Online June 26, 2021
Journal of Neuroendovascular Therapy 2022; 16: 116–122 DOI: 10.5797/jnet.cr.2021-0027

Case Report

Multiple Thrombectomies for Cerebral and Coronary Artery Occlusion in Trousseau Syndrome

Shota Sakai,[1] Yuichiro Tsurusaki,[1] Takao Morita,[1] Kenji Miki,[2] Daisuke Inoue,[2] Sei Haga,[2] and Shoji Arihiro[1]

Objective: Trousseau syndrome (TS) is a condition of systemic thrombosis generally associated with an underlying malignancy. An ischemic stroke is a representative thrombotic event. Thrombectomy is a useful procedure for the treatment of cerebral large vessel occlusion, and anticoagulation therapy is the main preventive treatment for TS. This case report describes a woman with terminal pancreatic tumor presenting with repeated occlusions of cerebral and coronary arteries necessitating multiple thrombectomies.

Case Presentation: A 67-year-old woman was admitted to our hospital with severe right hemiplegia and global aphasia. MRI revealed left M1 occlusion; therefore, a thrombectomy was performed. Her symptoms recovered completely. Body contrast CT revealed pancreatic cancer with multiple metastases, and she was diagnosed with TS. On day 4 after thrombectomy, the same neurological symptoms occurred and re-occlusion of the left M1 was confirmed. Endothelial injury was suspected, and thrombectomy was repeated. Despite continuing anticoagulation therapy, the coronary artery was occluded and she underwent percutaneous coronary intervention on day 13. To treat the primary pancreatic lesion, she was transferred to the Surgery unit on day 20.

Conclusion: Hypercoagulability associated with TS and endothelial damage due to rough procedure resulted in repeated vessel occlusions in this case. Careful thrombectomy and anticoagulation therapy with strict monitoring are needed in TS patients.

Keywords Trousseau syndrome, endothelial damage, re-occlusion, coronary artery

Introduction

Trousseau syndrome (TS) is a condition characterized by systemic thrombosis related to hypercoagulability due to an underlying terminal malignancy.[1)] Ischemic stroke is one of the main thrombotic events, and small size lesions are usually detected in this syndrome.[2)] Several reports have also described occasional large vessel occlusion (LVO) requiring mechanical thrombectomy (MT).[3,4)] Although thrombotic events are sometimes recurrent, anticoagulants represent the main prophylaxis for TS.[1)] Herein, we report a case that required repeated thrombectomy not only due to re-occlusion of the same cerebral vessel but also for occlusion of the coronary artery in a TS patient despite receiving anticoagulation therapy.

Case Presentation

A 67-year-old woman was transferred to our hospital because of sudden onset of consciousness disturbance. She had no history except for herpes zoster. The blood pressure, pulse rate, and temperature were 186/103 mmHg, 74 bpm, and 37°C, respectively. The neurological examination revealed global aphasia, severe right hemiparesis, and left conjugate deviation. The National Institutes of Health Stroke Scale (NIHSS) score was 25. Blood tests showed elevation of alkaline phosphatase (1565 U/L), γ-glutamyl

[1]*Department of Cerebrovascular Medicine, Kyushu Rosai Hospital, Kitakyushu, Fukuoka, Japan*
[2]*Department of Neurosurgery, Kyushu Rosai Hospital, Kitakyushu, Fukuoka, Japan*

Received: March 1, 2021; Accepted: May 18, 2021
Corresponding author: Shota Sakai. Department of Cerebrovascular Medicine, Kyushu Rosai Hospital, 1-1, Sonekitamachi, Kokuraminami-ku, Kitakyushu, Fukuoka 800-0296, Japan
Email: shoooo0725@gmail.com

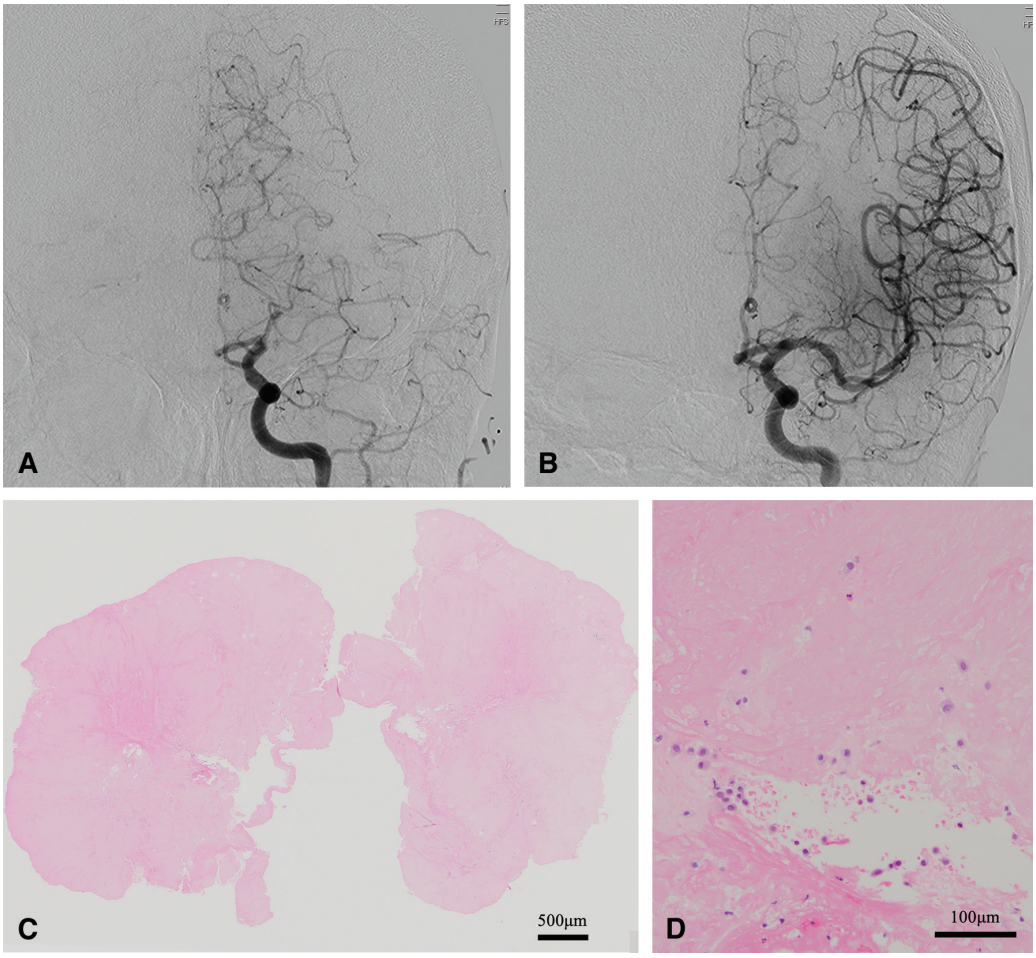

Fig. 1 Initial conventional angiography revealed the occlusion of left M1 (**A**). After the thrombectomy, almost complete recanalization of left MCA was confirmed (**B**). Histopathology with hematoxylin–eosin staining showed that retrieved thrombus mainly consists of fibrin (**C** and **D**). MCA: middle cerebral artery

transpeptidase (431 U/L), C-reactive protein (5.58 mg/dL), D-dimer (19.7 μg/mL), and fibrin degradation products (61.5 μg/mL). The electrocardiogram (ECG) showed that heart rate was 75 bpm, with sinus rhythm and left axis deviation. Head CT showed no hemorrhage or early signs of ischemia. From the symptoms, cerebral LVO was strongly suspected; therefore, she received infusion with tissue-plasminogen activator and underwent a cerebral angiogram immediately. Under local anesthesia, a 9F long sheath was inserted in the left femoral artery, and 9F Optimo (Tokai Medical Products, Aichi, Japan) was placed in the left internal carotid artery (ICA) with systematic heparinization. An angiogram revealed occlusion of the M1 portion of the left middle cerebral artery (MCA) (**Fig. 1A**). A Marksman microcatheter (Medtronic, Minneapolis, MN, USA) was navigated to the distal site of the occluded vessel with a CHIKAI 14 microguidewire (Asahi Intecc, Aichi, Japan), and a Solitaire Platinum 4 × 40 mm (Medtronic) stent retriever (SR) was deployed at a position with its center at the site of occlusion. After an AXS Catalyst 7 catheter (Stryker, Kalamazoo, MI, USA) was navigated coaxially to the top of the ICA and continuous aspiration was started, the Solitaire and the Catalyst 7 were removed, but recanalization could not be achieved. The same devices were used again and the Solitaire was deployed from a more distal site. The Solitaire and the Catalyst 7 were removed using the same technique, and a whitish and elastic embolus adhering to the strut of the Solitaire was retrieved. An angiography showed partial recanalization of the left MCA (thrombolysis in cerebral infarction [TICI] 2C[5]) (**Fig. 1B**). After the procedure, the neurological deficits recovered completely and she was put on continuous infusion of unfractionated heparin at 10000 units/day. MRI performed the next day showed left basal ganglia and corona radiata infarction and confirmed left MCA recanalization (**Fig. 2A**–**2C**). Contrast-enhanced CT of the body revealed

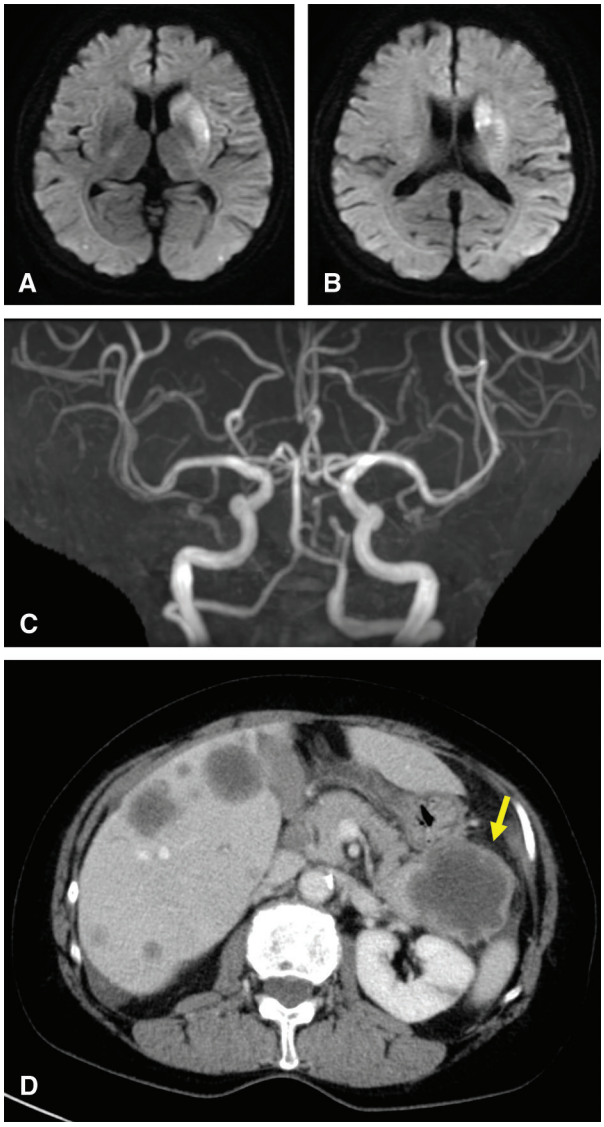

Fig. 2 Diffusion-weighted image revealed high-intensity lesion on the left basal ganglia and corona radiata (**A** and **B**). MRA showed no abnormal findings (**C**). Contrast-enhanced CT revealed pancreatic cancer (arrow) with multiple metastases to liver, lung, and peritoneal dissemination (**D**).

pancreatic cancer with multiple metastases to the liver and lung, with peritoneal dissemination (**Fig. 2D**). A pathology examination of the retrieved thrombus indicated mainly the presence of fibrin, with no tumor cells (**Fig. 1C** and **1D**). Because no other embolic sources were detected, the patient was diagnosed with TS. Ultrasonography showed a deep venous thrombus on both lower extremities; thus, heparin was switched to edoxaban 30 mg/day on day 4. On the same day, she complained of a weakness of the right upper extremity, and the NIHSS score was 1. Head MRI revealed a new spot lesion on left frontal lobe, and MRA revealed poor visualization of the left M1 portion (**Fig. 3A** and **3B**). The site where the thrombectomy was performed was poorly visualized; therefore, an endothelial injury was suspected. Aspirin 200 mg and infusion of an ozagrel were added immediately; nonetheless after 1 hour, global aphasia, severe right hemiparesis, and left conjugate deviation appeared again. An angiogram revealed re-occlusion of the left M1 portion (**Fig. 3C**). A Marksman was navigated to the periphery of the occluded vessel with a CHIKAI 14, and an AXS Catalyst 7 was navigated coaxially to the proximal side of thrombus. Continuous aspiration was started, and the Catalyst 7 was removed. There was no thrombus detected in the devices, but subsequent angiography again confirmed partial recanalization of the left MCA (TICI 2C). Clopidogrel 300 mg was administered through the nasal tube, and angiography 25 min after the recanalization showed no evidence of re-occlusion (**Fig. 3D**). On the next day, bloody stool was observed and the all antithrombotic drugs were stopped temporarily. Lower gastrointestinal endoscopy showed no active bleeding, and thus continuous infusion with unfractionated heparin was resumed with 10000 units/day. Because the patient desired to be discharged, unfractionated heparin was switched from continuous infusion to subcutaneous injection with 15000 units/day. Although neurological deficits recovered completely, on day 13, she complained of chest pain. ECG showed ST-segment elevation in leads II, III, and V3–5. Myocardial infarction was suspected and she underwent percutaneous coronary intervention. A coronary angiogram revealed occlusion of seven segments of the left anterior descending branch (**Fig. 4A**). Aspiration was performed and recanalization was achieved (**Fig. 4B**). The thrombus included mainly fibrin with no tumor cells in the pathological findings, similar to the first thrombus retrieved from the cerebral vessel (**Fig. 4C** and **4D**). Continuous infusion of unfractionated heparin was started again with 20000 units/day. She was transferred to the Surgery unit on day 20 with modified Rankin Scale 1; she succumbed to the primary lesion on day 71.

Discussion

In 1865, Armand Trousseau reported a superficial thrombophlebitis caused by a hypercoagulation state associated with malignant tumors for the first time.[6] Today, cancer-related thrombosis is known as TS, and the pathology is understood to be caused by thrombotic events due to disseminated intravascular coagulation or nonbacterial thrombotic endocarditis (NBTE) in terminal cancer patients.[7]

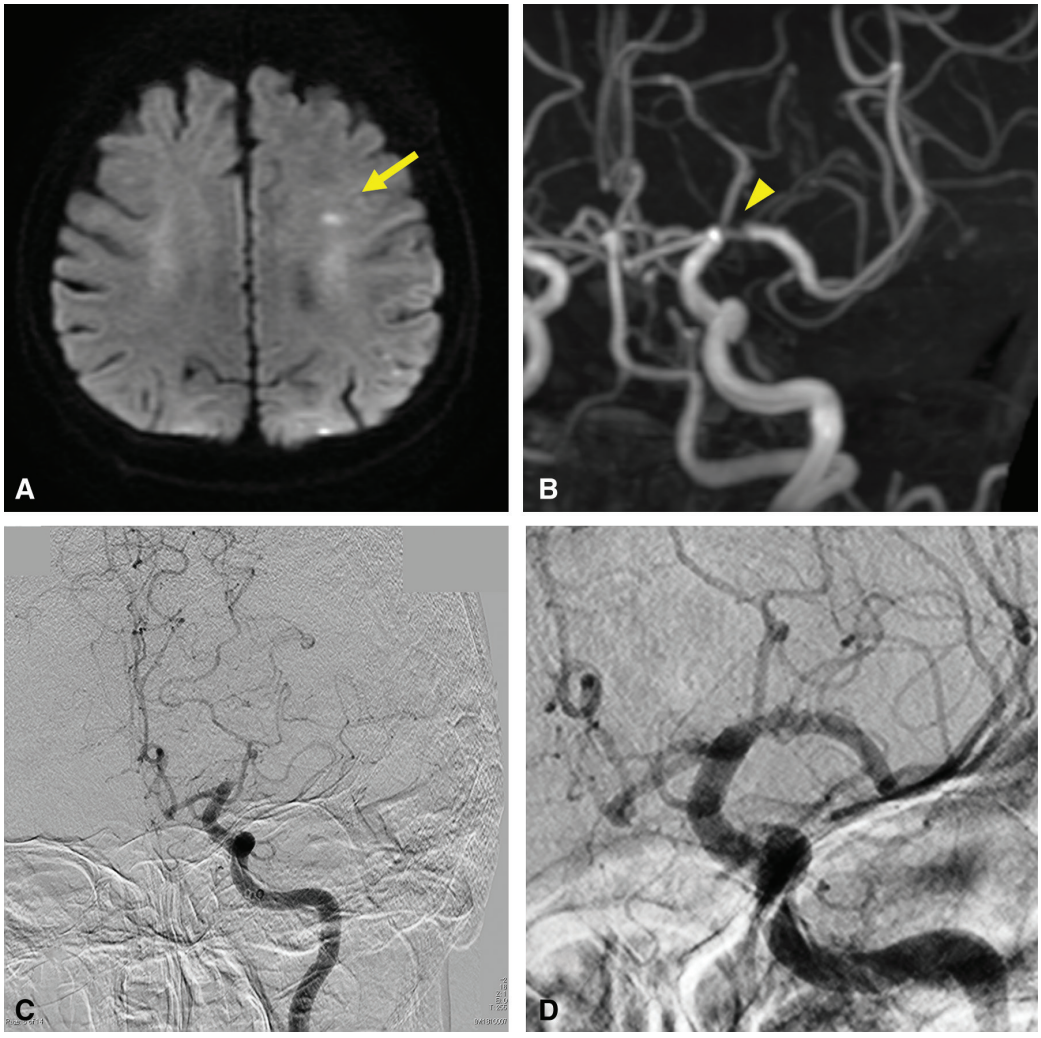

Fig. 3 MRI revealed a new spot lesion (arrow) on the left frontal lobe (**A**) and MRA showed abnormal visualization (arrowhead) of the left M1 (**B**). Angiography revealed re-occlusion of the left M1 (**C**), and thrombectomy was performed again and successfully achieved recanalization. After 25 min of thrombectomy, there was no evidence of re-occlusion (**D**).

TS usually induces small multiple cerebral ischemic lesions[2] but occasionally may develop LVO. Several clinical trials have proven the efficacy of MT for LVO,[8–12] and empirically, re-occlusion events are rarely experienced. Indeed, the prevalence of re-occlusion after the MT has been reported to be 2%–9% for any type of ischemic stroke.[13,14] In these studies, risk factors of re-occlusion included the number of device passes, missed residual thrombus or stenosis on the past angiography after thrombectomy, intracranial ICA or M2 occlusion, stroke of undetermined cause, and statin pretreatment.[13,14]

According to our research, there are 14 reported incidences of TS treated by MT with available literature[2–4,13,15–22] (**Table 1**). Of half of the cases that experienced re-occlusion of the cerebral large vessels, five cases involved the same vessels.

With regard to the mechanisms involved in re-occlusion, Shinohara et al. suspected the association of NBTE, or endothelial damage caused by the SR,[2] and Wassef et al. described arterial dissection as the cause.[22] Cicilioni et al. proposed the presence of circulating extracellular vesicles, which is associated with the activation of neutrophil extracellular traps and thrombus formation in the presence of an underlying malignancy.[19] Only two of these five cases described required retreatment. One case underwent contact aspiration (CA) again, while the other was performed stenting.

With respect to serial changes on MRA imaging in this case, we speculated that the re-occlusion could be attributed to endothelial damage in first procedure rather than from an embolism caused by hypercoagulability. Although there was a time lag of 3 days from the first treatment to the

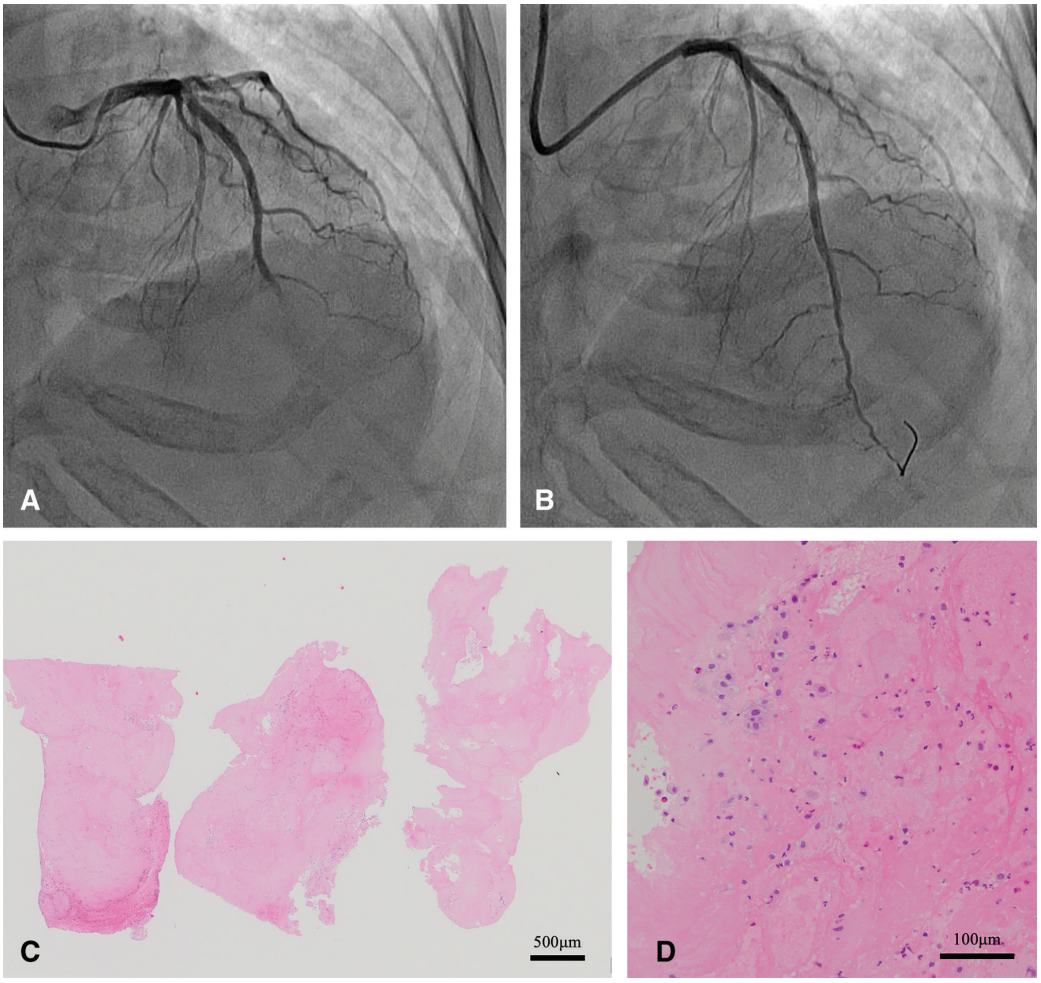

Fig. 4 Coronary angiography showing occlusion of the left anterior descending branch (**A**). After thrombectomy, a complete recanalization was observed (**B**). Thrombus included mainly fibrin in pathological findings (**C** and **D**).

re-occlusion in our case, the stenosis or occlusion due to endothelial damage may not always occur soon after the first maneuver, but may occur after several months.[23] The endothelial damage may have been a result of using the SR or due to thrombus stiffness, or both. Thrombi, mainly composed of fibrin, are solid and sticky, and the frictional resistance may cause vessel injury, such as endothelial damage or dissection.[3] When endothelial damage is suspected, as in our case, simple CA is one of the choice for retreatment strategy since the aspiration device scarcely touches the injured vessel wall using this technique. Jeon et al. have evaluated the efficacy and safety of MT by comparing the SR and CA technique for LVO in patients with active cancer.[24] They have reported that the characteristics of fibrin and platelet-rich thrombi make MT difficult to perform successfully, and compared with SR, CA reduces friction during the maneuver by suctioning the thrombi with a large bore-catheter. On the other hand, the complications such as hemorrhage and arterial dissection were not significantly different between the two groups.

Lee et al. have described that cancer-related stroke induces an unfavorable prognosis, especially in patients with higher serum D-dimer levels and baseline NIHSS score.[25] The primary cause of death within a short-term period in such patients is usually stroke; thus, actively performing MT for LVO in a selected group of patients with cancer has been recommended. In our patient, although the D-dimer level and baseline NIHSS score were high, death could have been avoided within the short-term period following the thrombectomies.

The medical treatment of TS recommends anticoagulation, especially subcutaneous injection of low-molecular weight heparin.[1] However, conservative strategies are still unclear and controversial. Sakuta et al. reported cerebral LVO with acute myocardial infarction (AMI) in TS.[15] After successful endovascular therapy for both arteries,

Table 1 Summary of existing case reports of Trousseau syndrome treated by thrombectomy

Author (year)	Age (years)	Sex	Primary cancer	Number of occlusions	Location	Procedure	Prognosis
Matsumoto et al. (2016)[17]	67	M	Stomach	1	BA	SR	N.A.
	84	F	Pancreas	1	Lt.MCA	SR	N.A.
Balci et al. (2019)[20]	57	M	Lung	1	Lt.M1	Aspiration	mRS 1 after 2 months
	60	M	Lung	1	Rt.M1	Aspiration	mRS 1 after 1 month
Marto et al. (2019)[13]	55	F	Ovary	1	Lt.M1 + coronary artery	SR + angioplasty (PCI)	mRS 1 after 3 months
Kuroda et al. (2019)[3]	75	F	Ovary	1	Lt.M1	SR + aspiration	Died on day 98
Murahashi et al. (2020)[18]	59	F	Liver	1	Rt.M1	SR + aspiration	Transferred to rehabilitation unit
Inoue et al. (2016)[16]	66	M	Lung	2	1. Rt.M1 2. Lt.M1	1.aspiration 2.aspiration	Died on day 87
Nishimuta et al. (2017)[4]	65	F	Stomach	2	1. BA, Rt.A1 2. Rt.M2	1. SR 2. SR	Died on day 31
Sakuta et al. (2019)[15]	55	F	N.A.	2	1. M1-2 2. M2	N.A.	mRS 3 after 3 months
Laible et al. (2015)[21]	57	M	Stomach	3	1. Lt.M1 2. Lt.M2 3. Lt.M2	N.A.	Died on day 10
Shinohara et al. (2017)[2]	86	F	Pancreas	3	1. Lt.M1 2. Lt.M1 3. Rt.M1	1. SR, aspiration 2. No treatment 3. No treatment	Died on day 35
Wassef et al. (2020)[22]	41	M	Pancreas	3	1. Lt.M1 2. Lt.ICA 3. Lt.ICA	1. Aspiration + t-PA + SR 2. Aspiration + t-PA 3. Stenting	Died 3.5 months after
Cicilioni et al. (2020)[19]	71	F	Lung	3	1. Lt.M1 2. Lt.M1 3. Rt.M2	1. Aspiration 2. Aspiration 3. SR + aspiration	Improved clinically and started chemo-therapy
Current case	67	F	Pancreas	3	1. Lt.M1 2. Lt.M1 3. Coronary artery	1. SR + aspiration 2. Aspiration 3. Aspiration (PCI)	Died on day 71

BA: basilar artery; F: female; ICA: internal carotid artery; Lt: left; M: male; MCA: middle cerebral artery; mRS: modified Rankin Scale; N.A.: not available; PCI: percutaneous coronary intervention; Rt: right; SR: stent retriever; t-PA: tissue-type plasminogen activator

subcutaneous heparin injection was started and no recurrence of infarction was observed. In our case, the thrombotic event occurred in the coronary artery despite treatment with subcutaneous unfractionated heparin injection. After changing the method of heparin infusion, the patient's course was uneventful. Despite continuous infusion being an ideal method to maintain stable drug concentrations,[4] it is unsuitable for long-term administration. Therefore, when we changed to subcutaneous injection, it required careful and strict management of heparinization by monitoring the activated partial thromboplastin time and D-dimer[19] to prevent thrombosis. Clinicians should recognize the risk of ischemic events and determine to what degree anticoagulation therapy is needed in TS patients. Nonetheless, the difficulty of medical therapy may depend on the progression or state of the primary lesion.[18,19]

Conclusion

Endothelial damage induced re-occlusion of the cerebral arteries and hypercoagulation caused occlusion of the coronary artery in a patient with TS. Careful thrombectomy and anticoagulation therapy are necessary for optimal management of TS.

Acknowledgment

We would like to thank Editage (www.editage.jp) for English language editing.

Disclosure Statement

The authors declare they have no conflicts of interest.

References

1) Navi BB, Iadecola C. Ischemic stroke in cancer patients: a review of an underappreciated pathology. *Ann Neurol* 2018; 83: 873–883.
2) Shinohara T, Tsumura M, Hasegawa A, et al. A case of mechanical thrombectomy for middle cerebral artery occlusion with Trousseau syndrome. *JNET J Neuroendovasc Ther* 2017; 11: 485–491.
3) Kuroda N, Hiramatsu H, Mori M, et al. Mechanical thrombectomy for trousseau syndrome in a terminally ill cancer patient. *J Pain Symptom Manage* 2019; 57: 688–694.
4) Nishimuta Y, Nagayama T, Hiwatari T, et al. A patient with cerebral embolism related to Trousseau's syndrome. *JNET J Neuroendovasc Ther* 2017; 11: 575–580.
5) Almekhlafi MA, Mishra S, Desai JA, et al. Not all "successful" angiographic reperfusion patients are an equal validation of a modified TICI scoring system. *Interv Neuroradiol* 2014; 20: 21–27.
6) Trousseau A. A phlegmasia alba dolens. *Lectures Clin Med* 1865; 5: 281–332.
7) Kuramoto K, Matsushita S, Yamanouchi H. Nonbacterial thrombotic endocarditis as a cause of cerebral and myocardial infarction. *Jpn Circ J* 1984; 48: 1000–1006.
8) Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med* 2015; 372: 11–20.
9) Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med* 2015; 372: 1019–1030.
10) Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med* 2015; 372: 1009–1018.
11) Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med* 2015; 372: 2285–2295.
12) Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med* 2015; 372: 2296–2306.
13) Marto JP, Strambo D, Hajdu SD, et al. Twenty-four-hour reocclusion after successful mechanical thrombectomy: associated factors and long-term prognosis. *Stroke* 2019; 50: 2960–2963.
14) Mosimann PJ, Kaesmacher J, Gautschi D, et al. Predictors of unexpected early reocclusion after successful mechanical thrombectomy in acute ischemic stroke patients. *Stroke* 2018; 49: 2643–2651.
15) Sakuta K, Mukai T, Fujii A, et al. Endovascular therapy for concurrent cardio-cerebral infarction in a patient with trousseau syndrome. *Front Neurol* 2019; 10: 965.
16) Inoue S, Fujita A, Mizowaki T, et al. Successful treatment of repeated bilateral middle cerebral artery occlusion by performing mechanical thrombectomy in a patient with trousseau syndrome. *No Shinkei Geka* 2016; 44: 501–506. (in Japanese)
17) Matsumoto N, Fukuda H, Handa A, et al. Histological examination of trousseau syndrome-related thrombus retrieved through acute endovascular thrombectomy: report of 2 cases. *J Stroke Cerebrovasc Dis* 2016; 25: e227–e230.
18) Murahashi S, Takeuchi Y, Hayashida S, et al. Trousseau syndrome with intrahepatic cholangiocarcinoma that could be removed radically after endovascular treatment: report of a case. *Brain Behav* 2020; 10: e01660.
19) Cicilioni K, Cristiano B, Jacobson JP, et al. Multiple thrombectomies in the same patient within one month: case report of a patient with Trousseau syndrome and acute ischemic stroke. *Brain Sci* 2020; 10: 590.
20) Balci S, Arsava EM, Topcuoglu MA, et al. Floating aortic thrombus: a rare cause of acute ischemic stroke necessitating modification of access route for thrombectomy. *J Stroke Cerebrovasc Dis* 2019; 28: 104291.
21) Laible M, Möhlenbruch M, Hacke W, et al. Repeated intraarterial thrombectomy within 72 hours in a patient with a clear contraindication for intravenous thrombolysis. *Case Rep Vasc Med* 2015; 2015: 872817.
22) Wassef C, Grenga A, Goldman B, et al. Triple thrombectomy for Trousseau syndrome: case report and review of the literature of stroke intervention in cancer-associated thrombus. *JNET J Neuroendovasc Ther* 2020; 14: 301–306.
23) Kim S, Ohtaki M, Tsuda H, et al. A case of delayed symptomatic middle cerebral artery stenosis following mechanical thrombectomy. *JNET J Neuroendovasc Ther* 2016; 10: 138–143.
24) Jeon Y, Baik SH, Jung C, et al. Mechanical thrombectomy in patients with acute cancer-related stroke: is the stent retriever alone effective? *J Neurointerv Surg* 2021; 13: 318–323.
25) Lee EJ, Bae J, Jeong HB, et al. Effectiveness of mechanical thrombectomy in cancer-related stroke and associated factors with unfavorable outcome. *BMC Neurol* 2021; 21: 57.