatic effect and do not affect the progression of the disease. Disease-modifying therapy is under active development. An alternative approach to pharmacotherapy is the use of drugs that mimic the effects of endogenous neurotrophic factors, such as Cerebrolysin, a peptide drug that affects various mechanisms of the pathological cascade in Alzheimer's disease.

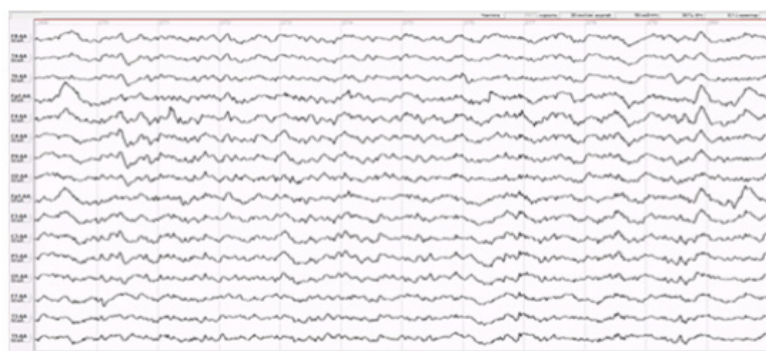


Figure 1: Background EEG of Patient K. During the Initial Examination.

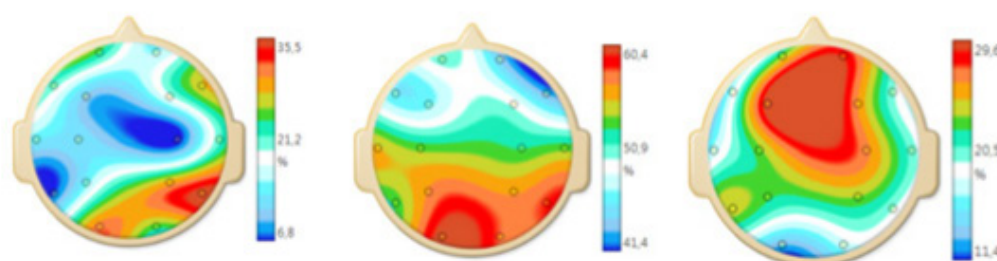


Figure 2: Delta, Theta and Alpha activity index maps - the result of computer processing of the background EEG in the periodometric analysis mode.

The long-term history of the use of Cerebrolysin includes numerous clinical multicenter studies with a pronounced positive effect at various stages of dementia development. It has been convincingly shown that Cerebrolysin is safe and effective in the treatment of Alzheimer's disease. Acting as a multipurpose peptidergic drug with a neurotrophic mechanism of action, Cerebrolysin has a long-term therapeutic effect, which may reflect its potential usefulness for modifying the disease even at the stages of moderate and severe dementia [12-14]. There is evidence of the effectiveness of Cerebrolysin as monotherapy [15]. But this point has a minimum of supporters. Combination therapy is considered to be a promising option at the present stage. The good tolerability of Cerebrolysin and memantine, the proven safety and tolerability of their combined use with cholinesterase inhibitors with potentiation of positive and reduction of negative effects allow us to recommend the use of a combination of these groups of drugs in the treatment of Alzheimer's disease [16,17].

Table 3: The results of the study of the content of CNS damage markers in the blood serum of patient K. before and after the course of treatment with Cerebrolysin.

Marker	Blood norm values, pg/ml	Before treatment	After treatment
A β 42	8-10*	38	16,4
A β 40	30-40*	59,8	61
Phosphorylated tau protein	8-10*	21	18

Note*: values below and above the specified range are considered pathological.

A meta-analysis of randomized, double-blind, placebo-controlled trials showed that intravenous administration of 30 ml/ day of Cerebrolysin to patients with mild to moderate Alzheimer's disease demonstrates a combined effect leading to global clinical changes and improved cognitive function. Cerebrolysin was significantly more

effective than placebo in terms of cognitive function after 4 weeks ($p=0.031$) and 6 months ($p=0.1710$) of follow-up, with respect to global clinical changes ($p=0.0212$ and $p=0.0150$, respectively) [13]. Neuropsychological testing remains the most accessible tool for tracking cognitive function dynamics in patients with dementia and Alzheimer's disease. In the clinical case under consideration, the ADAS-cog+ and MMSE data clearly correlated with the results of assessment of brain structural changes, the level of amyloid proteins A β 40, A β 42, phosphorylated tau protein in blood serum, and data on the frequency-spatial distribution of brain bioelectric activity. Minimally invasive methods are of particular importance for diagnosis and dynamic observation in clinical practice: the study of neurodegeneration proteins in the blood, neurophysiological parameters.

The detection of pathological values of neurodegeneration markers in the blood of patients suffering from dementia with Alzheimer's disease is an established fact [18]. Most researchers identify two key processes that determine the development and progression of Alzheimer's disease: amyloidosis and neurodegeneration (tauopathy) [19]. According to the tau concept, the main causes of neurodegeneration are disorders in the structure of neurons. They are associated with hyperphosphorylation of the microtubule binding protein (tau protein). This leads to the collapse of intracellular transport, disruption of synaptic transmission and deposition of neurofibrillary tangles in the parenchyma of the brain. According to the amyloid concept, the cause of pathological processes in the central nervous system is the formation of "amyloid plaques" in the glia from insoluble A β 42 peptide and deposition of toxic A β 40 peptide in the wall of cerebral vessels. In the presented clinical case, the clinical effect in the form of some improvement in cognitive functions (improvement of self-care skills, concentration of attention, speech) correlated with the positive dynamics of blood levels of amyloids and phosphorylated tau protein.

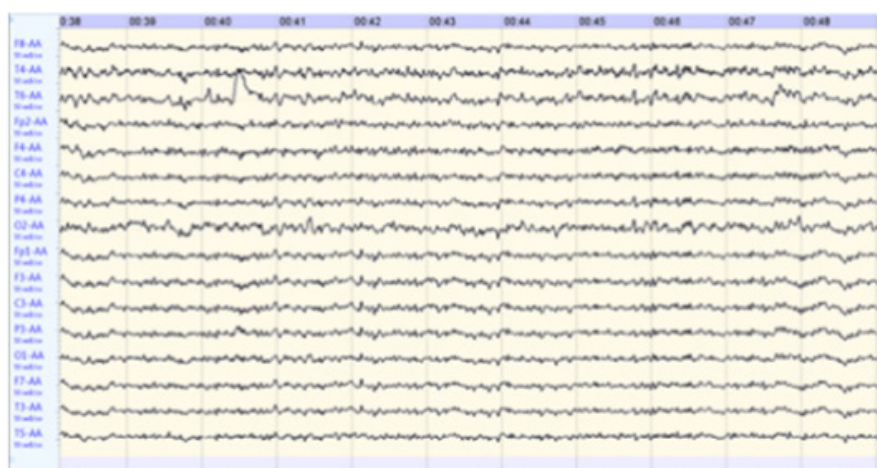


Figure 3: Background EEG of patient K. during repeated examination after the course of treatment with Cerebrolysin

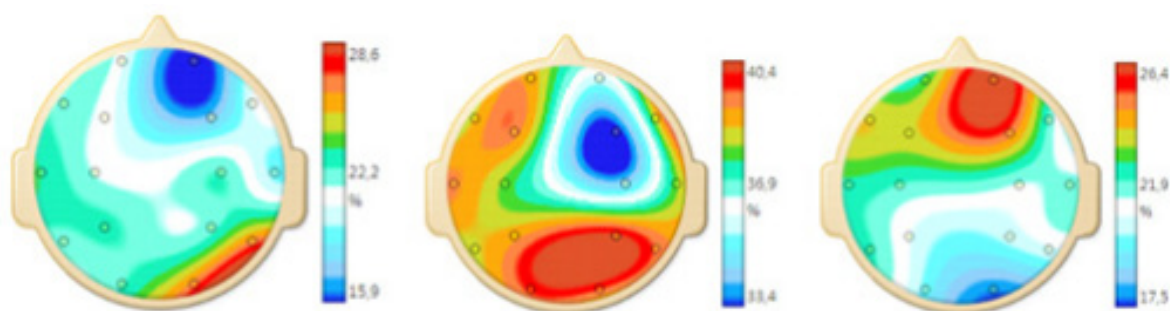


Figure 4: delta, theta and alpha activity index maps - the result of computer processing of the background EEG in the periodometric analysis mode.

According to contemporary neurophysiological researchers, computed electroencephalography (EEG) has become an affordable method with high temporal resolution, the parameters of which demonstrate high diagnostic value in Alzheimer's disease [20]. Currently, EEG analysis of the bioelectric activity of the brain has evolved from a method based solely on visual viewing to a quantitative one, significantly reducing the degree of subjectivity. Literature data demonstrate that the EEG in Alzheimer's disease is characterized by high power delta and theta rhythms, as well as low power alpha and/or beta rhythms in the occipital regions [21-23].

There is a correlation between the severity of dementia and the severity of changes in the EEG in the form of a decrease in the frequency of the basic rhythm and an increase in the index of slow-wave activity [24]. Some authors suggest using a decrease in the theta activity index during dynamic monitoring as a predictor of response to anticholinesterase therapy [25-26]. It has also been shown that the power spectrum of the occipital alpha rhythm correlates with the cognitive status of patients measured using the ADAS-cog scale: the lower the power of the alpha range, the worse the cognitive status [27]. In patient K. Under the influence of Cerebrolysin therapy, there was a tendency to reduce pathological computer EEG patterns (Figures 2 and 4). In general, the ADAS-cog+ test data improved, the alpha activity index increased, and the level of A β 42 and phosphorylated tau protein decreased in patient K.

These results suggest that all of the listed markers of the activity of the pathological process can be used alone or in combination to examine patients with dementia in Alzheimer's disease [26]. Along with neurocognitive tests, the use of biomarkers is becoming an important part of clinical practice as new treatments are introduced that alter the course of the disease.

Conclusion

Cerebrolysin used in the treatment of a patient suffering from dementia with Alzheimer's disease during a "Post-marketing observational prospective study to evaluate the clinical outcomes and tolerability of the drug Cerebrolysin, solution for injection, ampoules of 5 ml, 10 ml and 20 ml, manufactured by EVER Neuro Pharma GmbH, Austria, in patients with vascular dementia and dementia with Alzheimer's disease", had a positive effect on cognitive status, the functional state of the central nervous system and the dynamics of markers of neurodegeneration.

CASE SUMMARY



Patient

• 82 years • Alzheimer's disease dementia



Challenge

• Moderate dementia with loss of daily living skills



Treatment

• Cerebrolysin 20 mL/day IV x 20 days



Outcome

• ADAS-cog 61.3 → 58.6 • Improved self-care and concentration



Take Home Message

Cerebrolysin treatment was associated with improved cognitive and functional status, including better self-care, attention, and speech, accompanied by changes in biomarkers and neurophysiological parameters in a patient with moderate Alzheimer's dementia.

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References

Acute Ischemic Stroke - Alexander Borisevich

1. Zhang D, Dong Y, Li Y, Chen J, Wang J, Hou L. Efficacy and Safety of Cerebrolysin for Acute Ischemic Stroke: A Meta-Analysis of Randomized Controlled Trials. *Biomed Res Int.* 2017;2017:4191670. 10.1155/2017/4191670
2. Muresanu DF, Heiss WD, Hoernberg V et al. Cerebrolysin and Recovery After Stroke (CARS) A randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47(1):151-159.
3. Ziganshina LE, Abakumova T, Vernay L. Cerebrolysin for acute ischemic stroke. *Cochrane Database Syst Rev.* 2017;4(4):CD007026. 10.1002/14651858
4. Gharagozli K, Harandi AA, Houshmand S, et al. Efficacy and safety of Cerebrolysin treatment in early recovery after acute ischemic stroke: a randomized, placebo-controlled, double-blinded, multicenter clinical trial. *J Med Life.* 2017;10(3):153-160.
5. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018;39(4):629-640. 10.1007/s10072-017-3214-0
6. Guekht A, Vester J, Heiss WD, et al. Safety and efficacy of Cerebrolysin in motor function recovery after stroke: a meta-analysis of the CARS trials. *Neurol Sci.* 2017;38(10):1761-1769. 10.1007/s10072-017-3037-z
7. Mekaj YH, Daci FT, Mekaj AY. New insights into the mechanisms of action of aspirin and its use in the prevention and treatment of arterial and venous thromboembolism. *Ther Clin Risk Manag.* 2015;11:1449-1456. 10.2147/TCRM.S92222
8. Mach F, Baigent C, Catapano AL, et al. Scientific Document Group. 2019 ESC/EAS Guidelines for the management of dyslipidaemias: lipid modification to reduce cardiovascular risk. *Eur Heart J.* 2020;41(1):111-188. 10.1093/eurheartj/ehz455
9. Berger C, Stauder A, Xia F, Sommer C, Schwab S. Neuroprotection and glutamate attenuation by acetylsalicylic acid in temporary but not in permanent cerebral ischemia. *Exp Neurol.* 2008;210:543-548. 10.1016/j.expneurol.2007.12.002
10. Wei Z, Chigurupati S, Arumugam TV, Jo DG, Li H, Chan SL. Notch activation enhances the microglia-mediated inflammatory response associated with focal cerebral ischemia. *Stroke.* 2011;42(9):2589-2594. 10.1161/STROKEAHA.111.614834

Acute Ischemic Stroke - Anaal Awni Moh'd El-Khasawneh

1. Dukkupati S, et al. Complications of diagnostic cardiac catheterization and percutaneous coronary interventions. *Cardiol Clin.* 2013;31(1):1-9.
2. Fuchs S, et al. Stroke complicating percutaneous coronary interventions: Incidence, predictors, and prognostic implications. *Circulation.* 2002;106(1):86-91.
3. Powers WJ, et al. 2019 Guidelines for the early management of patients with acute ischemic stroke. *Stroke.* 2019;50:e344-e418.
4. Muresanu DF, et al. Cerebrolysin and Recovery After Stroke (CARS): A randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47(1):151-159.
5. Bornstein NM, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: A meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018;39(4):629-640.
6. Ziganshina LE, et al. Cerebrolysin for acute ischemic stroke. *Cochrane Database Syst Rev.* 2020;7:CD007026.
7. Muresanu DF, et al. Neurotrophic factors and neuroplasticity in stroke recovery. *J Neurol Sci.* 2019;398:1-8
8. Brainin M. Cerebrolysin: a multi-target drug for recovery after stroke. *Expert Rev Neurother.* 2018 Aug;18(8):681-687. doi: 10.1080/14737175.2018.1500459. Epub 2018 Jul 18. PMID: 30004268.

Acute Ischemic Stroke - Benjamin WY Lo

1. Fiani B, Covarrubias C, Wong A, et al. Cerebrolysin for stroke, neurodegeneration, and traumatic brain injury: review of the literature and outcomes. *Neurol Sci.* 2021;42(4):1345-53.
2. Kang DH, Choi BY, Lee SH, et al. Effects of cerebrolysin on hippocampal neuronal death after pilocarpine-induced seizure. *Front Neurosci.* 2020. <https://doi.org/10.3389/fnins.2020.568813>.
3. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and recovery after stroke (CARS). *Stroke.* 2016;47(1):151-159.
4. Homberg V, Jianu DC, Stan A, et al. Speech therapy combined with Cerebrolysin in enhancing nonfluent aphasia recovery after acute ischemic stroke: ESCAS randomized pilot study. *Stroke.* 2025;56:937-947.
5. Beghi E, Binder H, Birle C, et al. European Academy of Neurology guideline on pharmacological support in early motor rehabilitation after acute ischaemic stroke. *Eur J Neurol.* 2021;28(9):2831-2845.

Acute Ischemic Stroke - Romany Hosni Gabra

1. Feigin VL, Brainin M, Norrving B, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke.* 2022;17(1):18-29.
2. Powers WJ, Rabinstein AA, Ackerson T, et al. 2019 Guidelines for the Early Management of Patients With Acute Ischemic Stroke. *Stroke.* 2019;50(12):e344-e418.
3. Adams HP Jr, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial (TOAST). *Stroke.* 1993;24(1):35-41.
4. Rowland LP, Pedley TA. *Merritt's Neurology.* 13th ed. Philadelphia: Wolters Kluwer; 2016.

5. Casa DJ, Armstrong LE, Hillman SK, et al. National Athletic Trainers' Association Position Statement: Fluid Replacement for Athletes. *J Athl Train.* 2000;35(2):212–224.
6. Wang Y, Lim LL, Levi C, Heller RF, Fisher J. Influence of admission body temperature on stroke mortality. *Stroke.* 2000;31(2):404–409.
7. Bouchama A, Knochel JP. Heat stroke. *N Engl J Med.* 2002;346(25):1978–1988.
8. Heiss WD. The ischemic penumbra: correlates in imaging and implications for treatment of ischemic stroke. *Cerebrovasc Dis.* 2011;32(4):307–320.
9. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of randomized controlled trials. *Stroke.* 2018;49(6):1516–1524.
10. Zhang L, Chopp M, Meier DH, et al. Neurorestorative therapies for stroke: underlying mechanisms and translation to the clinic. *Lancet Neurol.* 2019;18(7):647–659.
11. Hankey GJ. Stroke. *Lancet.* 2017;389(10069):641–654.
12. Steiner T, Böhm M, Dichgans M, et al. Recommendations for the management of intracranial haemorrhage—part I. *Cerebrovasc Dis.* 2006;22(4):294–316.

Acute Ischemic Stroke - Vien C Le

1. Donkor ES. Stroke in the 21(st) century: a snapshot of the bur-den, epidemiology, and quality of life. *Stroke Res Treat* 2018; 2018: 3238165.
2. Heinsius T, Bogousslavsky J and Van Melle G. Large infarcts in the middle cerebral artery territory etiology and outcome patterns. *Neurology* 1998; 50(2): 341–350.
3. Misra V, Ritchie MM, Stone LL, et al. Stem cell therapy in ischemic stroke: role of IV and intra-arterial therapy. *Neurology* 2012; 79: S207–212.
4. Prasad K, Sharma A, Garg A, et al. Intravenous autologous bone marrow mononuclear stem cell therapy for ischemic stroke: a multicentric, randomized trial. *Stroke* 2014; 45(12): 3618–3624.
5. Ghali AA, Yousef MK, Ragab OA, et al. Intra-arterial infusion of autologous bone marrow mononuclear stem cells in subacute ischemic stroke patients. *Front Neurol* 2016; 7: 228.
6. Chang WH, Park C-H, Kim D, et al. Cerebrolysin combined with rehabilitation promotes motor recovery in patients with severe motor impairment after stroke. *BMC Neurol* 2016; 16: 31.
7. Lyden P. Using the National Institutes of Health Stroke Scale 2017; 48: 513–519.
8. Gregson JM, Leathley MJ, Moore AP, et al. Reliability of measurements of muscle tone and muscle power in stroke patients. *Age Ageing* 2000; 29(3): 223–228.
9. James M. Use of the medical research council muscle strength grading system in the upper extremity. *J Hand Surg Am* 2007; 32(2): 154–156.
10. Jang SH and Chang MC. Motor outcomes of patients with a complete middle cerebral artery territory infarct. *Neural Regeneration Research* 2013; 8: 1892–1897.
11. Naghdi S, Ansari NN, Mansouri K, et al. A neurophysiological and clinical study of Brunnstrom recovery stages in the upper limb following stroke. *Brain Inj* 2010; 24(11): 1372–1378.
12. Broderick JP, Adeoye O and Elm J. Evolution of the Modified Rankin Scale and its use in Future Stroke Trials. *Stroke* 2017; 48(7): 2007–2012.
13. Mahoney FI and Barthel DW. Functional evaluation: the Barthel Index. *Maryland State Med J* 1965; 14: 61–65.
14. Chen J, Li Y, Katakowski M, et al. Intravenous bone marrow stromal cell therapy reduces apoptosis and promotes endogenous cell proliferation after stroke in female rat. *J Neurosci Res* 2003; 73: 778–786.
15. Carbajal-Galarza M, Chinchihualpa N, Abanto-Perez S, et al. Effectiveness of technological interventions to improve upper limb motor function in people with stroke in low- and middle-income countries: protocol for a systematic review and meta-analysis, 2020, <https://www.medrxiv.org/content/10.1101/2020.11.10.20209197v1.full.pdf>
16. Wang H, Arceo R, Chen S, et al. Effectiveness of interventions to improve hand motor function in individuals with moderate to severe stroke: a systematic review protocol. *BMJ Open* 2019; 9: e032413.
17. Ranzani R, Lamercy O, Metzger JC, et al. Neurocognitive robot-assisted rehabilitation of hand function: a randomized control trial on motor recovery in subacute stroke. *J Neuroeng Rehabil* 2020; 17: 115.
18. Ito A, Kubo N, Liang N, et al. Regenerative rehabilitation for stroke recovery by inducing synergistic effects of cell therapy and neurorehabilitation on motor function: a narrative review of pre-clinical studies. *Int J Mol Sci* 2020; 21: 3135.
19. Muresanu DF, Heiss W-D, Hoemberg V, et al. Cerebrolysin
20. and recovery after stroke (CARS). *Stroke* 2016; 47: 151–159. 20. Muresanu DF, Florian S, Hömberg V, et al. Efficacy and safety of cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial. *Neurol Sci* 2020; 41(5): 1171–1181.
21. Zhang Y, Chopp M, Zhang Y, et al. Randomized controlled trial of Cerebrolysin's effects on long-term histological outcomes and functional recovery in rats with moderate closed head injury. *J Neurosurg.* Epub ahead of print 6 September 2019. DOI: 10.3171/2019.6.Jns191027.

CERECAP - Natan Bornstein

1. Ribó M, Staszewski J, Zeiler SR, Michalak S, El Bassiouny A, Gongora-Rivera F, Poljakovic Z, Khasanova DR, Kalinin MN, Chutinet A, Eichel R, Kojder K, Ong M, Bedeković MR, Chang CH, Lee M, Quitasol P, Tsiskaridse A, Bornstein NM. Cerebroprotection in acute ischemic stroke: Perspectives on combining cerebrolysin with recanalization therapy. *J Stroke Cerebrovasc Dis.* 2026 Jan;35(1):108515. doi: 10.1016/j.jstrokecerebrovasdis.2025.108515. Epub 2025 Dec 3.

CERECAP - Alex Chang

1. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723-1731. doi:10.1016/S0140-6736(16)00163-X
2. Saver JL, Goyal M, van der Lugt A, et al. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: a meta-analysis. *JAMA*. 2016;316(12):1279-1288. doi:10.1001/jama.2016.13647
3. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. *Stroke*. 2019;50(12):e344-e418. doi:10.1161/STR.0000000000000211
4. Hong JM, Kim DS, Kim M. Hemorrhagic transformation after ischemic stroke: mechanisms and management. *Front Neurol*. 2021;12:703258. doi:10.3389/fneur.2021.703258
5. Dammavalam V, Lin S, Nessa S, Daksla N, Stefanowski K, Costa A, et al. Neuroprotection during thrombectomy for acute ischemic stroke: a review of future therapies. *Int J Mol Sci*. 2024;25(2):891. doi:10.3390/ijms25020891
6. Kalinin MN, Khasanova DR. Heterogeneous treatment effects of Cerebrolysin as an early add-on to reperfusion therapy: post hoc analysis of the CEREHETIS trial. *Front Pharmacol*. 2024;14:1288718. doi:10.3389/fphar.2023.1288718
7. Staszewski J, Dębiec A, Gniadek-Olejniczak K, et al. Cerebrolysin after endovascular thrombectomy in stroke: 12-month functional outcomes in a propensity-matched cohort. *Transl Stroke Res*. 2026;17:28. doi:10.1007/s12975-026-01414-z
8. Khasanova DR, Kalinin MN. Cerebrolysin as an early add-on to reperfusion therapy: risk of hemorrhagic transformation after ischemic stroke (CEREHETIS), a prospective, randomized, multicenter pilot study. *BMC Neurol*. 2023;23:121. doi:10.1186/s12883-023-03159-w
9. Kalinin MN, Khasanova DR. Cerebrolysin, hemorrhagic transformation, and anticoagulation timing after reperfusion therapy in stroke: post hoc secondary analysis of the CEREHETIS trial. *Front Pharmacol*. 2026;16:1725255. doi:10.3389/fphar.2025.1725255

CERECAP - Daniel Šaňák

1. Prabhakaran S, Gonzales N, Zachrison K, et al. 2026 Guideline for the early management of patients with acute ischemic stroke: A guideline from American Heart Association/American Stroke Association. *Stroke* 2026; 57: e00-e00. doi: 10.1161/STR.0000000000000513
2. Aguiar de Sousa D, Katsanos A, Li L, et al. ESO annual stroke evidence update 2025. *Eur Stroke J* 2026, 11(2), 1–16 <https://doi.org/10.1093/esj/aakag009>
3. Muresanu DF, Buzoianu A, Florian SI, et al. Towards a roadmap in brain protection and recovery. *J Cell Mol Med* 2012; 16(12): 2861-71.
4. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischemic stroke: a meta-analysis of individual patient data from five randomized trials. *Lancet* 2016; 387(10029):1723-31. doi: 10.1016/S0140-6736(16)00163-X.
5. Chollet F, Cramer SC, Stinear C, et al. Pharmacological therapies in post stroke recovery: recommendations for future clinical trials. *J Neurol* 2014; 261(8): 1461-8.
6. Engelter ST. Safety in pharmacological enhancement of stroke rehabilitation. *Eur J Phys Rehabil Med* 2013 ; 49(2): 261-7.
7. Yan M, Yang S, Zhao B, et al. Sonic hedgehog pathway: molecular mechanisms and therapeutic potentials in ischemic stroke recovery. *Biochem Pharmacol* 2025; 242(1):117235.
8. Sahota P, Savitz SI. Investigational therapies for ischemic stroke: neuroprotection and neurorecovery. *Neurotherapeutics* 2011; 8(3): 434-51
9. Riley C, Hutter-Paier B, Windisch M, et al. A peptide preparation protects cells in organotypic brain slices against cell death after glutamate intoxication. *J Neural Transm* 2006; 113(1):103-10
10. Brainin M. Cerebrolysin: a multi-target drug for recovery after stroke. *Exp Rev Neurother* 2018; 18(8): 681-687.
11. Ploughman M, Windle V, MacLellan CL, White N, Dore JJ, Corbett D. Brain-derived neurotrophic factor contributes to recovery of skilled reaching after focal ischemia in rats. *Stroke* 2009; 40(4):1490-1495.
12. Cook DJ, Nguyen C, Chun HN, I LL, Chiu AS, Machnicki M et al. Hydrogel-delivered brain-derived neurotrophic factor promotes tissue repair and recovery after stroke. *J Cereb Blood Flow Metab*. 2017; 37(3):1030-1045.
13. Jeffers MS, Corbett D. Synergistic effects of enriched environment and task-specific reach training on poststroke recovery of motor function. *Stroke* 2018; 49(6):1496-1503.
14. Veerbeek JM, Van Wegen E, Van Peppen R, van der Wees PJ, Hendricks E, Rietbert M, et al. What is the evidence for physical therapy poststroke? A systematic review and meta-analysis. *PLOS one* 2014; 9(2):879-887.
15. Vosko M, Sanak D, Do Y, et al. C-REGS2-A multinational, high-quality comparative effectiveness study of Cerebrolysin in moderate acute ischemic stroke. *Int J Stroke* 2025; 20(9):1060-1070.

CERECAP - Samajarn Jitrada

1. Feigin VL, Brainin M, Norrving B, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *Int J Stroke*. 2022;17(1):18–29.
2. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387:1723–1731.
3. Kang SY, Kim JS. Anterior cerebral artery infarction: stroke mechanism and clinical-imaging study in 100 patients. *Neurology*. 2008;70:2386–2393.

4. Dirnagl U, Iadecola C, Moskowitz MA. Pathobiology of ischaemic stroke: an integrated view. *Trends Neurosci.* 1999;22:391–397.
5. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and Recovery After Stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47:151–159.
6. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018;39:629–640.

CERECAP - Marina Roje-Bedekovic

1. Schonewille WJ, Wijman CA, Michel P, Rueckert CM, Weimar C, Mattle HP, et al; BASICS study group. Treatment and outcomes of acute basilar artery occlusion in the Basilar Artery International Cooperation Study (BASICS): a prospective registry study. *Lancet Neurol.* 2009 Aug;8(8):724–30. doi: 10.1016/S1474-4422(09)70173-5
 2. Tao C, Nogueira RG, Zhu Y, Sun J, Han H, Yuan G, et al; ATTENTION Investigators. Trial of Endovascular Treatment of Acute Basilar-Artery Occlusion. *N Engl J Med.* 2022 Oct 13;387(15):1361–1372. doi: 10.1056/NEJMoa2206317
 3. Jovin TG, Li C, Wu L, Wu C, Chen J, Jiang C, et al; BAOCHE Investigators. Trial of Thrombectomy 6 to 24 Hours after Stroke Due to Basilar-Artery Occlusion. *N Engl J Med.* 2022 Oct 13;387(15):1373–1384. doi: 10.1056/NEJMoa2207576
 4. Adusumilli G, Kobeissi H, Ghozy S, Hardy N, Kallmes KM, Hutchison K, et al. Endovascular thrombectomy after acute ischemic stroke of the basilar artery: a meta-analysis of four randomized controlled trials. *J Neurointerv Surg.* 2023 Dec 21;15(e3):e446–e451. doi: 10.1136/jnis-2022-019776
 5. Hawkes MA, Blaginykh E, Ruff MW, Burrus T, Wijdicks EFM, Rabinstein AA. Long-term mortality, disability and stroke recurrence in patients with basilar artery occlusion. *Eur J Neurol.* 2020;27(3):579–585. doi:10.1111/ene.14126
 6. Heiss WD, Brainin M, Bornstein NM, Tuomilehto J, Hong Z; CASTA Investigators. Cerebrolysin in patients with acute ischemic stroke in Asia: results of a double-blind, placebo-controlled randomized trial. *Stroke.* 2012;43(3):630–636. doi:10.1161/STROKEAHA.111.628537
 7. Khasanova DR, Kalinin MN. Cerebrolysin as an early add-on to reperfusion therapy: risk of hemorrhagic transformation after ischemic stroke (CEREHETIS), a prospective, randomized, multicenter pilot study. *BMC Neurol.* 2023;23(1):121. doi:10.1186/s12883-023-03159-w
 8. Muresanu DF, Heiss WD, Hoernberg V, Bajenaru O, Popescu CD, Vester JC, et al. Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial. *Stroke.* 2016 Jan;47(1):151–9. doi: 10.1161/STROKEAHA.115.009416
 9. Stan A, Birle C, Blesneag A, Iancu M. Cerebrolysin and early neurorehabilitation in patients with acute ischemic stroke: a prospective, randomized, placebo-controlled clinical study. *J Med Life.* 2017;10(4):216–222.
 10. Chang WH, Lee J, Shin YI, Ko MH, Kim DY, Sohn MK, et al. Cerebrolysin Combined with Rehabilitation Enhances Motor Recovery and Prevents Neural Network Degeneration in Ischemic Stroke Patients with Severe Motor Deficits. *J Pers Med.* 2021 Jun 11;11(6):545. doi: 10.3390/jpm11060545
 11. Lang W, Stadler CH, Poljakovic Z, Fleet D; Lyse Study Group. A prospective, randomized, placebo-controlled, double-blind trial about safety and efficacy of combined treatment with alteplase (rt-PA) and Cerebrolysin in acute ischaemic hemispheric stroke. *Int J Stroke.* 2013;8(2):95–104. doi:10.1111/j.1747-4949.2012.00901.x
 12. Bornstein NM, Guekht A, Vester J, Heiss WD, Gusev E, Hömberg V, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018 Apr;39(4):629–640. doi: 10.1007/s10072-017-3214-0
 13. Writing Group for the BASILAR Group; Zi W, Qiu Z, Wu D, Li F, Liu H, et al. Assessment of Endovascular Treatment for Acute Basilar Artery Occlusion via a Nationwide Prospective Registry. *JAMA Neurol.* 2020 May 1;77(5):561–573. doi: 10.1001/jamaneurol.2020.0156
 14. Shen H, Killingsworth MC, Bhaskar SMM. Comprehensive meta-analysis of futile recanalization in acute ischemic stroke patients undergoing endovascular thrombectomy: prevalence, factors, and clinical outcomes. *Life.* 2023;13(10):1965. doi:10.3390/life13101965
 15. Bouslama M, Haussen DC, Aghaebrahim A, Grossberg JA, Walker G, Rangaraju S, et al. Predictors of Good Outcome After Endovascular Therapy for Vertebrobasilar Occlusion Stroke. *Stroke.* 2017 Dec;48(12):3252–3257. doi: 10.1161/STROKEAHA.117.018270
 16. Mokin M, Sonig A, Sivakanthan S, Ren Z, Eljovich L, Arthur A, et al. Clinical and Procedural Predictors of Outcomes From the Endovascular Treatment of Posterior Circulation Strokes. *Stroke.* 2016 Mar;47(3):782–8. doi: 10.1161/STROKEAHA.115.011598
 17. Moskowitz MA, Lo EH, Iadecola C. The science of stroke: mechanisms in search of treatments. *Neuron.* 2010;67(2):181–198. doi:10.1016/j.neuron.2010.07.002
 18. Nouh A, Remke J, Ruland S. Ischemic posterior circulation stroke: a review of anatomy, clinical presentations, diagnosis, and current management. *Front Neurol.* 2014;5:30. doi:10.3389/fneur.2014.00030
 19. Poljakovic Z, Supe S, Ljevak J, Starcevic K, Peric I, Blazevic N, et al. Efficacy and safety of Cerebrolysin after futile recanalisation therapy in patients with severe stroke. *Clin Neurol Neurosurg.* 2021 Aug;207:106767. doi: 10.1016/j.clineuro.2021.106767
 20. Ribó M, Staszewski J, Zeiler SR, Michalak S, El Bassiouny A, Gongora-Rivera F, et al. Cerebroprotection in acute ischemic stroke: Perspectives on combining cerebrolysin with recanalization therapy. *J Stroke Cerebrovasc Dis.* 2026 Jan;35(1):108515. doi: 10.1016/j.jstrokecerebrovasdis.2025.108515
-

CERECAP - Michal Karlinski

1. A. J. Ferrari, D. F. Santomauro, A. Aali et al., "Global Incidence, Prevalence, Years Lived with Disability (YLDs), Disability-Adjusted Life-Years (DALYs), and Healthy Life Expectancy (HALE) for 371 Diseases and Injuries in 204 Countries and Territories and 811 Subnational Locations, 1990–2021: A Systematic Analysis for the Global Burden of Disease Study 2021," *Lancet*, vol. 403, no. 10440, pp. 2133–2161, 2024.
2. A. Safouris, L. Palaiodimou, A. H. Katsanos et al., "Overview of Systematic Reviews Comparing Endovascular to Best Medical Treatment for Large-Vessel Occlusion Acute Ischaemic Stroke: An Umbrella Review," *Therapeutic Advances in Neurological Disorders*, vol. 17, p. 17562864241246938, 2024.
3. J. Staszewski, A. Dębiec, S. Strilciuc et al., "Efficacy of Cerebrolysin Treatment as an Add-on therapy to Mechanical thrombectomy in Patients With Acute Ischemic Stroke due to Large Vessel Occlusion in Anterior Circulation: Results of a 3-Month Follow-up of a Prospective, Open Label, Single-Center Study," *Translational Stroke Research*, vol. 16, no. 6, pp. 1931–1946, 2025.
4. P. Lyden, A. Buchan, J. Boltze et al., "Top Priorities for Cerebroprotective Studies—A Paradigm Shift: Report From STAIR XI," *Stroke*, vol. 52, no. 9, pp. 3063–3071, 2021.
5. S. Alamowitch, G. Turc, L. Palaiodimou et al., "European Stroke Organisation (ESO) Expedited Recommendation on Tenecteplase for Acute Ischaemic Stroke," *European Stroke Journal*, vol. 8, no. 1, pp. 8–54, 2023.
6. S. Afridi, F. Ali, M. U. Ghani et al., "Efficacy and Safety of Cerebrolysin as an Adjunct to Mechanical thrombectomy in Acute Ischemic Stroke: A Systematic Review and Meta-Analysis of Observational Studies," *Brain and Behavior*, vol. 16, no. 3, p. e71252, 2026.
7. M. Ribó, J. Staszewski, S. Zeiler et al., "Cerebroprotection in Acute Ischemic Stroke: Perspectives on Combining Cerebrolysin With Recanalization therapy," *Journal of Stroke and Cerebrovascular Diseases*, vol. 35, no. 1, p. 108515, 2026.
8. K. Rejdak, H. Sienkiewicz-Jarosz, P. Bienkowski, and A. Alvarez, "Modulation of Neurotrophic Factors in the Treatment of Dementia, Stroke and TBI: Effects of Cerebrolysin," *Medicinal Research Reviews*, vol. 43, no. 5, pp. 1668–1700, 2023.
9. N. M. Bornstein, A. Guekht, J. Vester et al., "Safety and Efficacy of Cerebrolysin in Early Post-Stroke Recovery: A Meta-Analysis of Nine Randomized Clinical Trials," *Neurological Sciences*, vol. 39, no. 4, pp. 629–640, 2018.
10. L. E. Ziganshina, T. Abakumova, D. Nurkhametova, and K. Ivanchenko, "Cerebrolysin for Acute Ischaemic Stroke," *CDSR*, vol. 2023, no. 10, 2023.
11. A. Guekht, J. Vester, W. D. Heiss et al., "Safety and Efficacy of Cerebrolysin in Motor Function Recovery After Stroke: A Meta-Analysis of the CARS Trials," *Neurological Sciences*, vol. 38, no. 10, pp. 1761–1769, 2017.
12. V. Homberg, D. C. Jianu, A. Stan et al., "Speech therapy Combined With Cerebrolysin in Enhancing Nonfluent Aphasia Recovery After Acute Ischemic Stroke: ESCAS Randomized Pilot Study," *Stroke*, vol. 56, no. 4, pp. 937–947, 2025.
13. M. R. Vosko, D. Sanak, Y. Do et al., "C-REGS2—A Multinational, High-Quality Comparative Effectiveness Study of Cerebrolysin in Moderate Acute Ischemic Stroke," *International Journal of Stroke*, vol. 20, no. 9, pp. 1060–1070, 2025.
14. Z. Poljakovic, S. Supe, J. Ljevak et al., "Efficacy and Safety of Cerebrolysin After Futile Recanalisation Therapy in Patients With Severe Stroke," *Clinical Neurology and Neurosurgery*, vol. 207, p. 106767, 2021.
15. D. R. Khasanova and M. N. Kalinin, "Cerebrolysin as an Early Add-on to Reperfusion therapy: Risk of Hemorrhagic Transformation After Ischemic Stroke (CEREHETIS), a Prospective, Randomized, Multicenter Pilot Study," *BMC Neurology*, vol. 23, no. 1, p. 121, 2023.
16. A. ElBassiouny, M. S. A. Shehata, A. S. Zaki, R. Y. Bedros, A. H. El-Sudany, and A. A. Nasser, "Cerebrolysin as an Adjuvant therapy After Mechanical thrombectomy in Large Vessel Occlusion Cardioembolic Stroke: A Propensity Score Matching Analysis," *Frontiers in Neurology*, vol. 16, p. 1510284, 2025.
17. E. Beghi, H. Binder, C. Birle et al., "European Academy of Neurology and European Federation of Neurorehabilitation Societies Guideline on Pharmacological Support in Early Motor Rehabilitation After Acute Ischaemic Stroke," *European Journal of Neurology*, vol. 28, no. 9, pp. 2831–2845, 2021.

CERECAP - Mikhail Kalinin & Dina Khasanova

1. Majoie CB, Cavalcante F, Gralla J, et al. Value of intravenous thrombolysis in endovascular treatment for large-vessel anterior circulation stroke: individual participant data meta-analysis of six randomised trials. *Lancet*. 2023;402(10406):965-974. doi:10.1016/S0140-6736(23)01142-X
2. Fischer U, Kaesmacher J, Strbian D, et al. Thrombectomy alone versus intravenous alteplase plus thrombectomy in patients with stroke: an open-label, blinded-outcome, randomised non-inferiority trial. *Lancet*. 2022;400(10346):104-115. doi:10.1016/S0140-6736(22)00537-2
3. Khasanova DR, Kalinin MN. Cerebrolysin as an early add-on to reperfusion therapy: risk of hemorrhagic transformation after ischemic stroke (CEREHETIS), a prospective, randomized, multicenter pilot study. *BMC Neurol*. 2023;23(1):121. doi:10.1186/s12883-023-03159-w
4. Kalinin MN, Khasanova DR. Heterogeneous treatment effects of Cerebrolysin as an early add-on to reperfusion therapy: post hoc analysis of the CEREHETIS trial. *Front Pharmacol*. 2024;14:1288718. doi:10.3389/fphar.2023.1288718
5. Kalinin MN, Khasanova DR. Cerebrolysin, hemorrhagic transformation, and anticoagulation timing after reperfusion therapy in stroke: post hoc secondary analysis of the CEREHETIS trial. *Front Pharmacol*. 2026;16:1725255. doi:10.3389/fphar.2025.1725255

6. Staszewski J, Dębiec A, Strlicuc S, et al. Efficacy of Cerebrolysin treatment as an add-on therapy to mechanical thrombectomy in patients with acute ischemic stroke due to large vessel occlusion in anterior circulation: results of a 3-month follow-up of a prospective, open label, single-center study. *Transl Stroke Res.* 2025;16(6):1931-1946. doi:10.1007/s12975-025-01355-z
7. Staszewski J, Dębiec A, Gniadek-Olejniczak K, et al. Cerebrolysin after endovascular thrombectomy in stroke: 12-month functional outcomes in a propensity-matched cohort. *Transl Stroke Res.* 2026;17(2):28. doi:10.1007/s12975-026-01414-z
8. ElBassiouny A, Shehata MSA, Zaki AS, Bedros RY, El-Sudany AH, Nasser AA. Cerebrolysin as an adjuvant therapy after mechanical thrombectomy in large vessel occlusion cardioembolic stroke: a propensity score matching analysis. *Front Neurol.* 2025;16:1510284. doi:10.3389/fneur.2025.1510284
9. Poljakovic Z, Supe S, Ljevak J, et al. Efficacy and safety of Cerebrolysin after futile recanalisation therapy in patients with severe stroke. *Clin Neurol Neurosurg.* 2021;207:106767. doi:10.1016/j.clineuro.2021.106767
10. Kalinin MN, Khasanova DR, Ibatullin MM. The hemorrhagic transformation index score: a prediction tool in middle cerebral artery ischemic stroke. *BMC Neurol.* 2017;17(1):177. doi:10.1186/s12883-017-0958-3

CERECAP - Roni Eichel

1. Goyal M, Menon BK, van Zwam WH, et al; HERMES Collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet.* 2016;387(10029):1723–1731.
2. Yang X, Sun D, Huo X, et al. Futile reperfusion of endovascular treatment for acute anterior circulation large vessel occlusion in the ANGEL-ACT registry. *J Neurointerv Surg.* 2023;15:e363–e368.
3. Nie X, Leng X, Miao Z, Fisher M, Liu L. Clinically ineffective reperfusion after endovascular therapy in acute ischemic stroke. *Stroke.* 2023;54(3):873–881.
4. Mujanovic A, Ng F, Meinel TR, et al. No-reflow phenomenon in stroke patients: a systematic literature review and meta-analysis of clinical data. *Int J Stroke.* 2024;19(1):58–67.
5. Rubiera M, Garcia-Tornel A, Olive-Gadea M, et al. Computed tomography perfusion after thrombectomy: an immediate surrogate marker of outcome after recanalization in acute stroke. *Stroke.* 2020;51(6):1736–1742.
6. ter Schiphorst A, Blaquièrre M, Moynier M, et al. Hypoperfusion on early MRI despite successful thrombectomy: a prospective imaging and inflammatory biomarkers study. *Stroke.* 2024 (online first).
7. Albers GW, Marks MP, Kemp S, et al; DEFUSE 3 Investigators. Thrombectomy for stroke at 6 to 16 hours with selection by perfusion imaging. *N Engl J Med.* 2018;378(8):708–718.
8. Heiss WD, Brainin M, Bornstein NM, Tuomilehto J, Hong Z; CASTA Investigators. Cerebrolysin in patients with acute ischemic stroke in Asia: results of a double-blind, placebo-controlled randomized trial. *Stroke.* 2012;43(3):630–636.
9. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and Recovery After Stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47(1):151–159.
10. Lang W, Stadler CH, Poljakovic Z, Fleet D; Lyse Study Group. A prospective, randomized, placebo-controlled, double-blind trial about safety and efficacy of combined treatment with alteplase (rt-PA) and Cerebrolysin in acute ischaemic hemispheric stroke. *Int J Stroke.* 2013;8(2):95–104.
11. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018;39:629–640.
12. Poljakovic Z, Supe S, Ljevak J, et al. Efficacy and safety of Cerebrolysin after futile recanalisation therapy in patients with severe stroke. *Clin Neurol Neurosurg.* 2021;207:106767.
13. Khasanova DR, Kalinin MN. Cerebrolysin as an early add-on to reperfusion therapy: risk of hemorrhagic transformation after ischemic stroke (CEREHETIS), a prospective, randomized, multicenter pilot study. *BMC Neurol.* 2023;23(1):121.
14. Shen H, Killingsworth MC, Bhaskar SMM. Comprehensive meta-analysis of futile recanalization in acute ischemic stroke patients undergoing endovascular thrombectomy: prevalence, factors, and clinical outcomes. *Life.* 2023;13(10):1965.
15. Eichel R, Teitcher M, Mausbach S, Poplavska A, Shqair S, Eichel R, Ben David E, Bornstein N. Post-endovascular thrombectomy CT perfusion imaging as a prognostic biomarker and patient-selection tool for adjuvant therapy: a systematic review, meta-analysis, and clinical threshold framework. 2026 (manuscript submitted).

Acute Ischemic Stroke - Sergey Marchenko

1. Fujinami J, Ohara T, Kitani-Morii F, et al. Cancer-associated hypercoagulation increases the risk of early recurrent stroke in patients with active cancer. *Cerebrovascular Diseases.* 2018;46(1-2):46-51. <https://doi.org/10.1159/000491436>
2. Kim K, Lee JH. Risk factors and biomarkers of ischemic stroke in cancer patients. *Journal of Stroke.* 2014;16(2):91-96. <https://doi.org/10.5853/jos.2014.16.2.91>
3. Homberg V, Jianu DC, Stan A, et al. Speech therapy combined with Cerebrolysin in enhancing nonfluent aphasia recovery after acute ischemic stroke: ESCAS randomized pilot study. *Stroke.* 2025;56(4):937-947. <https://doi.org/10.1161/STROKEAHA.124.049834>
4. Strlicuc S, Radu C, Grad DA, et al. Cost-effectiveness of Cerebrolysin after ischemic stroke: secondary analysis of the CARS study. *Healthcare (Basel).* 2023;11(10):1497. <https://doi.org/10.3390/healthcare11101497>
5. Kalinin MN, Khasanova DR. Cerebrolysin in combination with reperfusion therapy for ischemic stroke: a prospective analysis of multimodal neuroimaging data in the CEREHETIS study. *S.S. Korsakov Journal of Neurology and Psychiatry.* 2025;125(6):84-98. <https://doi.org/10.17116/jnevro202512506184>

6. Khasanova DR, Kalinin MN. Effects of simultaneous use of Cerebrolysin and alteplase on hemorrhagic transformation of brain infarction and functional outcome in stroke patients: CEREHETIS, a randomized multicenter pilot trial. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2023;123(8-2):60-69. <https://doi.org/10.17116/jnevro202312308260>
7. Teng H, Li C, Zhang Y, et al. Therapeutic effect of Cerebrolysin on reducing impaired cerebral endothelial cell permeability. *Neuroreport*. 2021;32(5):359-366. <https://doi.org/10.1097/WNR.0000000000001598>
8. Zhang Y, Chopp M, Meng Y, et al. Improvement in functional recovery with administration of Cerebrolysin after experimental closed head injury. *Journal of Neurosurgery*. 2013;118(6):1343-1355. <https://doi.org/10.3171/2013.3.JNS122061>
9. Yeşilot N, Ekizoğlu E, Çoban O. Clinical features of cancer-associated ischemic stroke. *Noro Psikiyatr Ars*. 2018;55(2):113-117. <https://doi.org/10.29399/npa.22999>

Hemorrhagic Stroke - Alfredo Arellano Ramirez

1. Wessels T, Möller-Hartmann W, Noth J, Klötzsch C. CT findings and clinical features as markers for patient outcome in primary pontine hemorrhage. *AJNR Am J Neuroradiol*. 2004;25:257-260.
2. Takeuchi S, Suzuki G, Takasato Y, Masaoka H, Hayakawa T, Otani N, et al. Prognostic factors in patients with primary brainstem hemorrhage. *Clin Neurol Neurosurg*. 2013;115:732-735.
3. Huang KB, Ji Z, Ding K, Li H, Gao PY, Wang YH. Predictors of 30-day mortality and 90-day functional recovery after primary pontine hemorrhage. *J Stroke Cerebrovasc Dis*. 2017;26:145-150.
4. Zhang L, Chopp M, Meier DH, Winter S, Wang L, Szalad A, et al. Cerebrolysin enhances neurogenesis in the ischemic brain and improves functional outcome after stroke. *J Neurosci Res*. 2010;88:3275-3281.
5. Alcántara-González F, Gutiérrez-Vargas JA, Mena R, et al. Neuroprotective mechanisms of Cerebrolysin in experimental brain injury models. *CNS Neurol Disord Drug Targets*. 2019;18:38-49.
6. Bornstein NM, Guekht A, Vester J, Heiss WD, Gusev E, Hömberg V, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: A meta-analysis of randomized clinical trials. *Stroke*. 2018;49:151-159.
7. Rockenstein E, Mante M, Adame A, Crews L, Moessler H, Masliah E. Neuroprotective effects of Cerebrolysin in models of neurodegeneration. *J Neural Transm*. 2006;113:629-645.
8. Heiss WD, Brainin M, Bornstein NM, Tuomilehto J, Hong Z. Cerebrolysin in patients with acute ischemic stroke in Asia: Results of a double-blind, placebo-controlled trial. *Stroke*. 2012;43:630-636.
9. Muresanu DF, Heiss WD, Hömberg V, Bajenaru O, Popescu CD, Vester JC, et al. Cerebrolysin and recovery after stroke (CARS): A randomized, placebo-controlled trial. *Stroke*. 2016;47:151-159.
10. Muresanu DF, Ciurea AV, Gorgan RM, et al. A prospective, randomized, double-blind trial of Cerebrolysin in moderate and severe traumatic brain injury. *J Neurol Sci*. 2020;420:117259.
11. Xiong Y, Mahmood A, Chopp M. Neurorestorative treatments for traumatic brain injury. *Nat Rev Neurol*. 2010;6:560-570.
12. Hutter-Paier B, Grygar E, Windisch M. Death of cultured cortical neurons induced by glutamate is reduced by Cerebrolysin. *J Neural Transm Suppl*. 1998;53:267-273.
13. Poon W, Vos PE, Muresanu DF, Vester JC, von Wild K, Hömberg V, et al. Cerebrolysin Asian-Pacific Trial in Acute Brain Injury and Neurorecovery (CAPTAIN): rationale and design. *J Neurotrauma*. 2021;38:3185-3193.
14. Muresanu DF, Vester JC, Burneo JG, et al. Neurotrophic treatment and recovery of consciousness after severe brain injury: emerging evidence and future directions. *Front Neurol*. 2023;14:1188762.

Hemorrhagic Stroke - Juan Carlos Pérez García

1. Yepez Yerovi FE, Noroña Guevara GE. Hemorragia subaracnoidea revisión bibliográfica. *Ciencia Latina Rev Cient Multidiscip*. 2023;7(1):9279-9293. Doi: doi.org/10.37811/cl_rcm.v7i1.5049
2. Parra Quintana, J., Arce Chariguaman, W. P., Yuniz Molina, N. A., & Villagrán, L. E. 2021. Abordaje diagnóstico y terapéutico de la hemorragia subaracnoidea. *Journal of American Health*. Recuperado a partir de <https://jah-journal.com/index.php/jah/article/view/73>
3. Kojder K, Jarosz K, Andrzejewska A, Solek-Pastuszka J, Skonieczna-Żydecka K, Kaczmarczyk M, Jurczak A. Cerebrolysin in Patients Diagnosed with Subarachnoid Hemorrhage-The Results of an Observational Cohort Study. *Biomedicines*. 2024 Oct 30;12(11):2492. doi: 10.3390/biomedicines12112492.
4. Park YK, Yi HJ, Choi KS, Lee YJ, Kim DW, Kwon SM. Cerebrolysin for the Treatment of Aneurysmal Subarachnoid Hemorrhage in Adults: A Retrospective Chart Review. *Adv Ther*. 2018 Dec;35(12):2224-2235. doi: 10.1007/s12325-018-0832-8.
5. Zhang G, Zhang W, Chang H, Shen Y, Ma C, Mao L, Li Z, Lu H. Endovascular treatment of multiple intracranial aneurysms in patients with subarachnoid hemorrhage: one or multiple sessions? *Front Neurol*. 2023 Jun 20;14:1196725. doi: 10.3389/fneur.2023.1196725.

Hemorrhagic Stroke - Chi Tun Tang

1. Sacco RL, Kasner SE, Broderick JP, Caplan LR, Connors JJ, Culebras A, et al. An updated definition of stroke for the 21st century. *Stroke*. 2013;44(7):2064-89.
2. Murata Y, Yamaguchi S, Kajikawa H, Yamamura K, Sumioka S, Nakamura S. Relationship between the clinical manifestations, CT findings and outcome in 80 patients with primary pontine hemorrhage. *J Neurol Sci*. 1999;167(2):107-11.

- Wessels T, Möller-Hartmann W, Noth J, Klötzsch C. CT findings and clinical features as markers for patient outcome in primary pontine hemorrhage. *AJNR Am J Neuroradiol.* 2004;25(2):257–60.
- Matsukawa H, Shinoda M, Fujii M, Takahashi O, Murakata A. Risk factors for mortality in patients with non-traumatic pontine hemorrhage. *Acta Neurol Scand.* 2015;131(4):240–5.
- Nishizaki T, Ikeda N, Nakano S, Sakakura T, Abiko M, Okamura T. Factors determining the outcome of pontine hemorrhage in the absence of surgical intervention. *Open J Mod Neurosurg.* 2012;2(2):17–20.
- Shrestha BK, Ma L, Lan ZG, et al. Surgical management of spontaneous hypertensive brainstem hemorrhage. *Interdiscip Neurosurg.* 2015;2:145–8.
- Hemphill JC 3rd, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke.* 2015;46(7):2032–60.

Hemorrhagic Stroke - Shady Safwat Hassan

- American Heart Association/American Stroke Association. Greenberg SM, Ziai WC, Cordonnier C, Dowlatshahi D, Francis B, Goldstein JN, et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage. *Stroke.* 2022;53(7):e282–e361.
- European Stroke Organisation. Steiner T, Al-Shahi Salman R, Beer R, Christensen H, Cordonnier C, Csiba L, et al. European Stroke Organisation (ESO) guidelines for the management of spontaneous intracerebral hemorrhage. *Int J Stroke.* 2014;9(7):840–855.
- World Health Organization. Hypertension. Geneva: WHO; 2023.
- O'Donnell MJ, Chin SL, Rangarajan S, Xavier D, Liu L, Zhang H, et al. Global and regional effects of potentially modifiable risk factors associated with acute stroke in 32 countries (INTERSTROKE): a case-control study. *Lancet.* 2016;388(10046):761–775.
- Qureshi AI, Palesch YY, Barsan WG, Hanley DF, Hsu CY, Martin RL, et al. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *N Engl J Med.* 2016;375(11):1033–1043.
- Anderson CS, Heeley E, Huang Y, Wang JG, Stapf C, Delcourt C, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. *N Engl J Med.* 2013;368(25):2355–2365.
- Hemphill JC III, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the management of spontaneous intracerebral hemorrhage. *Stroke.* 2015;46(7):2032–2060.
- Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, et al. Global, regional, and national burden of stroke and its risk factors, 1990–2019. *Lancet Neurol.* 2021;20(10):795–820.
- Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery. *Stroke.* 2016;47(6):e98–e169.
- Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2019 Update to the 2018 Guidelines for the Early Management of Acute Ischemic Stroke. *Stroke.* 2019;50:e344–e418.
- American Diabetes Association Professional Practice Committee. Standards of Care in Diabetes—2024. *Diabetes Care.* 2024;47(Suppl 1):S1–S350.
- GBD 2019 Stroke Collaborators. Global, regional, and national burden of stroke and risk factors, 1990–2019. *Lancet Neurol.* 2021;20(10):795–820.
- Poon MTC, Fonville AF, Al-Shahi Salman R. Long-term prognosis after intracerebral haemorrhage: systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry.* 2014;85(6):660–667.
- Dodick DW, Johnston KC, Levine SR. Management of acute intracerebral hemorrhage. *Neurol Clin.* 2008;26(4):1037–1054.
- Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. *J Clin Epidemiol.* 2017;89:218–235.

Hemorrhagic Stroke - Kyi Hlaing

- Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. *J Neurosurg.* 1986;65(4):476–483.
- van Beijnum J, et al. Outcome after spontaneous and arteriovenous malformation-related intracerebral haemorrhage. *Stroke.* 2011;42(8):2355–2359.
- Krakauer JW, Carmichael ST. Neural plasticity and recovery after brain injury. *Neuron.* 2012;76(5):871–884.

Hemorrhagic Stroke - Zdravka Poljakovic

- Hoh BL, Ko NU, Amin-Hanjani S, et al. 2023 Guideline for the Management of Patients With Aneurysmal Subarachnoid Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. *Stroke.* 2023;54:e314–e370. doi:10.1161/STR.0000000000000436.
- Woo PYM, Ho JWK, Ko NMW, et al. Randomized, placebo-controlled, double-blind, pilot trial to investigate safety and efficacy of Cerebrolysin in patients with aneurysmal subarachnoid hemorrhage. *BMC Neurol.* 2020;20:401. doi:10.1186/s12883-020-01908-9.
- Teng H, Li C, Zhang Y, et al. Therapeutic effect of Cerebrolysin on reducing impaired cerebral endothelial cell permeability. *Neuroreport.* 2021;32:359–366. doi:10.1097/WNR.0000000000001598.
- Kojder K, Jarosz K, Bosiacki M, et al. Cerebrolysin in patients with subarachnoid hemorrhage: a systematic review and meta-analysis. *J Clin Med.* 2023;12:6638. doi:10.3390/jcm12206638.

5. Hoang Ngoc N, Van Tuyen N. Using low-dose tissue plasminogen activator through external ventricular drain and Cerebrolysin for the treatment of severe intraventricular hemorrhage: a case report. *SAGE Open Med Case Rep*. 2020;8:2050313X20981464. doi:10.1177/2050313X20981464.

Neurorehabilitation - Adina Stan

1. Feigin VL, Brainin M, Norrving B, Martins S, Sacco RL, Hacke W, et al. World Stroke Organization (WSO): global stroke fact sheet 2022. *Int J Stroke*. 2022;17(1):18–29.
2. Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, et al. 2019 update to the 2018 guidelines for the early management of acute ischemic stroke. *Stroke*. 2019;50(12):e344–418.
3. Momjian-Mayor I, Baron JC. The pathophysiology of watershed infarction in internal carotid artery disease. *Stroke*. 2005;36(3):567–77.
4. Hart RG, Diener HC, Coutts SB, Easton JD, Granger CB, O'Donnell MJ, et al. Embolic strokes of undetermined source. *Lancet Neurol*. 2014;13(4):429–38.
5. Cramer SC. Repairing the human brain after stroke: I. Mechanisms of spontaneous recovery. *Ann Neurol*. 2008;63(3):272–87.
6. Caplan LR, Hennerici M. Impaired clearance of emboli (washout) is an important link between hypoperfusion, embolism, and ischemic stroke. *Arch Neurol*. 1998;55(11):1475–82.
7. Kang DW, Chalela JA, Ezzeddine MA, Warach S. Association of ischemic lesion patterns on diffusion-weighted imaging with TOAST stroke subtypes. *Arch Neurol*. 2003;60(12):1730–4.
8. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery. *Stroke*. 2016;47(6):e98–169.
9. Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu BO, Vester JC, et al. Cerebrolysin and recovery after stroke (CARS): a randomized, placebo-controlled trial. *Stroke*. 2016;47(1):151–9.
10. Beghi E, Binder H, Birle C, Bornstein N, Diserens K, Groppa S, et al. European Academy of Neurology and European Federation of Neurorehabilitation Societies guideline on pharmacological support in early motor rehabilitation after acute ischaemic stroke. *Eur J Neurol*. 2021;28(9):2831–45.

Neurorehabilitation - Claudio Soto

1. Dziewas R, Glahn J, Helfer C, et al. Neurogenic Dysphagia Guideline. *Neurological Research and Practice*. 2021.
2. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery. *Stroke*. 2012.
3. Cramer SC. Repairing the human brain after stroke. *N Engl J Med*. 2010.
4. Muresanu DF, Heiss WD, Hoemberg V, et al. Cerebrolysin and recovery after stroke: systematic review and meta-analysis. *J Neural Transm*. 2020.

Neurorehabilitation - Melecio M. Peña

1. Murray CJ, Lopez AD. Measuring the global burden of disease. *N Engl J Med*. 2013;369:448–457.
2. Wardlaw JM, Murray V, Berge E, del Zoppo GJ. Thrombolysis for acute ischemic stroke. *Stroke*. 2014;45:e225.
3. Masliah E, Díez-Tejedor E. The pharmacology of neurotrophic treatment with Cerebrolysin: brain protection and repair to counteract pathologies of acute and chronic neurological disorders. *Drugs Today*. 2012;48(Suppl A):3–24.
4. Muresanu DF, Buzoianu A, Florian SI, von Wild T. Towards a roadmap in brain protection and recovery. *J Cell Mol Med*. 2012;16:2861–2871.
5. Ren J, Sietsma D, Qiu S, Moessler H, Finklestein SP. Cerebrolysin enhances functional recovery following focal cerebral infarction in rats. *Restor Neurol Neurosci*. 2007;25:25–31.
6. Zhang C, Chopp M, Cui Y, et al. Cerebrolysin enhances neurogenesis in the ischemic brain and improves functional outcome after stroke. *J Neurosci Res*. 2010;88:3275–3281.
7. Heiss WD, Brainin M, Bornstein NM, Tuomilehto J, Hong Z; CASTA Investigators. Cerebrolysin in patients with acute ischemic stroke in Asia: results of a double-blind, placebo-controlled randomized trial. *Stroke*. 2012;43:630–636.
8. Muresanu DF, Heiss WD, Hoemberg V, et al. Cerebrolysin and Recovery After Stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke*. 2016;47:151–159.
9. Muresanu DF, et al. Role and impact of Cerebrolysin for ischemic stroke care. *J Clin Med*. 2022;11:1273.

Neurorehabilitation - Paschenelle B. Celis

1. Flowers HL, Skoretz SA, Silver FL, Rochon E, Fang J, Flamand-Roze C, Martino R. Poststroke aphasia frequency, recovery, and outcomes: a systematic review and meta-analysis. *Arch Phys Med Rehabil*. 2016;97(12):2188–2201.e8. doi:10.1016/j.apmr.2016.03.006.
2. Martino R, Foley N, Bhogal S, Diamant N, Speechley M, Teasell R. Dysphagia after stroke: incidence, diagnosis, and pulmonary complications. *Stroke*. 2005;36(12):2756–2763. doi:10.1161/01.STR.0000190056.76543.eb.
3. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, et al. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47(6). doi:10.1161/STR.0000000000000098.
4. Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev*. 2016;(6). doi:10.1002/14651858.CD000425.pub4.
5. Gonzalez-Suarez C, Grimmer K, Alipio I, Anoto-Canencia EG, Santos-Carpio ML, Dizon JM, et al. Stroke rehabilitation in the Philippines: an audit study. *Disabil CBR Incl Dev*. 2015;26(3):44–67. doi:10.5463/DCID.v26i3.446.

6. Collantes MEV, Zuñiga YH, Granada CN, Uezono DR, De Castillo LC, Enriquez CG, et al. Current state of stroke care in the Philippines. *Front Neurol*. 2021;12:665086. doi:10.3389/fneur.2021.665086.
7. Philippine Association of Speech-Language Pathologists. Spaces in the profession: SLPs in provinces and hospitals [Internet]. Manila: Philippine Association of Speech-Language Pathologists; 2021 Dec 10 [cited 2026 Aug 10]. Available from: <https://www.pasp.org.ph/post/spaces-in-the-profession-slp-in-provinces-and-hospitals>.
8. Zhang D, Dong Y, Li Y, Chen J, Wang J, Hou L. Efficacy and safety of Cerebrolysin for acute ischemic stroke: a meta-analysis of randomized controlled trials. *Biomed Res Int*. 2017;2017:4191670. doi:10.1155/2017/4191670.
9. Homberg V, Jianu DC, Stan A, Strilciuc S, Chelaru VF, Karliński M, et al. Speech therapy combined with Cerebrolysin in enhancing nonfluent aphasia recovery after acute ischemic stroke: ESCAS randomized pilot study. *Stroke*. 2025;56(4):937-947. doi:10.1161/STROKEAHA.124.049834.
10. Logan A, Faeldon L, Kent B, Ong A, Marsden J. A scoping review of stroke services within the Philippines. *BMC Health Serv Res*. 2024;24:1006. doi:10.1186/s12913-024-11334-z.
11. Wilson SM, Eriksson DK, Schneck SM, Lucanie JM. A quick aphasia battery for efficient, reliable, and multidimensional assessment of language function. *PLoS One*. 2018;13(2). doi:10.1371/journal.pone.0192773.
12. Trapl M, Enderle P, Nowotny M, Teuschl Y, Matz K, Dachenhausen A, Brainin M. Dysphagia bedside screening for acute-stroke patients: the Gugging Swallowing Screen. *Stroke*. 2007;38(11):2948-2952. doi:10.1161/STROKEAHA.107.483933.
13. Quinn TJ, Dawson J, Walters MR, Lees KR. Reliability of the modified Rankin Scale: a systematic review. *Stroke*. 2009;40(10):3393-3395. doi:10.1161/STROKEAHA.109.557256.
14. Quinn TJ, Dawson J, Walters MR, Lees KR. Exploring the reliability of the modified Rankin Scale. *Stroke*. 2009;40(3):762-766. doi:10.1161/STROKEAHA.108.522516.
15. Gregson JM, Leathley MJ, Moore AP, Smith TL, Sharma AK, Watkins CL. Reliability of the Tone Assessment Scale and the modified Ashworth scale as clinical tools for assessing poststroke spasticity. *Arch Phys Med Rehabil*. 1999;80(9):1013-1016. doi:10.1016/S0003-9993(99)90053-9.
16. Harb A, Kishner S. Modified Ashworth Scale. *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
17. Ladurner G, Kalvach P, Moessler H; Cerebrolysin Study Group. Neuroprotective treatment with Cerebrolysin in patients with acute stroke: a randomised controlled trial. *J Neural Transm (Vienna)*. 2005;112(3):415-428. doi:10.1007/s00702-004-0248-2.
18. Hien NM, Duc DP. The AVANT rehabilitation program and Cerebrolysin for treatment of post-stroke dysphagia: a case report. *J Med Life*. 2019;12(3):236-238. doi:10.25122/jml-2019-1008.
19. Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, et al. Cerebrolysin and recovery after stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke*. 2016;47(1):151-159. doi:10.1161/STROKEAHA.115.009416.
20. Maillard Dewarrat G, Annoni JM, Fornari E, Carota A, Bogousslavsky J, Maeder P. Acute aphasia after right hemisphere stroke. *J Neurol*. 2009;256(9):1461-1467. doi:10.1007/s00415-009-5137-z.

Neurorehabilitation - Ratanapat Chanubol

1. Catanese L, Tarsia J, Fisher M. Acute ischemic stroke therapy overview. *CircRes*. 2017;120(3):541-58
 2. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke: 2019 update to the 2018 guidelines for the early management of acute ischemic stroke: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2019;50(12):e344-418
 3. Kwakkel G, van Peppen R, Wagenaar RC, et al. Effects of augmented exercise therapy time after stroke: A meta-analysis. *Stroke*. 2004;35(11):2529-39
 4. Alcántara-González F, Mendoza-Perez CR, Zaragoza N, et al. Combined administration of cerebrolysin and donepezil induces plastic changes in pre-frontal cortex in aged mice. *Synapse*. 2012;66:938-49
 5. Zhang C, Chopp M, Cui Y, et al. Cerebrolysin enhances neurogenesis in the ischemic brain and improves functional outcome after stroke. *J Neurosci Res*. 2010;88(15):3275-81
 6. Zhang L, Chopp M, Meier DH, et al. Sonic hedgehog signaling pathway mediates cerebrolysin-improved neurological function after stroke. *Stroke* 2013; 44(7):1965-72
 7. Bornstein NM, Guekht A, Vester J, et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: A meta-analysis of nine randomized clinical trials. *Neurol Sci*. 2018;39:629-40
 8. Chang WH, Park CH, Kim DY, et al. Cerebrolysin combined with rehabilitation promotes motor recovery in patients with severe motor impairment after stroke. *BMC Neurol*. 2016;16: 31
 9. Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47(6):e98-169
 10. Ziganshina LE, Abakumova T, Vernay L. Cerebrolysin for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2017;4(4):CD007026
 11. Heiss WD, Brainin M, Bornstein NM, et al. Cerebrolysin in patients with acute ischemic stroke in Asia: Results of a double-blind, placebo-controlled randomized trial. *Stroke*. 2012;43(3):630-36
 12. Lang W, Stadler CH, Poljakovic Z, Fleet D. A prospective, randomized, placebo-controlled, double-blind trial about safety and efficacy of combined treatment with alteplase (rt-PA) and Cerebrolysin in acute ischaemic hemi-spheric stroke. *Int J Stroke*. 2013;8(2):95-104
-

13. Chang WH, Park CH, Kim DY, et al. Cerebrolysin combined with rehabilitation promotes motor recovery in patients with severe motor impairment after stroke. *BMC Neurol.* 2016;16: 31
14. Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: A Guideline for Healthcare Professionals from the American Heart Association/American Stroke Association. *Stroke.* 2016;47(6):e98-169
15. Ziganshina LE, Abakumova T, Vernay L. Cerebrolysin for acute ischaemic stroke. *Cochrane Database Syst Rev.* 2017;4(4):CD007026
16. Heiss WD, Brainin M, Bornstein NM, et al. Cerebrolysin in patients with acute ischemic stroke in Asia: Results of a double-blind, placebo-controlled randomized trial. *Stroke.* 2012;43(3):630-36
17. Lang W, Stadler CH, Poljakovic Z, Fleet D. A prospective, randomized, placebo-controlled, double-blind trial about safety and efficacy of combined treatment with alteplase (rt-PA) and Cerebrolysin in acute ischaemic hemi-spheric stroke. *Int J Stroke.* 2013;8(2):95-104
18. Gharagozli K, Harandi AA, Houshmand S, et al. Efficacy and safety of Cerebrolysin treatment in early recovery after acute ischemic stroke: A randomized, placebo-controlled, double-blinded, multicenter clinical trial. *J Med Life.* 2017;10(3):153-60
19. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and recovery after stroke (CARS): A randomized, placebo-controlled, double-blind, multi-center trial. *Stroke.* 2016;47(1):151-59
20. Guekht A, Heiss D, Gusev E, et al. Cerebrolysin and recovery after stroke (CARS 2): A randomized, placebo-controlled, double-blind, multicenter clinical study. *J Neurol Sci.* 2015;357:e103
21. Martinez RM. Efficacy of Cerebrolysin in the reduction of spasticity during stroke rehabilitation. *J Med Life.* 2017;10(3):161-66
22. Kim JY, Kim HJ, Choi HS, et al. Effects of Cerebrolysin® in patients with minimally conscious state after stroke: an observational retrospective clinical study. *Front Neurol.* 2019;10:803
23. Woo PYM, Ho JWK, Ko NMW, et al. Randomized, placebo-controlled, double-blind, pilot trial to investigate safety and efficacy of Cerebrolysin in patients with aneurysmal subarachnoid hemorrhage. *BMC Neurol.* 2020;20(1):401
24. Chen CC, Weiv ST, Tsai SC, et al. Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: Double-blind, placebo-controlled, randomized study. *Br J Neurosurg.* 2013;27(6):803-7
25. Gavrilova SI, Alvarez A. Cerebrolysin in the therapy of mild cognitive impairment and dementia due to Alzheimer's disease: 30 years of clinical use. *Med Res Rev.* 2020 [Online ahead of print]
26. Adams HP Jr., Davis PH, Leira EC, et al. Baseline NIH Stroke Scale score strongly predicts outcome after stroke: A report of the Trial of Org 10172 in Acute Stroke Treatment (TOAST). *Neurology.* 1999;53(1):126-31
27. Jørgensen HS, Nakayama H, Raaschou HO, et al. Outcome and time course of recovery in stroke. Part II: Time course of recovery. The Copenhagen Stroke Study. *Arch Phys Med Rehabil.* 1995;76(5):406-12
28. Masliah E, Diez-Tejedor E. The pharmacology of neurotrophic treatment with Cerebrolysin: Brain protection and repair to counteract pathologies of acute and chronic neurological disorders. *Drugs Today (Barc).* 2012;48(Suppl. A):3-24
29. Zhang L, Chopp M, Wang C, et al. Prospective, double blinded, comparative assessment of the pharmacological activity of Cerebrolysin and distinct peptide preparations for the treatment of embolic stroke. *J Neurol Sci.* 2019;398:22-26

Neurorehabilitation - Sindi Mitrovic

1. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery: A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association. *Stroke.* 2016;47:e98-e169. doi:10.1161/STR.0000000000000098.
2. Bernhardt J, Hayward KS, Kwakkel G, et al. Agreed definitions and a shared vision for new standards in stroke recovery research: The Stroke Recovery and Rehabilitation Roundtable taskforce. *Int J Stroke.* 2017;12:444-450. doi:10.1177/1747493017711816.
3. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial. *Stroke.* 2016;47:151-159. doi:10.1161/STROKEAHA.115.009416.
4. Beghi E, Binder H, Birle C, et al. European Academy of Neurology and European Federation of NeuroRehabilitation Societies guideline on pharmacological support in early motor rehabilitation after acute ischaemic stroke. *Eur J Neurol.* 2021;28:2831-2845. doi:10.1111/ene.14936.
5. Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. A method for evaluation of physical performance. *Scand J Rehabil Med.* 1975;7:13-31.
6. van der Lee JH, De Groot V, Beckerman H, Wagenaar RC, Lankhorst GJ, Bouter LM. The intra- and interrater reliability of the Action Research Arm Test: a practical test of upper extremity function in patients with stroke. *Arch Phys Med Rehabil.* 2001;82:14-19.
7. Langhorne P, Bernhardt J, Kwakkel G. Stroke rehabilitation. *Lancet.* 2011;377:1693-1702. doi:10.1016/S0140-6736(11)60325-5.
8. Berg K, Wood-Dauphinee S, Williams JL, Maki B. Measuring balance in the elderly: validation of an instrument. *Can J Public Health.* 1992;83(Suppl 2):S7-S11.

Aphasia - Laura Eszhanova

1. Rejdak K, Sienkiewicz-Jaroszy H, Bienkowski P, Alvarez A. Modulation of neurotrophic factors in the treatment of dementia, stroke and TBI: Effects of Cerebrolysin. *Med Res Rev.* 2023 Sep;43(5):1668-1700.
2. Bornstein, N.M., Guekht, A., Vester, J. et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci* 39, 629–640 (2018). <https://doi.org/10.1007/s10072-017-3214-0>

1. Rejdak K, Sienkiewicz-Jarosz H, Bienkowski P, Alvarez A. Modulation of neurotrophic factors in the treatment of dementia, stroke and TBI: Effects of Cerebrolysin. *Med Res Rev*. 2023 Sep;43(5):1668-1700.
2. Bornstein, N.M., Guekht, A., Vester, J. et al. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci* 39, 629–640 (2018). <https://doi.org/10.1007/s10072-017-3214-0>
3. Homberg, Volker, et al. Speech therapy combined with cerebrolysin in enhancing nonfluent aphasia recovery after acute ischemic stroke: ESCAS randomized pilot study. *Stroke*, 2025, 56.4: 937-947.
4. Aida Kondybayeva. (2024). Socially Significant Aspects of Stroke in Kazakhstan. *Research reviews*, (5). Available at <https://ojs.scipub.de/index.php/RR/article/view/3046>
5. Quinn TJ, Richard E, Teuschl Y, et al. European Stroke Organisation and European Academy of Neurology joint guidelines on post-stroke cognitive impairment. *Eur Stroke J*. 2021;6(3)–XXXVIII. doi:10.1177/23969873211042192.
6. Nicholls JK, Ince J, Minhas JS, Chung EML. Emerging Detection Techniques for Large Vessel Occlusion Stroke: A Scoping Review. *Front Neurol*. 2022;12:780324. doi:10.3389/fneur.2021.780324.
7. El Hussein N, Katzan IL, Rost NS, et al. Cognitive Impairment After Ischemic and Hemorrhagic Stroke: A Scientific Statement From the American Heart Association/American Stroke Association. *Stroke*. 2023;54(6)–e291. doi:10.1161/STR.0000000000000430.

Aphasia - Marina Romano

1. Daras G, Beber BC, Cassol K. Impact of post-stroke aphasia on functional communication, quality of life, and symptoms of depression. *Rev Neurol*. 2024;78(8):231-238. Disponible en: <https://pubmed.ncbi.nlm.nih.gov/38095330/>
2. Mureşanu DF, Heiss WD, Hoang DG, Chopp M, Guekht AB, Vester JC, et al. Case report: A 38-year-old female patient with acute Wernicke's aphasia and right-sided hemiparesis following an ischemic stroke treated with Cerebrolysin. *Front Neurol*. 2022;13:845321. doi: 10.3389/fneur.2022.845321
3. Mureşanu DF, Heiss WD, Hoang DG, Chopp M, Guekht AB, Vester JC, et al. Speech Therapy Combined With Cerebrolysin in Enhancing Poststroke Aphasia Recovery: The ESCAS Randomized Clinical Trial. *Stroke*. 2025;56(3):612-622. doi: 10.1161/STROKEAHA.124.049834
4. Berthier ML, Green C, Lara JP, Higuera Y, Albert ML, López-Barroso D, et al. Memantine and constraint-induced aphasia therapy in chronic poststroke aphasia. *Ann Neurol*. 2009 May;65(5):577-85. doi: 10.1002/ana.21597. PMID: 19475666.
5. Berthier ML, Green C, Higuera Y, Fernández I, Hinojosa JA, Martín MC, et al. A randomized, placebo-controlled study of donepezil in chronic poststroke aphasia. *Neurology*. 2006 Nov 14;67(9):1687-9. doi: 10.1212/01.wnl.0000242626.69666.e2. PMID: 17101908. [1]
6. Pigretti SG, Isaac C, Cea C, et al. Farmacoterapia en rehabilitación temprana posterior el accidente cerebrovascular isquémico [Pharmacological treatment in early rehabilitation after ischemic stroke]. *Medicina (B Aires)*. 2023;83 Suppl 3:1-40.
7. Atallah A, Fustinoni O, Zurru M, Beigelman R, Cirio J, Ameriso S, et al. Identifying Barriers in Acute Stroke Therapy in Argentina: ARENAS Registry. *Neurology*. 2014 Apr;82(10 Supplement):P2.014.
8. Prabhakaran S, Gonzalez NR, Zachrisson KS, et al. 2026 Guideline for the Early Management of Patients With Acute Ischemic Stroke: A Guideline From the American Heart Association/American Stroke Association. *Stroke*. Published online January 26, 2026. doi:10.1161/STR.0000000000000513
9. Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet [Internet]*. 2016 [cited 2026 Apr 4];387(10029):1723-31. Available from: doi.org
10. Ribó M, Staszewski J, Zeiler SR, Michalak S, El Bassiouny A, Gongora-Rivera F, Poljakovic Z, Khasanova DR, Kalinin MN, Chutinet A, Eichel R, Kojder K, Ong M, Bedeković MR, Chang CH, Lee M, Quitalol P, Tsiskaridse A, Bornstein NM. Cerebroprotection in acute ischemic stroke: Perspectives on combining cerebrolysin with recanalization therapy. *J Stroke Cerebrovasc Dis*. 2026 Jan;35(1):108515. doi: 10.1016/j.jstrokecerebrovasdis.2025.108515. Epub 2025 Dec 3. PMID: 41349847.
11. Ya-Chi Chuang, Chuan-Ching Liu, I-Ching Yu, Yu-Lin Tsai, Shin-Tsu Chang. Shifting of global aphasia to Wernicke's aphasia in a patient with intact motor function: a case report. *BMC Neurology* 2021 Mar 11;21(1):111. doi: 10.1186/s12883-021-02131-w.
12. Yu-Hsuan Chen, Ying-Hsuan Tsai, Ta-Chung Chao, Li-Fan Lin, Chia-Ying Lai, Shin-Tsu Chang. Pure dysarthria in a young adult with deficit of the cerebral perfusion of the left frontal-parietal circuit. *Journal of Neurology and Neuroscience Research* 2024 June 25; 5(1):44-48. DOI: 10.5281/zenodo.12526239. <https://www.scienipublishers.com/journal-of-neurology-and-neuroscience-research-volume-5-issue-1/>
13. Ying-Hsuan Tsai, Yu-Hsuan Chen, Ta-Chung Chao, Li-Fan Lin. Shin-Tsu Chang. New type of lacunar stroke presenting in brain perfusion images: A case report. *World Journal of Neurology* 2024 December 31; 10(1): 98672. DOI: 10.5316/wjn.v10.i1.98672.
14. Lyden P, Raman R, Liu L, Emr M, Warren M, Marler J. National Institutes of Health Stroke Scale certification is reliable across multiple venues. *Stroke*. 2009;40(7):2507-11.
15. Kertesz A. Western Aphasia Battery-Revised (WAB-R). San Antonio (TX): PsychCorp; 2006.
16. van Swieten JC, Koudstaal PJ, Visser MC, Schouten HJ, van Gijn J. Interobserver agreement for the assessment of handicap in stroke patients. *Stroke*. 1988 May;19(5):604-7.
17. Mahoney FI, Barthel DW. Functional evaluation: the Barthel Index. *Md State Med J*. 1965 Feb;14:56-61.[A4.1]

Aphasia - S.E. Khatkova

1. Wolf S, Gerloff C, Backhaus W. Predictive Value of Upper Extremity Outcome Measures After Stroke-A Systematic Review and Metaregression Analysis. *Front Neurol*. 2021 Jun 10;12:675255. doi: 10.3389/fneur.2021.675255. PMID: 34177780; PMCID: PMC8222610.
2. Yanishevsky SN, Khatkova SE. A progressive view on the treatment and rehabilitation of acute ischemic stroke. S.S. Korsakov Journal of Neurology and Psychiatry. 2022;122(12-2):50-54. (In Russ.). <https://doi.org/10.17116/jnevro202212212250>
3. Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, Rahlfs VW, Doppler E, Meier D, Moessler H, Guekht A. Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial. *Stroke*. 2016 Jan;47(1):151-9. doi: 10.1161/STROKEAHA.115.009416. Epub 2015 Nov 12. PMID: 26564102; PMCID: PMC4689177.
4. Chang WH, Park CH, Kim DY, Shin YI, Ko MH, Lee A, Jang SY, Kim YH. Cerebrolysin combined with rehabilitation promotes motor recovery in patients with severe motor impairment after stroke. *BMC Neurol*. 2016 Mar 2;16:31. doi: 10.1186/s12883-016-0553-z. PMID: 26934986; PMCID: PMC4776414.
5. Homberg V, Jianu DC, Stan A, Strilciuc S, Chelaru VF, Karliński M, Brainin M, Heiss WD, Muresanu DF, Enderby PM. Speech Therapy Combined With Cerebrolysin in Enhancing Nonfluent Aphasia Recovery After Acute Ischemic Stroke: ESCAS Randomized Pilot Study. *Stroke*. 2025 Apr;56(4):937-947. doi: 10.1161/STROKEAHA.124.049834. Epub 2025 Feb 17. PMID: 39957612; PMCID: PMC11932442.
6. Bonifacio GB, Ward NS, Emsley HCA, et al. Optimising rehabilitation and recovery after a stroke. *Pract Neurol*. 2022;22(6):478-485. doi:10.1136/practneurol-2021-003004. PMID: 35896376.
7. Karaganova I, Mindova S. Neuroplasticity after stroke: Adaptive and maladaptive mechanisms in evidence-based rehabilitation. *J Stroke Cerebrovasc Dis*. 2026 Jun;35(6):108634. doi: 10.1016/j.jstrokecerebrovasdis.2026.108634. Epub 2026 Apr 11. PMID: 41967694.
8. Teng H, Li C, Zhang Y, Lu M, Chopp M, Zhang ZG, Melcher-Mourgas M, Fleckenstein B. Therapeutic effect of Cerebrolysin on reducing impaired cerebral endothelial cell permeability. *Neuroreport*. 2021 Mar 24;32(5):359-366. doi: 10.1097/WNR.0000000000001598. PMID: 33661804.
9. Varvarousis ND, Martzivanou C, Dimopoulos D, et al. The effectiveness of botulinum toxin on spasticity and gait of hemiplegic patients after stroke: A systematic review and meta-analysis. *Toxicon*. 2021;203:74-84. doi:10.1016/j.toxicon.2021.09.020. PMID: 34626599.
10. Doan TN, Kuo MY, Chou LW. Efficacy and Optimal Dose of Botulinum Toxin A in Post-Stroke Lower Extremity Spasticity: A Systematic Review and Meta-Analysis. *Toxins (Basel)*. 2021;13(6):428. doi:10.3390/toxins13060428. PMID: 34207357.

Aphasia - Svitlana Oleksandrivna Medvedkova

1. Brady MC, Mills C, Prag Øra H, et al. European Stroke Organisation (ESO) guideline on aphasia rehabilitation. *European Stroke Journal*. 2025;0(0). doi:10.1177/23969873241311025
2. Feigin VL, Brainin M, Norrving B, et al. World Stroke Organization (WSO): Global Stroke Fact Sheet 2022. *International Journal of Stroke*. 2022;17(1):18-29. doi:10.1177/17474930211065917
3. Worrall, L., Simmons-Mackie, N., Wallace, S. J., Rose, T., Brady, M. C., Kong, A. P., Murray, L., & Hallowell, B. (2016). Let's call it „aphasia“: Rationales for eliminating the term „dysphasia“. *International journal of stroke : official journal of the International Stroke Society*, 11(8), 848–851. <https://doi.org/10.1177/1747493016654487>
4. Dickey, L., Kagan, A., Lindsay, M. P., Fang, J., Rowland, A., & Black, S. (2010). Incidence and profile of inpatient stroke-induced aphasia in Ontario, Canada. *Archives of physical medicine and rehabilitation*, 91(2), 196–202. <https://doi.org/10.1016/j.apmr.2009.09.020>
5. Brady MC, Ali M, VandenBerg K, Williams LJ, Williams LR, Abo M, Becker F, Bowen A, Brandenburg C, Breitenstein C, et al. Complex Speech-Language Therapy Interventions for Stroke-Related Aphasia: The RELEASE Study Incorporating a Systematic Review and Individual Participant Data Network Meta-Analysis. *National Institute for Health and Care Research*; 2022. Accessed March 12, 2024. <http://www.ncbi.nlm.nih.gov/books/NBK584830/>
6. Marebwa BK, Fridriksson J, Yourganov G, Feenaughty L, Rorden C, Bonilha L. Chronic post-stroke aphasia severity is determined by fragmentation of residual white matter networks. *Sci Rep*. 2017;7:8188. doi: 10.1038/s41598-017-07607-9
7. Brady MC, Kelly H, Godwin J, Enderby P, Campbell P. Speech and language therapy for aphasia following stroke. *Cochrane Database Syst Rev*. 2016;2016:CD000425. doi: 10.1002/14651858.CD000425.pub4
8. Homberg V, Jianu DC, Stan A, Strilciuc S, Chelaru VF, Karliński M, Brainin M, Heiss WD, Muresanu DF, Enderby PM. Speech Therapy Combined With Cerebrolysin in Enhancing Nonfluent Aphasia Recovery After Acute Ischemic Stroke: ESCAS Randomized Pilot Study. *Stroke*. 2025;56(4):937–947. doi:10.1161/STROKEAHA.124.049834

Acute traumatic brain and spinal cord injury - Adrian-Gheorghe M. Vasilcovi

1. Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol*. 2017;16(12):987-1048. doi:10.1016/S1474-4422(17)30371-X.
2. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery*. 2017;80(1):6-15. doi:10.1227/NEU.0000000000001432.
3. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley DS; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *J Clin Epidemiol*. 2014;67(1):46-51. doi:10.1016/j.jclinepi.2013.08.003.i

4. Poon W, Matula C, Vos PE, et al. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I - a randomized, placebo-controlled, double-blind, Asian-Pacific trial. *Neurol Sci.* 2020;41(2):281-293. doi:10.1007/s10072-019-04053-5.
5. Muresanu DF, Florian S, Hömberg V, et al. Efficacy and safety of Cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial. *Neurol Sci.* 2020;41(5):1171-1181. doi:10.1007/s10072-019-04181-y.
6. Vester JC, Buzoianu AD, Florian SI, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci.* 2021;42(11):4531-4541. doi:10.1007/s10072-020-04974-6.

Acute traumatic brain and spinal cord injury - Andrii Shevchuk

1. Shuanglong Z. et al. A meta-analysis of cognitive and functional outcomes in severe brain trauma cases. *Frontiers in Behavioral Neuroscience*, 2024; 18: 1349672.
2. Dewan M.C. et al. Estimating the global incidence of traumatic brain injury. *Journal of Neurosurgery*, 2018; 130(4), 1080–1097.
3. Sariaslan A. et al. Long-Term Outcomes Associated with Traumatic Brain Injury in Childhood and Adolescence: A Nationwide Swedish Cohort Study of a Wide Range of Medical and Social Outcomes. *PloS Medicine*, 2016; 13(8): e1002103.
4. Vester J.C. et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurological Sciences*, 2021; 42, 4531-4541.

Acute traumatic brain and spinal cord injury - Helmut Trimmel

1. Stocker RA. Intensive care in traumatic brain injury including multimodal monitoring and neuroprotection. *Med Sci.* 2019;7(3):37. doi:10.3390/medsci7030037
2. Mauritz W, Brazinova A, Majdan M, Leitgeb J. Epidemiology of traumatic brain injury in Austria. *Wien Klin Wochenschr.* 2014;126(1–2):42–52. doi:10.1007/s00508-013-0456-6
3. Mauritz W, Brazinova A, Majdan M, Rehorkikova V, Leitgeb J. Deaths due to traumatic brain injury in Austria between 1980 and 2012. *Wien Klin Wochenschr.* 2014;128(23–24):1096–1101. doi:10.3109/02699052.2014.904522
4. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery.* 2017;80(1):6–15. doi:10.1227/NEU.0000000000001432
5. Marehbian J, Muehlschlegel S, Edlow BL, Hinson HE, Hwang DY. Medical management of the severe traumatic brain injury patient. *Neurocrit Care.* 2017;27(3):430–446. doi:10.1007/s12028-017-0408-5
6. Brazinova A, Majdan M, Leitgeb J, Trimmel H, Mauritz W; Austrian Working Group on Improvement of Early TBI Care. Factors that may improve outcomes of early traumatic brain injury care: prospective multicenter study in Austria. *Scand J Trauma Resusc Emerg Med.* 2015;23(1):53. doi:10.1186/s13049-015-0133-z
7. Kabadi SV, Faden AI. Neuroprotective strategies for traumatic brain injury: improving clinical translation. *Int J Mol Sci.* 2014;15(1):1216–1236. doi:10.3390/ijms15011216
8. McGeown JP, Hume PA, Theadom A, Quarrie KL, Borotkanics R. Nutritional interventions to improve neurophysiological impairments following traumatic brain injury: a systematic review. *J Neurosci Res.* 2021;99(2):573–603. doi:10.1002/jnr.24746
9. Muresanu DF, Ciurea AV, Gorgan RM, et al. A retrospective, multicenter cohort study evaluating the severity-related effects of Cerebrolysin treatment on clinical outcomes in traumatic brain injury. *CNS Neurol Disord Drug Targets.* 2015;14(5):587–599. doi:10.2174/1871527314666150430162531
10. Trimmel H, Majdan M, Wodak A, Herzer G, Csomor D, Brazinova A. Citicoline in severe traumatic brain injury: indications for improved outcome: a retrospective matched-pair analysis from 14 Austrian trauma centers. *Wien Klin Wochenschr.* 2018;130(1–2):37–44. doi:10.1007/s00508-017-1240-9
11. Poon W, Matula C, Vos PE, et al. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I—a randomized, placebo-controlled, double-blind, Asian-Pacific trial. *Neurol Sci.* 2020;41(2):281–293. doi:10.1007/s10072-019-04053-5
12. Muresanu DF, Florian S, Hömberg V, et al. Efficacy and safety of Cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial. *Neurol Sci.* 2020;41(5):1171–1181. doi:10.1007/s10072-019-04181-y
13. Sayed IE, Zaki A, Fayed AM, Shehata GM, Abdelmonem S. A meta-analysis of the effect of different neuroprotective drugs in management of patients with traumatic brain injury. *Neurosurg Rev.* 2018;41(2):427–438. doi:10.1007/s10143-016-0775-y
14. Zafonte RD, Bagiella E, Ansel BM, et al. Effect of citicoline on functional and cognitive status among patients with traumatic brain injury: Citicoline Brain Injury Treatment Trial (COBRIT). *JAMA.* 2012;308(19):1993–2000. doi:10.1001/jama.2012.13256
15. Grieb P. Neuroprotective properties of citicoline: facts, doubts and unresolved issues. *CNS Drugs.* 2014;28(3):185–193. doi:10.1007/s40263-014-0144-8
16. Thoenen H, Edgar D. Neurotrophic factors. *Science.* 1985;229(4710):238–242. doi:10.1126/science.2409599

17. Puderbaugh M, Emmady PD. *Neuroplasticity*. StatPearls Publishing; 2020. Accessed March 4, 2021. <https://www.ncbi.nlm.nih.gov/books/NBK557811/>
18. Teng H, Li C, Zhang Y, et al. Therapeutic effect of Cerebrolysin on reducing impaired cerebral endothelial cell permeability. *Neuroreport*. 2021;32:359–366. doi:10.1097/WNR.0000000000001598
19. Secades JJ. Citicoline: pharmacological and clinical review, 2016 update. *Rev Neurol*. 2016;63(S03):S1–S73.
20. Secades JJ. Role of citicoline in the management of traumatic brain injury. *Pharmaceuticals*. 2021;14(5):410. doi:10.3390/ph14050410
21. Varadaraju DN, Ananthakishan A. Effect of cerebroprotein hydrolysate with citicoline versus citicoline alone in the initial management of head injury and its clinical outcome: a prospective randomized comparative study. *J Evid Based Med Healthc*. 2017;4(47):2835–2837. doi:10.18410/jebmh/2017/562
22. Adibhatla RM, Hatcher JF. Cytidine 5'-diphosphocholine (CDP-choline) in stroke and other CNS disorders. *Neurochem Res*. 2005;30(1):15–23. doi:10.1007/s11064-004-9681-8
23. Secades JJ. Citicoline: pharmacological and clinical review, 2010 update. *Rev Neurol*. 2011;52(Suppl 2):S1–S62.
24. Ghaffarpasand F, Torabi S, Rasti A, et al. Effects of Cerebrolysin on functional outcome of patients with traumatic brain injury: a systematic review and meta-analysis. *Neuropsychiatr Dis Treat*. 2018;15:127–135. doi:10.2147/NDT.S186865
25. Muresanu D. *Neurotrophic Factors*. 2003.

Acute traumatic brain and spinal cord injury - Ignacio Previgliano

1. Santurro A, et al. Integrative Diagnostic and Prognostic Paradigms in Diffuse Axonal Injury: Insights from Clinical, Histopathological, Biomolecular, Radiological, and AI-Based Perspectives. *Int J Mol Sci*. 2025;26:7808.
2. Bruggeman GF, et al. Traumatic axonal injury (TAI): definitions, pathophysiology and imaging—a narrative review. *Acta Neurochir (Wien)*. 2021;163:31-44.
3. Sanker V, et al. Frequency of Diffuse Axonal Injury and Its Outcomes in Severe Traumatic Brain Injury (sTBI): A Systematic Review and Meta-Analysis. *J Neurotrauma*. 2025;42(15-16):1243-1255.
4. Adams JH, Graham DI, Murray LS, Scott G. Diffuse axonal injury due to nonmissile head injury in humans: an analysis of 45 cases. *Ann Neurol*. 1982;12:557-563.
5. Gennarelli TA, Thibault LE, Adams JH, Graham DI, Thompson CJ, Marcincin RP. Diffuse axonal injury and traumatic coma in the primate. *Ann Neurol*. 1982;12:564-574.
6. Delteil C, et al. Traumatic axonal injury: Clinic, forensic and biomechanics perspectives. *Leg Med (Tokyo)*. 2024;70:102465.
7. Hilario A, et al. Hallazgos de imagen en el traumatismo craneoencefálico grave. *Radiología*. 2025;67:331-342.
8. Lampros M, et al. The Role of Novel Imaging and Biofluid Biomarkers in Traumatic Axonal Injury: An Updated Review. *Biomedicines*. 2023;11:2312.
9. Moen KG, et al. The prognostic importance of traumatic axonal injury on early MRI: the Trondheim TAI-MRI grading and quantitative models. *Eur Radiol*. 2024;34:8015-8029.
10. Almeida Vieira RC, et al. The Relationship between Injury Characteristics and Post-Traumatic Recovery after Diffuse Axonal Injury. *Biomedicines*. 2024;12:311.
11. Muresanu DF, et al. CAPTAIN II trial. [Complete citation to be added].
12. Muresanu DF, et al. Cerebrolysin and traumatic brain injury: meta-analysis of randomized clinical trials. [Complete citation to be added].
13. Taccone FS, De Oliveira Manoel AL, Robba C, et al. Use a “GHOST-CAP” in acute brain injury. *Crit Care*. 2020;24:89.
14. Robba C, McCredie V, Chesnut RM, et al. Traumatic brain injury management in the intensive care unit: standard of care and knowledge gaps. *Intensive Care Med*. 2025;51:1112-1127.
15. Taccone FS, Rodriguez EE, Zaccarelli M, Sterchele ED. The neurovanguard concept and real-world embracement. *Crit Care*. 2024;28:153.
16. Liu M, Li C, Zhang Z, Mei H, Ban G. Application of GHOST-CAP strategy combined with multimodal monitoring in the treatment of a patient with polytrauma complicated by severe traumatic brain injury: a case report. *Front Med*. 2026;13:1748816.

Acute traumatic brain and spinal cord injury - Jacek Staszewski

1. Sandoval JJ, De Jesus O. Anterior Spinal Artery Syndrome. *StatPearls*. Treasure Island (FL): StatPearls Publishing; updated 2024 Jun 7.
2. Caton MT, Huff JS. Spinal Cord Ischemia. *StatPearls*. Treasure Island (FL): StatPearls Publishing; updated 2023 Aug 14.
3. Yogendranathan N, Herath HMMTB, Pahalagamage SP, Kulatunga A. A case of anterior spinal cord syndrome in a patient with unruptured thoracic aortic aneurysm with a mural thrombus. *BMC Cardiovasc Disord*. 2018;18:44. doi:10.1186/s12872-018-0786-4.
4. McBride F, Anketell J, McDonnell GV, Maguire S, Doherty KM. Non-surgical spinal cord infarction: case series and long-term follow-up of functional outcome. *Spinal Cord Ser Cases*. 2024;10:73.
5. Ramineni KK, Kandragu SS, Jakkani RK, Alwala S. Imaging highlights of anterior spinal cord infarction: Owl's eye sign. *Curr J Neurol*. 2021;20(2):118-119. doi:10.18502/cjn.v20i2.6749.

6. Dokponou YCH, Ontsi Obame FL, Takoutsing B, Mustapha MJ, Nyalundja AD, Saad MS, et al. Spinal cord infarction: a systematic review and meta-analysis of patient's characteristics, diagnosis accuracy, management, and outcome. *Surg Neurol Int.* 2024;15:325. doi:10.25259/SNI_477_2024.
7. Muresanu DF, Heiss WD, Hoernberg V, Bajenaru O, Popescu CD, Vester JC, et al. Cerebrolysin and Recovery After Stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47(1):151-159. doi:10.1161/STROKEAHA.115.009416.
8. Patel PN, et al. Safety and efficacy of Cerebrolysin for neurorecovery after acute ischemic stroke: a systematic review and meta-analysis of 14 randomized controlled trials. *Cureus.* 2025;17(8):e91054. doi:10.7759/cureus.91054.
9. Bartanusz V, Jezova D, Alajajian B, Digicaylioglu M. The blood-spinal cord barrier: morphology and clinical implications. *Ann Neurol.* 2011;70(2):194-206. doi:10.1002/ana.22421.
10. Jin LY, Li J, Wang KF, Xia WW, Zhu ZQ, Wang CR, Li XF, Liu HY. Blood-spinal cord barrier in spinal cord injury: a review. *J Neurotrauma.* 2021;38:1203-1224. doi:10.1089/neu.2020.7413.
11. Teng H, Li C, Zhang Y, et al. Therapeutic effect of Cerebrolysin on reducing impaired cerebral endothelial cell permeability. *NeuroReport.* 2021;32:359-366. doi:10.1097/WNR.0000000000001598.
12. Staszewski J, Dębiec A, Strlicius S, Gniadek-Olejniczak K, Piusinska-Macoch R, Balo D, et al. Efficacy of Cerebrolysin treatment as an add-on therapy to mechanical thrombectomy in patients with acute ischemic stroke due to large vessel occlusion in anterior circulation: results of a 3-month follow-up of a prospective, open-label, single-center study. *Transl Stroke Res.* 2025;16:1931-1946. doi:10.1007/s12975-025-01355-z.
13. Staszewski J, Dębiec A, Gniadek-Olejniczak K, Stępień A, Piusinska-Macoch R, Strlicius S, et al. Cerebrolysin after endovascular thrombectomy in stroke: 12-month functional outcomes in a propensity-matched cohort. *Transl Stroke Res.* 2026;17(2):28. doi:10.1007/s12975-026-01414-z.
14. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *J Med Case Rep.* 2013;7:223. doi:10.1186/1752-1947-7-223.
15. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. *J Clin Epidemiol.* 2017;89:218-235. doi:10.1016/j.jclinepi.2017.04.026.

Acute traumatic brain and spinal cord injury - Jose Daniel Salvador Ruiz González

1. Muresanu DF. Brain recovery--an unified theory. *J Cell Mol Med.* 2010 Mar;14(3):455-6. doi: 10.1111/j.1582-4934.2010.01020.x
2. Ohmura K, Tomita H, Hara A. Peritumoral Edema in Gliomas: A Review of Mechanisms and Management. *Biomedicines.* 2023 Oct 9;11(10):2731. doi: 10.3390/biomedicines11102731
3. Bramlett HM, Dietrich WD. Pathophysiology of cerebral ischemia and brain trauma: similarities and differences. *J Cereb Blood Flow Metab.* 2004 Feb;24(2):133-50. doi: 10.1097/01.WCB.0000111614.19196.04
4. Alvarez XA, Sampedro C, Figueroa J, Tellado I, González A, García-Fantini M, Cacabelos R, Muresanu D, Moessler H. Reductions in qEEG slowing over 1 year and after treatment with Cerebrolysin in patients with moderate-severe traumatic brain injury. *J Neural Transm (Vienna).* 2008 May;115(5):683-92. doi: 10.1007/s00702-008-0024-9
5. Alvarez XA, Sampedro C, Pérez P, Laredo M, Couceiro V, Hernández A, et al. Positive effects of cerebrolysin on electroencephalogram slowing, cognition and clinical outcome in patients with postacute traumatic brain injury: an exploratory study. *Int Clin Psychopharmacol.* 2003 Sep;18(5):271-8. doi: 10.1097/00004850-200309000-00003
6. Asghari AM, Salehpour F, Aghazadeh J, Shakeri M, Shokohi G, Ebrahimi N, Bazazi AM, Pourhajshokr N. Investigation of the effect of Cerebrolysin on patients with head trauma and diffuse axonal injury. *Int J Curr Res Acad Rev.* 2014;2(8):62-9.
7. Chen CC, Wei ST, Tsai SC, Chen XX, Cho DY. Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: double-blind, placebo-controlled, randomized study. *Br J Neurosurg.* 2013 Dec;27(6):803-7. doi: 10.3109/02688697.2013.793287
8. Wong GK, Zhu XL, Poon WS. Beneficial effect of cerebrolysin on moderate and severe head injury patients: result of a cohort study. *Acta Neurochir Suppl.* 2005;95:59-60. doi: 10.1007/3-211-32318-x_13
9. Zhang Y, Chopp M, Meng Y, Zhang ZG, Doppler E, Mahmood A, Xiong Y. Improvement in functional recovery with administration of Cerebrolysin after experimental closed head injury. *J Neurosurg.* 2013 Jun;118(6):1343-55. doi: 10.3171/2013.3.JNS122061
10. Alam A, Hana Z, Jin Z, Suen KC, Ma D. Surgery, neuroinflammation and cognitive impairment. *EBioMedicine.* 2018 Nov;37:547-556. doi: 10.1016/j.ebiom.2018.10.021
11. Denes A, Pradillo JM, Drake C, Buggey H, Rothwell NJ, Allan SM. Surgical manipulation compromises leukocyte mobilization responses and inflammation after experimental cerebral ischemia in mice. *Front Neurosci.* 2014 Jan 17;7:271. doi: 10.3389/fnins.2013.00271
12. Selianina NV, Karakulova IuV. [The effect of neurotrophic treatment on the activation of reparative processes in patients with acute traumatic brain injury]. *Zh Nevrol Psikhiatr Im S S Korsakova.* 2012;112(5):46-9
13. Lyden PD. Cerebroprotection for Acute Ischemic Stroke: Looking Ahead. *Stroke.* 2021 Aug;52(9):3033-3044. doi: 10.1161/STROKEAHA.121.032241
14. Vester JC, Buzoianu AD, Florian SI, Hömberg V, Kim SH, Lee TMC, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci.* 2021 Nov;42(11):4531-4541. doi: 10.1007/s10072-020-04974-6
15. Zhivolupov SA, Shapkova Elu, Samartsev IN, Iurin AA. [The comparative analysis of neyromidin and cerebrolysin effects on neurodynamic processes during craniocerebral injury]. *Zh Nevrol Psikhiatr Im S S Korsakova.* 2011;111(4):31-6. Russian

16. Werner C, Engelhard K. Pathophysiology of traumatic brain injury. *Br J Anaesth*. 2007 Jul;99(1):4-9. doi: 10.1093/bja/aem131
17. Lo EH, Dalkara T, Moskowitz MA. Mechanisms, challenges and opportunities in stroke. *Nat Rev Neurosci*. 2003 May;4(5):399-415. doi: 10.1038/nrn1106

Acute traumatic brain and spinal cord injury - Junhyun Choi

1. Pedersen PM, Vinter K, Olsen TS. Aphasia after stroke: type, severity and prognosis. *The Copenhagen aphasia study. Cerebrovasc Dis*. 2004;17(1):35-43. doi: 10.1159/000073896
2. Tani J, Wen YT, Hu CJ, Sung JY. Current and Potential Pharmacologic Therapies for Traumatic Brain Injury. *Pharmaceuticals (Basel)*. 2022 Jul 6;15(7):838. doi: 10.3390/ph15070838
3. Giacino JT, Whyte J, Bagiella E, Kalmar K, Childs N, Khademi A, et al. Placebo-controlled trial of amantadine for severe traumatic brain injury. *N Engl J Med*. 2012 Mar 1;366(9):819-26. doi: 10.1056/NEJMoa1102609
4. Alvarez XA, Sampedro C, Pérez P, Laredo M, Couceiro V, Hernández A, et al. Positive effects of cerebrolysin on electroencephalogram slowing, cognition and clinical outcome in patients with postacute traumatic brain injury: an exploratory study. *Int Clin Psychopharmacol*. 2003 Sep;18(5):271-8. doi: 10.1097/00004850-200309000-00003
5. Ren J, Sietsma D, Qiu S, Moessler H, Finklestein SP. Cerebrolysin enhances functional recovery following focal cerebral infarction in rats. *Restor Neurol Neurosci*. 2007;25(1):25-31.
6. Homberg V, Jianu DC, Stan A, Strilciuc S, Chelaru VF, Karliński M, et al. Speech Therapy Combined With Cerebrolysin in Enhancing Nonfluent Aphasia Recovery After Acute Ischemic Stroke: ESCAS Randomized Pilot Study. *Stroke*. 2025 Apr;56(4):937-947. doi: 10.1161/STROKEAHA.124.049834
7. Riley DS, Barber MS, Kienle GS, Aronson JK, von Schoen-Angerer T, Tugwell P, et al. CARE guidelines for case reports: explanation and elaboration document. *J Clin Epidemiol*. 2017 Sep;89:218-235. doi: 10.1016/j.jclinepi.2017.04.026
8. Rejdak K, Sienkiewicz-Jarosz H, Bienkowski P, Alvarez A. Modulation of neurotrophic factors in the treatment of dementia, stroke and TBI: Effects of Cerebrolysin. *Med Res Rev*. 2023 Sep;43(5):1668-1700. doi: 10.1002/med.21960
9. Muresanu DF, Heiss WD, Hoemberg V, Bajenaru O, Popescu CD, Vester JC, et al. Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial. *Stroke*. 2016 Jan;47(1):151-9. doi: 10.1161/STROKEAHA.115.009416
10. Gharagozli K, Harandi AA, Houshmand S, Akbari N, Muresanu DF, Vester J, et al. Efficacy and safety of Cerebrolysin treatment in early recovery after acute ischemic stroke: a randomized, placebo-controlled, double-blinded, multicenter clinical trial. *J Med Life*. 2017 Jul-Sep;10(3):153-160.
11. Vester JC, Buzoianu AD, Florian SI, Hömberg V, Kim SH, Lee TMC, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci*. 2021 Nov;42(11):4531-4541. doi: 10.1007/s10072-020-04974-6

Acute traumatic brain and spinal cord injury - Mohammed Hammad Eltantawy

1. Fiani B, Covarrubias C, Wong A, Doan T, Reardon T, Nikolaidis D, et al. Cerebrolysin for stroke, neurodegeneration, and traumatic brain injury: review of the literature and outcomes. *Neurol Sci*. 2021;42(4):1345–1353.
2. Ghaffarparasand F, Torabi S, Rasti A, Niakan MH, Aghabaklou S, Pakzad F, et al. Effects of Cerebrolysin on functional outcome of patients with traumatic brain injury: a systematic review and meta-analysis. *Neuropsychiatr Dis Treat*. 2019;15:127–135.
3. Muresanu DF, et al. Neurotrophic and neuroprotective mechanisms of Cerebrolysin in neurological recovery. *Neurol Sci*. 2021;42:1345–1353.
4. Sahib S, Sharma HS, Menon PK, Muresanu DF, Castellani RJ, Nozari A, et al. Cerebrolysin enhances spinal cord conduction and reduces blood-spinal cord barrier breakdown, edema formation, immediate early gene expression and cord pathology after injury. *Prog Brain Res*. 2020;258:483–507.
5. Menon PK, Muresanu DF, Sharma A, Mössler H, Sharma HS. Cerebrolysin, a mixture of neurotrophic factors, induces marked neuroprotection in spinal cord injury following intoxication of engineered nanoparticles from metals. *Recent Pat CNS Drug Discov*. 2012;7(1):40–49.
6. Poon WS, Matula C, Vos PE, Muresanu DF, von Steinbüchel N, von Wild K, et al. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I randomized placebo-controlled trial. *Neurol Sci*. 2020;41:281–293.
7. Vester JC, Buzoianu AD, Florian SI, Hömberg V, Kim SH, Lee TMC, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci*. 2021;42(11):4531–4541.
8. Muresanu DF, Heiss WD, Hoemberg V, et al. Cerebrolysin and neurorecovery after acute central nervous system injury: current evidence and future directions. *J Neural Transm*. 2019;126(Suppl 1):S1–S10.

Acute traumatic brain and spinal cord injury - Sahid Muradovich Annanepesov

1. Greenberg MS. *Greenberg's Handbook of Neurosurgery*. 10th ed. New York: Thieme; 2023.
2. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery*. 2017;80(1):6-15. doi:10.1227/NEU.0000000000001432.
3. Powers WJ, Rabinstein AA, Ackerson T, et al. Guidelines for the early management of patients with acute ischemic stroke. *Stroke*. 2019;50:e344-e418.
4. Winstein CJ, Stein J, Arena R, et al. Guidelines for Adult Stroke Rehabilitation and Recovery. *Stroke*. 2016;47:e98-e169.

5. Muresanu DF, Florian S, Hömberg V, et al. Efficacy and safety of Cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial. *Neurol Sci.* 2020;41:1171-1181. doi:10.1007/s10072-019-04181-y.
6. Poon W, Matula C, Vos PE, et al. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I - a randomized, placebo-controlled, double-blind, Asian-Pacific trial. *Neurol Sci.* 2020;41:281-293. doi:10.1007/s10072-019-04137-2.
7. Vester JC, Buzoianu AD, Florian SI, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci.* 2021;42:4531-4541. doi:10.1007/s10072-020-04974-6.
8. Chen CC, Wei ST, Tsaia SC, Chen XX, Cho DY. Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: double-blind, placebo-controlled, randomized study. *Br J Neurosurg.* 2013;27(6):803-807. PMID:23656173.
9. Muresanu DF, Heiss WD, Hoemberg V, et al. Cerebrolysin and Recovery After Stroke (CARs): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke.* 2016;47(1):151-159. doi:10.1161/STROKEAHA.115.009416.
10. Stan A, Birla C, Blesneag A, Iancu M. Cerebrolysin and early neurorehabilitation in patients with acute ischemic stroke: a prospective, randomized, placebo-controlled clinical study. *J Med Life.* 2017;10(4):216-222.
11. EVER Neuro Pharma GmbH. Cerebrolysin Product Monograph. 2021. Contraindications include epilepsy and severe renal impairment. Prescribing information may vary by country.
12. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D; CARE Group. The CARE guidelines: consensus-based clinical case reporting guideline development. *J Clin Epidemiol.* 2014;67(1):46-51. doi:10.1016/j.jclinepi.2013.08.003.

Acute traumatic brain and spinal cord injury - Silvina Ilut

1. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery.* 2017;80(1):6-15. doi:10.1227/NEU.0000000000001432.
2. Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol.* 2017;16(12):987-1048. doi:10.1016/S1474-4422(17)30371-X.
3. Poon W, Matula C, Vos PE, et al. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I - a randomized, placebo-controlled, double-blind, Asian-Pacific trial. *Neurol Sci.* 2020;41(2):281-293. doi:10.1007/s10072-019-04053-5.
4. Muresanu DF, Florian SI, Hömberg V, et al. Efficacy and safety of Cerebrolysin in neurorecovery after moderate-severe traumatic brain injury: results from the CAPTAIN II trial. *Neurol Sci.* 2020;41(5):1171-1181. doi:10.1007/s10072-019-04181-y.
5. Vester JC, Buzoianu AD, Florian SI, et al. Cerebrolysin after moderate to severe traumatic brain injury: prospective meta-analysis of the CAPTAIN trial series. *Neurol Sci.* 2021;42(11):4531-4541. doi:10.1007/s10072-020-04974-6.
6. Gagnier JJ, Kienle G, Altman DG, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. *J Med Case Rep.* 2013;7:223. doi:10.1186/1752-1947-7-223.

Acute traumatic brain and spinal cord injury - Vitalie Lisnic

1. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the Management of Severe Traumatic Brain Injury, Fourth Edition. *Neurosurgery.* 2017;80(1):6-15. doi:10.1227/NEU.0000000000001432.
2. Hawryluk GWJ, Rubiano AM, Totten AM, et al. Guidelines for the Management of Severe Traumatic Brain Injury: 2020 Update of the Decompressive Craniectomy Recommendations. *Neurosurgery.* 2020;87(3):427-434. doi:10.1093/neuros/nyaa278.
3. Hutchinson PJ, Koliass AG, Timofeev IS, et al. Trial of Decompressive Craniectomy for Traumatic Intracranial Hypertension. *N Engl J Med.* 2016;375(12):1119-1130. doi:10.1056/NEJMoa1605215.
4. Mele C, Pingue V, Caputo M, et al. Impact of Cranioplasty on Rehabilitation Course of Patients with Traumatic or Hemorrhagic Brain Injury. *Brain Sci.* 2023;13(1):89. doi:10.3390/brainsci13010089.
5. Ozoner B. Cranioplasty Following Severe Traumatic Brain Injury: Role in Neurorecovery. *Curr Neurol Neurosci Rep.* 2021;21(11):62. doi:10.1007/s11910-021-01147-6.
6. Sveikata L, Vasung L, El Rahal A, et al. Syndrome of the trephined: clinical spectrum, risk factors, and impact of cranioplasty on neurologic recovery in a prospective cohort. *Neurosurg Rev.* 2022;45(2):1431-1443. doi:10.1007/s10143-021-01680-3.
7. Ashayeri K, Jackson EM, Huang J, Brem H, Gordon CR. Syndrome of the Trephined: A Systematic Review. *Neurosurgery.* 2016;79(4):525-534. doi:10.1227/NEU.0000000000001366.
8. Iaccarino C, Koliass AG, Roumy LG, Fountas K, Adeleye AO. Cranioplasty Following Decompressive Craniectomy. *Front Neurol.* 2020;10:1357. doi:10.3389/fneur.2019.01357.
9. Henry J, Amoo M, Taylor J, O'Brien DP. Complications of cranioplasty in relationship to traumatic brain injury: a systematic review and meta-analysis. *Acta Neurochir (Wien).* 2021;163:1421-1435.
10. Maas AIR, Menon DK, Adelson PD, et al. Traumatic brain injury: integrated approaches to improve prevention, clinical care, and research. *Lancet Neurol.* 2017;16(12):987-1048. doi:10.1016/S1474-4422(17)30371-X.
11. Wilson L, Stewart W, Dams-O'Connor K, et al. The chronic and evolving neurological consequences of traumatic brain injury. *Lancet Neurol.* 2017;16(10):813-825. doi:10.1016/S1474-4422(17)30279-X.
12. Frontera JA, Gilmore EJ, Johnson EL, et al. Guidelines for Seizure Prophylaxis in Adults Hospitalized with Moderate-Severe Traumatic Brain Injury: A Clinical Practice Guideline for Health Care Professionals from the Neurocritical Care Society. *Neurocrit Care.* 2024;40(3):819-844. doi:10.1007/s12028-023-01907-x.

Functional and Cognitive Recovery in neurological disorders - Elena Krikun

1. Letter to the Editor, published on April 17, 2020, at NEJM.org. *N Engl J Med* 2020; 382:2574-2576 DOI: 10.1056/NEJMc2009191 <https://www.nejm.org/doi/full/10.1056/NEJMc2009191>
2. Webb S. et al Guillain-Barré syndrome following COVID-19: a newly emerging post-infectious complication. *BMJ Case Rep* 2020;13:e236182. doi:10.1136/bcr-2020-236182
3. Trujillo Gittermann et al Relation between COVID-19 and Guillain-Barré syndrome in adults: a systematic review DOI: 10.1016/j.nrleng.2020.07.005 <https://www.elsevier.es/en-revista-neurologia-english-edition--495-avance-resumen-relation-between-covid-19-guillain-barre-syndrome-S2173580820302145>
4. Zhao et al Guillain-Barré syndrome associated with SARS-CoV-2 infection: causality or coincidence? *The Lancet Neurology*. Published: April 01, 2020 DOI: [https://doi.org/10.1016/S1474-4422\(20\)30109-5](https://doi.org/10.1016/S1474-4422(20)30109-5)
5. Levin et al *Clinical scales in neurology*. ISBN 978-5-00030-641-3. –M.: MEDpress-inform, 2019. – 192 p.

Functional and Cognitive Recovery in neurological disorders - N.U. Makhkamova

1. World Health Organization. *Global report on hypertension: the race against a silent killer*. Geneva: WHO; 2023.
2. Brainin M, Tuomilehto J, Heiss WD, Bornstein N, et al. Post-stroke cognitive decline: an update and perspectives for clinical research. *Eur J Neurol*. 2015;22(2):229–238.
3. Masserini F, Gendarini C, Baso G, Salvadori E, Pantoni L. Therapeutic strategies in vascular cognitive impairment: a systematic review and meta-analysis. *Alzheimers Dement*. 2025;21(11).
4. Zhu Z, Duan S, Sun X. A review of hypertension and vascular cognitive impairment. *Brain Heart*. 2025;3(1):44.
5. Smith EE, Aparicio HJ, Gottesman RF, et al. Vascular contributions to cognitive impairment and dementia in the United States: a scientific statement from the American Heart Association. *Stroke*. 2025;56–e330.
6. Kalaria RN, Akinyemi RO, Paddick SM, Ihara M. Current perspectives on the prevention of vascular cognitive impairment and the promotion of vascular brain health. *Expert Rev Neurother*. 2024;24(1):25–44.
7. Guekht AB, Moessler H, Novak PH, Gusev EI; Cerebrolysin Investigators. Cerebrolysin in vascular dementia: improvement of clinical outcome in a randomized, double-blind, placebo-controlled multicenter trial. *J Stroke Cerebrovasc Dis*. 2011;20(4):310–318. doi:10.1016/j.jstrokecerebrovasdis.2010.01.012.
8. Bath PM, Gray LJ, Bath-Hextall FJ, et al. Cerebrolysin for vascular dementia. *Cochrane Database Syst Rev*. 2019.
9. Vosko MR, Sanak D, Do Y, et al. C-REGS2—a multinational, high-quality comparative effectiveness study of Cerebrolysin in moderate acute ischemic stroke. *Int J Stroke*. 2025;20(9):1060–1070. doi:10.1177/17474930251375439.
10. Vosko MR, Sanak D, Vester JC, Brainin M, et al. Improved cognitive trajectory after acute ischemic stroke: insights from C-REGS2 trial. *Eur Stroke J*. 2026;11(Suppl 1).
11. Al-Kuraishy HM, Al-Gareeb AI, et al. The possible role of Cerebrolysin in the management of vascular dementia: leveraging concepts. *Neuroscience*. 2025;568:202–208. doi:10.1016/j.neuroscience.2025.01.040.

Functional and Cognitive Recovery in neurological disorders - Rana Samadova

1. Jurcau A, Ardelean IA. Molecular pathophysiological mechanisms of ischemia/reperfusion injuries after recanalization therapy for acute ischemic stroke. *J Integr Neurosci*. 2021 Sep 30;20(3):727-744. doi: 10.31083/j.jin2003078. PMID: 34645107.
2. Mureșanu DF, Livinț Popa L, Chira D, Dăbală V, Hapca E, Vlad I, Văcăraș V, Popescu BO, Cherecheș R, Strilciuc Ș, Brainin M. Role and Impact of Cerebrolysin for Ischemic Stroke Care. *J Clin Med*. 2022 Feb 25;11(5):1273. doi: 10.3390/jcm11051273. PMID: 35268364; PMCID: PMC8911124.
3. Feigin VL, Owolabi MO; World Stroke Organization–Lancet Neurology Commission Stroke Collaboration Group. Pragmatic solutions to reduce the global burden of stroke: a World Stroke Organization-Lancet Neurology Commission. *Lancet Neurol*. 2023 Dec;22(12):1160-1206. doi: 10.1016/S1474-4422(23)00277-6. Epub 2023 Oct 9. Erratum in: *Lancet Neurol*. 2023 Dec;22(12):e13. doi: 10.1016/S1474-4422(23)00425-8. PMID: 37827183; PMCID: PMC10715732.
4. Jurcau A, Ardelean IA. Molecular pathophysiological mechanisms of ischemia/reperfusion injuries after recanalization therapy for acute ischemic stroke. *J Integr Neurosci*. 2021 Sep 30;20(3):727-744. doi: 10.31083/j.jin2003078. PMID: 34645107.
5. Ma Y, Yang S, He Q, Zhang D, Chang J. The Role of Immune Cells in Post-Stroke Angiogenesis and Neuronal Remodeling: The Known and the Unknown. *Front Immunol*. 2021 Dec 16;12:784098. doi: 10.3389/fimmu.2021.784098. PMID: 34975872; PMCID: PMC8716409.

Functional and Cognitive Recovery in neurological disorders - Soo Hwan Yim

1. Vora NM, Holman RC, Mehal JM, Steiner CA, Blanton J, Sejvar J. Burden of encephalitis-associated hospitalizations in the United States, 1998-2010. *Neurology*. 2014 Feb 4;82(5):443-51. doi: 10.1212/WNL.0000000000000086
2. Venkatesan A. Epidemiology and outcomes of acute encephalitis. *Curr Opin Neurol*. 2015 Jun;28(3):277-82. doi: 10.1097/WCO.0000000000000199
3. Solomon T, Michael BD, Smith PE, Sanderson F, Davies NW, Hart IJ, et al; National Encephalitis Guidelines Development and Stakeholder Groups. Management of suspected viral encephalitis in adults--Association of British Neurologists and British Infection Association National Guidelines. *J Infect*. 2012 Apr;64(4):347-73. doi: 10.1016/j.jinf.2011.11.014
4. Piret J, Boivin G. Immunomodulatory Strategies in Herpes Simplex Virus Encephalitis. *Clin Microbiol Rev*. 2020 Feb 12;33(2):e00105-19. doi: 10.1128/CMR.00105-19

5. Rejdak K, Sienkiewicz-Jarosz H, Bienkowski P, Alvarez A. Modulation of neurotrophic factors in the treatment of dementia, stroke and TBI: Effects of Cerebrolysin. *Med Res Rev.* 2023 Sep;43(5):1668-1700. doi: 10.1002/med.21960.
6. Toader LE, Roşu GC, Cătălin B, Pirici I, Gîlceavă IC, Albu VC, et al. Cerebrolysin increases motor recovery and decreases inflammation in a mouse model of autoimmune encephalitis. *Rom J Morphol Embryol.* 2018;59(3):755-762.
7. Panisset M, Gauthier S, Moessler H, Windisch M; Cerebrolysin Study Group. Cerebrolysin in Alzheimer's disease: a randomized, double-blind, placebo-controlled trial with a neurotrophic agent. *J Neural Transm (Vienna).* 2002 Jul;109(7-8):1089-104. doi: 10.1007/s007020200092
8. Brainin M. Cerebrolysin: a multi-target drug for recovery after stroke. *Expert RevNeurother.* 2018 Aug;18(8):681-687. doi: 10.1080/14737175.2018.1500459
9. Fiani B, Covarrubias C, Wong A, Doan T, Reardon T, Nikolaidis D, et al. Cerebrolysin for stroke, neurodegeneration, and traumatic brain injury: review of the literature and outcomes. *Neurol Sci.* 2021 Apr;42(4):1345-1353. doi: 10.1007/s10072-021-05089-2
10. Kojder K, Jarosz K, Bosiacki M, Andrzejewska A, Zacha S, Solek-Pastuszka J, et al. Cerebrolysin in Patients with Subarachnoid Hemorrhage: A Systematic Review and Meta-Analysis. *J Clin Med.* 2023 Oct 20;12(20):6638. doi: 10.3390/jcm12206638
11. Bornstein NM, Guekht A, Vester J, Heiss WD, Gusev E, Hömberg V, Rahlfs VW, Bajenaru O, Popescu BO, Muresanu D. Safety and efficacy of Cerebrolysin in early post-stroke recovery: a meta-analysis of nine randomized clinical trials. *Neurol Sci.* 2018 Apr;39(4):629-640. doi: 10.1007/s10072-017-3214-0
12. Bohmwald K, Andrade CA, Gálvez NMS, Mora VP, Muñoz JT, Kalergis AM. The Causes and Long-Term Consequences of Viral Encephalitis. *Front Cell Neurosci.* 2021 Nov 30;15:755875. doi: 10.3389/fncel.2021.755875

Functional and Cognitive Recovery in neurological disorders - Tatsiana V. Dakukina

1. Kolykhalov IV (2016) Current approaches to optimize treatment of dementia and Alzheimer's disease. *Korsakov S.S. Journal of Neurology and Psychiatry* 116(6): 87-92.
 2. Allegri RF and Guekht A (2012) Cerebrolysin improves symptoms and delays progression in patients with Alzheimer's disease and vascular dementia. *Drugs Today (Barc)* 48(Suppl A): 25-41.
 3. Gauthier S, Proaño JV, Jia J, Froelich L, Vester JC, et al (2015) Cerebrolysin in mild-to-moderate Alzheimer's disease: a meta-analysis of randomized controlled clinical trials. *Dement Geriatr Cogn Disord* 39(5-6): 332-347.
 4. Negoda SV (2013) Cerebrolysin: evidence base and clinical use in cognitive disorders. *Polyclinic doctor's Handbook* 7(8): 46-48.
 5. Clinical protocol "Providing medical care to patients with organic, including symptomatic, mental disorders (adult and child populations)". Resolution of the Ministry of Health of the Republic of Belarus dated. 108: 10-14.
 6. (2022) The standard of medical care for elderly and senile patients with cognitive disorders (diagnosis and treatment). Appendix to the Order of the Ministry of Health of the Russian Federation dated 81n.
 7. Ruiz A, Pesini P, Espinosa A, Grijalba VP, Valero S, et al (2013) Blood amyloid beta levels in healthy, mild cognitive impairment and Alzheimer's disease individuals: replication of diastolic blood pressure correlations and analysis of critical covariates. *PLoS One* 27; 8(11): e81334.
 8. Shaw LM, Korecka M, Figurski M, Toledo J, Irwin D, et al (2020) Detection of Alzheimer Disease Pathology in Patients Using Biochemical Biomarkers: Prospects and Challenges for Use in Clinical Practice. *J Appl Lab Med* 5(1): 183-193.
 9. Astashenok AN, Poleshchuk NN, Dokukina TV, et al (2015) Identification of neurodegeneration marker proteins in patients with cognitive impairments and detection of protease-resistant prion protein (PrP) in various dementia conditions. *Psychiatry, psychotherapy and clinical psychology* 2(20): 11-21.
 10. (2018) mhGAP intervention guide for mental, neurological and substance use disorders in non-specialized health settings: mental health Gap Action Programme (mhGAP) – version 20: 174 C.
 11. (2013) Instruction for medical use of the drug Cerebrolysin. Approved by the Ministry of Health. Order of the Ministry of Health dated 1452.
 12. (2021) Cerebrolysin in Alzheimer disease. Product monograph Cerebrolysin Reconnecting neurons. Empowering for life 57-69.
 13. Gavrilova SI and Alvarez A (2021) Cerebrolysin in the therapy of mild cognitive impairment and dementia due to Alzheimer's disease: 30 years of clinical use. *Med Res Rev* 41(5): 2775-2803.
 14. Álvarez AX and Fuentes P (2011) Cerebrolysin in Alzheimer's disease. *Drugs Today (Barc)* 47(7): 487-513.
 15. Dolphin H, Dyer AH, Morrison L, Shenkin SD, Welsh T, et al (2024) New horizons in the diagnosis and management of Alzheimer's Disease in older adults. *Age Ageing* 53(2): afae005.
 16. Vasenina EE, Trusova NA, Gankina OA, et al (2014) Combination therapy of Alzheimer's disease. *Neuronews* 4(59): 7.
 17. Doppler E, Alvarez X, (2009) et al. Synergistic treatment effects with Cerebrolysin and donepezil: Results from a randomized, double-blind, multicenter trial to compare safety and efficacy of Cerebrolysin, donepezil and a combination treatment in patients with probable Alzheimer's disease. *Alzheimers & Dementia* 5(4).
 18. Ritchie C, Smailagic N, Noel Storr AH, Ukoumunne O, Ladds EC, et al (2017) CSF tau and the CSF tau/ABeta ratio for the diagnosis of Alzheimer's disease dementia and other dementias in people with mild cognitive impairment (MCI). *Cochrane Database Syst Rev* 3(3): CD010803.
 19. Gulisano W, Maugeri D, Baltrons MA, Fà M, Amato A, et al (2018) Role of Amyloid-β and Tau Proteins in Alzheimer's Disease: Confuting the Amyloid Cascade. *J Alzheimers Dis* 64(s1): S611-S631.
-

20. Cojocaru AB, Azhigova AM and Larkina ES (2023) Application of Eeg in the Assessment of Functional Changes in the Brain in Cognitive Disorders 78-83.
21. Ding Y, Chu Y, Liu M, Ling Z, Wang S, et al (2022) Fully automated discrimination of Alzheimer's disease using resting-state electroencephalography signals. *Quant Imaging Med Surg* 12(2): 1063-1078.
22. Simfukwe C, Han SH, Jeong HT and Youn YC et al (2023) qEEG as Biomarker for Alzheimer's Disease: Investigating Relative PSD Difference and Coherence Analysis. *Neuropsychiatr Dis Treat* 19: 2423-2437.
23. Dakuukina T and Misiuk N.
24. Adamis D, Sahu S and Treloar A (2005) The utility of EEG in dementia: a clinical perspective. *Int J Geriatr Psychiatry* 20(11): 1038-1045.
25. Adler G, Brassen S, Chwalek K, Dieter B, Teufel M (2004) Prediction of treatment response to rivastigmine in Alzheimer's dementia. *J Neurol Neurosurg Psychiatry* 75(2): 292-294.
26. Babiloni C, Lizio R, Marzano N, Capotosto P, Soricelli A, et al. (2016) Brain neural synchronization and functional coupling in Alzheimer's disease as revealed by resting state EEG rhythms. *Int J Psychophysiol* 103: 88-102.
27. Burd SG, Lebedeva AV, Rubleva Yu V, Pantina EF, et al (2024) EEG chhanges in patients itch Alzhheimer's Disease. S..S. *Korsakov Journal of Neurology and Psychiatry* 124 (42): 7276
28. Dolphin H, Dyer AH, Morrison L, Shenkin SD, Welsh T, et al. (2024) New horizons in the diagnosis and management of Alzheimer's Disease in older adults. *Age Ageing* 53(2): afae005.

CERECAP - Nguyen Hoang Ngoc

1. Rordorf G and McDonald C. Spontaneous intracerebral hem-orrhage: prognosis and treatment, 2011, <https://somepomed.org/articulos/contents/mobipreview.htm?34/47/35569>
2. Morgenstern LB, Hemphill JC 3rd, Anderson C, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2010; 41(9): 2108–2129.
3. Morgan T, Awad I, Keyl P, et al. Preliminary report of the Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage (CLEAR-IVH) Clinical Trial. *Acta Neurochir Suppl* 2008; 105: 217–220.
4. Hanley DF, Lane K, McBee N, et al. Thrombolytic removal of intraventricular haemorrhage in treatment of severe stroke: results of the randomised, multicentre, multiregion, placebo-controlled CLEAR III trial. *Lancet* 2017; 389(10069): 603–611.
5. Kumar S, Selim MH and Caplan LR. Medical complications after stroke. *Lancet Neurol* 2010; 9(1): 105–118.
6. Muresanu DF, Heiss WD, Hoernberg V, et al. Cerebrolysin and recovery after stroke (CARS): a randomized, placebo-controlled, double-blind, multicenter trial. *Stroke* 2016; 47(1): 151–159.
7. Winkler A, Schandl I, Galoppi M, et al. AVANT: stroke-reha-bilitation program in Vietnam: report of progress after 3 years of implementation. In: Dettmers C, Schönle PW and Weiller C (eds) *Neurology & rehabilitation*. Bad Honnef: Hippocampus Verlag e.K, 2019, p. S15.
8. Teasdale G and Jennett B. Assessment of coma and impaired consciousness: a practical scale. *Lancet* 1974; 304: 81–84.
9. Wilson JL, Hareendran A, Grant M, et al. Improving the assessment of outcomes in stroke: use of a structured inter-view to assign grades on the Modified Rankin Scale. *Stroke* 2002; 33(9): 2243–2246.
10. Ortiz GA and Sacco LR. National Institutes of Health Stroke Scale (NIHSS). In: Balakrishnan N, Colton T, veritt B, et al. (eds) *Wiley StatsRef: statistics reference online*, 2014. DOI: 10.1002/9781118445112.stat06823.
11. Graeb DA, Robertson WD, Lapointe JS, et al. Computed tomo-graphic diagnosis of intraventricular hemorrhage. *Radiology* 1982; 143(1): 91–96.

Informed Consent

Written informed consent for publication of the clinical information and any accompanying images or other potentially identifiable material was obtained from all patients described in this book or, where applicable, from their legally authorized representatives. All case reports were prepared and presented in accordance with applicable ethical principles and with appropriate measures to protect patient confidentiality and anonymity.

