A Case of Mechanical Thrombectomy for Middle Cerebral Artery Occlusion with Trousseau Syndrome

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Objective and Case Presentation: The patient was an 86-year-old woman with histories of surgery for stomach, colon, and pancreatic cancers. In addition to left hemiparesis as a sequela of two past episodes of cerebral infarction, she newly developed right hemiplegia and acute cerebral infarction due to left middle cerebral artery (MCA) occlusion. Since the condition was not an indication for intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA), mechanical thrombectomy was immediately performed, and almost complete recanalization could be achieved about 5 hours after the onset. The retrieved thrombus was a white and elastic hard fibrin thrombus that contained no blood cells. Although temporary symptomatic relief was obtained, bilateral MCA occlusion occurred in succession, and the patient died on the 35th day of illness.

Conclusion: Accumulation of cases and pathological evaluation of retrieved thrombi are necessary for the elucidation of the optimal mechanical thrombectomy or antithrombotic therapy for acute cerebral infarction due to Trousseau syndrome.

Keywords ▶ Trousseau syndrome, thrombectomy, acute ischemic stroke, endovascular, histology

Introduction

Trousseau syndrome is a condition leading to stroke due to hypercoagulability associated with malignant neoplasm. Recently, evidence of mechanical thrombectomy for acute cerebral infarction due to major intracranial vessel occlusion has been established, but only three cases of Trousseau syndrome that underwent mechanical thrombectomy have been reported.1,2 In this report, we present a case that showed temporary improvement by mechanical thrombectomy but had multiple early recurrences and died.

Case Presentation

The patient was an 86-year-old woman with right hemiplegia and aphasia. Her history included stomach cancer (resected 19 years before), colon cancer (treated by endoscopic mucosal resection 3 years before), pancreatic cancer (resected 1 year before), liver metastasis (suspected to be from pancreatic cancer), brain tumor (observed), hypertension, and diabetes. She had left hemiparesis (left upper and lower extremities: Manual Muscle Test [MMT]4) as a sequela of the first episode of cerebral infarction, which occurred 3 months before, and needed a wheelchair for activities of daily life.

Three months before, she developed cerebral infarction in the right frontal lobe and was emergently transported to our hospital. No stenosis or occlusion of the major intracranial arteries was noted, and the administration of clopidogrel at 75 mg was started. She was transferred to the surgery department with left hemiparesis persisting and was scheduled to undergo surgery for liver metastasis but was found to have myocardial infarction, which was asymptomatic, on close preoperative examination 2 months before, and began to receive additional medication with aspirin at 100 mg. At this point, transthoracic echocardiography was performed, but
Ten days before, she newly developed dysarthria during inpatient chemotherapy for liver metastasis and showed *de novo* cerebral infarction in the left occipital lobe. With alleviation of symptoms, she was discharged to home, but on the next day (February, 2015), she suffered right hemiplegia and aphasia in the toilet at 8 am and was emergently transported to our hospital (onset-to-arrival time: 1 hour and 10 minutes).

On admission, she was 149 cm tall, weighed 31 kg, and showed a blood pressure of 167/62 mmHg, a heart rate of 60 bpm, regular, and a body temperature of 36.3°C. The level of consciousness was 100 on the Japan Coma Scale, and she showed left concomitant deviation and paralysis of the right upper (MMT1) and lower (MMT2) extremities. There was global aphasia, and the National Institute of Health Stroke Scale (NIHSS) score was 31.

Laboratory tests on admission showed a platelet count of $20.5 \times 10^4/\mu L$ and a prothrombin time-international normalized ratio (PT-INT) of 1.07, but fibrinogen degradation product (FDP) testing was not performed. The D dimer level was high at 19.8 µg/mL. Although the N-terminal pro b-type natriuretic peptide (NT-Pro BNP) was high at 4314 on the test 10 days before, no marked abnormality was observed on other blood chemistry tests, and the condition did not fulfill the diagnostic criteria for disseminated intravascular coagulation (DIC). Electrocardiogram (ECG) showed a heart rate of 79 bpm, sinus rhythm, ST elevation in leads II, III, and aVF, reflecting inferior wall infarction detected 2 months before, and negative T waves in leads V3–V6, but no change had been noted for 1 month prior to the present illness.

Head CT showed low-density areas at the sites of the past two episodes of cerebral infarction but no abnormality causing the new symptoms.

On diffusion-weighted imaging of head MRI, faint high-intensity areas were observed in the cortices of the temporal lobe, parietal lobe, and insula supplied by the left middle cerebral artery (MCA) (Alberta Stroke Program Early CT Score [ASPECTS]: 6). Head MRA demonstrated occlusion in a distal part of the horizontal part of the left MCA (arrival-to-imaging time: 1 hour and 20 minutes) (Fig. 1).

We judged that there was discrepancy between the ischemic area estimated from the occluded vessel and the infarcted area indicated by diffusion-weighted images. Since the patient had developed cerebral infarction 10 days before, the condition was not an indication for intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA), and although she needed assistance for activities of daily living (ADL) after the first episode of cerebral infarction, we immediately performed percutaneous thrombectomy in expectation of symptomatic alleviation.

![Fig. 1](A and B) Diffusion-weighted MRI and MRA 2 months before thrombectomy show ischemic stroke on right MCA area. (C and D) The same series 10 days before thrombectomy show ischemic stroke on left occipital lobe. (E, F, and G) The same series on admission show high-intensity lesion on left MCA area, and left distal MCA is occluded. MCA: middle cerebral artery.
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Partial recanalization of the posterior branch of the MCA was observed on angiography. Residual thrombus was observed in the blood vessel, and its retrieval was attempted using the forced suction technique by manual aspiration with a syringe after guiding a Penumbra 5MAX reperfusion catheter (Penumbra, Alameda, CA, USA) coaxially with a Penumbra 3MAX reperfusion catheter and a CHIKAI 14 by pressing the devices against the thrombus, but recanalization could not be achieved despite two aspirations. The Trevo provue 4.0/20 mm was deployed again by adjusting the center of the stent at the thrombus. Angiography was not performed immediately after deployment, but, on imaging after 5-minute waiting, the anterior branch of the MCA remained occluded. After thrombectomy, effective recanalization of thrombolysis in cerebral infarction (TICI) 2B was achieved (puncture-to-recanalization time: 1 hour and 29 minutes) (Fig. 2). A whitish, elastic hard thrombus, caught deep in the mesh of the stent, was retrieved. On histopathological examination, it consisted of...

Fig. 2 (A and B) Internal carotid angiogram shows left MCA occlusion. (A) Anteroposterior, (B) lateral view. (C, D, and E) After two passes with stent retriever, posterior trunk of left MCA is recanalized. Thrombus is left in the left MCA (arrow). (C) Anteroposterior view, (D) Lateral view, (E) Enlarged view of the C image. (F and G) Complete recanalization is obtained after three passes with stent retriever. (F) Anteroposterior, (G) lateral view. MCA: middle cerebral artery.
primarily of fibrin, and no blood or tumor cells were observed (Fig. 3).

After the procedure, aphasia was mitigated, and right hemiplegia improved to MMT3, but, because of left hemiplegia as a sequela of cerebral infarction that had occurred 3 months before, recovery was limited to NIHSS 20. Dual-antiplatelet therapy was continued, and transesophageal echocardiography was scheduled, but right hemiplegia was aggravated again on the 2nd day of illness. On head CT and MRI, a lesion of infarction was established in part of the area treated by thrombectomy (Fig. 4A and 4B). Since there were strong body movements, MRA could not be performed, but the symptoms suggested re-occlusion after recanalization. Some improvements were observed in paralysis after the first treatment, but as the patient already had quadriplegia, conservative treatment was performed without attempting thrombectomy again. Despite continuation of rehabilitation, the patient developed de novo cerebral infarction due to occlusion of the right MCA (Fig. 4C and 4D) on the 9th day and died on the 35th day of illness. Pathological autopsy was not performed as the family did not consent.

**Discussion**

Trousseau syndrome is a condition in which stroke is induced by hypercoagulability associated with malignant neoplasm, and non-bacterial thrombotic endocarditis (NBTE) has been reported as its common causative factor. The patient reported here repeatedly suffered cerebral infarction in a short period after the detection of liver metastasis of pancreatic cancer. Concerning the pathogenic mechanism in this patient, we have not performed Holter ECG, but no atrial fibrillation was noted by monitoring during treatment at the first episode of cerebral infarction or during the inpatient treatment at the surgery department, and transthoracic echocardiography performed 2 months before or 7 days before the onset showed no thrombus in the left ventricle. At the past two episodes of cerebral infarction, we suspected atherothrombotic infarction in consideration of her old age and histories of hypertension and diabetes and treated her accordingly. However, as no stenotic lesion was noted in the vessels supplying the infarcted area including the cervical carotid artery, the condition is considered to be classified according to the The trial of Org 10172 in Acute Stroke Treatment (TOAST) classification as stroke due to other causes including clotting abnormality. In this patient, we did not perform clinical autopsy. In addition, we did not perform transesophageal echocardiography during Valsalva maneuver, which is reportedly useful for the detection of patent foramen ovale, or lower extremity ultrasonography after thrombectomy due to exacerbation of the general condition. Therefore, deep venous thrombosis
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complicating hypercoagulability due to malignant neoplasm and associated paradoxical embolism could not be excluded. However, in consideration of the presence of advanced malignant neoplasm, recurrent cerebral infarction, the report by Reisner et al.7 that 19% of malignant neoplasms are complicated by NBTE, the primary cause of which is considered to be platelet-dominant and thrombus-dominant thrombi, and the properties of the retrieved thrombus consistent with NBTE, Trousseau syndrome with NBTE as the source of emboli was a probable diagnosis of our patient. Since thrombi derived from NBTE are small with a diameter of 3 mm or less, they cannot be detected by transthoracic echocardiography, and transesophageal echocardiography is considered necessary,4 but the detection rate is still reported to be only about 18%.6 In our patient, also, we could not demonstrate thrombi on transthoracic echocardiography at the time of myocardial infarction.

According to our review, there have been only two reports of three cases who underwent thrombectomy for occlusion of the major intracranial arteries due to Trousseau syndrome.1,2 Trousseau syndrome is considered to be caused frequently by small thrombi from NBTE, and they are likely to cause peripheral embolism without occluding the major arteries, but reports of similar cases are expected to increase in the future with the prevalence of thrombectomy devices and establishment of evidence of clot retrieval therapy. In our patient, partial recanalization could be achieved by performing a thrombectomy procedure using Trevo provue twice. Since the thrombus remaining after partial recanalization was found to be small, and since they were residual thrombi that could not be retrieved by the previous two procedures, we changed the device and attempted the forced suction technique5 using Penumbra 5MAX. Considering that thrombus retrieval might be possible by suctioning the thrombus into the catheter and extracting them together, we navigated the catheter to a position where it compressed the thrombus, but the thrombus could not be captured perhaps as the catheter was not positioned coaxially with the thrombus, and effective recanalization of TICI 2B could be achieved using Trevo provue again. Concerning the indications for thrombectomy in cancer patients, we consider that the treatment should be evaluated as a therapeutic option to maintain the quality of life (QOL) by improving the neurofunctional outcome.

In our patient, since the thrombus causing occlusion could not be removed completely, its overall properties are unclear. However, the thrombus that remained after partial recanalization and could be retrieved was a whitish fibrin-dominant thrombus with no red blood cell components. Fibrin-dominant thrombi with few red blood cell components have been reported to be hard,5,9 but soft parts of the thrombus may have been fragmented by the two procedures using Trevo provue, and only the fibrin-rich part of the thrombus may have remained. Although the residual thrombus could not be recovered with a suction catheter, it could be fortunately recovered as the stent struts bit deep into it. Matsumoto et al. pathologically examined the thrombi retrieved from two patients with major artery occlusion associated with Trousseau syndrome25 and reported that thrombi recovered from patients with cerebral infarction due to atherothombotic occlusion or non-valvular atrial fibrillation were rich in blood cell components and fragile, but that those recovered from two patients with Trousseau syndrome were both white thrombi, 90% or more of which consisted of fibrin. Concerning the properties of thrombi and thrombectomy devices, Yuki et al. reported that the necessary number of procedures was higher, and the recanalization rate was lower, in fibrin-dominant thrombi compared with red blood cell-dominant thrombi in animal experiments of thrombectomy using Merci retriever (Concentric Medical, Mountain View, CA, USA).10 However, using stent type thrombectomy devices, Ioku et al. reported that fibrin-dominant hard thrombi could be captured by the outer side of the stent struts and retrieved.12 In addition, Gunning et al. experimentally reported that friction resistance was higher as the thrombus was more fibrin-dominant with fewer red blood cell components.12 Therefore, if thrombi in Trousseau syndrome are hard fibrin-dominant thrombi with few red blood cell components as in the four patients including ours, the Trevo series with a vertical strut structure may be appropriate as thrombectomy devices for patients with this disorder. If the friction resistance is high, there is concern over catheter occlusion during treatment using Penumbra by the suction method with a separator, and a method to capture the thrombus and remove it with the catheter as reported in the forced suction technique5 and a direct aspiration first pass technique (ADAPT) technique13 is considered desirable. Also, in a case series of non-cancer patients, Eiken et al. pathologically examined verrucae in 30 patients who underwent cardiac valve surgery due to NBTE and reported that they were platelet- and fibrin-dominant verrucae in all patients.25 In consideration also of the above report by Reisner et al.7 since a cause of Trousseau syndrome is NBTE, it is necessary to evaluate NBTE due to malignant neoplasm as a possible differential
diagnosis if such a thrombus has been retrieved from a patient with embolic cerebral infarction with an unidentified source of the embolus.

Although treatment of the causative disease is the first priority for the prevention of recurrence of Trousseau syndrome, unfractionated or lower-molecular-weight heparin is reportedly useful for antithrombotic therapy. In Trousseau syndrome, the hypercoagulable state is caused by some pathways, and heparin is considered useful, but warfarin to be ineffective, for widely suppressing such pathways. There have been reports that deep venous thrombosis occurred after change of heparin to oral warfarin during treatment for this disease and that the recurrence of cerebral infarction could not be prevented with dabigatran, a direct thrombin inhibitor. In our patient, also, the recurrence of cerebral infarction could not be prevented by dual-antiplatelet therapy, resulting in major artery occlusion. We suspected Trousseau syndrome and planned to perform transesophageal echocardiography to detect NBTE after treatment and, due to anxiety over hemorrhagic complications in the established infarcted region, to begin administering heparin after demonstration of NBTE by transesophageal echocardiography, but early recurrence was observed after 2 days. As for the cause of the re-occlusion of the left MCA after 2 days, the possibility of endothelial damage due to multiple procedures primarily using stent type devices cannot be excluded due to the lack of pathological evidence, but we considered the condition to be re-embolization due to NBTE because an animal experiment denied the occurrence of endothelial damage sufficient to cause luminal stenosis and because the contralateral MCA was also occluded on the 9th day. Accumulation of cases and pathological examination of retrieved thrombi are awaited for the establishment of an appropriate antithrombotic therapy.

## Conclusion

A case of Trousseau syndrome in which mechanical thrombectomy was performed for MCA occlusion was presented. Accumulation of cases and pathological examination of retrieved thrombi are necessary to clarify the optimal thrombectomy and antithrombotic procedures for acute cerebral infarction due to this syndrome.

## Disclosure Statement

Neither the first author nor any of the coauthors have any conflicts of interest.

## References

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