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Case Report

A Case of Severe Common Carotid Artery Stenosis Who Developed Cerebellar Infarction after Cervical Irradiation

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Objective: We report a case of cerebellar infarction caused by radiation-induced common carotid artery stenosis.
Case Presentation: The patient was a 72-year-old man who underwent irradiation for hypopharyngeal carcinoma 13 years ago. He was referred for asymptomatic left common carotid artery stenosis, but was brought to our hospital by ambulance with transient dysarthria and right facial dysesthesia 2 days after referral. Magnetic resonance imaging (MRI) revealed acute infarction in the left cerebellar hemisphere, and digital subtraction angiography (DSA) demonstrated that the blood flow in the left internal carotid artery perfused the left posterior inferior cerebellar artery (PICA) retrogradely through the left posterior communicating artery. The patient underwent carotid artery stenting (CAS) for left common carotid artery stenosis and blood flow in the left PICA improved; however, in-stent restenosis was revealed during follow-up. Percutaneous transluminal angioplasty (PTA) for in-stent restenosis was performed 9 months after the surgery.
Conclusion: We reported a rare case of ischemia in the PICA area caused by radiation-induced common carotid artery stenosis. Although CAS is recommended for the treatment of radiation-induced carotid artery stenosis, careful treatment and follow-up are needed to prevent perioperative complications and detect in-stent restenosis after CAS.

Keywords ▶ radiation-induced common carotid artery stenosis, cerebellar infarction, carotid artery stenting, in-stent restenosis

Introduction

Following the improvement of the treatment results for the head and neck malignant tumors, postoperative radiotherapy has been selected in many cases. However, post-irradiation carotid artery stenosis has been reported as a late complication related to radiotherapy.[1,2] In this study, we report a case of cerebellar infarction caused by severe common carotid artery stenosis after cervical irradiation and review the literature.

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Case Presentation

The patient was a 72-year-old man. He underwent radiotherapy following surgery for hypopharyngeal cancer 13 years ago. Mild hoarseness and dysphagia remained, but he was independent in his daily life. To treat hypertension, drug therapy was administered at a local clinic. Computed tomography (CT) angiography for detailed examination of peripheral arterial disease demonstrated that the left common carotid artery was 90% area stenosis, although it was asymptomatic, and he was referred to our department. As a dermal finding, slight atrophy of the cervical skin was noted. On brain magnetic resonance angiography (MRA), the vertebrobasilar arteries were poorly visualized and cerebral angiography was scheduled for detailed examination (**Fig. 1a** and **1b**). However, transient dysarthria and right facial dysesthesia were noted 2 days after referral, and he was brought to our hospital by ambulance. The symptoms completely disappeared in 15 minutes. Subsequently, there was no new neurological finding. On diffusion- weighted magnetic resonance imaging (MRI), a high-signal-intensity area in the left cerebellar hemisphere was observed. Visualization of the left internal carotid artery to middle cerebral artery was poorer than on MRA at the time of initial

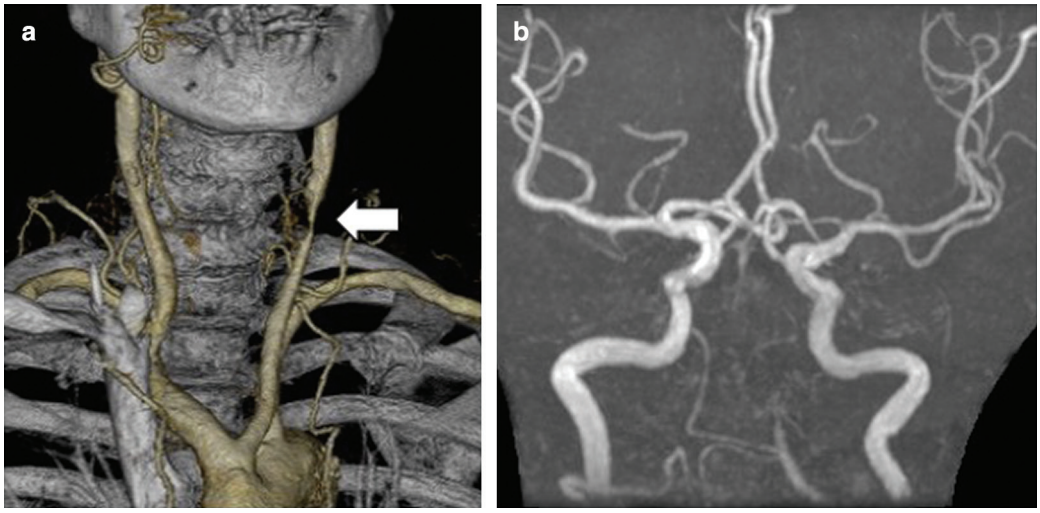

Fig. 1 (**a**) CT angiography and (**b**) MRA on the initial consultation. CT angiography on the initial consultation showed stenosis of the left common carotid artery, with 90% area stenosis (**a**, arrow). On MRA, the vertebrobasilar arteries were poorly visualized (**b**).

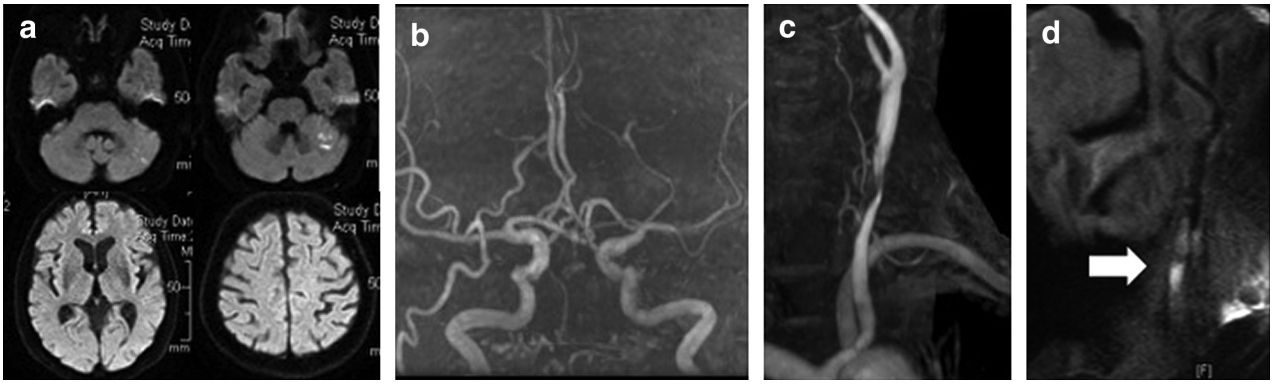

Fig. 2 Brain MRI and MRI of the carotid artery on admission (**a**: diffusion-weighted brain MRI, **b**: brain MRA, **c**: time-of-flight MRI of the carotid artery, **d**: Black blood MRI of the carotid artery). Diffusion-weighted MRI on admission revealed acute ischemic stroke in the left cerebellar hemisphere (**a**). On MRA, visualization of the left internal carotid artery to middle cerebral artery was poorer than on MRA at the time of initial consultation (**b**). Time-of-flight MRI of the carotid artery showed a slightly high signal intensity at the lesion site (**c**). Black blood MRI showed a markedly high signal intensity (**d**, arrow).

consultation (**Fig. 2a** and **2b**). MRI of the carotid artery with the black blood method revealed that plaque of the left common carotid artery comprised a high-brightness lesion, suggesting unstable plaque. The plaque volume was large (**Fig. 2c** and **2d**).

Cerebral angiography was performed. Left common carotid angiography confirmed severe stenosis of the common carotid artery (**Fig. 3a**). The blood flow in the left internal carotid artery perfused the basilar artery to left posterior inferior cerebellar artery (PICA) retrogradely through the left posterior communicating artery. However, the left PICA was poorly visualized due to severe stenosis of the left common carotid artery (**Fig. 3c**). Furthermore, perfusion in the left middle cerebral artery region was reduced (**Fig. 3b**). Congenital hypoplasia of the left vertebral artery was observed and selective left vertebral angiography was difficult; therefore, the left upper arm was pressurized with a manchette for angiography, but the left PICA was not visualized (**Fig. 3d** and **3e**). The right vertebral artery comprised the PICA end (**Fig. 3f** and **3g**). On right common carotid angiography, the fetal-type right posterior communicating artery was visualized, but there was no retrograde blood flow to the basilar artery.

We considered that hemodynamic ischemia of the left PICA related to severe stenosis of the left common carotid artery was an etiological factor for cerebellar infarction based on the following findings: there was no anterograde left PICA blood flow due to congenital hypoplasia of the left vertebral artery; and the blood flow in the left internal carotid artery perfused the left PICA retrogradely through

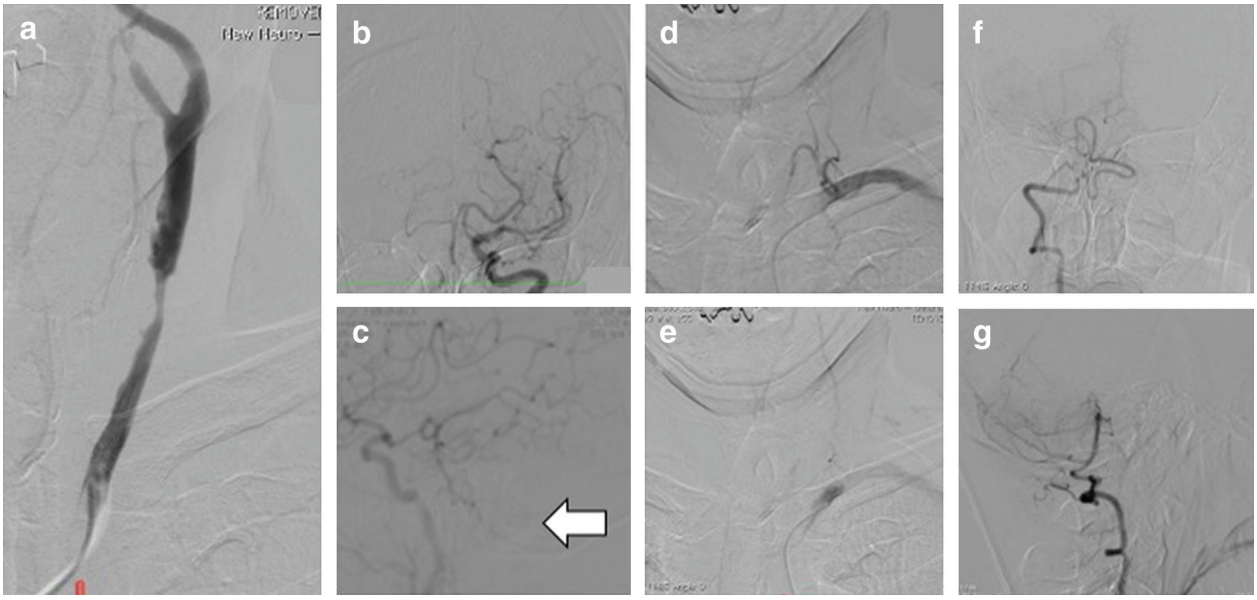

Fig. 3 Cerebral angiography on admission (**a**, **b**: frontal views on left common carotid angiography, **c**: lateral view on left common carotid angiography, **d**, **e**: origin of the left vertebral artery, **f**: frontal view on right vertebral angiography, **g**: lateral view on right vertebral angiography). Left common carotid angiography showed a stenotic lesion of the common carotid artery that was previously detected (**a**). Retrograde blood flow to the basilar artery via the posterior communicating artery was observed. The left PICA was poorly visualized (**b**, **c**, arrow). Angiography at the origin of the left vertebral artery showed congenital hypoplasia of the left vertebral artery (**d**, **e**). Right vertebral angiography revealed that the right vertebral artery comprised the PICA end (**f**, **g**). PICA: posterior inferior cerebellar artery

the left posterior communicating artery. After his admission, we started to treat. Stents were placed in the bilateral common iliac arteries to treat peripheral arterial disease, and aspirin at 100 mg/day and clopidogrel at 75 mg/day were orally administered. Therefore, the oral administration of the two antiplatelet drugs was continued, and sufficient fluid replacement was conducted under resting. There was no new symptom and carotid artery stenting (CAS) was performed 7 days after onset.

Under local anesthesia, the right femoral artery was punctured and an 8-Fr Flow Gate (Stryker Neurovascular, Fremont, CA, USA) was guided into the left common carotid artery coaxially with a 5-Fr MSK (Medikit, Tokyo, Japan) (**Fig. 4a**). Under proximal balloon protection, a FilterWire EZ (Boston Scientific, Natick, MA, USA) was carefully passed through the lesion site and deployed. Only at the time of lesion-site passage, the proximal balloon was dilated and flow reversal was induced through aspiration with a syringe. After deploying the FilterWire EZ, the procedure was performed under distal filter protection alone. The lesion measured 2.5 mm at the most stenotic site, with central- and peripheral-side common carotid artery diameters of 8.5 and 8.5–9.0 mm, respectively. The lesion length involving from proximal to distal ulcers was approximately 55 mm. Predilatation with a Sterling 3.5 mm × 20 mm (Boston Scientific) was conducted and two Carotid Wall Stents 8 mm × 21 mm (Boston Scientific) were overlapped/placed (**Fig. 4b**) Subsequently, postdilatation with a Sterling 5.5 mm × 20 mm (Boston Scientific) was conducted. Digital subtraction angiography (DSA) confirmed the absence of plaque protrusion after stenting. Left common carotid angiography confirmed the improvement of stenosis at the lesion site and favorable visualization of the left PICA, and the procedure was completed (**Fig. 4c** and **4d**).

Diffusion-weighted MRI the day after surgery demonstrated asymptomatic microinfarction in the left cerebral hemisphere, but visualization of the left internal carotid artery to middle cerebral artery was favorable on MRA (**Fig. 5a** and **5b**). The course was favorable and the patient was discharged 8 days after surgery. After discharge, the oral administration of the two antiplatelet drugs was continued and follow-up was conducted using carotid ultrasonography. On examination 6 months after surgery, in-stent plaque was not observed and the peak systolic flow velocity (PSV) of the common carotid artery was 107 cm/s. However, carotid ultrasonography 8 months after surgery revealed isoechoic in-stent plaque, with a PSV of 319 cm/s. Under a diagnosis of restenosis, the oral administration of the two antiplatelet drugs was continued and percutaneous transluminal angioplasty (PTA) was performed via a right brachial approach 9 months after surgery.

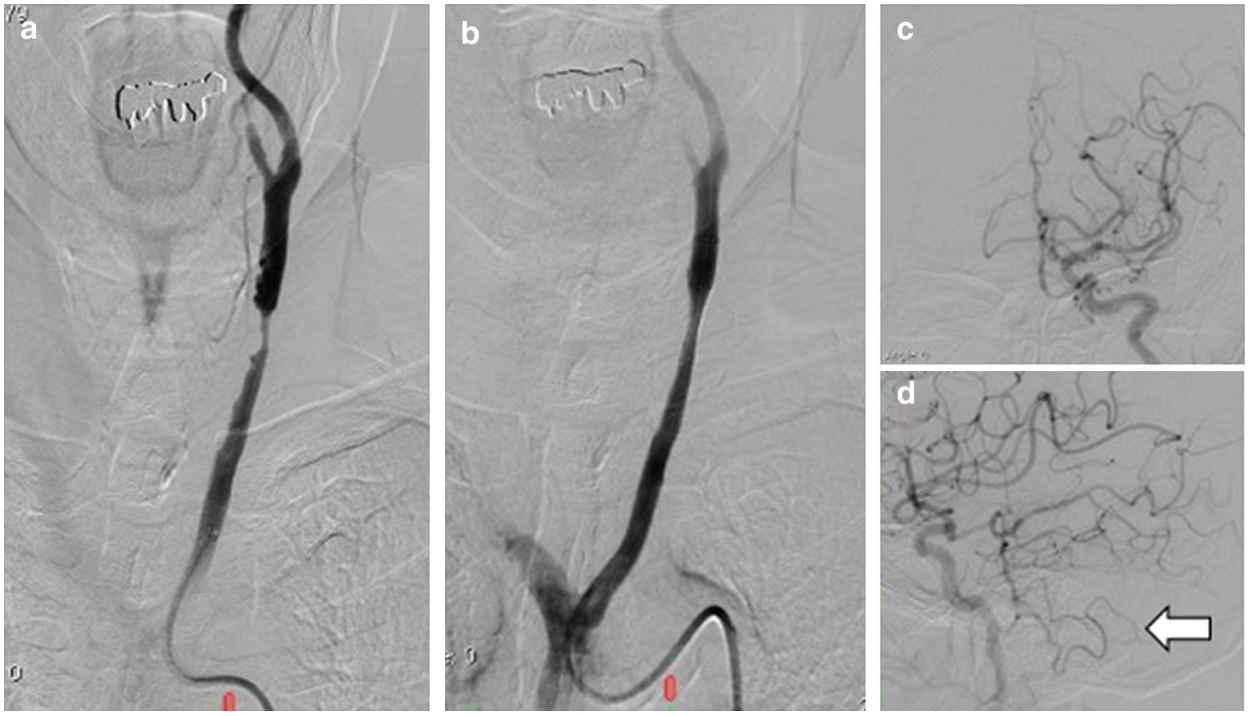

Fig. 4 CAS (**a**: before treatment, **b**: after treatment, **c**: posttreatment frontal view on left common carotid angiography, **d**: posttreatment lateral view on left common carotid angiography). Two Carotid Wall Stents were inserted, reducing stenosis (**a**, **b**). Improvements in intracranial perfusion/the visualization of the left PICA in comparison with those before treatment were confirmed (**c**, **d**, arrow). CAS: carotid artery stenting; PICA: posterior inferior cerebellar artery

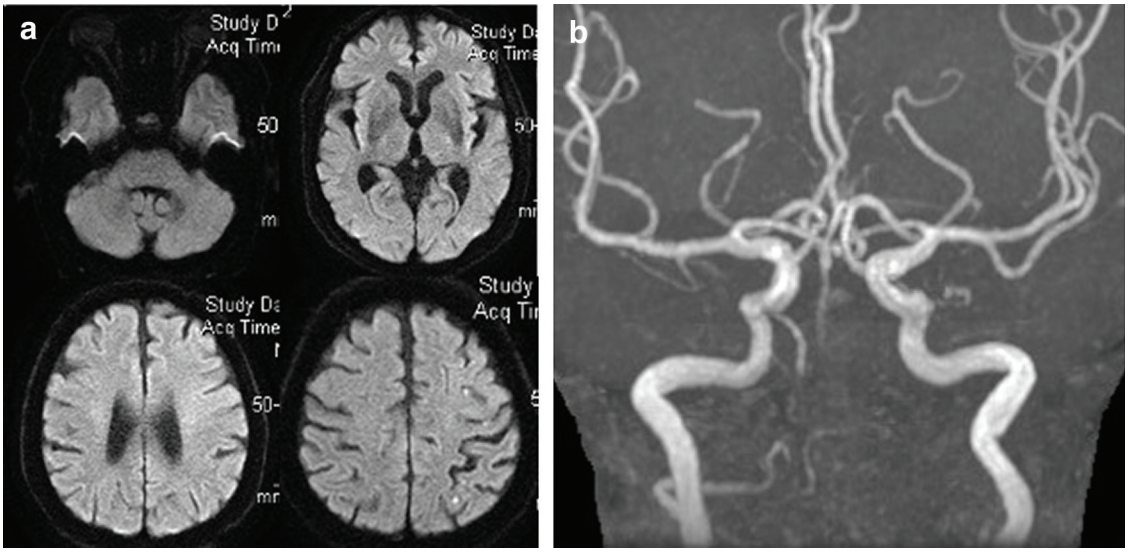

Fig. 5 MRI the day after treatment (**a**: diffusion-weighted MRI, **b**: MRA). Diffusion-weighted MRI the day after treatment showed embolic microinfarction in the left cerebral hemisphere (**a**). On MRA, the visualization of the left internal carotid artery to middle cerebral artery was better than on MRA before treatment (**b**).

Under local anesthesia, a 6-Fr Axcel Guide MSK (Medikit) was guided into the left common carotid artery coaxially with a 5-Fr MSK (Medikit) (**Fig. 6a**). Left common carotid angiography revealed hypoperfusion of the left PICA related to left common carotid artery stenosis. A FilterWire EZ (Boston Scientific) was carefully passed through the lesion site and deployed. PTA was performed using a Sterling 4.0 mm × 20 mm (Boston Scientific). As dilatation was insufficient, the Sterling was switched to a Sterling 6.0 mm × 20 mm (Boston Scien-

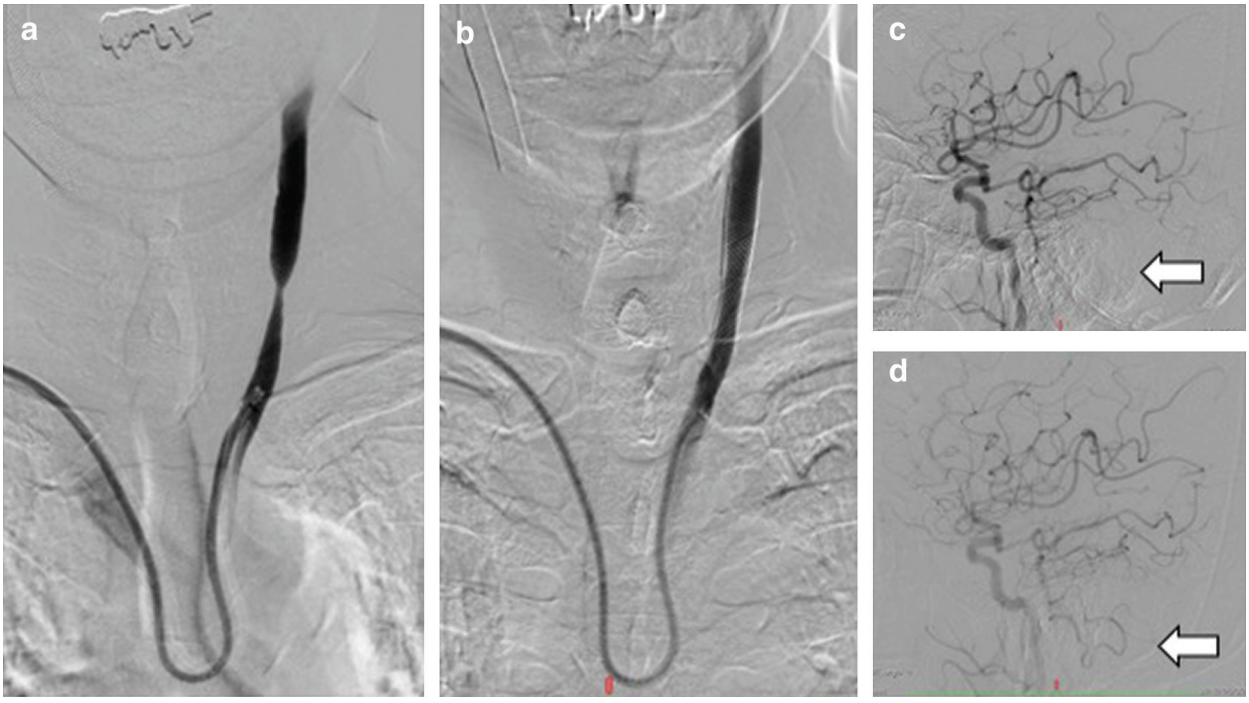

Fig. 6 PTA (**a**: before treatment, **b**: after treatment, **c**: pretreatment lateral view on left common carotid angiography, **d**: posttreatment lateral view on left common carotid angiography). Dilatation with a Sterling reduced stenosis (**a**, **b**). Improvement in the visualization of the left PICA in comparison with that before treatment was confirmed (**c**, **d**, arrow). PICA: posterior inferior cerebellar artery; PTA: percutaneous transluminal angioplasty

tific) and PTA was conducted again (**Fig. 6b**). After confirming the improvement of stenosis at the lesion site and favorable visualization of the left PICA, the procedure was completed (**Fig. 6c** and **6d**).

The postoperative course was favorable and there was no new neurological finding. The patient was discharged. Follow-up is still conducted at the outpatient clinic.

Discussion

Post-irradiation carotid artery stenosis is a known complication, but its mechanism remains to be clarified. Concerning the physiopathology of this disorder, Louis et al.[3] proposed the following mechanism: irradiation-related vasa vasorum disturbance induces ischemia of the elastic tissue or muscle fibers, being replaced by the fibrous tissue, the adventitia is then replaced by fibrous tissue, leading to the progression of arteriosclerotic changes through fibrous thickening. A recent study suggested the irradiation-related vascular endothelial cell injury causes inflammatory changes, inducing ischemic or fibrous changes of the media/adventitia.[4] As a risk factor, Cheng et al.[5] proposed the interval from irradiation. They reported that the risk of carotid artery stenosis progression in patients with an interval of ≥5 years after cervical irradiation was 8.5 times higher than that in those with an interval of <5 years. Furthermore, they reported that risk factors for severe carotid artery stenosis after irradiation included age, smoking, heart disease, and previous surgery for tumors as a primary disease.[6]

Regarding treatment, CAS is selected as a first-choice procedure in many cases, considering carotid endarterectomy (CEA)-related risks such as post-irradiation adhesion, nerve injury, and wound-site complications.[7] Several studies compared the results of CEA for post-irradiation carotid artery stenosis with those of CAS. Giannopoulos et al.[8] reported that the incidence of nerve injury after CEA was higher as a complication than after CAS within 30 days after surgery, and that there were no differences in the incidence of stroke or myocardial infarction, or mortality rate between the two procedures. Concerning the long-term outcome (mean follow-up: 50 months), the mortality rate was lower in the CEA group, whereas the incidence of restenosis was similar. On the other hand, another study reported that the incidence of stroke during long-term follow-up was higher in the CAS group.[9] Regarding the properties of plaque, according to a previous study,[10] symptomatic carotid artery stenosis after irradiation is characterized by unstable plaque in many cases and some lesions involve the central side of the common carotid artery; long lesions with a large volume of plaque. Based

on these studies, preoperative strategies must be carefully reviewed in patients with long lesions and/or a large volume of plaque even when performing CAS.

In the present case, the right vertebral artery comprised the PICA end and congenital hypoplasia of the left vertebral artery was noted. The blood flow in the left internal carotid artery perfused the basilar artery to left PICA retrogradely through the left posterior communicating artery, exhibiting rare hemodynamics. Hemodynamic cerebral ischemia involving the left PICA region initially occurred and we considered treatment to be indicated. Preoperative MRI of the carotid artery with the black blood method revealed a large volume of unstable plaque, and the lesion involved the central side of the common carotid artery; therefore, CAS was selected, also considering anatomical factors.

Concerning treatment, the risk of distal embolism was considered due to a large volume of unstable plaque. Furthermore, the bifurcation of the left common carotid artery comprised a bovine arch according to preoperative images, suggesting the difficulty of guiding a guiding catheter and instability of a guiding catheter during the procedure. Considering the risk of distal embolism for unstable plaque, the procedure under combined proximal and distal balloon protection was ideal. However, the hemodynamics in the present case suggested that the ischemic tolerance of the brain was low and the procedure was performed under distal filter protection because anterograde blood flow can be maintained during the procedure. Parodi et al.[11] reported the usefulness of the "seat belt and air bag" technique, in which the common/external carotid arteries are blocked only when a filter device passes through the lesion site, flow reversal is promoted through aspiration with a syringe, and the procedure is carried out while maintaining anterograde blood flow by releasing blockage after deploying the filter device in patients with contralateral carotid artery occlusion or severe collateral-pathway-free stenosis of the internal carotid artery. In the present case, in reference to this technique, the balloon of a guiding catheter was dilated for transient anterograde blood flow blockage when a FilterWire EZ passed through the lesion site, and aspiration was performed using a syringe during blockage to prevent plaque scattering. After deploying the FilterWire EZ, the balloon of the guiding catheter was shrunk and the procedure was performed while maintaining anterograde blood flow. Furthermore, the guiding catheter was anchored to the common carotid artery by dilating its balloon at an appropriate time on guiding-catheter insertion or stent deployment to prevent guiding-catheter slipping.

In the present case, the most stenotic site measured 2.5 mm and a PTA balloon for predilatation measuring 3.5 mm × 20 mm, larger than the size of the most stenotic site, which facilitates stent passage, was selected. However, when it passed through the origin of the left common carotid artery, the guiding catheter was kicked back. Regarding stent-size selection, a diameter of 10 mm was considered appropriate based on the diameter of the normal common carotid artery. Before surgery, the guiding catheter was expected to be unstable and we should have confirmed its instability by inserting only a stent measuring 10 mm in diameter through the guiding catheter prior to treatment. If the guiding catheter were kicked back, we should have switched the approach to a trans-brachial approach to examine the stability of the guiding catheter. However, based on the motion of the PTA balloon for predilatation, we selected a stent size of 8.0 mm (undersize) in diameter × 21 mm (shortest length). Due to the long lesion with unstable plaque, two closed-cell stents were used for the stent-in-stent technique. Myouchin et al.[12] reported the usefulness of the stent-in-stent technique with closed-cell stents for carotid artery stenosis with unstable plaque. They defined plaque with a signal intensity ratio of >1.25 to the sternocleidomastoid muscle as unstable using the MRI black blood method, and stated that the application of the stent-in-stent technique for lesions with unstable plaque reduced the free-cell size of a stent, suggesting its usefulness for the prevention of plaque protrusion. In the present case, the stent-in-stent technique with closed-cell stents was also selected and there was no postoperative ischemic complication, leading to a favorable course. Furthermore, a previous study reported that postdilatation induced the development of debris, causing symptomatic embolism in many cases.[13] In the present case, excessive postdilatation was avoided and a balloon size of 5.5 mm × 20 mm, corresponding to approximately 60% of the diameter of the normal common carotid artery, was selected.

Concerning the mid- to long-term results of CAS for carotid artery stenosis after irradiation, restenosis may occur. Ting et al.[14] reported that angioplasty/stenting for long lesions caused restenosis. As a mechanism of restenosis, hyperplasia of smooth muscle cells may be involved,[15] but post-CAS restenosis is reportedly asymptomatic in many cases. In the present case, CAS was performed based on the above therapeutic strategy. However, stents measuring 8 mm (undersize) in diameter were used and the stent-in-stent technique with closed-cell stents was selected; this may have led to restenosis. As described above, the instability

of the guiding catheter was expected before surgery and we should have sufficiently reviewed a therapeutic strategy to adopt stents measuring 10 mm in diameter, appropriate for the lesion in the present case. Furthermore, another study found that restenosis was more frequent when the percent residual stenosis after CAS was higher.[16] Residual stenosis after initial CAS may have led to restenosis. In the present case, additional treatment was conducted considering the risk of recurrent hemodynamic posterior circulation ischemia. There were other treatment options: angioplasty and the stent-in-stent technique. However, for the stent-in-stent technique, a total of three stents must be inserted and there was a possibility of the stents themselves exacerbating the percent stenosis; therefore, angioplasty was selected. Concerning the timing of additional treatment, the difficulty of treatment must be carefully considered in individual patients, as the purpose of treatment is to prevent recurrent cerebral infarction.

Conclusion

We reported a case of cerebellar infarction caused by radiation-induced severe common carotid artery stenosis for which CAS was performed, restenosis developed during follow-up, and additional treatment was conducted. For the treatment of carotid artery stenosis after irradiation of the head and neck, CAS is recommended, but therapeutic strategies must be carefully established based on the volume and properties of plaque, considering the risk of perioperative complications. Furthermore, postoperative restenosis may develop, and careful posttreatment follow-up and prompt treatment intervention should be necessary.

Disclosure Statement

The authors declare no conflicts of interest.

References

1) Bowers DC, McNeil DE, Liu Y, et al: Stroke as a late treatment effect of Hodgkin's Disease: a report from the Childhood Cancer Survivor Study. *J Clin Oncol* 2005; 23: 6508–6515.
2) Dorresteijn LD, Kappelle AC, Boogerd W, et al: Increased risk of ischemic stroke after radiotherapy on the neck in patients younger than 60 years. *J Clin Oncol* 2002; 20: 282–288.
3) Louis EL, McLoughlin MJ, Wortzman G: Chronic damage to medium and large arteries following irradiation. *J Can Assoc Radiol* 1974; 25: 94–104.
4) Plummer C, Henderson RD, O'Sullivan JD, et al: Ischemic stroke and transient ischemic attack after head and neck radiotherapy: a review. *Stroke* 2011; 42: 2410–2418.
5) Cheng SW, Wu LL, Ting AC, et al: Irradiation-induced extracranial carotid stenosis in patients with head and neck malignancies. *Am J Surg* 1999; 178: 323–328.
6) Cheng SW, Ting AC, Lam LK, et al: Carotid stenosis after radiotherapy for nasopharyngeal carcinoma. *Arch Otolaryngol Head Neck Surg* 2000; 126: 517–521.
7) Yadav JS, Wholey MH, Kuntz RE, et al: Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004; 351: 1493–1501.
8) Giannopoulos S, Texakalidis P, Jonnalagadda AK, et al: Revascularization of radiation-induced carotid artery stenosis with carotid endarterectomy vs. carotid artery stenting: A systematic review and meta-analysis. *Cardiovasc Revasc Med* 2018; 19: 638–644.
9) Tallarita T, Oderich GS, Lanzino G, et al: Outcomes of carotid artery stenting versus historical surgical controls for radiation-induced carotid stenosis. *J Vasc Surg* 2011; 53: 629–636.e1–5.
10) Cheng SW, Ting AC, Wu LL: Ultrasonic analysis of plaque characteristics and intimal-medial thickness in radiation-induced atherosclerotic carotid arteries. *Eur J Vasc Endovasc Surg* 2002; 24: 499–504.
11) Parodi JC, Schönholz C, Ferreira LM, et al: "Seat belt and air bag" technique for cerebral protection during carotid stenting. *J Endovasc Ther* 2002; 9: 20–24.
12) Myouchin K, Takayama K, Wada T, et al: Carotid artery stenting using a closed-cell stent-in-stent technique for unstable plaque. *J Endovasc Ther* 2019; 26: 565–571.
13) Ackerstaff RG, Suttorp MJ, van den Berg JC, et al: Prediction of early cerebral outcome by transcranial Doppler monitoring in carotid bifurcation angioplasty and stenting. *J Vasc Surg* 2005; 41: 618–624.
14) Ting AC, Cheng SW, Yeung KM, et al: Carotid stenting for radiation-induced extracranial carotid artery occlusive disease: efficacy and midterm outcomes. *J Endovasc Ther* 2004; 11: 53–59.
15) Fokkema M, den Hartog AG, Bots ML, et al: Stenting versus surgery in patients with carotid stenosis after previous cervical radiation therapy: systematic review and meta-analysis. *Stroke* 2012; 43: 793–801.
16) Clark DJ, Lessio S, O'Donoghue M, et al: Mechanisms and predictors of carotid artery stent restenosis: a serial intravascular ultrasound study. *J Am Coll Cardiol* 2006; 47: 2390–2396.