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Case Report

A Case of Carotid Artery Stenting after Aspiration of Thrombus and Unstable Plaque

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Objective: There is no established method for carotid artery stenting (CAS) for internal carotid artery stenosis with vulnerable plaque and thrombosis. We report a case in which CAS was performed by aspiration using the Penumbra system for thrombosis that increased in the subacute phase in symptomatic cervical internal carotid artery stenosis.

Case Presentations: A 59-year-old man with a history of lacunar infarction visited the emergency department with weakness in the right upper limb. He was admitted for cerebral infarction in the left corona radiata and basal ganglia. During the course, additional multiple cerebral infarctions developed in the left cerebral hemisphere. The patient was diagnosed with left internal carotid artery stenosis and underwent CAS. As mural thrombus increased compared with preoperative imaging, CAS was performed after thrombus aspiration using the Penumbra system. A large amount of plaque was observed in the aspirated blood.

Conclusion: Thrombus aspiration using the Penumbra system was effective as distal embolic protection during CAS for internal carotid artery stenosis with increased and shape-changing thrombus. The aspirated blood exhibited pathological findings of plaque tissue and thrombus.

Keywords ▶ carotid artery stenting, unstable plaque, aspiration of thrombus

Introduction

There is no established method for carotid artery stenting (CAS) for cervical internal carotid artery stenosis with vulnerable plaque accompanied by thrombosis. In the present patient, cervical internal carotid artery stenosis with vulnerable plaque demonstrating enlargement and morphological change of thrombus in the symptomatic subacute phase was successfully treated by aspiration using the Penumbra system followed by CAS.

Case Presentation

The patient was a 59-year-old male with numbness and muscle weakness of the right arm. His clinical history included transient ischemic attack at the age of 55 years, lacunar infarction of the left thalamus at the age of 57 years, hypertension, diabetes mellitus, and dyslipidemia.

He was orally administered cilostazol at 200 mg/day, azilsartan at 20 mg/day, amlodipine at 5 mg/day, rosuvastatin at 2.5 mg/day, esomeprazole magnesium hydrate at 20 mg/day, nifedipine at 10 mg/day, and bisoprolol fumarate at 5 mg/day.

As numbness of the right arm, which had persisted after left lacunar infarction 2 years prior, was exacerbated, and as muscle weakness appeared and gradually progressed, he consulted the emergency department, being capable of unassisted ambulation. On the visit, the JCS was 0, GCS was E4V5M6, blood pressure was 245/139 mmHg, heart rate was 102 beats/min, muscle weakness of the right arm with a manual muscle testing (MMT) score of 3 was

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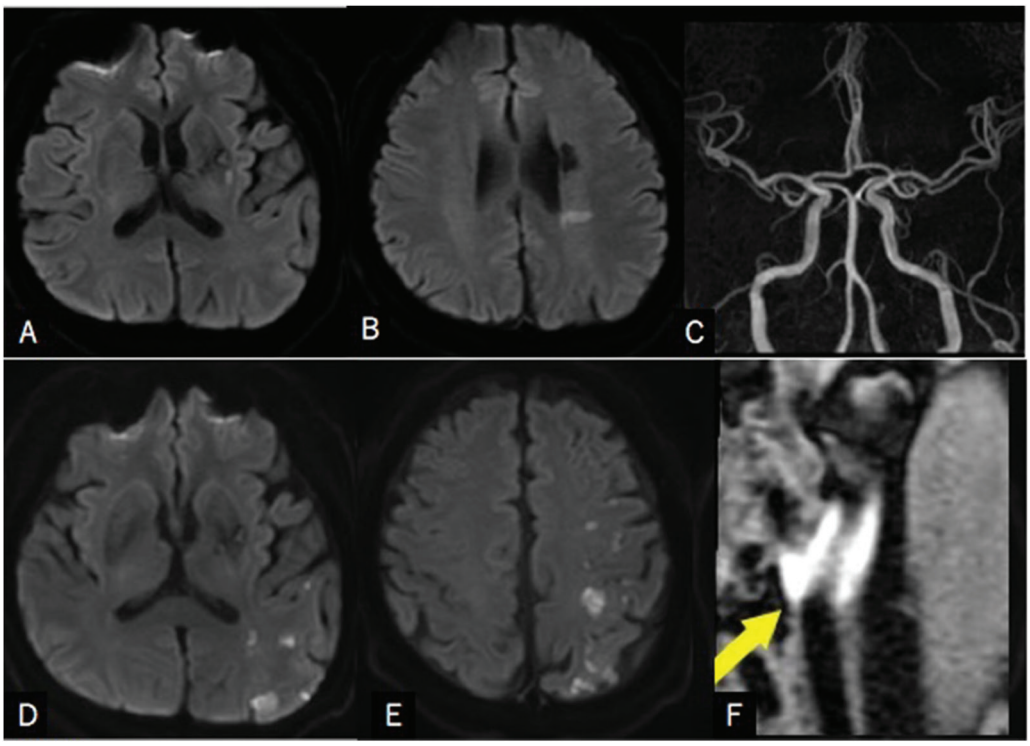


Fig. 1 (**A** and **B**) Diffusion-weighted head MRI on admission. Acute cerebral infarction was observed from the left putamen to the corona radiata. (**C**) Head MRA. No occlusion of major arteries was noted. (**D** and **E**) Diffusion-weighted head MRI on the 16th hospital day. Multiple cerebral infarctions not observed on admission appeared in the territory of the left meddle cerebral artery. (**F**) Black-blood MRI on the 17th hospital day. Sagittal T1WI. Hyper-intense vulnerable plaque was noted by T1WI in the left cervical internal carotid artery (arrow).

observed, and pain and temperature sensations were reduced. In the right leg, the MMT score was 5, and no sensory decline was noted. Diffusion-weighted head MRI revealed multiple acute small infarctions from the left basal ganglia to the corona radiata (**Fig. 1A** and **1B**). No stenosis was observed in the major intracranial arteries (**Fig. 1C**).

After admission, ozagrel sodium and edaravone were administered from the 1st hospital day. The oral administration of clopidogrel at 75 mg/day was initiated, and oral cilostazol at 200 mg/day was terminated on the 6th hospital day. On the 15th hospital day, exacerbation of weakness of the right arm (MMT score decreased from 5 to 3) was noted, and the oral administration of aspirin at 100 mg/day was added. When head MRI was performed on the 16th hospital day, multiple novel diffuse cerebral infarctions were detected in the territory of the left middle cerebral artery (**Fig. 1D** and **1E**), and carotid artery ultrasonography demonstrated North American Symptomatic Carotid Endarterectomy Trial (NASCET) 68% stenosis in the left cervical internal carotid artery. On black-blood MRI performed on the 17th hospital day, the plaque was hyper-intense on T1WI and was diagnosed as vulnerable (**Fig. 1F**). A diagnosis of NASCET 53% stenosis was made by cerebral angiography performed on the 19th hospital day (**Fig. 2A** and **2B**). Cilostazol administration at 100 mg/day was initiated on the 29th hospital day, and CAS was carried out on the 31st hospital day.

Endovascular surgery was performed as follows: An 8Fr 45-cm sheath was inserted into the right femoral artery under general anesthesia, and cerebral angiography was performed by placing an 8Fr Optimo 90 cm (Tokai Medical Products, Aichi, Japan) in the left common carotid artery, which revealed enlargement and morphological change of the thrombus compared with previous angiography (**Fig. 2C** and **2D**). We decided to aspirate the thrombus using the Penumbra system, followed by CAS. The balloon of the 8Fr Optimo 90 cm was inflated, and a Carotid GuardWire PS 300 cm (Medtronic, Minneapolis, Minnesota, USA) was advanced through the lesion while manually aspirating blood in the lumen of the 8Fr Optimo (**Fig. 3A-2**). The following procedure was carried out under distal protection by inflating the Carotid GuardWire PS on the distal side of the stenosed area of the internal carotid artery. The Penumbra 5MAX ACE68 (Penumbra Inc., Alameda, CA, USA)

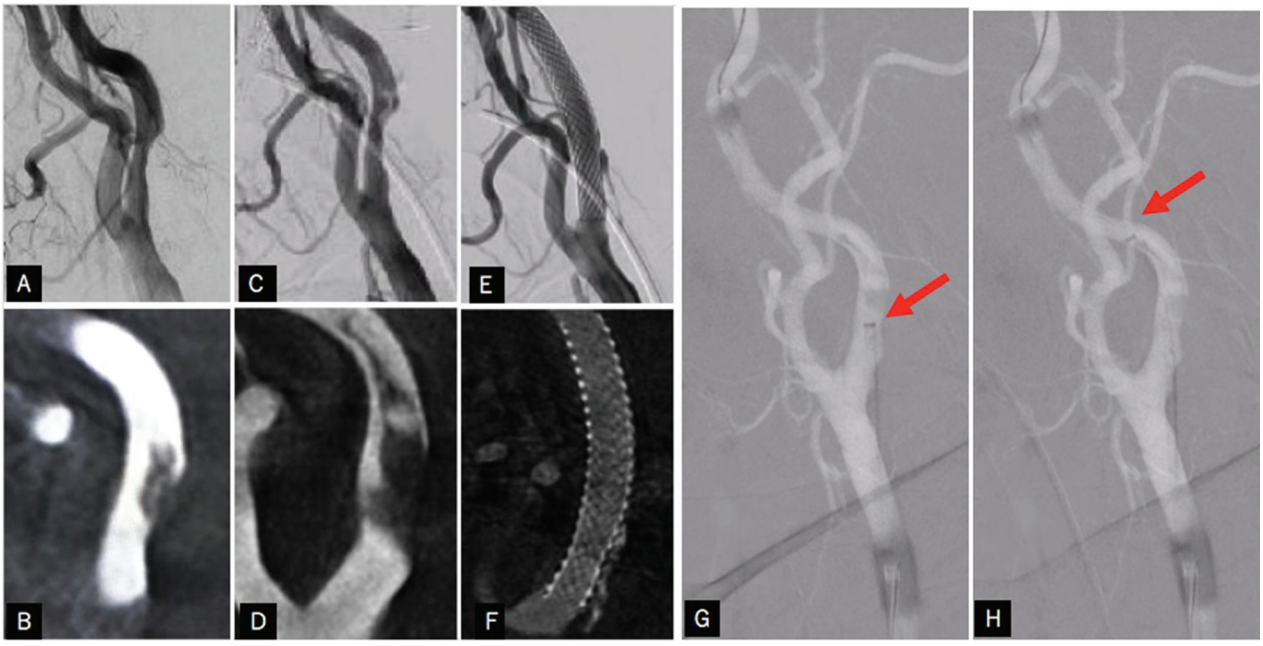


Fig. 2 (**A** and **B**) Cerebral angiography on the 19th hospital day. Left common carotid artery angiography. (**A**) Lateral view of the neck. (**B**) Slab MIP. Left cervical internal carotid artery stenosis (NASCET 52.9%). (**C** and **D**) Left common carotid artery angiography immediately before CAS on the 31st hospital day. (**C**) Lateral view of the neck. (**D**) Slab MIP. Progression of stenosis, and enlargement and morphological change of the thrombus were noted. (**E** and **F**) Left common carotid artery angiography after CAS. (**E**) Lateral view of the neck. (**F**) Slab MIP. The thrombus disappeared, and satisfactory dilation was observed. (**G** and **H**) Left common carotid artery angiography during CAS. The Optimo and Carotid GuardWire were inflated, and blood was aspirated while the Penumbra 5MAX ACE68 was moved from the proximal side to the distal side of the thrombus. (**G**) Aspiration was initiated on the proximal side. (**H**) Aspiration was ended on the distal side. CAS: carotid artery stenting; NASCET: North American Symptomatic Carotid Endarterectomy Trial

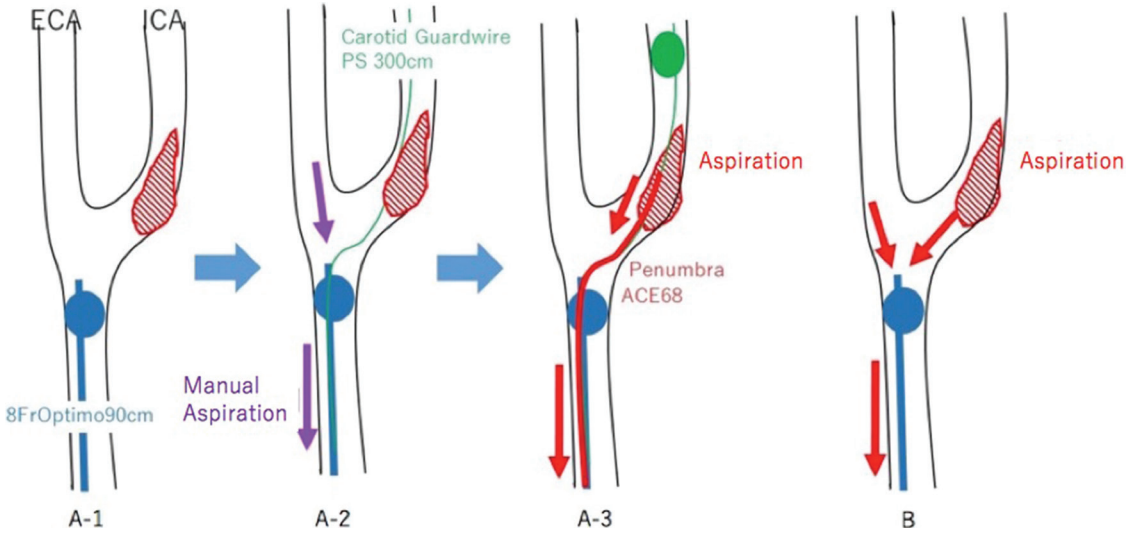


Fig. 3 (**A**) Procedure performed in the present case. After proximal occlusion with an 8Fr Optimo (**A-1**), the Carotid GuardWire PS 300 cm was advanced through the stenosed area while manually aspirating blood through the Optimo (**A-2**). A Penumbra 5MAX ACE68 was inserted in Carotid GuardWire PS and guided to a point proximal to the thrombus, and the thrombus and plaque were aspirated using the Penumbra aspiration pump (**A-3**). (**B**) Procedure of Bhogal P et al. CAS was performed while aspirating blood using the Penumbra aspiration pump directly through the guiding catheter with a balloon. CAS: carotid artery stenting

was inserted into Optimo coaxially with Carotid GuardWire PS, the Penumbra aspiration pump was connected, and 80 mL of blood was aspirated while moving the Penumbra 5MAX ACE68 from a point immediately after the bifurcation of the internal carotid artery distally to the thrombus (**Figs. 2G, 2H,** and **3A-3**). The Penumbra 5MAX ACE68 was removed, and percutaneous transluminal angioplasty (PTA) was performed before stenting using

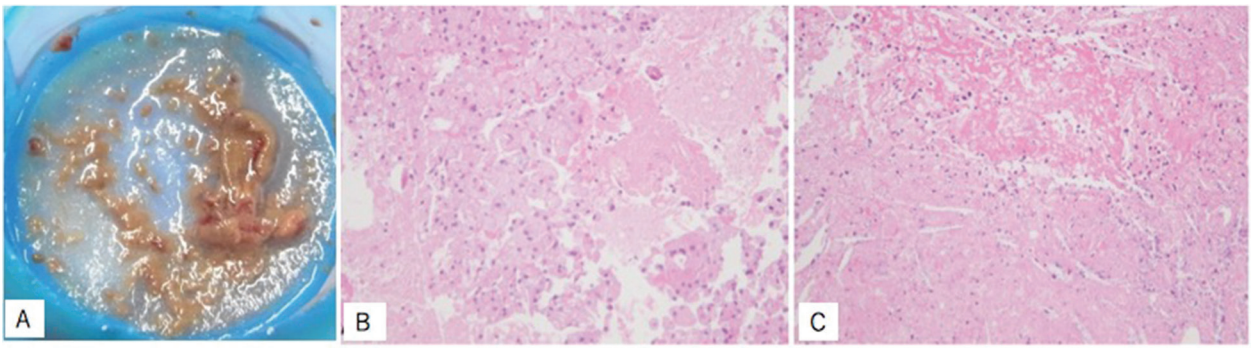
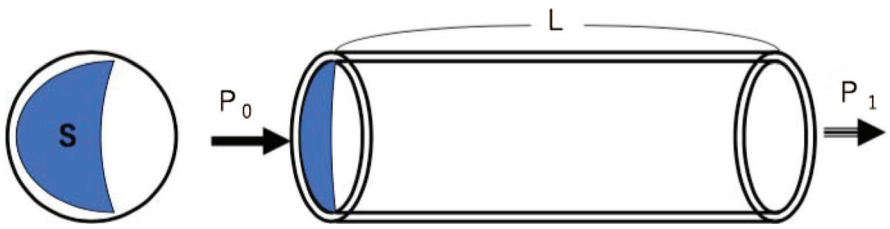


Fig. 4 (**A**) Muddy thrombus was observed in the blood aspirated by Penumbra 5MAX ACE68 and Penumbra aspiration pump. (**B** and **C**) Pathological findings in aspirated blood. HE staining. Object magnification ×20. (**B**) Macrophage aggregates and inflammatory cell infiltration were observed. (**C**) Fibrin thrombus and calcification were observed.

Makaira 5 mm × 20 mm (Kaneka Medix Corp., Osaka, Japan), A Carotid WALLSTENT 8 mm × 21 mm (Boston Scientific Natic, MA, USA) was placed in the stenosted area of the internal carotid artery, and PTA was performed after stenting using Makaira 5 mm × 20 mm. Using a 6Fr Export Advance (Medtronic, Minneapolis, Minnesota, USA), 220 mL of blood was aspirated until no gross debris was caught on the filter. Satisfactory dilation was confirmed by angiography after stenting (**Fig. 2E** and **F**). A large amount of muddy thrombus was observed in the blood aspirated by the Penumbra aspiration pump (**Fig. 4A**). No new cerebral infarction was noted on head MRI the day after surgery, and the patient was transferred to a recovery rehabilitation hospital with a modified Rankin scale of 3 on the 40th hospital day.

Discussion

There is no established method of CAS for carotid artery stenosis with vulnerable plaque. In the reported patient, the results of CAS after aspirating the thrombus using the Penumbra system were favorable for cervical carotid artery stenosis with vulnerable plaque that exhibited enlargement and morphological change of thrombus in the symptomatic subacute phase. The SAPPHIRE study of high-risk patients undergoing carotid endarterectomy (CEA) demonstrated that CAS using a distal embolic protection device (EPD) is not inferior to CEA in efficacy or safety.[1] The present patient did not correspond to the CEA high-risk group of the SAPPHIRE study and was diagnosed with vulnerable plaque by black-blood MRI. CEA is usually selected in patients with vulnerable plaque accompanied by thrombus, and we also considered CEA for this patient. However, the thrombus extended from the lower margin of the 3rd cervical vertebral body to the 2nd cervical vertebral body on lateral angiograms, and we selected CAS because we judged that the distal part of the thrombus may not be captured by CEA. As the patient had infarction in the territory of penetrating branches on admission, the presence of carotid artery stenosis was closely evaluated after recurrence. However, we should have initiated dual antiplatelet therapy (DAPT) in the acute period by diagnosing vulnerable plaque earlier. Regarding the time of therapeutic intervention, Topakian et al. reported that early CAS within 2 weeks after onset has a high risk.[2] As the progression after recurrence was able to be controlled by ozagrel sodium and three antiplatelet agents, we selected treatment in the subacute phase. Although enlargement and morphological change of the thrombus were confirmed by angiography during CAS, suggesting a high risk of distal embolization, we judged that treatment was necessary and continued the procedure. Plaque with such morphology is referred to as free-floating thrombi. Ferrero et al. considered CAS in such patients to be dangerous and treated them by CEA, but suggested that prompt treatment will lead to a favorable outcome.[3] Sawada et al. reported that a Carotid Guardwire PS (Medtronic, Santa Rosa, California, USA) or Mo.Ma Ultra (Medtronic, Minneapolis, Minnesota, USA) was effective at treating plaques suggested to be markedly vulnerable by black-blood MRI.[4] We treated the present patient using Carotid Guardwire PS based on the flow reversal concept of Mo.Ma Ultra (Medtronic, Minneapolis, Minnesota, USA). After occluding the distal internal carotid artery with a Carotid Guardwire PS, the recanalization catheter Penumbra 5MAX ACE68 was navigated coaxially with a Carotid Guardwire PS 300 cm to a site close to the thrombus, and it was aspirated by an aspiration pump. The performance of an aspiration catheter depends



$$Q = (Deq)^2 S(P0\text{-}P1)/32\mu L$$

$$Deq = 4S/A$$

$$Q = \underbrace{((P0\text{-}P1)/2\mu)}_{\text{Not dependent on catheter specifications (constant)}} \times \underbrace{(S^3/LA^2)}_{\text{Varies with catheter specifications}}$$

- Q :Flow volume (mm^3/sec)
- Deq :Equivalent diameter (mm)
- S :Cross-sectional area of the aspiration lumen (mm^2)
- A :Wetted perimeter (mm)
- (P0-P1) :Pressure gradient between tip and base-end of the catheter (Pa)
- μ :Viscosity of the aspirate (mPa・sec)
- L :Catheter length (mm)

Fig. 5 Theoretical calculation formula for ideal fluid. Formula expressing the flow volume when the cross-section of the aspiration lumen is not an exact circle. The flow volume is dependent on the luminal area and wetted perimeter of the catheter.

Table 1 Comparison of flow volume between ACE068 and Export Advance 6F

	ACE068	Export Advance 6F
Catheter internal diameter (mm)	1.73	1.09
GuardWire external diameter (mm)	0.356	0.356
Area S (mm^2)	2.25	0.83
Wetted perimeter A (mm)	6.55	4.54
Total length L (mm)	1320	1400
S^3/LA^2	2.01×10^{-4}	2.00×10^{-5}

Comparison of flow volume in aspiration using the 6Fr Export Advance and Penumbra 5MAX ACE68 each with a Carotid GuardWire PS 300 cm inserted using the theoretical calculation formula for ideal fluid. The flow volume obtained with the 6Fr Export Advance was only approximately 10% of that with the Penumbra 5MAX ACE68.

on two parameters: the thrombus removal force (TRF) and flow volume.[5] These two parameters were compared between the method employed for our patient and the method of aspiration by advancing the 6Fr Export Advance attached to the Carotid GuardWire PS 300 cm.

TRF is expressed as the product of the luminal area and aspiration pressure. The internal diameter of Penumbra 5Max ACE68 is 1.73 mm and that of 6Fr Export advance is 1.09 mm. If they are used with the Carotid GuardWire PS 300 cm as a guide, the luminal area of Penumbra 5MAX ACE68 is 2.25 mm^2 and that of 6Fr Export Advance is 0.83 mm^2, after subtraction of the area occupied by the Carotid GuardWire PS. As the pump provides a more stable aspiration pressure than manual aspiration, the method applied for our patient is considered superior in TRF even though the Carotid GuardWire PS 300 cm passes through the lumen. Regarding the flow volume, if the cross-section of the aspiration lumen, through which the Carotid GuardWire passes, is not an exact circle, the flow volume is expressed as in **Fig. 5**, and is dependent on the luminal area and wetted perimeter of the catheter. Using the formula shown in **Fig. 5**, the 6Fr Export Advance was considered to provide a flow volume of approximately 10% of that of Penumbra 5MAX ACE68 (**Table 1**). In addition, 220 mL of blood was aspirated after post-PTA, and there was concern over the progression of postoperative anemia. Although the hemoglobin concentration, which was 16.5 g/dL 2 days before surgery, decreased to 13.7 g/dL on the day after surgery, no decrease in blood pressure or tachycardia was observed.

Bhogal et al. reported a case in which CAS was performed for acute symptomatic carotid artery stenosis using the Penumbra aspiration pump.[6] Similar to our patient, irregular plaque was confirmed in this patient, and CAS

was performed during aspiration using the Penumbra aspiration pump through a guiding catheter with a balloon placed in the common carotid artery (**Fig. 3B**). In this method, the reperfusion catheter of the Penumbra system is not used, but PTA and stenting can be performed while continuing aspiration. On the other hand, the method applied for our patient has high ability to remove ruptured plaque and enlarged thrombus, which cannot be recovered completely by aspiration from the common carotid artery alone (**Fig. 3A, 3B**). Flow reversal, implemented by blocking the common carotid artery and external carotid artery, is another method for the prevention of distal embolization. Montorsi et al. performed CAS by randomly dividing patients with vulnerable plaque into those treated by filter protection and those treated by flow reversal, and observed and compared microembolic signals (MES) during surgery by transcranial ultrasonography. In the group treated by flow reversal, fewer MES were observed during surgery, but more were observed only immediately after deflation of the balloon used for occlusion.[7] As the absence of debris was confirmed by performing manual aspiration before deflating the balloon, debris that was unable to be removed by manual aspiration was considered to have existed. The method by which debris is removed with strong force is considered effective in patients with a large amount of vulnerable plaque such as our patient. Furthermore, Nakanishi et al. reported a patient who received CEA for restenosis after CAS. The stent and plaque were excised en bloc, and plaque accompanied by ulceration was formed in the area where stent dilation was restricted due to differences in wall properties.[8] The lack of uniform stent dilation is considered to be a risk factor for restenosis. In our patient, uniform dilation was achieved after post-PTA (**Fig. 2E** and **2F**), and a large amount of plaque was aspirated, resulting in the favorable outcome.

Pathological findings of carotid artery stenosis have been reported by analyzing lesions obtained by CEA. Fukao et al. noted ulceration, mural thrombus, or intraplaque hemorrhage in 19 of 27 symptomatic carotid artery stenosis patients with plaque, and reported that 90% or milder carotid artery stenosis can also be symptomatic, and that atherosclerotic ulcer and intraplaque hemorrhage are concurrent and correlated.[9] Hayashi et al. compared debris recovered by CAS with pathological specimens obtained by CEA, and identified the characteristics of debris. They classified debris into reddish thrombotic debris with sparse cell components, hematoxylinophillic polygonal calcified debris, yellowish lipid-rich debris with sparse cell components, fibrous debris consisting mainly of fibrous components, and cellular debris rich in cell components.[10] Compared with CEA specimens, the characteristics of thrombotic debris corresponded to intraplaque hemorrhage and mural thrombus, those of calcified debris corresponded to old plaque, those of lipid-rich debris corresponded to cholesterin crystals, those of fibrous debris corresponded to fibrous capsule, and those of cellular debris corresponded to inflammatory cell infiltration. This report compared the morphological characteristics of debris with findings in CEA specimens, but in our patient, plaque fragments were confirmed to the blood aspirated before PTA, and pathological findings normally obtained by CEA, such as fibrin, calcification, hyalinization, cholesterin clefts, macrophage aggregates, and inflammatory cell infiltration, were obtained (**Fig. 4A, 4B,** and **4C**). According to the classification by Hayashi et al., they are classified as thrombotic debris, calcified debris, lipid-rich debris, and cellular debris, respectively.[10] This suggests that the blood aspirated before destruction of plaque by the balloon contained not only thrombus but also plaque tissue itself due to atherosclerosis.

Based on these observations, in CAS for cervical internal carotid artery stenosis with vulnerable plaque accompanied by thrombosis, part of the thrombus and plaque is considered to be removed by aspiration using the Penumbra system in advance, improving the safety of the procedure. Concerning the off-label use of the Penumbra system, we did not request approval from the institutional review board, and explained this to the patient and his family after the procedure.

Conclusion

In a patient with cervical internal carotid artery stenosis with vulnerable plaque who exhibited enlargement and morphological change of the thrombus in the symptomatic subacute phase, CAS was performed in combination with aspiration using the Penumbra system. Thrombus and pathological features of plaque tissue were observed in the aspirate.

Disclosure Statement

There are no conflicts of interest to declare concerning this paper.

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