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Case Report

A Patient with a Large Aneurysm Complicated by Stenosis of the Internal Carotid Artery Distal to the Aneurysm in Whom Treatment Using a Pipeline Flex Was Performed

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Objective: We report a case of in-stent stenosis as a complication at 6 months after the deployment of Pipeline Flex. This case necessitated retreatment for parent artery occlusion.

Case Presentation: A 55-year-old woman with right-side visual disorder was referred to our hospital for the deployment of Pipeline Flex. Cerebral digital subtraction angiography (DSA) demonstrated a large right-side paraclinoid aneurysm in combination with severe internal carotid artery (ICA) stenosis just beyond the aneurysm. We deployed Pipeline Flex under general anesthesia. After deployment, we performed angioplasty through the Pipeline. Six months after deployment, this patient exhibited exacerbation of visual disorder. Follow-up DSA revealed in-stent stenosis at 6 months after the deployment of Pipeline Flex. Therefore, we performed parent artery occlusion. Right-side visual disorder was improved in this patient.

Conclusion: If Pipeline is deployed for patients with ICA stenosis just beyond an aneurysm, we need to be aware of in-stent stenosis after deployment.

Keywords▶ Pipeline, large aneurysm of the internal carotid artery, in-stent stenosis

Introduction

In some patients with large/giant cerebral or fusiform aneurysms, clipping under craniotomy or coil embolization is difficult, often requiring parent artery occlusion. In patients with proximal internal carotid artery (ICA) aneurysms, intra-/extracranial bypass in combination with the above procedures facilitates radical parent artery occlusion,[1] but invasive surgery, such as radial artery grafting, is sometimes required.[2] On the other hand, concerning endovascular treatment, the recanalization rate of large and wide-neck cerebral aneurysms after coil embolization alone is high,[3,4] and recanalization of large cerebral aneurysms is frequently needed even when balloon- or stent-assisted coil embolization is performed.[5]

In April 2015, a flow diverter (Pipeline Flex, Medtronic, Irvine, CA, USA) was approved in Japan. Since then, it has been applied to treat such refractory aneurysms in a limited number of institutions/by a limited number of surgeons. Currently, a modified flow diverter, Pipeline Shield (Medtronic), is available, and may further improve the results of treatment. In Japan, treatment using this flow diverter is indicated for intracranial ICA aneurysms (excluding the acute phase of rupture), measuring ≥10 mm, proximal to the posterior communicating artery bifurcation (guidelines for the correct use of intracranial artery stents [flow diverters for aneurysm treatment], 2nd edition). The Pipeline is an ideal device that facilitates angioplastic treatment in which a large/giant cerebral aneurysm, especially a fusiform aneurysm, alone is occluded while preserving a parent artery. The results of Pipeline placement in aneurysms that had been considered to be refractory were favorable.[6]

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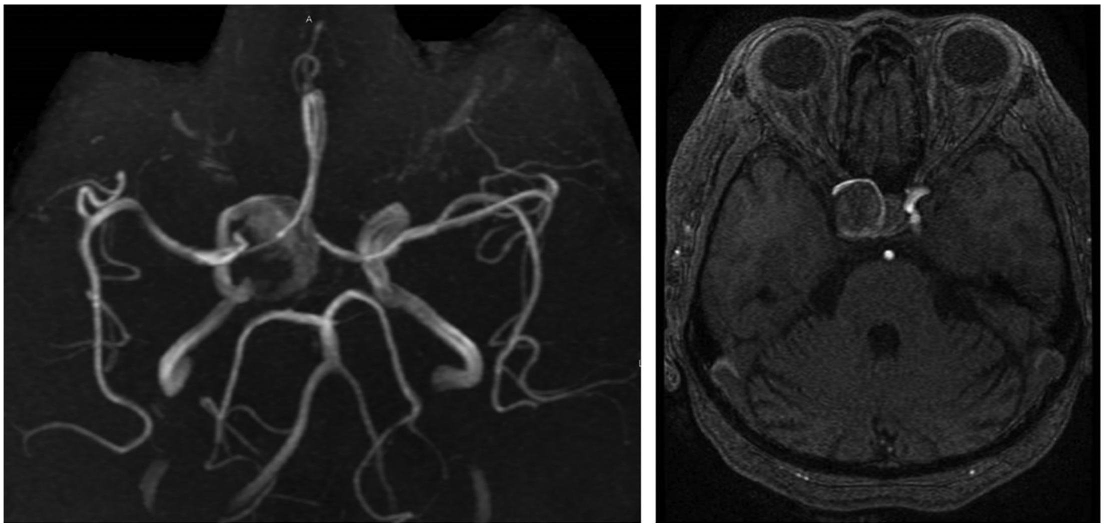

Fig. 1 Head MRA and original image (time-of-flight). MRA: magnetic resonance imaging

At our hospital, the deployment of Pipeline was performed in 69 patients (70 aneurysms) between June 2015 and December 2019. Of these, we report a patient with a large ICA paraclinoid aneurysm in whom in-stent stenosis developed after the deployment of Pipeline, requiring parent artery occlusion, and review the literature.

Case Presentation

Patient: A 55-year-old female.
Medical history: Autoimmune hepatitis.
Present illness: Head magnetic resonance imaging (MRI) at another hospital 7 years prior to presentation revealed a large intracranial right ICA aneurysm (**Fig. 1**), but it was asymptomatic, and follow-up was continued. Visual disorder of the right eye had persisted for the past 3 months, and she consulted the same hospital. Right quadrantanopia was noted. Its size and localization met indication criteria for the deployment of Pipeline Flex, and she was referred to our hospital. Digital subtraction angiography (DSA) demonstrated a large right ICA paraclinoid aneurysm measuring 16 mm in maximum diameter. In addition, severe stenosis of the ICA distal to the aneurysm was observed (**Fig. 2**). The large right ICA paraclinoid aneurysm was symptomatic, and its maximum diameter exceeded 10 mm; therefore, the deployment of Pipeline Flex was performed.
Initial surgery (the deployment of Pipeline): Under general anesthesia, a 6-Fr Shuttle sheath (Cook Medical, Bloomington, IN, USA) was inserted into the right femoral artery. Using a coaxial system consisting of a 5-Fr Navien (Medtronic), Marksman (Medtronic), and Traxcess 12-14 200 (Terumo Corporation, Aliso Viejo, CA, USA), the Navien was inserted into the petrous part of the ICA and the Marksman was guided into the right middle cerebral artery (M1). Concerning the position of deployment, a Pipeline Flex 4.5 mm × 20 mm was deployed through the end of the ICA beyond the site of marked ICA stenosis to sufficiently cover the aneurysmal neck (**Figs. 3A, 4B,** and **4D**). After deployment, the Marksman was placed in the Pipeline using a delivery wire, and the delivery wire was removed/exchanged for a CHIKAI 10 300. Subsequently, a HyperForm 7.0 mm × 7.0 mm (Medtronic) was guided, and angioplasty was performed to crimp the Pipeline to the vascular wall, slightly expanding stenosis of the ICA (**Fig. 4C** and **4E**). In addition, intra-aneurysmal stagnation of contrast medium (Eclipse sign) was observed (**Fig. 3B** and **3C**). To protect the optic nerves, 250 mg of SOL-MELCORT was intravenously administered twice a day from the day of surgery (during surgery) until 2 days after surgery.
Postoperative course: A slight improvement in right quadrantanopia was achieved the day after surgery, and there was no new neurological deficit. The patient was discharged. Right low vision developed 2 months after surgery, but no treatment was conducted based on her will. On admission to our hospital for follow-up DSA after 6 months, her right visual acuity had reduced to light perception. DSA demonstrated in-stent stenosis, which was consistent with the stenotic site (**Fig. 5A** and **5B**). Jet blood flow into the aneurysm due to loading on the Pipeline side related to blood flow passage disorder associated with severe in-stent stenosis was confirmed (**Fig. 5A**; white arrow). Severe stenosis may have increased the intra-aneurysmal pressure,

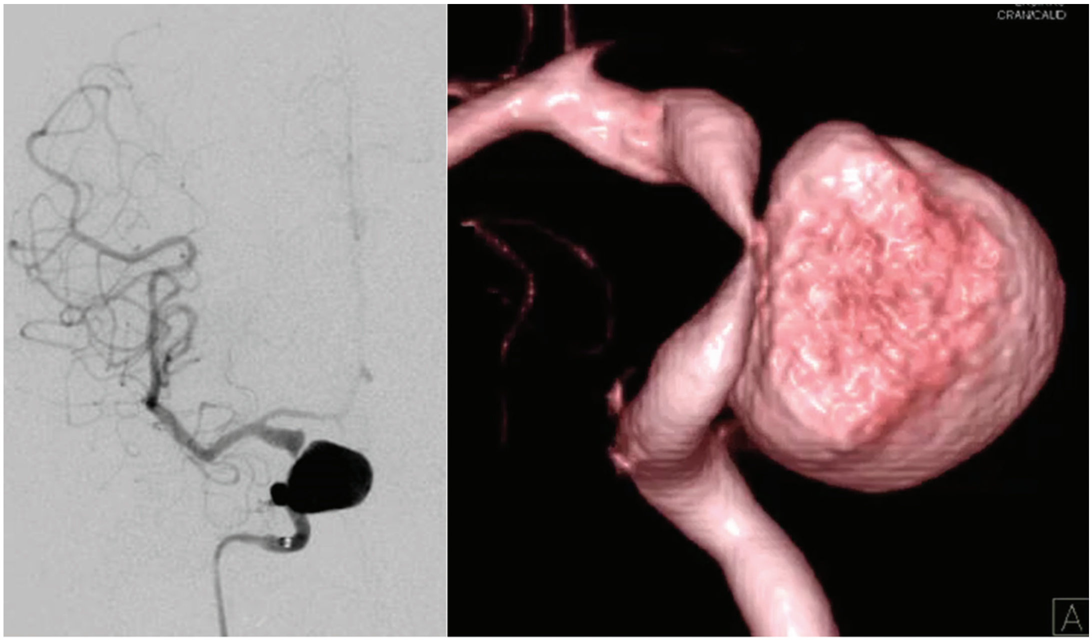

Fig. 2 DSA (frontal view) and three-dimensional rotational angiography. DSA: digital subtraction angiography

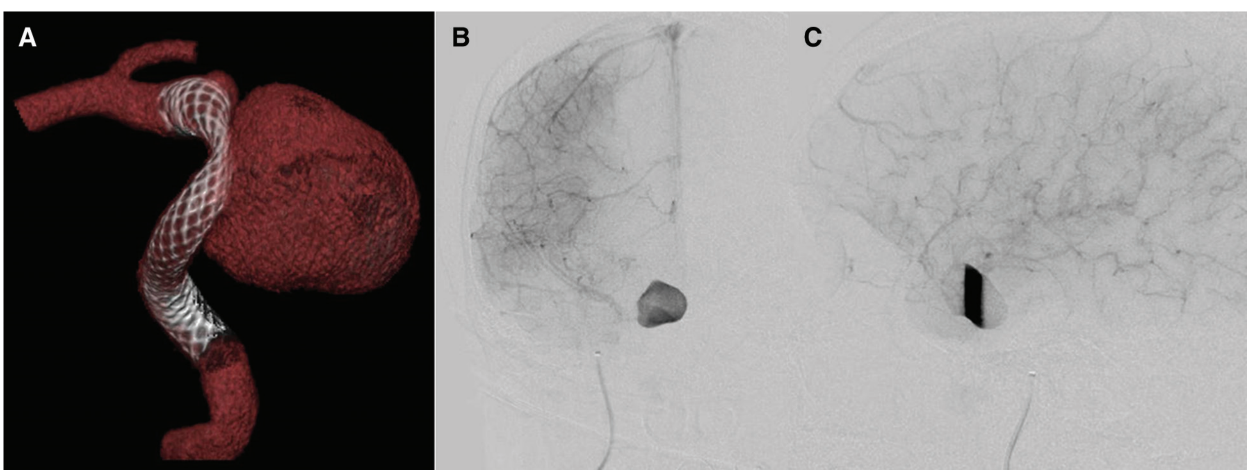

Fig. 3 Cone-beam CT image (**A**). Final DSA of the initial therapy showed the eclipse sign (frontal view = **B**, lateral view = **C**). CT: computed tomography; DSA: digital subtraction angiography

leading to the progression of visual disorder through compression of the right optic nerve. For initial treatment, angioplasty was performed after the deployment of Pipeline, but vascular stenosis expanded only slightly. As Pipeline overlapping following additional angioplasty is ineffective, we planned parent artery occlusion.

Additional surgery (balloon occlusion test (BOT) and parent artery occlusion): Additional surgery was performed 6.5 months after the deployment of Pipeline. A 5-Fr Envoy (Johnson & Johnson, Miami, FL, USA) was inserted into the right cervical ICA (C1 level) through a 5-Fr long sheath. Through this guiding catheter, a Shouryu 4.0 mm × 7.0 mm (Kaneka Medix Corp., Osaka, Japan) was guided into the petrous part of the right ICA. It was expanded in this artery for occlusion, and left cervical internal carotid and left vertebral angiography were performed using a 4-Fr OK-2M. The former confirmed cross flow mediated by the anterior communicating artery, and the latter revealed blood flow mediated by the posterior communicating artery. Subsequently, occlusion was continued for 30 minutes, but there was no symptom. Lastly, a tolerance test was conducted by reducing the blood pressure from 130 to ≤100 mmHg using nicardipine. There was no symptom, suggesting ischemic tolerance. Based on this, local anesthesia was switched to

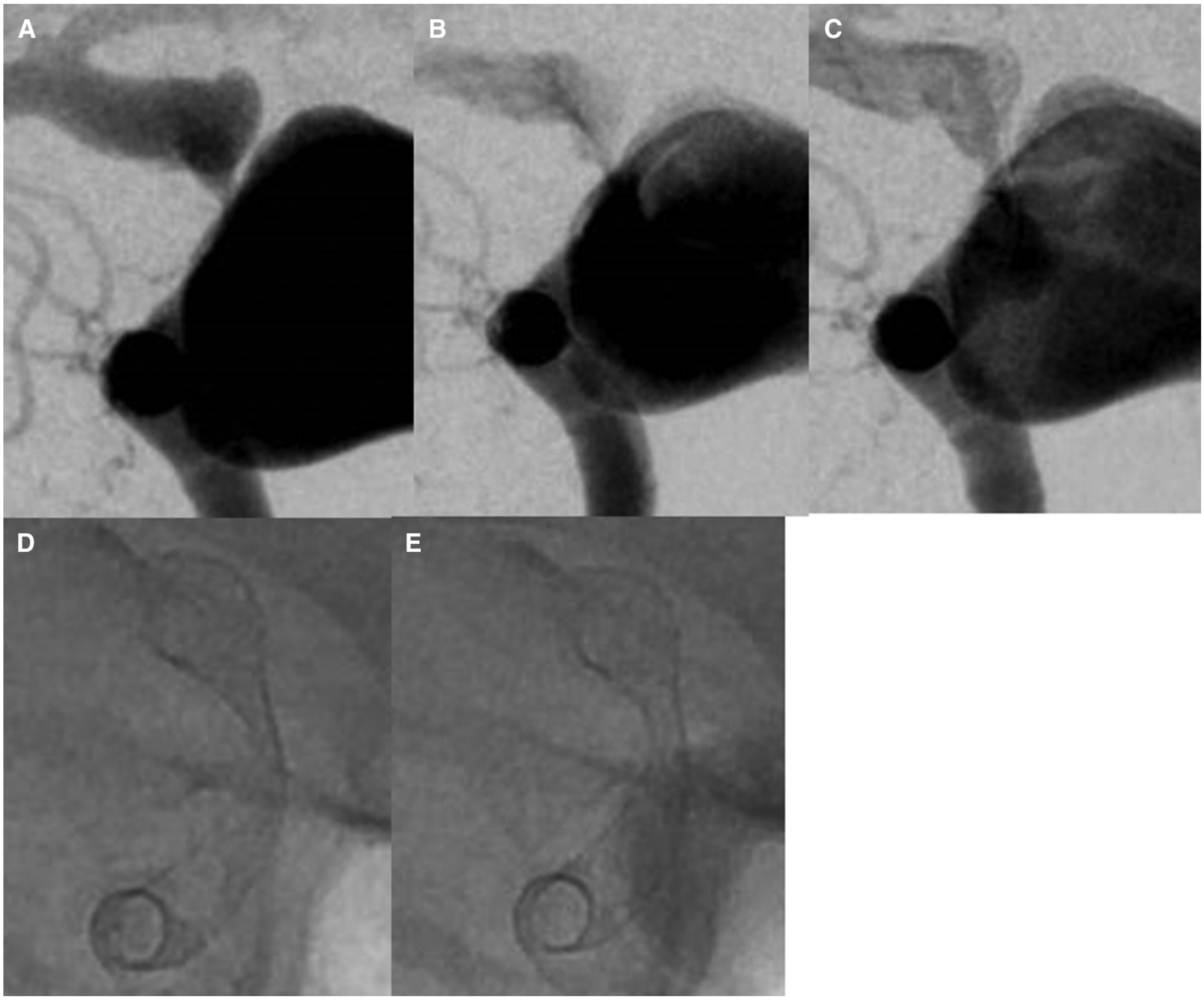

Fig. 4 Frontal working angle image before deployment of the Pipeline. There is severe stenosis of ICA just beyond the aneurysm neck. (**A**) Frontal working angle image just after deployment of the Pipeline. Further aggravation of severe ICA stenosis was observed just after deployment of the Pipeline. (**B**) Frontal working angle image just after angioplasty using a balloon catheter. (**C**) Improvement of severe stenosis was observed just after angioplasty (An exterior view of the Pipeline just before (**D**) and after (**E**) the angioplasty). ICA: internal carotid artery

general anesthesia for parent artery occlusion. Next, 8-Fr FlowGate (Stryker, Kalamazoo, MI, USA), 6-Fr JB-2, and RF 35 150 guiding catheters were guided/inserted into the right cervical ICA (C1 level) through an 8-Fr long sheath. A SL-10 STR and Headway 17 STR (Terumo Corporation, Aliso Viejo, CA, USA) were guided to the end of the ICA beyond the severe stenotic site of this artery through the 8-Fr FlowGate, and intra-aneurysmal-coil-insertion-free parent artery occlusion was performed by the double microcatheter method using 18 coils (**Fig. 5B**). On final angiography, the aneurysm and right ICA were not completely enhanced, and contralateral internal carotid angiography confirmed sufficient cross-flow mediated by the anterior communicating artery (**Fig. 6A**). Vertebral angiography demonstrated slight posterior-communicating-artery-mediated blood flow to the right anterior circulation (**Fig. 6B**). Surgery was completed. After surgery, there was no neurological deficit, and an improvement in right low vision, which had progressed, was achieved.

Discussion

In Japan, the deployment of Pipeline has been performed to treat intracranial ICA aneurysms measuring ≥10 mm (excluding the acute phase of rupture, proximal to the posterior communicating artery bifurcation) since April 2015. This treatment facilitates angioplastic parent artery preservation and occlusion of an aneurysm alone, especially in patients with large or giant ICA aneurysms, which are difficult to treat using conventional treatment methods, such

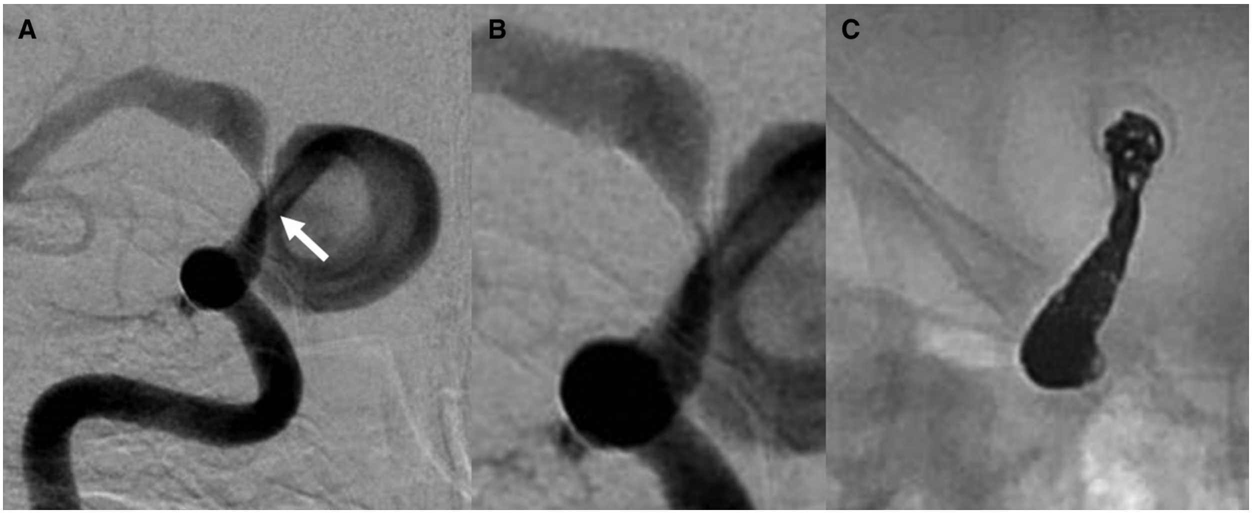

Fig. 5 In-stent stenosis was observed at 6 months after deployment of the Pipeline (**A**). Jet flow was noted in the aneurysm over the Pipeline (white arrow) (**B**). Frontal working view after parent artery occlusion using coils (**C**).

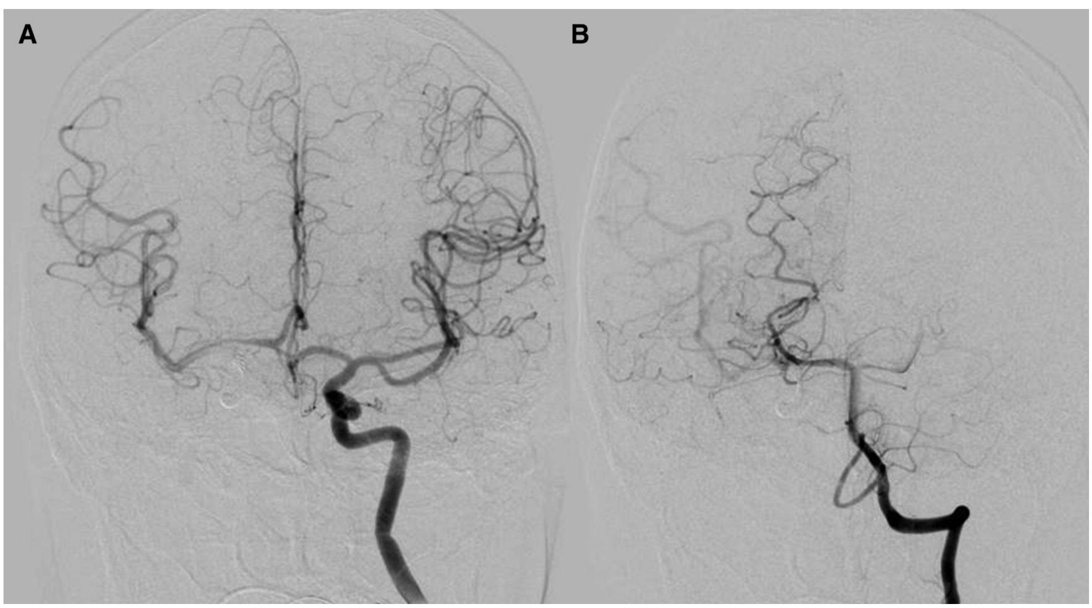

Fig. 6 Frontal view of Lt. carotid angiography (**A**) and Lt. vertebral angiography (**B**) after parent artery occlusion.

as our patient; it is an ideal treatment method. Many studies have demonstrated its safety and efficacy.[7–9] In addition, the results of a meta-analysis involving the comparison of clipping under craniotomy, coil embolization, and treatment using a flow diverter as treatments for ICA paraclinoid aneurysms with optic nerve disorder revealed that the improvement rating for optic nerve disorder after treatment using a flow diverter was significantly higher (clipping under craniotomy: 58%, coil embolization: 49%, and flow diverter: 71%)[10]; treatment with a flow diverter is useful in patients with cranial nerve symptoms.

As a complication related to the deployment of Pipeline, in-stent stenosis has been reported, but its incidence is low.[11–14] According to an article published in 2018 involving patients with in-stent stenosis after the deployment of Pipeline and a systematic review, in-stent stenosis developed in 12 (7.1%) of 155 patients (162 aneurysms) who underwent the deployment of Pipeline.[11] Furthermore, according to a systematic review regarding in-stent stenosis in this article, its mean incidence was 8.8% (0–39%). In 2018, Oishi et al. also reported the results of Pipeline insertion in 94 patients (100 aneurysms); in-stent stenosis developed in one patient.[6] Even when in-stent stenosis is observed after the deployment of Pipeline, it rarely becomes symptomatic, requiring additional treatment.[12] Furthermore, neo-intimal hyperplasia is considered to be an etiological factor for in-stent stenosis. A previous study suggested the involvement of cardiovascular risk factors such as smoking, dyslipidemia, and hypertension.[15]

In the present case, stenosis of the ICA distal to the aneurysm was observed. On initial treatment, angioplasty was performed after the deployment of Pipeline, and stenosis slightly expanded, but restenosis was noted later. The patient had a history of autoimmune hepatitis, but there were no cardiovascular risk factors. Angioplasty on initial treatment slightly expanded stenosis. Based on this condition, we suspected its relationship with the dural ring as the anatomical characteristic of this site, differing from routinely reported in-stent stenosis. Concerning the pathogenesis of low vision before additional treatment, the site of stenosis distal to the aneurysm may have affected blood outflow, influencing the intra-aneurysmal pressure through intra-aneurysmal jet blood flow beyond the Pipeline, thereby leading to optic nerve disorder. Therefore, as additional treatment, we did not selected Pipeline overlapping after the angioplasty. A BOT was conducted, suggesting ischemic tolerance. Thus, we selected parent artery occlusion.

Based on this experience, a BOT must always be conducted before the deployment of Pipeline to confirm the presence of ischemic tolerance in patients with stenosis of a parent blood vessel distal to an aneurysm. If sufficient dilation at the site of stenosis cannot be obtained by angioplasty following the deployment of Pipeline as initial treatment even in the presence of ischemic tolerance, parent artery occlusion should be considered in the phase of initial treatment. On the other hand, if there is no ischemic tolerance, the deployment of Pipeline should not be selected as initial treatment. In such cases, no therapeutic strategy has been established, but bypass-combined parent artery occlusion may be appropriate.

Conclusion

We reported a patient in whom the deployment of Pipeline was performed as initial treatment for a large ICA paraclinoid aneurysm with stenosis of this artery distal to the aneurysm, and in-stent stenosis developed after surgery, rapidly inducing visual disorder. In this patient, cerebral angiography confirmed intra-aneurysmal jet blood flow, suggesting an increase in the intra-aneurysmal pressure, and parent artery occlusion was performed after confirming ischemic tolerance using a BOT, reducing visual disorder. In the future, a BOT must always be conducted before the deployment of Pipeline to confirm the presence of ischemic tolerance when performing the deployment of Pipeline in patients with stenosis of the ICA distal to an aneurysm. If sufficient vasodilation at the site of stenosis cannot be obtained by angioplasty following the deployment of Pipeline even in the presence of ischemic tolerance, parent artery occlusion should be considered in the phase of initial treatment. On the other hand, if there is no ischemic tolerance, bypass-combined parent artery occlusion should be performed without selecting the deployment of Pipeline as initial treatment.

Disclosure Statement

The authors declare no conflict of interest.

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