Online October 13, 2020
Journal of Neuroendovascular Therapy 2021; 15: 181–188 DOI: 10.5797/jnet.cr.2020-0034

Case Report

Mechanical Thrombectomy for Internal Carotid Artery Occlusion in a Patient with POEMS Syndrome

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Objective: To report a case of mechanical thrombectomy (MT) for internal carotid artery (ICA) occlusion in a patient with polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome, a rare systemic disease associated with plasma cell proliferation.

Case Presentation: A 52-year-old woman was taking steroids due to autoimmune hepatitis. She was diagnosed with acute cerebral infarction due to left ICA occlusion. Although MT was performed, recanalization was not achieved. Therefore, recanalization was carried out using a vasodilator and percutaneous transluminal angioplasty (PTA) in combination.

Conclusion: PTA may be effective for large-vessel occlusion (LVO) in patients with POEMS syndrome.

Keywords ▶ mechanical thrombectomy, POEMS syndrome, stent retriever, PTA

Introduction

Mechanical thrombectomy (MT) is the gold standard for acute-phase treatment of intracranial main artery obstruction in addition to intravenous alteplase infusion (intravenous thrombolysis with recombinant tissue plasminogen activator; IV rt-PA). MT has been widely used since several randomized controlled trials (RCTs) demonstrated better outcomes with this procedure than with medical treatment, including IV rt-PA therapy, in patients meeting certain conditions between 2014 and 2015.[1)] The time to recanalization affects the prognosis, especially that of occlusion of large vessels such as the internal carotid artery (ICA) and middle cerebral artery (MCA).[2)] Therefore, accurate judgment is required within a short time during the procedure.

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Received: February 13, 2020; Accepted: August 4, 2020
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POEMS syndrome is a systemic disease related to plasma cell proliferation and is associated with a range of symptoms, including peripheral neuropathy, organomegaly, endocrine disorder, monoclonal gammopathy, and skin changes (POEMS).[3)] Although there are many reports of ischemic disease of the coronary and lower extremity arteries associated with POEMS syndrome,[4,5)] reports of cerebral infarction are markedly rare. The mechanism by which cerebral infarction develops in patients with POEMS syndrome is unknown. It occasionally occurs in the terminal artery region. In recent years, however, there have been some reports on the involvement of proximal vessels.[6)]

We report a patient who underwent thrombectomy for large-vessel occlusion (LVO) and was later diagnosed with POEMS syndrome as a result of further examination.

Case Presentation

A 52-year-old woman with a history of autoimmune hepatitis complicated by Sjögren's syndrome received prednisolone for 2 years. She had severe numbness in both lower extremities and gait disturbance for 6 months, and was scheduled to undergo a detailed examination for polyneuropathy. The last known time when she was clinically well was 8 a.m. on the day of onset. Upon returning home at 5:30 p.m., a family member found her lying on the floor and she was transferred to our hospital by ambulance at 7:00 p.m. Her consciousness was a score of 20 according to the Japan Coma Scale (JCS) when she arrived at the hospital. Her

blood pressure was 137/79 and pulse rate was 68 bpm, with no arrythmia. A manual muscle test for the right upper and lower extremities demonstrated MMT2/5 hemiparesis, total aphasia, and right hemispatial neglect. The National Institutes of Health Stroke Scale (NIHSS) score was 23.

Laboratory findings

Electrocardiography (ECG) revealed sinus rhythm. No abnormal findings were found on hematological examination, including the coagulation system, except for a slightly high triglyceride level of 239 mg/dL (**Table 1**). Diffusion-weighted imaging (DWI) MRI of the head revealed diffuse high-intensity areas in the left MCA (**Fig. 1A** and **1B**) and DWI-ASPECTS was 6 points. There was a mismatch between the high-intensity area on the FLAIR image and the high-intensity area on the DWI (**Fig. 1C** and **1D**). Magnetic resonance angiography (MRA) demonstrated occlusion of the left ICA at the siphon site, poor visualization of the bilateral anterior cerebral artery (ACA), and multiple stenoses of the intracranial large vessels such as right MCA M2 stenosis (**Fig. 2A**). However, stenosis of the cervical portion of the ICA was not noted (**Fig. 2B**). Arterial spin-labeling (ASL) images suggested extensive hypoperfusion of the left cerebral hemisphere (**Fig. 2C** and **2D**).

Table 1 Blood test

WBC	9680/μL
Hb	13.2 g/dL
Ht	42.6%
Plt	30.3×10^4/μL
d-dimer	0.8 μg/mL
Prothrombin time	12.1 sec
INR	1.01
APTT	30.0 sec
T.P	6.8 g/dL
Alb	3.5 g/dL
AST	22 IU/L
ALT	8 IU/L
LDH	166 IU/L
BUN	11.0 mg/dL
Cre	0.65 mg/dL
Na	139 mEq/dL
K	3.7 mEq/L
Cl	105 mEq/L
Ca	8.9 mg/dL
Fe	20 μg/dL
HDL-Chol.	52 mg/dL
LDL-Chol.	97 mg/dL
TG	239 mg/dL
UA	4.9 mg/dL
IgG	982 mg/dL
IgA	255 mg/dL
IgM	122 mg/dL
Immunoglobulin free L-chain κ/λ ratio	1.25
BNP	54.7 pg/mL
FT4	1.26 ng/dL
GH	3.12 ng/mL
PRL	30.5 ng/mL
Somatomedin C	70 ng/mL
Calcitonin	1.81 pg/mL
Rheumatoid factor	38 IU/mL
Serum complement level	30.6 CH50/mL
Anti-smooth muscle antibody	Negative
Mitochondrial antibody	Negative
Anti-cardiolipin antibody IgG	8 U/mL or less
P-ANCA	<1.0 U/mL
C-ANCA	<1.0 U/mL

Alb: albumin; ALT: alanine aminotransferase; ANCA: anti-neutrophil cytoplasmic antibody; APTT: activated partial thromboplastin time; AST: aspartate aminotransferase; BUN: blood urea nitrogen; GH: growth hormone; Hb: hemoglobin; HDL: high-density lipoprotein; Ht: hematocrit; INR: international normalized ratio; LDH: lactate dehydrogenase; LDL: low-density lipoprotein; Plt: platelet; Prl: prolactin; TG: triglyceride; T.P.: total protein; UA: uric acid; WBC: white blood cells

Endovascular treatment

Administration of alteplase was not indicated because the time of onset of cerebral infarction was unknown. No atrial fibrillation (AF) was noted on ECG and there were no risk factors for cerebral infarction such as hypertension (HT), hyperlipidemia (HLD), diabetes mellitus (DM), or smoking. The presence of multiple stenoses in the large vessel and occlusion of the left ICA suggested atherothrombotic cerebral infarction. MT was selected because she was a non-elderly patient with aphasia and right hemiparesis even though more than 10 hours had elapsed since the last known time when she was clinically well and there was a DWI/FLAIR mismatch. Prior to treatment, we informed the patient's family that it may be more difficult to achieve recanalization compared with thrombectomy for cardiogenic embolism, and of the possibility and risks of percutaneous transluminal angioplasty (PTA) and intra-arterial administration of drugs, and received consent for thrombectomy. After insertion of an 8Fr long sheath into the right femoral artery under local anesthesia, 2500 units of heparin was intravenously injected. Then, an 8-French FlowGate^2 (Stryker Neurovascular, Fremont, CA, USA) was guided to the left common carotid artery and angiography was performed. Although there was no significant stenosis at the bifurcation of the cervical ICA, occlusion at the left internal carotid-ocular artery bifurcation and beyond was observed (**Fig. 3A**). Next, arteriography of the right ICA was carried out, revealing no right MCA stenosis (which was suspected on MRA) (**Fig. 3B**). To perform MT, the

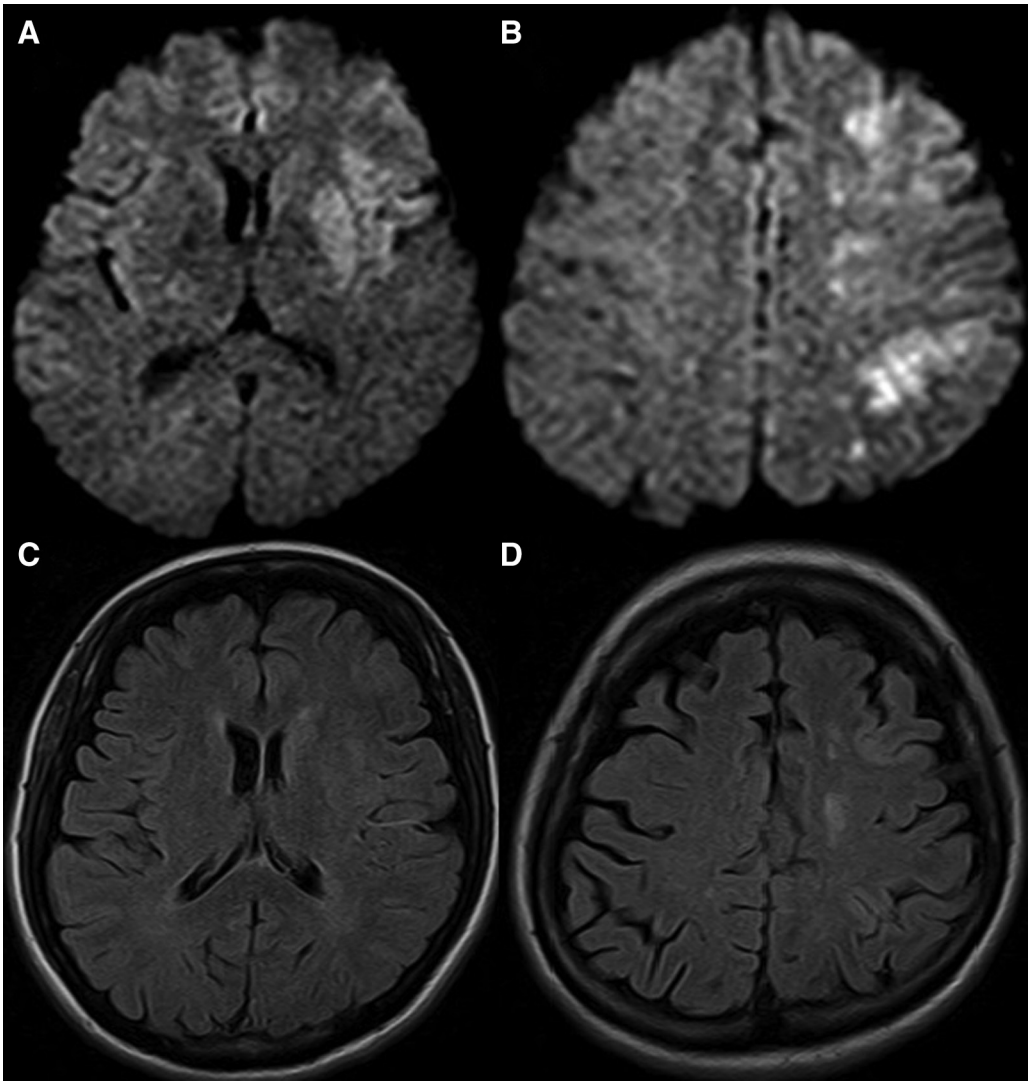

Fig. 1 DWI MRI showed multiple hyper-intensity lesions (**A** and **B**). MRI FLAIR did not show as extensive hyper-intensity lesions as DWIs (**C** and **D**). DWI/FLAIR mismatch was determined. DWI: diffusion-weighed imaging; MRI: magnetic resonance imaging

FlowGate[2] was placed again in the left ICA, and an Excelsior XT-27 (Stryker Neurovascular) and CHIKAI 14 (Asahi Intecc, Nagoya, Aichi, Japan) were navigated into a Penumbra ACE 60 (Penumbra, Alameda, CA, USA). An XT-27 was then guided to the MCA M2 segment. At this point, simultaneous imaging from XT-27 and Penumbra ACE 60 confirmed occlusion from the left ICA to the proximal MCA. An attempt to retrieve thrombi using the Penumbra ACE 60 and Trevo XP (4 mm × 30 mm; Stryker Neurovascular) resulted in recanalization with one pass (**Fig. 4A**). However, there was no thrombus in the retrieved stent. Internal carotid angiography performed 5 minutes later revealed stenosis at the proximal MCA and proximal ACA (**Fig. 4B**). Moreover, the left MCA was occluded again 10 minutes later and the stenosis of the left ICA was aggravated (**Fig. 4C**). As no thrombus was retrieved and stenosis rapidly aggravated on angiography after recanalization, LVO was judged to not be due to cardiogenic embolism and that recanalization was achieved by temporary vasodilation as a result of the deployment of Trevo XP. In consideration of the possibility of mechanical vasospasm due to the stent, intra-arterial injection of 40 mg of papaverine hydrochloride was performed from the end of the ICA and recanalization was achieved. However, the effect did not last long and reocclusion occurred after 10 minutes. A mechanism analogous to vasospasm was suspected because the intra-arterial administration of papaverine hydrochloride was effective. As the possibility of atherothrombotic infarction was unable to be excluded, PTA was performed twice at a pressure of 8 atm for 30 seconds using

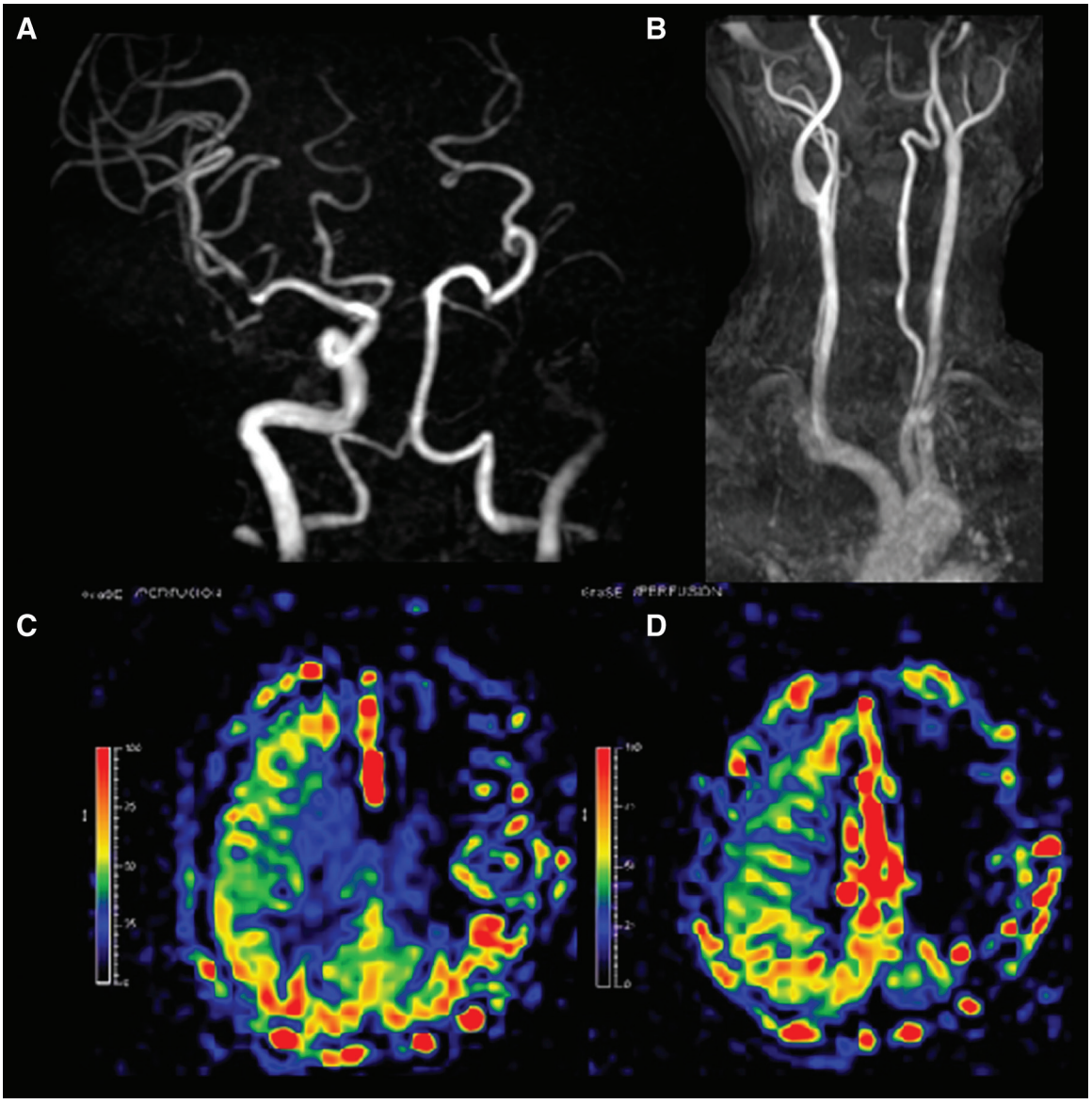

Fig. 2 MRA revealed occlusion of the left ICA (**A** and **B**). MRI ASL images suggested extensive hypoperfusion of the left cerebral hemisphere (**C** and **D**). ASL: arterial spin-labeling; ICA: internal carotid artery; MRA: magnetic resonance angiography; MRI: magnetic resonance imaging

a Gateway PTA balloon catheter (2 mm × 9 mm; Stryker Neurovascular) after administration of antiplatelet agents (clopidogrel 300 mg + aspirin 100 mg) (**Fig. 5A**). Recanalization of the MCA was maintained for 30 minutes and the procedure was finished (**Fig. 5B**).

Postoperative course

After endovascular treatment, FLAIR images demonstrated an extensive high-intensity area in the left MCA region (**Fig. 6A** and **6B**), but consciousness disturbance gradually improved. Two weeks later, the consciousness level of the patient was score 3 of JCS, with right hemiparesis (upper extremity: MMT3/5; lower extremity: MMT4/5) and moderate motor aphasia. Simple communication became possible. MRI 1 month after surgery revealed no new stenosis or occlusion of the left ICA (**Fig. 6C**). Oral administration of clopidogrel at 75 mg and Bayaspirin at 100 mg was started, but the medication was changed later to Bayaspirin at 100 mg alone.

The cause of cerebral infarction due to LVO was investigated in detail after the patient's neurological symptoms stabilized. No AF was noted on Holter ECG. When we interviewed her again about her medical history, she told us that she had been aware of sensory disturbance and weakness in both lower extremities since 2 months before admission. Therefore, multiple neuropathy symptoms were

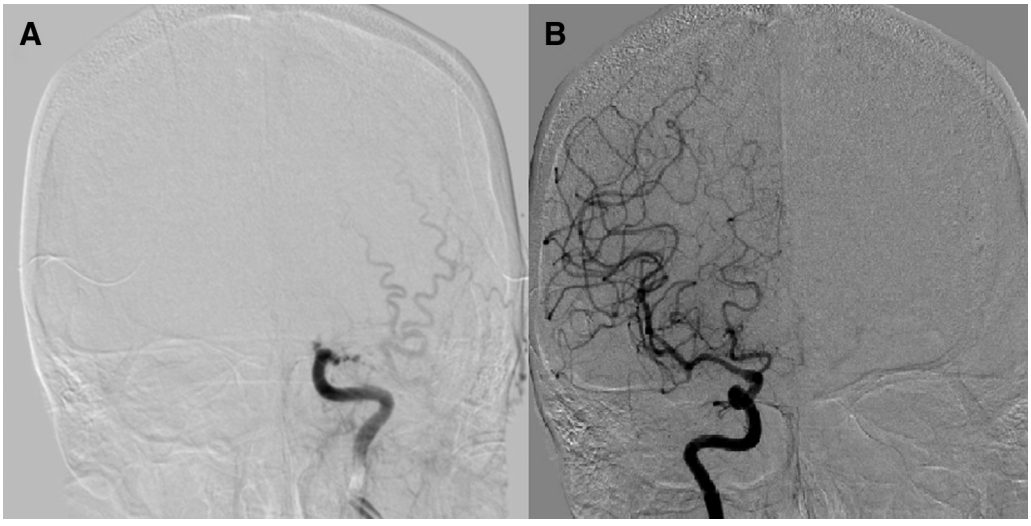

Fig. 3 Bilateral internal carotid angiography showed no right MCA stenosis, (**A**) but there was occlusion of the distal left ICA (**B**). ICA: internal carotid artery; MCA: middle carotid artery

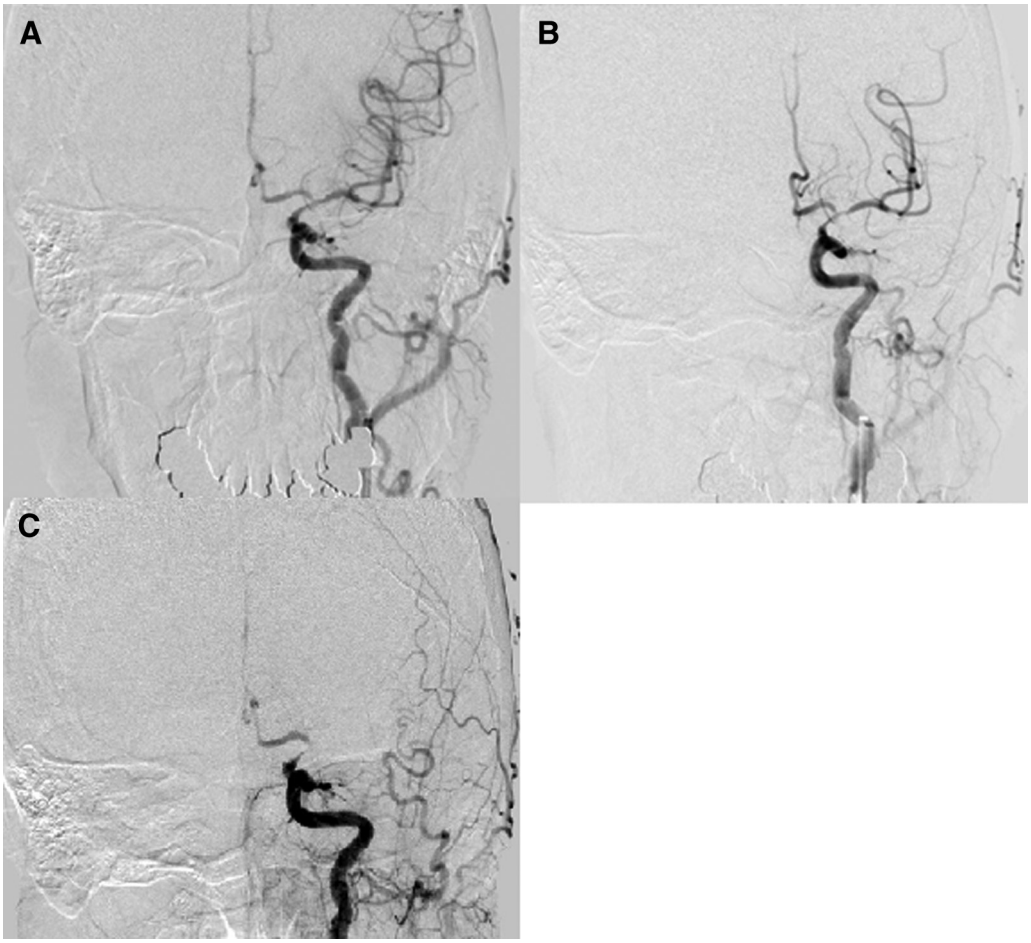

Fig. 4 Recanalization was achieved with one pass during thrombectomy, but stenosis was observed in the proximal portion of the left MCA/ACA (**A**). Five minutes after recanalization, left MCA/ACA stenosis was exacerbated (**B**). Fifteen minutes after recanalization, left MCA occlusion and left ICA stenosis were further exacerbated (**C**). ACA: anterior cerebral artery; ICA: internal carotid artery; MCA: middle carotid artery

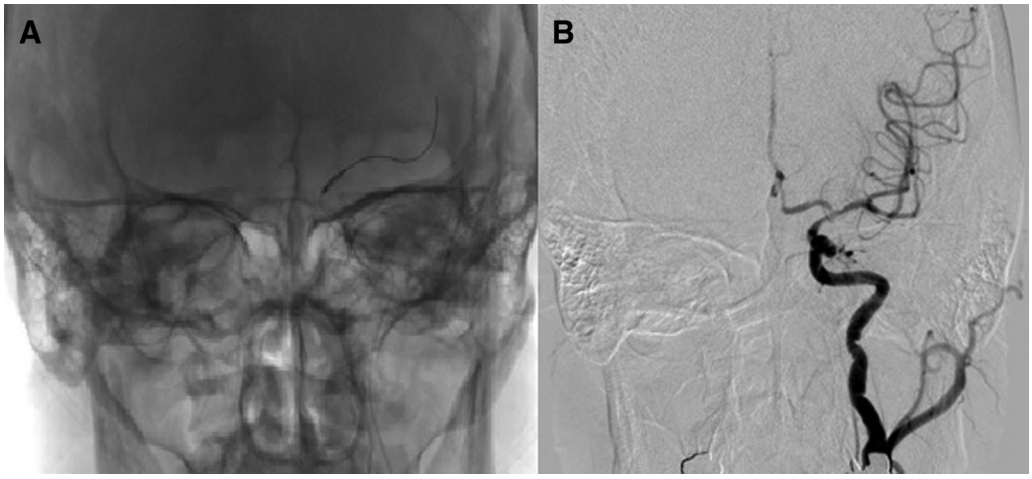

Fig. 5 Vasodilation was maintained using a Gateway PTA balloon catheter (2 mm × 9 mm) (**A** and **B**). PTA: percutaneous transluminal angioplasty

suspected and a nerve conduction test was performed, based on which a diagnosis of demyelinating polyneuropathy was made. Furthermore, pleural effusion, ascites, hepatosplenomegaly, cutaneous hemangioma in the back, and pelvic osteosclerotic lesion were confirmed by CT. The serum vascular endothelial growth factor (VEGF) level was abnormally high at 1900 pg/mL. Bone marrow biopsy demonstrated no monoclonal immunoglobulin. Based on the above clinical course and laboratory findings, the condition of the patient was considered "probable" according to the diagnostic criteria for POEMS syndrome (**Table 2**).

Chemotherapy for POEMS syndrome was considered during hospitalization, but we prioritized antiplatelet therapy and rehabilitation taking into account the potential risks of adverse reactions. Neurological symptoms improved subsequently, and the patient was discharged from the hospital 130 days after the onset. She was able to walk with a cane. The condition of POEMS syndrome was judged to be stable as the serum VEGF value was normal (256 pg/mL) at 6 months after disease onset. Her serum VEGF level will be measured on a regular basis, and at the time of disease progression, chemotherapy will be provided according to the condition of multiple myeloma.

Discussion

In the present case, vascular stenosis occurred repeatedly during thrombectomy for acute LVO and angioplasty was successful. Detailed history-taking and postoperative examination led to a diagnosis of main artery obstruction associated with POEMS syndrome. Our patient was relatively young (52 years old) and had no history of HT, HLD, DM, or heart disease, including AF. AF or other causes of embolism were not identified. Thus, many findings were inconsistent with typical LVO due to thromboembolism. There are several possible explanations for the LVO in our patient: (1) atherosclerotic lesions, (2) vasospasm following the use of a stent-type thrombectomy device, and (3) reversible cerebral vasoconstriction syndrome (RCVS). First, the possibility of atherosclerotic lesions was precluded based on the patient's history and background factors. Angiographic findings obtained when recanalization was achieved with one pass of Trevo XP also negated the possibility of atherosclerotic lesions. As for the second possibility of vasospasm, reocclusion after recanalization can be explained by stent-induced vasospasm, but not the onset of the disease. Lastly, RCVS was also an unlikely cause because the patient had no symptoms, such as headache, during the course and no vascular stenosis was observed at any other site. Thus, she was diagnosed with rare cerebral infarction due to LVO associated with POEMS syndrome.

POEMS syndrome is a rare systemic disease related to plasma cell proliferation and is associated with a range of symptoms, including peripheral neuropathy, organomegaly, endocrine disorder, monoclonal gammopathy, and cutaneous changes.[7] For diagnosis, polyneuropathy is a requirement, and cases are categorized by the level of certainty into "definite," "probable," and "possible" based on other major and minor criteria (**Table 2**).[8] The prevalence of this rare syndrome in Japan was estimated to be 0.3 per 100,000 persons in a national survey conducted in 2003.[9] POEMS syndrome was reported to be complicated by cerebral infarction in 13.4% of cases. In general, cerebral infarction associated with POEMS syndrome mainly

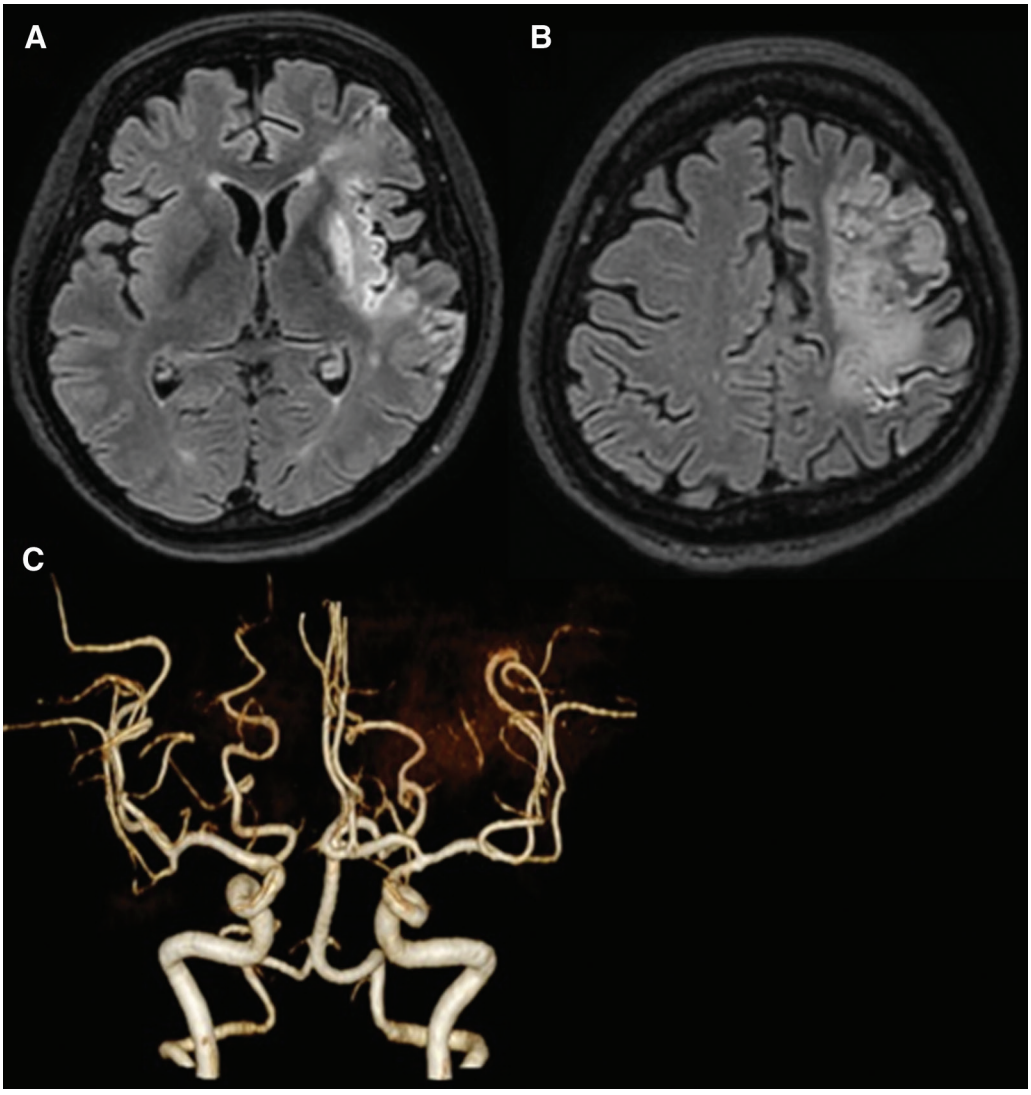

Fig. 6 Cerebral infarction was observed in a part of the left MCA region (**A** and **B**). MRA 1 month after PTA showed no restenosis of the left ICA(**C**). ICA: internal carotid artery; MCA: middle carotid artery; MRA: magnetic resonance angiography; PTA: percutaneous transluminal angioplasty

involves the terminal artery, and cervical or proximal intracranial vascular stenosis is common.[6] A possible mechanism related to POEMS syndrome is the involvement of pro-inflammatory cytokines. A recent hypothesis is that pro-inflammatory cytokines, such as interleukin (IL)-1β, IL-6, tumor necrosis factor (TNF)-α, and VEGF, induce cerebral infarction by inflammatory damage to the walls of the great vessels of the brain.[10] Although endothelial cell hyperplasia in the peripheral nerve vessels was previously reported in a patient with POEMS syndrome who had a high serum VEGF level,[11] there have been no reports on the histopathological investigation of stenosis or occlusion of the major arteries. POEMS syndrome may be related to arterial occlusion considering the presence of underlying plasma cell monoclonal proliferation and abnormally high serum levels of VEGF in patients with this syndrome. The definitive cause is however debatable. As described above, there are many uncertainties about the mechanism of cerebral infarction associated with POEMS syndrome.

In the present case, it is unclear whether thrombectomy using a stent retriever was the best choice. Recanalization was achieved with one pass, but there was no thrombus in the retrieved stent and reocclusion occurred soon afterwards. Intra-arterial administration of papaverine hydrochloride and PTA were effective for reocclusion.

Recanalization was achieved with a door-to-recanalization time of 125 minutes, but extensive infarction developed postoperatively. Regarding the present case, PTA may have been

Table 2 Diagnostic criteria and categories

Diagnostic criteria	
Major criteria:	
Polyneuropathy (required)	
High serum VEGF level (≥1000 pg/mL)	
Monoclonal immunoglobulin (serum or urine test-positive [as confirmed by immunofixation electrophoresis])	
Minor criteria:	
Osteosclerotic lesion, Castleman's disease, organomegaly, edema, pleural effusion, ascites, pericardial effusion, endocrine abnormalities (adrenal, thyroid, pituitary, gonadal, parathyroid, and pancreatic function), skin abnormalities (pigment deposition, stiff bristles, hemangiomas, cyanosis, and pallor of the nail bed), papilledema, and thrombocytosis	
*However, thyroid function abnormality or pancreatic function abnormality alone is not a minor criterion because they are highly prevalent.	
Diagnostic categories	
Definite	All three major criteria AND one or more of the minor criteria are met
Probable	Two of the three major criteria, namely peripheral neuropathy (polyneuropathy) and high serum VEGF level, AND one or more of the minor criteria are met
Possible	One of the three major criteria, namely peripheral neuropathy (polyneuropathy), AND two or more of the minor criteria are met

VEGF: vascular endothelial growth factor

more useful than MT for recanalization of LVO. Performing PTA upfront may have enabled recanalization in a shorter time. However, it is not practical to employ PTA for initial treatment because of the difficulty in diagnosing POEMS syndrome before surgery. In cases where reocclusion occurs soon after thrombectomy using a stent retriever, the potential presence of pre-existing conditions should be suspected, as in the present case, in addition to atherosclerotic lesions. A better treatment choice can be achieved by taking the medical history as much as possible before surgery and by keeping this condition in mind. It is of importance to consider the potential presence of a range of diseases and possible treatment options within a limited amount of time available during thrombectomy to improve the outcomes.

Conclusion

PTA for LVO was successful in a patient with POEMS syndrome.

Disclosure Statement

The authors declare no conflict of interest.

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