A Patient with Hyperperfusion-related Cerebral Hemorrhage after Neuroendovascular Treatment for Vertebral Artery Stenosis

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Objective: We report a patient with hyperperfusion-related cerebral hemorrhage after neuroendovascular treatment for symptomatic vertebral artery stenosis.

Case Presentation: The patient was a 75-year-old male, who presented with repeated attacks of vertigo. He was diagnosed with vertebral-basilar insufficiency. Subsequently, medical treatment involving the administration of an antiplatelet drug was performed, but brainstem infarction developed. Cerebral angiography showed occlusion of the left vertebral artery and stenosis at the origin and intracranial area of the right vertebral artery. Cerebral blood flow scintigraphy revealed a reduction in cerebellar blood flow as well as the site of infarction. The patient was considered to be resistant to medical treatment, and angioplasty was performed at two stenotic sites of the left vertebral artery. Despite strict blood pressure control, brainstem hemorrhage occurred 4 hours after surgery. The postoperative cerebral blood flow scintigraphy findings suggested hyperperfusion-related hemorrhage.

Conclusion: For endovascular treatment of vertebral artery stenosis with cerebral blood flow failure, postoperative hyperperfusion-related cerebral hemorrhage may not be prevented by blood pressure control alone. Therapeutic strategies, such as a staged angioplasty, should be established based on cerebral blood flow examination findings.

Keywords ► angioplasty, hyperperfusion, vertebral artery

Introduction

Carotid endarterectomy (CEA) and carotid artery stenting (CAS) for symptomatic carotid artery stenosis are more advantageous than drug therapy from the viewpoint of recurrent cerebral infarction prevention.^{1,2)} However, concerning subclavian or vertebral artery revascularization, no large-scale clinical trial has been conducted, and its efficacy and safety remain controversial.

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We report a patient with hyperperfusion-related cerebral hemorrhage after endovascular treatment for symptomatic vertebral artery stenosis. We also discuss the efficacy and safety of revascularization for posterior cerebral circulation.

Case Presentation

A 75-year-old male with a history of hypertension and diabetes mellitus consulted the outpatient clinic of our department with repeated vertigo in July 2014. MRI did not reveal any cerebral infarction, but the left vertebral artery was not visualized on MRA, and stenosis of the right vertebral artery was suggested. Under a diagnosis of vertebral-basilar insufficiency, 81 mg/day of aspirin was initially administered. However, the symptom was repeatedly observed, and 200 mg/day of cilostazol was additionally administered. However, brainstem infarction occurred on September 24, 2014, and the patient was admitted.

Diffusion-weighted MRI on admission revealed fresh cerebral infarction in the right pons (**Fig. 1A**). The left

Fig. 1 (A) Diffusion-weighted imaging showing acute infarction in the right cerebellum. (B) MRA showing the stenosis of the intracranial right vertebral artery (arrow). The left vertebral artery was not visualized.

Fig. 2 (A) The right vertebral angiogram (anterior-posterior view) demonstrating severe stenosis of the intracranial right vertebral artery. (B) The right vertebral angiogram (lateral view) demonstrating severe stenosis of the intracranial right vertebral artery. The right PICA was absent. (C) The left vertebral angiogram (anterior-posterior view) demonstrating occlusion of the left vertebral artery after branching the left PICA. (D) The right innominate angiogram showing severe stenosis at the origin of the right vertebral artery. PICA: posterior inferior cerebellar artery

Fig. 3 N-isopropyl-p-[^{123}I]-iodoamphetamine single-photon emission computed tomography scans showing decrease in the blood flow in the right cerebellar hemisphere.

vertebral artery was not visualized on MRA, and stenosis of the right vertebral artery was suggested (**Fig. 1B**). Subsequently, cerebral angiography showed stenosis at the origin of the right vertebral artery, as well as marked stenosis of the intracranial right vertebral artery. The right posterior inferior cerebellar artery was not visualized (**Fig. 2A, 2B, and 2D**). On the other hand, the left vertebral artery was occluded immediately after branching the left posterior inferior cerebellar artery, and there was no collateral blood flow from the anterior circulation via the posterior communicating artery (**Fig. 2C**). N-isopropyl-p-[^{123}I]-iodoamphetamine (IMP) single-photon emission computed tomography (SPECT) revealed a marked reduction in blood flow in the right cerebellum other than the site of infarction (**Fig. 3**).

Based on these findings, a diagnosis of symptomatic vertebral artery stenosis resistant to medical treatment was made, and endovascular treatment was scheduled (October 17).

Neuroendovascular treatment

As antiplatelet therapy, aspirin and cilostazol were continuously administered, and 5000 units of heparin were intravenously injected by inserting an 8 Fr sheath introducer to the right inguinal region under local anesthesia. An 8 Fr Launcher (Medtronic, Minneapolis, MN, USA) was transiently inserted into the right subclavian artery, and a 4.2 Fr FUBUKI 125 cm (Asahi Intecc Co., Ltd, Aichi, Japan) was coaxially inserted to guide the Launcher into the right vertebral artery. Subsequently, the 4.2Fr FUBUKI 125 cm was removed, and a Gateway 2.5 × 15 mm (Stryker, Kalamazoo, MI, USA) was guided to the intracranial stenotic site using a 0.014-inch CHIKAI (Asahi Intecc). Initially, the site was dilated at 6 atm, but dilation was insufficient, and the site was again dilated at 8 atm. As arterial dissection was suspected, stenting, as an emergency management strategy to prevent acute vascular occlusion, was explained to the patient, and his consent was obtained. Using a Prowler Select Plus (Codman & Shurtleff, Johnson & Johnson, Raynham,

Fig. 4 (A) The right vertebral angiogram after the balloon angioplasty and the stenting showing sufficient dilatation of the vertebral artery. (B) The right innominate angiogram after the endovascular therapy showing dilatation of the stenotic lesion at the origin of the right vertebral artery.

MA, USA), an Enterprise 4.5 × 28 mm (Codman & Shurtleff, Johnson & Johnson) was inserted to the same site. Right vertebral artery angiography confirmed sufficient dilation of the stenotic site (**Fig. 4A**) although the right posterior inferior cerebellar artery was not visualized. Subsequently, a PALMAZ Genesis 5.0 × 15 mm (Cordis, Miami Lakes, FL, USA) was inserted to the origin of the vertebral artery to confirm favorable dilation of the stenotic site. The procedure was completed without neutralizing heparin (**Fig. 4B**).

After treatment, the patient's condition was favorable, and there was no deterioration of neurological findings. Subsequently, the patient was admitted to the intensive care unit. To prevent hyperperfusion, blood pressure control was conducted under sedation so that the systolic blood pressure might be ≤120 mmHg. However, the consciousness level suddenly worsened 4 hours after treatment. CT revealed hemorrhage of the right midbrain and cerebellum (**Fig. 5**). IMP SPECT the day after treatment showed the disappearance of right cerebellar blood flow attenuation, which was observed before surgery, as well as bilateral cerebellar and partial brainstem hyperperfusion in comparison with the cerebral hemisphere (**Fig. 6**).

Subsequently, rehabilitation was performed. Dysphagia and right incomplete paralysis remained, and the patient was transferred to another hospital 6 months after treatment.

Discussion

In patients with symptomatic vertebral or basilar artery stenosis, the recurrence rate of stroke is considered to be

Fig. 5 A CT scan showing hemorrhage in the right mid-brain and the right cerebellum.

relatively high.³⁾ For this reason, some studies recommended angioplasty by endovascular treatment, and it was reported that the success rate of this procedure was high, and that the incidence of complications was relatively low.⁴⁻⁶⁾ As a frequent complication, post-treatment restenosis has been indicated, and recently, drug-eluting stents have been used to overcome this issue.^{7,8)}

However, there is no evidence regarding the efficacy of angioplasty by endovascular treatment for vertebral artery stenosis in comparison with drug therapy although various clinical studies demonstrated the usefulness of CEA or CAS for symptomatic carotid artery stenosis for the prevention of recurrent stroke.⁹⁻¹¹⁾ In the only randomized

Fig. 6 N-isopropyl-p-[¹²³I]-iodoamphetamine single-photon emission computed tomography scans showing increase in the blood flow in the cerebellum and in the brain stem.

clinical study, there was no difference in the long-term prognosis between endovascular and medical treatments.¹²⁾ Therefore, angioplasty for vertebral artery stenosis must be carefully indicated.

In the present case, hyperperfusion rather than hemorrhagic infarction may have been involved in the pathogenesis of cerebral hemorrhage for the following reasons: cerebral infarction was localized in the penetrating vessel area, with an interval of 1 month from the onset, and the site of hemorrhage differed from that of infarction. The incidence of cerebral hemorrhage related to hyperperfusion after carotid artery revascularization is approximately 1%, but most sequelae are serious. Many studies investigated the association between cerebral blood flow and hyperperfusion,¹³⁾ and post-treatment hyperperfusion-related cerebral hemorrhage is considered to be associated with a reduction in cerebral blood flow or vascular responsiveness before treatment.¹⁴⁾ Another study reported a patient with post-treatment hyperperfusion-related hemorrhage at

the site of pretreatment cerebral blood flow or vascular responsiveness attenuation after treatment for subclavian artery stenosis.¹⁵⁾ Taken together, there may also be a similar association after revascularization by posterior circulation endovascular treatment.

In the present case, blood pressure control was strictly performed in the intensive care unit, considering the risk of post-treatment hyperperfusion, but cerebral hemorrhage occurred. According to previous studies, blood pressure was controlled properly in all patients with hyperperfusion-related intracerebral hemorrhage after posterior circulation endovascular treatment.^{16–18)} These findings suggest that hyperperfusion-related hemorrhage cannot be completely prevented by blood pressure control alone in patients with blood flow failure before surgery.

A previous study reported a patient with hemorrhage after simultaneous endovascular treatment of the bilateral vertebral arteries.¹⁸⁾ In our patient, vertebral artery stenosis at the origin and intracranial region was also simultaneously

treated, leading to hemorrhage. In contrast, according to another case report, postoperative hyperperfusion after angioplasty did not cause cerebral hemorrhage for an insufficient improvement of vertebral artery stenosis in a patient with a reduction in cerebellar blood flow on pre-treatment SPECT.¹⁹⁾ These results suggest that a rapid improvement in blood flow for vertebral artery stenosis induces serious hyperperfusion, which may lead to hemorrhage.

Several studies indicated that when performing CEA or CAS for marked stenosis of the cervical internal carotid artery, two-stage treatment for avoiding postoperative hyperperfusion was safer in patients with a reduction in affected-side cerebral blood flow or vascular responsiveness on preoperative SPECT.^{20,21)} When treating patients with vertebral artery stenosis and a reduction in cerebral blood flow, strategies, such as step-by-step blood flow improvement, should be established to prevent hyperperfusion-related hemorrhage.

Conclusion

We reported a patient with vertebral artery stenosis and a reduction in cerebellar and brainstem blood flow before treatment in whom angioplasty was performed, and postoperative hyperperfusion-related cerebral hemorrhage occurred. No method to completely prevent hyperperfusion has been established in the treatment of severe vertebral artery stenosis, and therapeutic strategies, such as a staged angioplasty, should be devised based on the results of cerebral blood flow examination.

Disclosure Statement

There is no conflict of interest.

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