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Case Report

Endovascular Treatment for Basilar Artery Occlusion Caused by Radiation-induced Vertebral Artery Stenosis: Case Report

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Objective: We report endovascular treatment of a patient with acute basilar artery occlusion considered to be due to an embolus from radiation-induced vertebral artery stenosis.

Case Presentation: The patient was a 46-year-old male with a history of neck irradiation. He developed basilar artery occlusion. Temporary recanalization achieved by intravenous alteplase therapy and revascularization was followed by relapse. The origin of the vertebral artery was stenosed, and basilar artery was considered to have been embolized by a thrombus formed on the proximal side of the vertebral artery, where blood flow was stagnated due to reduced antegrade flow from the distal side of the stenotic vertebral artery and the increased collateral flow from the deep cervical artery. Recurrence of cerebellar infarction could be prevented by revascularization and occlusion of the parent artery.

Conclusion: Acute basilar artery occlusion considered to be due to an embolus from radiation-induced vertebral artery stenosis is a rare condition, but it must be recognized as a possible cause of posterior circulation infarction.

Keywords ▶ radiation therapy, vertebral artery stump syndrome, basilar artery occlusion, thrombectomy

Introduction

One cause of posterior circulation infarction is embolism due to a thrombus formed by acute occlusion at the origin of the vertebral artery. This condition, called vertebral artery stump syndrome, has been reported to be likely to recur and have a poor functional prognosis.[1–3] Occlusion at the origin of the vertebral artery is considered to be caused by disorders including atherosclerosis, aortitis syndrome, vertebral artery dissection, and trauma.[4–6] While it is most often caused by atherosclerosis, radiation-induced cases have also been reported.[7,8]

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We treated a case of basilar artery occlusion due to vertebral artery stump syndrome considered to have been caused by radiation-induced stenosis at the origin of the vertebral artery by two steps of endoscopic treatment.

Case Presentation

The patient was a 46-year-old male who presented with dysarthria, numbness of the bilateral upper extremities, and dizziness. He had undergone radiotherapy for nasopharyngeal carcinoma at 66 Gy/33 Fr in X-9 (**Fig. 1A**). He was irradiated from the bilateral clavicular regions to the neck. Bilateral vertebral artery stenosis was detected in May X (**Fig. 1B** and **1C**), and oral antiplatelet therapy (clopidogrel) was initiated. Concerning atherosclerotic risk factors, he had no hypertension, diabetes, dyslipidemia, or smoking history.

Course of the present illness: At 7:30 on November Y, X, the patient suddenly developed dysarthria, numbness of the bilateral upper extremities, and dizziness and was transported to a local hospital. He was rated as E3V4M6 by the Glasgow Coma Scale (GCS) and showed paralysis of the left upper and lower extremities, dysarthria, and oculomotor dysfunction. The National Institute of Health

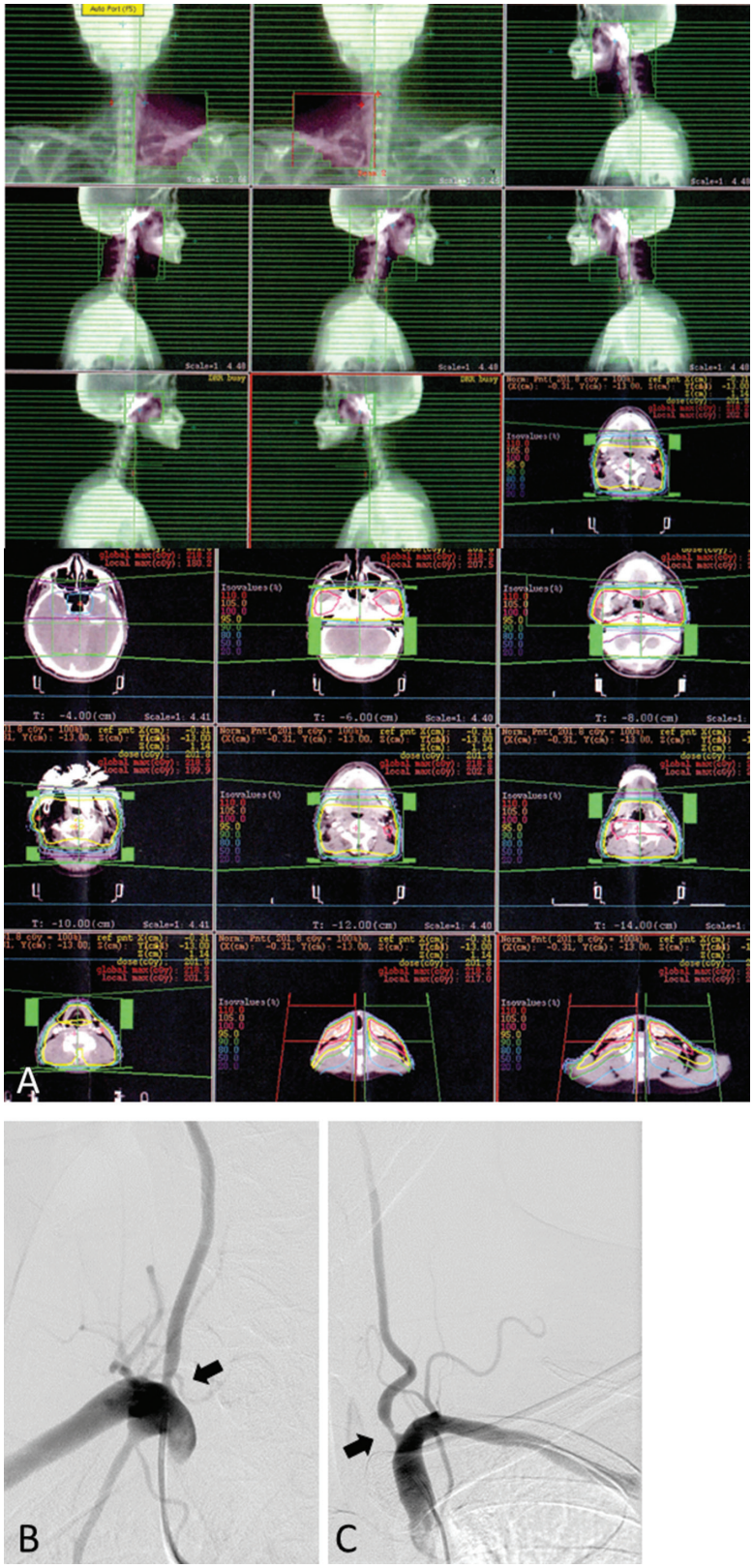

Fig. 1 (**A**) Radiotherapy plan for nasopharyngeal cancer. Irradiation was made to the bilateral clavicular regions. (**B**) Anterior-posterior view of the right subclavian angiogram (May X). Mild stenosis is observed at the origin of the right vertebral artery (arrow). (**C**) Anterior-posterior view of the left subclavian angiogram (May X). Moderate stenosis was observed in the left vertebral artery (arrow).

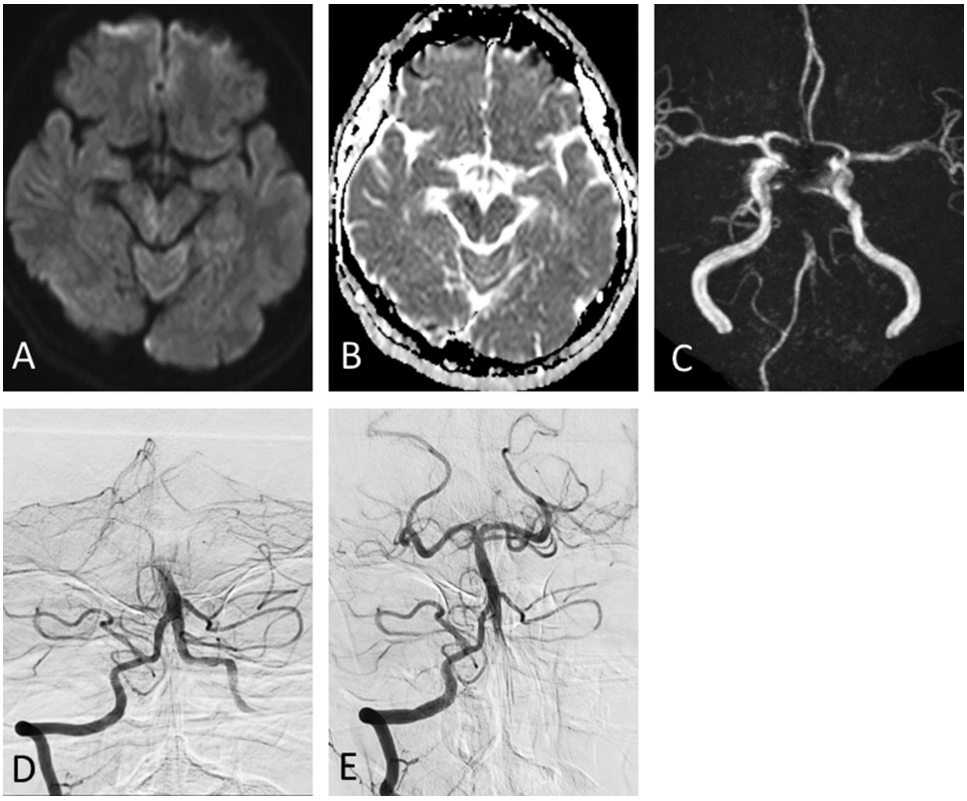

Fig. 2 (**A–C**) MRI at emergency transport (**A**) diffusion-weighted image, (**B**) apparent diffusion coefficient and MRA (**C**). MRI showed acute infarction in the right midbrain, and MRA showed occluded basilar artery and left vertebral artery. (**D**) Anterior-posterior view of the right vertebral angiogram after t-PA administration. The basilar artery trunk was occluded. (**E**) Anterior-posterior view of the right vertebral angiogram after revascularization. The basilar artery was recanalized (TICI 2b). t-PA: tissue plasminogen activator; TICI: thrombolysis in cerebral infarction

Stroke Scale (NIHSS) score was 17. Electrocardiogram (ECG) showed no arrhythmia. Plain MRI of the head by diffusion weighted image (DWI) showed mild hyperintensity in the right midbrain, and hypointensity was noted in the same region by apparent diffusion coefficient (ADC) mapping (**Fig. 2A** and **2B**). On MRA, delineation of the left vertebral and basilar arteries was poor (**Fig. 2C**). A diagnosis of acute infarction of the right midbrain due to basilar artery occlusion was made, intravenous thrombolysis with recombinant tissue plasminogen activator (t-PA) therapy was initiated 122 minutes after the onset, and the patient was transported to our hospital.

Neurologic findings on admission: The level of consciousness was GCS E4V4M6. Incomplete palsy of the extremities, impaired adduction of the right eye, impaired abduction of the left eye, severe left facial paralysis, and dysarthria were observed, and the NIHSS score was 10.

Blood chemistry tests: The platelet count was $36 \times 10^4/\mu L$, fibrin degradation product (FDP) level was 10.4 μg/mL, and D-dimer level was 5.1 μg/mL.

Angiography: At the origin of the right vertebral artery, 50% stenosis was demonstrated, the left vertebral artery was retrogradely contrasted at the vertebrobasilar union, and the tip of the basilar artery was occluded. Vascular dissection at the origin of the left vertebral artery could not be completely excluded, but as no false lumen or irregularity of the vascular wall suggestive of dissection was noted, a diagnosis of pseudo-occlusion due to marked stenosis was made.

First endovascular treatment: He was indicated for revascularization, and, after systemic heparinization (5000 units), a 6 Fr. Envoy guiding catheter (Johnson & Johnson, Miami, FL, USA) was placed in the right vertebral artery using a coaxial system via the right femoral artery. A Marksman catheter (eV3; Covidien, Irvine, CA, USA) was guided to the right posterior cerebral artery, and Solitaire FR 4 mm × 20 mm (eV3) was deployed from the right posterior cerebral artery to the basilar artery. Intermediate flow restoration (IFR) was confirmed, and the stent was retrieved, resulting in retrieval of a soft thrombus.

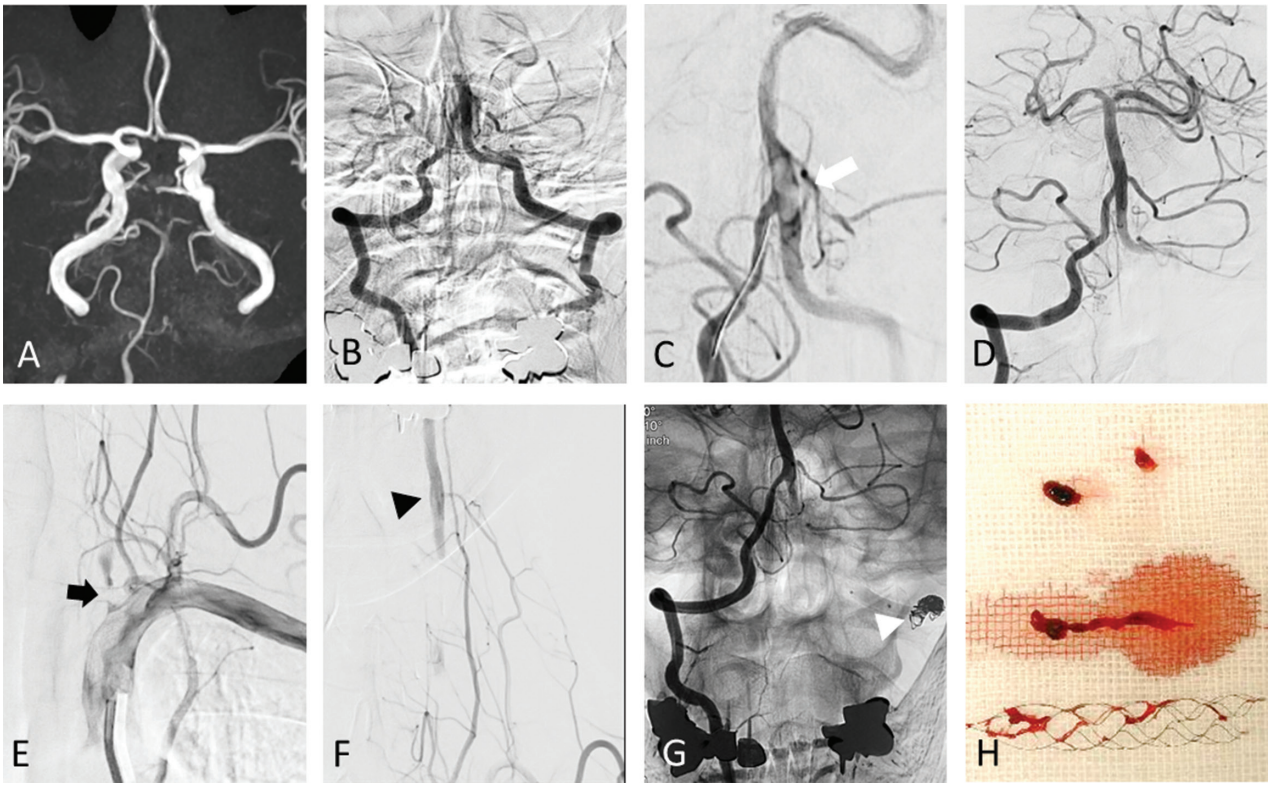

Fig. 3 (**A**) MRA at recurrence. The basilar artery was re-occluded. (**B**) Anterior-posterior view of the right vertebral angiogram. The trunk of the basilar artery was occluded. (**C** and **D**) Revascularization. When the stent retriever was deployed, a filling defect due to thrombus was observed from the left vertebral artery to the basilar artery (**C**) white arrow. The trunk of the basilar artery was recanalized (**D**). (**E** and **F**) Anterior-posterior view of the left subclavian angiogram. Pseudo-occlusion was noted at the origin of the left vertebral artery (**E**) black arrow. Antegrade blood flow of the left vertebral artery stagnated by collaterals via the deep cervical artery was observed (**F**) black arrowhead. (**G**) Anterior-posterior view of the right vertebral angiogram after parent artery occlusion of the left vertebral artery. Parent artery occlusion of the left vertebral artery was performed from the right vertebral artery via the union (white arrowhead). (**H**) Retrieved red thrombus.

The basilar artery could be recanalized, and the procedure was ended with thrombolysis in cerebral infarction (TICI) grade 2b (**Fig. 2D** and **2E**).

Postprocedural course: The NIHSS score improved to 3 immediately after the procedure. Occlusion of the basilar artery was suspected to be caused by stump syndrome from the origin of the left vertebral artery, but pseudo-occlusion of the origin of the left vertebral artery was treated conservatively (heparin administration). After revascularization, no exacerbation of neurologic symptoms or arrhythmia was noted. However, at about 9:40 on November Y + 1, exacerbation of neurologic symptoms with GCS scores of E1V2M3 and a NIHSS score of 27 was observed. Plain MRI of the head showed new foci of infarction in the thalamus, brainstem, and bilateral cerebellar hemispheres, and MRA confirmed occlusion of the basilar artery (**Fig. 3A**).

Second endovascular treatment: After systemic heparinization (5000 units), a 6 Fr. Roadmaster (Goodman, Aichi, Japan) was guided to the right vertebral artery using a coaxial system via the left femoral artery. Similar to the previous treatment, the basilar artery was occluded from the trunk to the tip. A Marksman was guided to the left posterior cerebral artery across the site of occlusion, and when a Solitaire FR 4 mm × 20 mm was deployed from the left posterior cerebral artery to the basilar artery, IFR was confirmed. A filling defect due to thrombus was noted from the left vertebral artery to the basilar artery, and TICI 3 recanalization was obtained by retrieving the stent (**Fig. 3B–3D**). As for the cause of embolism, since arrhythmia was not confirmed, and since angiography showed stagnation of blood flow from the distal side of the stenosed area of the vertebral artery to the anastomosis of the deep cervical artery, this area was diagnosed to be the source of the embolus (**Fig. 3E** and **3F**). Occlusion of the parent artery was planned to treat the left vertebral artery as the site of thrombus formation. Excelsior SL-10 (Stryker Neurovascular, Kalamazoo, MI, USA) was inserted retrogradely to the left vertebral artery from the right vertebral artery and guided to the V3 segment. The parent artery of the left vertebral artery was occluded by

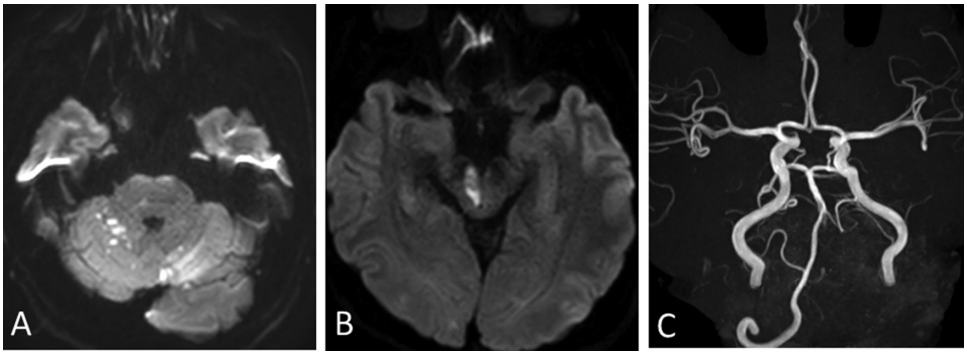

Fig. 4 (**A** and **B**) Diffusion-weighted MRI after treatment. Infarction was observed in the cerebellum and brainstem. (**C**) MRA after treatment. The basilar artery was recanalized, and the left vertebral artery was occluded.

inserting three Hydrosoft 4 mm × 10 cm (Terumo Corporation, Tokyo, Japan), three Hydrosoft 3 mm × 10 cm, and one 2.5 mm × 6 cm coils (**Fig. 3G**). The retrieved thrombus was a relatively fresh red thrombus that consisted primarily of red blood cells and fibrin, contained a small number of neutrophils, but was generally poor in cell components (**Fig. 3H**).

Postprocedural course: After the procedure, the NIHSS score improved to 4. Postprocedural MRI showed multiple infarction in the bilateral cerebellar hemispheres, midbrain, and right thalamus, but no new infarction due to basilar artery occlusion were detected after the second treatment (**Fig. 4A** and **4B**). Also, occlusion of the left vertebral artery and recanalization of the basilar artery were confirmed by MRA (**Fig. 4C**). Anticoagulant therapy using heparin was performed after the procedure. Since the D-dimer level improved, and since no recurrence of cerebellar infarction was noted, anticoagulant therapy was ended on the 5th postprocedural day. No recurrence of infarction was noted 3 months after the onset. Dysarthria and cerebellar ataxia persisted, and the modified Rankin Scale score 3 months after the onset was 3.

Discussion

In vertebral artery stump syndrome, thrombus is induced in the vertebral artery after occlusion at its origin by stagnation of blood flow on the proximal side of the occluded area due to collaterals such as those from the deep cervical artery, and embolic infarction occurs in the vertebrobasilar system.[1–3] It accounts for only 1.4% of the causes of infarction of the posterior circulation territory, but there has been a report that its recurrence rate is high at 25% and that the functional outcome is poor in 25%.[3] In our patient, pseudo-occlusion was observed at the origin of the left vertebral artery, and embolism is considered to have been caused by a thrombus formed on the distal side of the occluded artery and carried by blood flow via collaterals.

It is widely known that stenotic or occlusive lesions may develop in head and neck blood vessels after irradiation of the head and neck region. Such lesions occur mostly in the carotid artery, being reportedly observed in 12%–36% of the patients who underwent radiotherapy for head and neck cancer.[9–11] Although the pathogenic mechanism of vascular stenosis after radiotherapy has not been elucidated, damage of the elastic membranes, intimal thickening, plaque formation, and fibrosis as well as hyalinization of the vascular wall and formation of atheromatous plaques in the intima, leading to structural change of elastic fibers and muscle fibers in the artery and resulting in fibrosis, have been reported by animal experiments.[12,13] The period until the development of carotid artery stenosis or cerebral infarction after radiotherapy of the head and neck has been reported to be about 10 years or longer.[9,10] Regarding the irradiation dose, atheroma formation is reportedly promoted at 40 Gy or above.[9] Lam et al.[14] evaluated vascular stenosis using ultrasonography after radiotherapy for head and neck tumors and reported that 50% or severer carotid artery stenosis was observed in 29.6% of the patients but that vertebral artery stenosis was rare, being noted in only 5.6%. On the other hand, Zhou et al.[15] evaluated the presence or absence of vascular stenosis using contrast-enhanced MRA in 72 patients 3 years or longer after radiotherapy for nasopharyngeal cancer and reported that 50% or severer carotid artery stenosis was noted in 37.5% and that vertebral artery stenosis was noted in 34.7%, suggesting that the latter is not a rare condition. While the common carotid artery stenosis is a frequent

carotid artery lesion observed after radiotherapy of the head and neck, no characteristic findings have been reported regarding vertebral artery lesions.[16] In addition, stenosis after radiotherapy has been reported to progress more rapidly than atherosclerotic lesions.[17] Prefasi et al.[7] reported a patient who suffered cerebral infarction due to vertebral artery stenosis 20 years after radiotherapy for nasopharyngeal cancer at 70 Gy. Miyahara et al.[8] also reported a patient who underwent vascular surgery for bilateral vertebral artery stenosis that occurred 11 years after radiotherapy for nasopharyngeal cancer at 65 Gy. Our patient had no risk factor for atherosclerosis, and atherosclerosis was considered unlikely to be the cause of vertebral artery stump syndrome. The differential diagnosis of whether occlusion is caused by vertebral artery dissection or vertebral artery origin stenosis is difficult by cerebral angiography alone, but we diagnosed that the possibility of vertebral artery stump syndrome due to radiation-induced stenosis of the vertebral artery origin was high because the patient had no history of trauma, had undergone radiotherapy for head and neck cancer at 66 Gy, and had been known to have stenosis at the origin of the left vertebral artery. Although the carotid artery was included in the irradiation area, no carotid artery stenosis was noted. Since there is a possibility of future stenosis, periodic follow-up is considered necessary.

Cerebral embolism may be cardiogenic or caused by conditions that invite embolism such as Trousseau syndrome and heparin-induced thrombocytopenia (HIT). Cardiogenic embolism was excluded because no arrhythmia was detected by ECG monitoring. HIT was also excluded because the patient developed infarction before heparin administration. An involvement of Trousseau syndrome could not be excluded because clotting abnormalities such as increases in FDP and D-dimer were observed. However, as there was no finding suggestive of recurrence of nasopharyngeal cancer, the possibility of its involvement was considered low.[18,19]

There have been no reports to our knowledge about revascularization for cerebellar embolism due to vertebral artery stump syndrome. Stenotic lesions that can be approached from the contralateral side are treated from the contralateral side. If the lesion is impossible to approach, angioplasty is performed first, but, in this event, measures to prevent distal embolism must be taken. As treatment for the prevention of recurrence of vertebral artery stump syndrome, antiplatelet therapy, anticoagulant therapy, and endovascular treatment have been reported, but antiplatelet therapy is not considered very effective. Anticoagulant therapy is reported by Kawano et al.[3] to be effective, but recurrence was observed in 3 of the 11 patients administered heparin, and sufficient management of anticoagulation is necessary. Reports regarding endovascular treatment are few, and it should be performed in patients who have suffered recurrence even by anticoagulant therapy.[1,2] Nguyen et al. reported occlusion of the parent artery via collaterals or from the contralateral vertebral artery (VA) via the union.[1] In our patient, occlusion of the parent artery was performed in the left vertebral artery for the prevention of recurrence after thrombectomy. We considered stenting of the origin of the left vertebral artery, but we selected occlusion of the parent artery for greater safety and consistency because the distal end of stenosis could not be confirmed. In parent artery occlusion for vertebral artery stump syndrome, a point of attention is that embolization must be performed after locating the site of anastomosis with the vertebral artery because new stump syndrome may develop if embolization is performed on the proximal side of the site of anastomosis of vessels that can serve as collaterals such as the occipital artery.

Although vertebral artery stenosis after radiotherapy is rare, the condition, which is called vertebral artery stump syndrome, must be recognized as a possible cause of infarction of the posterior circulation territory.

Conclusion

We treated a patient with basilar artery occlusion secondary to vertebral artery stenosis after radiotherapy of the neck by revascularization and parent artery occlusion of the vertebral artery. While it is a rare disorder, it must be recognized as a possible cause of infarction of the posterior circulation territory.

Disclosure Statement

Yuji Matsumaru has received payments including lecture fees from Japan Medtronic, Terumo Corporation, and Johnson & Johnson. No other coauthor has conflicts of interest.

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