Staged Angioplasty and Stenting for Severe Cervical Internal Carotid Artery Stenosis in the Setting of Acute Ischemic Stroke

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Objective: We report two patients who underwent two-stage angioplasty and carotid artery stenting (CAS) for marked stenosis of the cervical internal carotid artery (ICA) related to acute intracranial artery occlusion.

Case Presentations: In Case 1, thrombectomy and angioplasty for cervical ICA occlusion were performed. Although the M2 region of the middle cerebral artery was occluded, thrombectomy led to recanalization. Later, CAS was conducted. In Case 2, angioplasty for stenosis at the ICA origin was performed, leading to recanalization of the main intracranial artery. Later, CAS was conducted.

Conclusion: Staged angioplasty may be selected as an option for stenosis of the cervical ICA with acute intracranial artery occlusion.

Keywords ▶ carotid artery stenting, carotid artery occlusion, hyperperfusion phenomenon, acute ischemic stroke, embolectomy

Introduction

Neither the efficacy nor the safety of endovascular treatment for marked stenosis of the cervical internal carotid artery (ICA) related to acute intracranial artery occlusion has been established. Several studies have reported one-stage treatment involving cervical ICA stenting, but potent postoperative antithrombotic therapy is required, and acute-phase intracranial hemorrhage may occur.

In this study, we report two patients with marked stenosis of the cervical ICA related to acute intracranial occlusion, for whom recanalization for intracranial occlusion was primarily performed in the acute phase, and percutaneous transluminal angioplasty (PTA) and carotid artery stenting (CAS) were conducted step by step to treat cervical ICA stenosis, considering the hemodynamics. PTA alone was performed in the acute phase, followed by two-stage CAS, leading to a favorable outcome. We also introduce the serial changes in cerebral blood flow after recanalization therapy.

Case Presentations

Case 1

A 77-year-old male was brought to our hospital by ambulance with gait disorder on waking up. On the initial consultation, the Japan Coma Scale (JCS) score was 1-2, and left hemiplegia was noted. The National Institute of Health Stroke Scale (NIHSS) score was 17, suggesting wake-up stroke. Intravenous thrombolysis with recombinant tissue plasminogen activator (rt-PA) was not indicated. On MRA, the visualization of the right ICA and M2 region of the middle cerebral artery was unfavorable (Figs. 1C and 1D). On MRI, diffusion-weighted images (DWI) showed acute infarction in the same area. The Alberta Stroke Programme Early CT Score (ASPECTS)-DWI was 8 points, suggesting DWI-perfusion-weighted image (PWI) and DWI-FLAIR mismatches. Endovascular treatment was performed.
After systemic heparinization, a 9F balloon guiding catheter (Optimo, Tokai Medical, Aichi, Japan) was inserted into the right common carotid artery (CCA). DSA revealed occlusion at the cervical ICA origin (Fig. 1E). A 0.014-inch microguidewire (Chikai 14 black, Asahi Intec, Aichi, Japan) was guided to the site of occlusion, but wire movement suggested the patency of the distal cervical ICA. A microcatheter (Marksman, Covidien, Irvine, CA, USA) was inserted, and DSA was performed. The translucency suggested thrombus formation at the distal end of the site of occlusion at the ICA origin. In the same site, a stent retriever (Solitaire, 6 mm × 30 mm, Covidien) was developed, and a red thrombus measuring 2 cm was removed through one pass. DSA confirmed recanalization in the same site, but occlusion related to marked stenosis was noted. Considering the necessity of angioplasty for maintaining the patency, 80 mg of Ozagrel sodium (Ozagrel Na) was intravenously administered. The oral administration of an antiplatelet drug was not performed because it was impossible to insert a transnasal gastric tube. Under proximal blockage, PTA (6 atm) was performed using a PTA balloon (Jackal RX, 4 mm × 4 cm, Kaneka Medical Products, Osaka, Japan), leading to the resumption of favorable anterograde blood flow (Fig. 1F). Subsequently, intracranial DSA revealed occlusion of the middle cerebral artery (M2 region) (Fig. 1G). An Optimo was inserted into the distal cervical ICA beyond the stenotic site at the ICA origin, and the stent retriever was developed in the site of middle cerebral artery occlusion to achieve complete recanalization through one pass (Fig. 1H). Immediately after surgery, aspirin (Bayaspirin, 300 mg) was loaded, and continued thereafter. Furthermore, aragatoban (Novastan HI injection, 60 mg/day) was intravenously administered for 2 days after surgery, and the oral administration of rosuvastatin (Crestor, 2.5 mg/day) was started. DWI the day after surgery did not show any significant increase in the infarcted area (Fig. 2A), but PWI showed an increase in the volume of cerebral blood flow involving an extensive area on the affected side (Fig. 2B). On days 6 and 10, there were also increases in the volume of cerebral blood flow locally, but hypoperfusion was noted on day 21. On day 13, clopidogrel (Plavix, 75 mg/day) was additionally administered, and CAS was performed on day 24. Under distal filter protection with a Filterwire EZ (Boston Scientific, Natick, MA, USA), predilation was conducted using a Sterling MR 3 mm 4 cm (Boston Scientific), and a closed-cell stent (Carotid Wallstent 8 mm × 29 mm, Boston Scientific) was deployed.
Inoue S, et al. 10000 units/day) was administered for 6 days. The oral administration of rosuvastatin (2.5 mg/day) was started. On DWI the day after surgery, there was no significant increase in the infarcted area (Fig. 4A). However, PWI showed an increase in the cerebral blood flow in the affected side beyond the extent of infarction (Fig. 4B). The cerebral blood flow reached a peak on day 4, and there was also an increase in the cerebral blood flow locally on day 12. However, hypoperfusion was noted on day 24. On day 17, clopidogrel (75 mg/day) was additionally administered. On day 28, CAS was performed. Under distal filter protection with a Filterwire EZ, predilation was performed using a Jackal RX 3.5 mm × 2 cm, and a Carotid Wallstent 8 mm × 29 mm was deployed and post-dilation was performed with a Sterling MR 4 mm × 3 cm. On PWI the day after CAS, there was no increase in the cerebral blood flow on the affected side (Fig. 4C). On day 38, the patient was referred to another hospital, with an mRS score of 2. There was no history of antiplatelet drug prescription before onset in either patient. During the course, there were no clinical symptoms suggestive of recurrent cerebral infarction, intracranial hemorrhage, or hyperperfusion syndrome.

Discussion
Stenosis of the cervical ICA is asymptomatic or causes relatively mild symptoms alone in most cases. However, the prognosis of patients with severe acute ischemic stroke (AIS) is unfavorable, and rt-PA administration is usually ineffective. Emergency PTA or CAS of the cerebral ICA in the acute phase of AIS is indicated for Class IIb/Level of Evidence C patients according to the guidelines in 2013 published by the American Heart Association/American
Stroke Association, and for Grade C1/Level 4 patients according to the Japanese Guidelines for the Management of Stroke 2015 (Japan Stroke Society). Furthermore, it is controversial which procedure, PTA or CAS, should be selected. The former may induce restenosis, and the latter may lead to dual-antiplatelet therapy (DAPT)-related hemorrhage.\(^2\,^3\) Few studies have compared the two procedures, and the results are inconsistent.\(^3\,^7\) Choudhri et al.\(^7\) reported that the prognosis in the PTA group was more favorable than in the CAS group (incidence of postoperative intracranial hemorrhage: 35%, mortality rate: 29%). In contrast, according to a study

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**Fig. 3** MRI, MRA, and DSA images of Case 2 on admission. (A) DWI showed acute ischemic lesion in the left MCA area. (B) PWI showed a diffuse reduction of CBF in the left MCA and ACA area. (C and D) MRA showed left M2 occlusion and severe left cervical ICA stenosis. (E and F) CCA angiogram before (E) and after (F) angioplasty. (G) Intracranial angiogram after the angioplasty showed no occlusive lesion in the major vessels. ACA: anterior cerebral artery; CBF: cerebral blood flow; CCA: common carotid artery; DWI: diffusion-weighted imaging; ICA: internal carotid artery; MCA: middle cerebral artery; PWI: perfusion-weighted imaging

**Fig. 4** Follow-up images of Case 2. (A and B) On the next day of admission, DWI (A) showed no apparent enlargement of ischemic lesion, and PWI (B) showed a diffuse increase in CBF in the right MCA and ACA area. (C) PWI on the next day of the CAS (day 29) showed no laterality of CBF. ACA: anterior cerebral artery; CAS: carotid artery stenting; CBF: cerebral blood flow; DWI: diffusion-weighted imaging; MCA: middle cerebral artery; PWI: perfusion-weighted imaging
based on the national database in the United States, the incidence of postoperative stroke and mortality rate in the PTA group were significantly higher than in the CAS group (3.9% vs. 1.9% and 9.0% vs. 3.8%, respectively), suggesting that PTA alone is insufficient.

In this study, we performed the following procedures for cervical ICA stenosis with AIS, leading to a favorable outcome without ischemic/hemorrhagic complications during the course: 1) initially, PTA alone was performed, 2) recanalization therapy for concomitant intracranial occlusive lesions was conducted, 3) in the acute phase, an antiplatelet drug alone was administered, and 4) after elective DAPT, stenting was performed. With respect to such two-stage treatment, Fargen et al. also recommended similar strategies. Two-stage treatment for stenosis of the cervical ICA was first reported by Yoshimura et al. as staged angioplasty to avoid hyperperfusion. For staged angioplasty, DAPT is introduced before initial treatment, but DAPT introduction in the presence of re- or luxury-perfusion may induce hemorrhage when performing emergency CAS for AIS. Our method has the following merits: hyperperfusion syndrome can be avoided, and DAPT in the acute phase can be avoided.

Concerning the timing of therapeutic intervention after the onset of AIS, CAS within 48 hours after onset is more dangerous than ≥49 hours after onset. Furthermore, the incidence of stroke and mortality rate related to CAS/carotid endarterectomy on the day of intravenous thrombolysis with rt-PA are significantly higher than in the absence of rt-PA therapy or ≥3 days or more after its administration. Therefore, Adachi et al. recommended that PTA alone should be performed within 3 days after rt-PA administration, and that CAS should be conducted 4 days or more after rt-PA administration. These findings are consistent with our method in which PTA alone is initially performed in the acute phase after onset.

Concerning the timing of two-stage stenting, the cerebral blood flow of the affected side increased in the two patients treated in this study, reaching a peak on days 2 to 4 and persisting in the infarcted area for 10 to 12 days. On days 21 to 24, the blood flow volume became lower than on the unaffected side. Few studies regarding emergency CAS have reported hyperperfusion syndrome. For staged angioplasty, as described above, it is recommended that CAS should be performed 2 weeks to 2 months after PTA. Based on these results, we consider that DAPT should be introduced 2 weeks or more after initial PTA, followed by CAS, but further examination is necessary.

Concerning the balloon diameter on initial PTA, only emergency PTA balloons measuring 4 or 5 mm in diameter were stocked in our hospital on treating our patients; we used balloons measuring 4 mm in diameter. These balloons were useful for the prevention of restenosis or treatment of tandem lesions because it was necessary to guide a 9F guiding catheter (outer diameter: 3 mm). However, they may have been too large to prevent hyperperfusion. Yoshimura et al. targeted a vascular lumen diameter of ≥2 mm using PTA balloons measuring 2.5 to 3 mm in diameter. In the future, initial treatment with a balloon measuring 3 mm in diameter should be considered when encountering similar patients.

With respect to the selection of one- or two-stage stenting for the cervical ICA, there was no history of antiplatelet drug therapy before onset in Case 1, and primary disease-related difficulty in patient cooperation and environmental factors in the angiography room made antiplatelet drug loading with a transnasal gastric tube impossible. As a result, we avoided stenting, and selected two-stage treatment. Since then, in our hospital, two-stage treatment has been selected as a first choice. In Case 2, it was initially adopted. In addition, two-stage treatment should also be considered for patients with extensive infarction on preoperative diagnostic imaging or those in whom intracranial hemorrhage related to the treatment of a tandem lesion is suspected. However, two-stage treatment may lead to acute occlusion; the presence or absence of neurological symptoms or abnormal diagnostic imaging findings must be examined. On the other hand, one-stage stenting should be performed when sufficient vasodilation is not achieved by PTA alone or when restenosis/reocclusion, a residual thrombus, or vascular dissociation is present.

In Case 1, a red thrombus measuring 2 cm was retrieved through a stent retriever at the site of cervical ICA occlusion. Before collection, DSA with a microcatheter at the distal occlusion site showed translucency, suggesting a thrombus at the occlusion site; the possibility of embolic occlusion could not be ruled out, and a stent retriever was initially used. However, PTA may be appropriate for patients with occlusion related to plaque rupture and secondary thrombus formation. Furthermore, the influence of a stent retriever on plaque must be considered. It is important to differentiate embolic occlusion of the cervical ICA from atherosclerotic occlusion for evaluating the condition and selecting therapeutic strategies. If possible, preoperative assessment using carotid artery ultrasonography may be useful. In addition, when an intracranial tandem lesion is present, PTA alone should be performed in the cervical
region to eliminate the lesion; the interval may be the shortest. On the other hand, when a secondary thrombus remains in a stenotic lesion after PTA, additional treatment, such as thrombectomy or stenting at this site, may be required. In our patients, thrombectomy was conducted using a stent retriever, but a study reported the use of a Penumbra system. This system may induce distal embolism, and caution is needed so that blood vessels in which thrombectomy is more difficult, such as the anterior cerebral or posterior communicating arteries, may not be occluded in the presence of occlusion of the middle cerebral artery.

To treat tandem lesions, it is necessary to guide a guiding catheter to the site of ICA stenosis, as demonstrated in Case 1. Considering the risk of distal embolism, a guiding catheter should be guided after stenting when adopting an antegrade approach. In contrast, a study recommended a thrombectomy-first approach in which stenting is performed after the treatment of intracranial lesions. An operation to guide a guiding catheter to the stenotic site may not directly contribute to the deterioration of the prognosis. In Case 2, the visualization of the M2 region of the middle cerebral artery was unfavorable on MRA, and FLAIR showed a hyperintense MCA branch sign, but DSA after cervical PTA did not confirm occlusion at the same site. A study reported that revascularization for cervical ICA occlusion alone led to spontaneous recanalization in the intracranial tandem lesion site. However, in our patients, we could not evaluate whether PTA of the cervical ICA resulted in spontaneous recanalization in the tandem lesion site, whether rt-PA alone led to recanalization, or whether the finding was solely related to a reduction in blood flow.

Concerning antiplatelet therapy, in the two patients, aspirin loading was conducted in the acute phase, and clopidogrel was additionally administered before CAS. However, cilostazol is more useful than aspirin for preventing post-stroke intracranial hemorrhage, and it should be positively considered in cases in which hemorrhagic changes may occur, including our patients.

Strategies to treat ICA stenosis with AIS must be examined, considering the timing of intervention and presence or absence of rt-PA administration. For patients requiring treatment early after onset, this method may become an option.

### Conclusion

Two-stage angioplasty may become a treatment option for cervical ICA stenosis with AIS. In the future, a larger number of patients should be investigated.

### Disclosure Statement

There is no conflict of interest for the author and coauthors.

### References