De novo expansion formation in the outer curvature of the internal carotid artery after flow diverter deployment for an infectious cavernous carotid aneurysm: illustrative case

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BACKGROUND Infectious aneurysms very rarely occur in the cavernous carotid artery. Recently, treatment by flow diverter implantation with preservation of the parent artery has been the treatment of choice.

OBSERVATIONS A 64-year-old woman presented with stenosis at the C5 segment of the left internal carotid artery (ICA), followed by ocular symptoms within 2 weeks, with a de novo aneurysm in the left cavernous carotid artery and wall irregularity with stenosis from the C2 to C5 segments of the left ICA. Antimicrobial therapy was given for 6 weeks, and a Pipeline Flex Shield was implanted. Angiography 6 months after treatment showed complete obliteration of the infectious aneurysm and improvement of the stenosis. However, de novo expansions were formed in the outer curvature of C3 and C4 segments of the ICA where the Pipeline device had been deployed.

LESSONS Aneurysms that develop rapidly and show shape changes over time, accompanied by fever and inflammation, may be associated with an infection. Because of the fragility in the irregular wall of the parent vessel associated with infectious aneurysms, de novo expansion may form in the outer curvature of the parent vessel after flow diverter placement; thus, careful follow-up is necessary.

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KEYWORDS infectious aneurysm; flow diverter; expansion formation; outer curvature

Infectious intracranial aneurysms are uncommon and account for 0.5%–6.5% of all aneurysms arising from cerebral vessels.1 Furthermore, infectious aneurysms very rarely form in the cavernous carotid artery, with fewer than 50 cases reported. Infective endocarditis is responsible for 65% of infectious intracranial aneurysms; however, it is a rare cause of a cavernous carotid artery aneurysm.3 Depending on the site and shape, parent artery occlusion is often observed in infectious aneurysms, and in recent years, endovascular treatment has become more common.1 Endovascular treatment by flow diverter implantation with preservation of the parent vessel is chosen for infectious aneurysms in the cavernous carotid artery.4,6

Herein, we report a case of an infectious aneurysm in the cavernous carotid artery, which had rapidly increased in size and changed shape. It was treated with Pipeline device implantation, and the targeted aneurysm disappeared. However, de novo expansions were observed in the outer curvature of the internal carotid artery (ICA).

Illustrative Case

History and Examination
A 64-year-old woman with no specific medical history presented to her local doctor on day 4 after the onset of headache and blurred left-eye vision. She was afebrile; however, her leukocyte count increased to 7800 cells/µL and her C-reactive protein (CRP) level increased to 6.8 mg/dL. Magnetic resonance angiography (MRA) showed stenosis of the C5 segment of the left ICA; however, no aneurysm was detected (Fig. 1A). Fourteen days after symptom onset, she was febrile (38°C) and had a leukocyte count of 16,100 cells/µL and CRP of 28.3 mg/dL, which further increased. Antibiotic therapy

ABBREVIATIONS CRP = C-reactive protein; CT = computed tomography; ICA = internal carotid artery; MRA = magnetic resonance angiography; PED = Pipeline embolization device.

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Fig. 2A: MRA on day 4 after the onset of symptoms shows stenosis in the C5 segment of the left ICA. B: MRA on day 20 after onset shows new aneurysm formation in the C4 segment of the left ICA, stenosis in the C2 segment, and mild improvement of stenosis in the C5 segment. C: CT angiography (CTA) on day 23 after onset shows an irregular aneurysm with a maximum diameter of 13.2 mm. D: CTA on day 58 after onset shows that the aneurysm has increased to a maximum diameter of 15.7 mm.

with meropenem was started. Two sets of blood cultures were taken, and both showed Streptococcus milleri; thus, treatment with ampicillin was continued. On day 21 after onset, left ptosis and left-eye movement disorder emerged. MRA demonstrated a 12-mm aneurysm in the cavernous portion of the left ICA and wall irregularity from the C2 to C5 segments of the ICA (Fig. 1B). There were no findings diagnostic of cavernous thrombophlebitis.

The patient was referred to our hospital on day 24 from symptom onset for close examination and treatment. On admission to our hospital, she had dilated left-eye pupil and left-eye abduction disorder but no chemosis or conjunctival infection. Echocardiography revealed no endocardial damage or verrucae. After admission to our hospital, 2 sets of blood cultures were taken, which were negative. Duke’s criteria did not confirm the diagnosis of infective endocarditis because only 2 of the subcriteria were met. Since the aneurysm was rapidly forming with fever and inflammations, it was suspected to be an infectious aneurysm. Based on the blood culture sensitivity, the aneurysm was treated with penicillin G for 6 weeks. Computed tomography (CT) angiography showed the aneurysm growth over time (maximum diameter of 15.6 mm) and improvement of the stenosis in the C5 segment of the ICA (Fig. 1C and D). Cerebral angiography on day 25 after onset showed that the aneurysm was irregularly shaped, as large as 8.14 mm in the neck, 7.32 mm in height, and 11.33 mm in the dome, and stenosis was observed at the C2 and C5 segments of the left ICA (Fig. 2A–C). The CRP level and leukocyte count decreased, and the blood culture was negative, so she underwent flow diverter implantation with preservation of the parent vessel. Aspirin 100 mg/day and clopidogrel 75 mg/day were administered 2 weeks before the surgery (day 4T).

Endovascular Surgery

Endovascular surgery was performed under general anesthesia on day 61 after symptom onset. Heparin was administered intravenously, and the intraoperative activating clotting time was maintained at ≥ 250 seconds. A 6-Fr Fubuki Dilator Kit (Asahi Intec) was inserted into the right femoral artery and was advanced to the left cervical ICA. Compared with the findings of cerebral angiography on day 25, the shape of the aneurysm and C2 to C5 segments of the ICA were altered (Fig. 2D–F). The size of the aneurysm increased: neck, 8.55 mm; height, 6.87 mm; and dome, 15.76 mm x 11.50 mm. The stenosis in the C2 and C5 segments of the left ICA improved; however, severe stenosis appeared in the C4 segment of the ICA proximal to the aneurysm neck, and blood flow distal to the stenosis was delayed. Through the catheter, a 5-Fr Navien support catheter (Medtronic) was placed in the C5 segment of the ICA and a Phenom 27 catheter (Medtronic) was advanced to the middle cerebral artery. A Pipeline Flex Shield (3.5 mm x 30 mm, Pipeline embolization device [PED], Medtronic) was deployed from the C2 to C4 segments of the ICA, and the stenosis was easily diluted by PED deployment. A Transform SC balloon catheter (4 mm x 7 mm, Stryker Neurovascular) was advanced, and balloon angioplasty was performed from the distal to the proximal end of the PED. The contrast was stagnant in the aneurysm, and an eclipse sign was observed (Fig. 2G and H). Cone-beam CT showed good adhesion of the PED to the vessel wall (Fig. 2I). Left internal carotid angiography revealed that a delay in blood flow distal to the C4 segment of ICA had been improved with dilation of the stenosis.

Postoperative Course

No new neurological disorder was found postoperatively. The patient was discharged home on day 8 after the surgery, with left pupillary dilation, ocular motility disorder, and ptosis remaining. Her ocular symptoms improved with time after the surgery; however, she still had mild abduction disorder, mild ptosis, and a dilated pupil 3 months after the surgery.

Cerebral angiography 6 months after surgery showed complete obliteration of the targeted aneurysm in the C4 segment of the ICA and improvement of the stenosis proximal and distal to the aneurysm. However, a de novo flat expansion with a maximum diameter of 8.06 mm was formed in the outer curvature in the C3 segment of the ICA and a de novo small expansion in the outer curvature in the C4 segment of the ICA (Fig. 3A and B). She took aspirin 100 mg per day and finished taking clopidogrel.

Cerebral angiography was performed 1 year after the surgery and showed no change in the de novo expansions at the C3 and C4 segments of the ICA (Fig. 3C and D). One year after the surgery, the ptosis had almost disappeared; however, a mild left pupillary dilation and abduction disorder remained. The patient has been followed up with periodic MRA and contrast-enhanced CT, and no aneurysmal changes have been observed. The targeted aneurysm that presented ocular symptoms has disappeared,
and the patient did not present with symptoms due to the new expansion at the outer curvature. We concluded that there was no potential for further enlargement since there were no changes on cerebral angiography from 6 months to 1 year later, and no infection was noted.

**Patient Informed Consent**

The necessary patient informed consent was obtained in this study.

**Discussion**

**Observations**

In this case, aneurysm formation was confirmed after a rapid course of approximately 2 weeks, and we strongly suspected an infectious aneurysm based on the clinical course, blood tests, and culture results. Two mechanisms for the formation of infectious aneurysms are generally known: endovascular and extravascular. In the endovascular mechanism, an aneurysm is formed when septic emboli cause cerebral infarction and surrounding infection, whereas
in the extravascular mechanism, an aneurysm is formed when infection close to the artery spreads to the vessel wall. It is unlikely that the aneurysm was formed with an endovascular mechanism because no infectious endocarditis was diagnosed and no clinical or imaging findings suggested ICA occlusion or stenosis caused by septic embolization. In this case, aneurysm formation and irregular vessel walls were observed from the C2 to the C5 segments of the ICA, and the infection possibly spread widely to the vessel wall in that area. Since infective endocarditis is a relatively rare cause of infectious aneurysms in the cavernous carotid artery, no sinusitis was observed, and the lesions were widely spread on the C2 to C5 segments of the ICA, infections such as cavernous thrombophlebitis were suspected to spread directly to the ICA and formed infectious aneurysms with an extravascular mechanism.

Since the patient was going to have endovascular surgery with stent deployment and the infectious vessel wall was fragile, antibiotic therapy was administered first. Endovascular surgery was performed at a time when infection was controlled, the shape of the aneurysms and parent vessel were almost unchanged, and vascular fragility appeared to have improved. In addition, it was an epidural aneurysm and rupture would not be fatal; thus, surgery was deferred until the completion of antibiotic therapy. If the aneurysm was ruptured during the antibiotic therapy, we would have considered a parent artery occlusion. Coil embolization with high packing density would not improve the ocular symptoms; thus, we chose to treat the aneurysm with a flow diverter to preserve the parent vessel and improve the ocular symptoms. Several cases of infectious aneurysms in the cavernous carotid artery have been treated with a flow diverter, and all of them showed complete obliteration of the aneurysm and improvement of cranial nerve symptoms.1-6

For patients with internal carotid aneurysms presenting with cranial nerve symptoms, significant improvement of the symptoms has been reported after treatment with the flow diverter less than 6 months after symptom onset.6 In infectious aneurysms, owing to the rapid formation of aneurysms and symptom onset, the time from the onset of cranial nerve symptoms to treatment may be shorter than that in other aneurysms. However, depending on the infection site, direct cranial nerve damage may be possible because of inflammation in addition to nerve compression with the aneurysm. In this case, long-term antibiotic therapy was necessary; thus, endovascular surgery was performed on day 61 after the onset of ocular symptoms. Despite surgery with a flow diverter less than 6 months after symptom onset, her left pupil remained dilated, and she had abducens disorder 1 year after surgery. The ocular symptoms were considered to have been caused by rapid formation and enlargement of the aneurysm, and direct cranial nerve damage due to inflammation such as cavernous thrombophlebitis may have been the cause of the residual ocular symptoms.

In this case, complete obliteration of the targeted aneurysm and improvement of the stenosis of the parent artery were achieved. To our knowledge, this is the first report of a de novo expansion formation in the outer curvature of the parent vessel where a flow diverter was deployed. A study reported that treatment with a flow diverter often results in incomplete occlusion of aneurysms in the outer curvature. Metal coverage over the aneurysm neck varies from 19% to 63%, depending on the bending angle of the flow diverter, which affects incomplete occlusion of aneurysms. In this case, de novo expansion was formed despite flow diverter deployment in the C3 and C4 segments of the ICA. The new formation of the expansion may have been related to its location in the outer curvature of the vessel, the fragility of the vessel wall due to infection, the endoleak that appeared with the vessels dilated as the infection healed in spite of good apposition immediately after flow diverter implantation, and increased blood flow because of the improvement of ICA stenosis and the decrease in intra-aneurysmal flow associated with aneurysm occlusion.

According to the findings of the change in shape, vascular fragility associated with an infection may have existed from the C2 to the C5 segments of the ICA in this case. Therefore, the patient might have been at risk for subarachnoid hemorrhage due to aneurysm formation in the C2 segment. Since the flow diverter was not deployed on the proximal side of the C5 segment of the ICA, it may have been necessary to deploy the flow diverter including the area where the vascular fragility existed.

The overlapping of 2 flow diverters is expected to increase the metal coverage of the aneurysm neck and improve the occlusion rate.7 In this case, it might have been better to deploy 2 overlapping

**FIG. 3.** The asterisk indicates the neck of the targeted aneurysm, the arrow indicates the outer curvature of C3 segment, and the arrowhead indicates the outer curvature of the C4 segment. Angiography (A) and 3D reconstruction (B) of frontal views of the left ICA 6 months after surgery show a de novo expansion in the outer curvature of the C3 (arrow) and C4 (arrowhead) segments of the ICA. Frontal view of angiography (C) and 3D reconstruction (D) of the left ICA 1 year after surgery shows no change in the shape of the expansion in the outer curvature of the C3 (arrow) and C4 (arrowhead) segments.
flow diverters in the outer curvature of the artery. It was an infectious aneurysm with a fragile vessel wall, and parent artery occlusion is still considered an option. If an infectious aneurysm is treated with preservation of the parent artery, careful follow-up is necessary because changes may be observed even after surgery. Thus, the parent vessel near the aneurysm being infectious and the fragility of the vessel wall must be considered in infectious aneurysms.

Lessons
Aneurysms that develop rapidly and show shape changes and enlargement with time, accompanied by fever and inflammation, may be associated with an infection. Since vascular fragility exists in the irregular wall of the parent artery associated with infectious aneurysms, de novo expansion may form in the outer curvature of the artery after the deployment of a flow diverter; thus, careful follow-up is necessary.

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References

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