Late Embolism Following Recanalization of Occluded Extracranial Internal Carotid Artery Dissection

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Objective: The clinical course of extracranial internal carotid artery dissection (eICAD) treated with medical therapy alone is usually benign, but late embolism may cause intracranial large artery occlusion (iLAO). We report a new procedure to treat iLAO caused by eICAD.

Case Presentation: A 47-year-old man patient presented with two episodes of transient right hemiparesis and mild neck pain. An emergent MRI detected a left internal carotid artery (ICA) occlusion but no new infarction. Because it was strongly suspected that eICAD was the cause, medical therapy was started, and the patient's neurological condition was frequently checked to ensure prompt response if a late embolism developed. One day after onset, a follow-up MRI revealed recanalization of the ICA occlusion and eICAD without a new infarction. Unfortunately, a late embolism of the left middle cerebral artery occurred 2 days after onset. We started intravenous tissue plasminogen activator administration immediately after a CT scan. We performed a mechanical thrombectomy (MT), resulting in thrombolysis in cerebral infarction (TICI) score of 3. Subsequently, we performed carotid artery stenting (CAS) for eICAD. Ten days after the stroke, the patient's National Institutes of Health Stroke Scale (NIHSS) score was 2.

Conclusion: When treating iLAO due to eICAD by MT and CAS, further vascular injury and intracranial embolism must be prevented. We used proximal and distal protection in combination, employing an aspiration catheter to withdraw the stent retriever and deliver a distal embolic protection device before CAS. As a result, the patient's condition improved.

Keywords ▶ extracranial internal carotid artery dissection, endovascular surgery, late embolism

Introduction

Extracranial internal carotid artery dissection (eICAD) is an important cause of ischemic stroke in young adults under 45 years old.¹ The clinical course is usually benign with medical therapy alone.² In some cases, however, eICAD may cause internal carotid artery (ICA) occlusion, embolic intracranial large artery occlusion (iLAO), and/or hemodynamic impairment.³ In such cases, acute phase surgical intervention may be required. Recently, the effectiveness of endovascular surgery (EVS) in acute iLAO due to eICAD has been reported.⁴,⁵ At each step during the EVS, we must prevent further vascular injury at the eICAD and intracranial embolism. In this report, we report a new procedure to treat iLAO caused by eICAD and prevent intraoperative further vascular injury and distal embolization.

Case Presentation

A 47-year-old male patient presented with two episodes of transient right hemiparesis and mild neck pain. When he presented to our emergency room, his neurological condition was completely restored (National Institutes of Health Stroke Scale [NIHSS] 0). Emergent MRI (SIGNA Explorer 1.5T; GE Healthcare, Chicago, IL, USA) detected no new ischemic lesion (Fig. 1A), but there was a left ICA occlusion at 1.4 cm distal to the ICA origin (Fig. 1B) with good collateral flow via an anterior communicating artery (Fig. 1C). He had no
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A continuous infusion of argatroban was continued, as the patient was still neurologically asymptomatic. However, 1 day after the recanalization, even under a continuous infusion of argatroban, he experienced sudden-onset right hemiparesis, aphasia, and loss of consciousness (NIHSS 21). An emergent non-enhanced CT (Optima CT660, GE Healthcare) scan of his brain revealed a hyperdense left MCA sign without intracranial hemorrhage (Fig. 1F).

The value of APTT and prothrombin time-international normalized ratio (PT-INR) just before the neurological deterioration was 36.1 seconds and 1.3, respectively. Since there were no other contraindications, intravenous tissue plasminogen activator (IV-tPA) was initiated 20 min after the onset of symptoms. He was transferred to our angiography suite immediately, and EVS was started within 45 min after the onset of symptoms.

Fig. 1 (A) Initial DWI showing no new ischemic lesions. (B) Cervical MRA showing a left ICA occlusion, 1.4 cm distal to the ICA origin (arrow). (C) MRA showing a good collateral flow of the intradural portion of the left ICA via an anterior communicating artery. (D) Follow-up MRA showing recanalization of the left ICA. (E) Follow-up cervical MRA showing an eccentric, smooth, and tapered stenosis with intramural hematoma and an intimal flap at the cervical portion of the left ICA (dotted arrow). (F) Emergent non-enhanced CT scan of the brain showing a hyperdense left MCA sign without intracranial hemorrhage. DWI: diffusion weighted image; ICA: internal carotid artery; MCA: middle cerebral artery
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A long 9-Fr guide sheath was placed in his right femoral artery under local anesthesia. Systemic heparinization was performed. DSA using a twin flat-panel angiographic system (Innova IGS 630, GE healthcare) revealed occlusion of the left MCA and ICA stenosis caused by eICAD, which started from the distal aspect of the carotid bulb and extended slightly proximal to the petrous portion of the left ICA, with a wall-adherent thrombus (Fig. 2A). Afterward, a 9-Fr balloon-guide catheter (Optimo; Tokai Medical Products, Inc., Aichi, Japan) was placed in the left ICA at the proximal edge of the eICAD under road mapping. The ICA stenosis was passed with a coaxial configuration of an aspiration catheter (Penumbra 5Max ACE60; Penumbra, Alameda, CA, USA), a 0.021 inch microcatheter (Markman microcatheter; Medtronic, Minneapolis, MN, USA), and a 0.014 inch wire (CHIKAI guide wire; Asahi Intecc Co., Ltd., Aichi, Japan), with the left ICA temporarily occluded by inflating the balloon of the balloon guide catheter as a proximal flow control to prevent further intracranial embolism from the wall-adherent thrombus at the eICAD, shown in Fig. 2A. From then on, the proximal flow control of each step was performed by temporarily occluding the internal carotid artery proximal to the eICAD. After confirming placement beyond the clot via gentle contrast injection through the microcatheter, a 6 × 25 mm Trevo XP ProVue stent (Stryker, Kalamazoo, MI, USA) was introduced through the microcatheter. Left internal carotid angiography via an aspiration catheter showing the embolic protection device (arrow) placed at the distal aspect of the eICAD in the lateral view. (E) Lateral cervical view showing two stents deployed in place overlapping from the origin of the ICA to slightly before the petrous portion of the ICA. (F) Left common carotid angiogram via guide catheter showing the eICAD is successfully treated. eICAD: extracranial internal carotid artery dissection; ICA: internal carotid artery; MCA: middle cerebral artery.

Fig. 2 Endovascular surgery. (A) Left internal carotid angiogram showing an eICAD with a wall-adherent thrombus (dotted arrow), observed from the distal carotid bulb to slightly proximal to the petrous portion of the left ICA. An acute MCA occlusion (arrow) is also seen in the anterior–posterior view. (B) Left internal carotid angiogram via aspiration catheter (dotted arrow) placed in the C1 portion of the ICA. Stent retriever placement and immediate flow restoration of the left MCA (arrow) in the anterior–posterior view are shown. (C) Left internal carotid angiogram via aspiration catheter placed in the C1 portion of the ICA. Successful recanalization of the left MCA in the anterior–posterior view is shown. (D) Left internal carotid angiogram performed via guide catheter showing the embolic protection device (arrow) placed at the distal aspect of the eICAD in the lateral view. (E) Lateral cervical view showing two stents deployed in place overlapping from the origin of the ICA to slightly before the petrous portion of the ICA. (F) Left common carotid angiogram via guide catheter showing the eICAD is successfully treated. eICAD: extracranial internal carotid artery dissection; ICA: internal carotid artery; MCA: middle cerebral artery.
place for 3 min, whereas the microcatheter was removed from the body through the aspiration catheter, whose tip was positioned away from the distal end of the eICAD. Then, the aspiration pump was turned on. Thereafter, under proximal flow control, the fully deployed stent retriever was slowly pulled back and removed through the aspiration catheter to avoid the stent retriever passing and damaging the eICAD. A small red thrombus was retrieved with the stent retriever after a single pass. A post-thrombectomy control angiogram demonstrated thrombolysis in cerebral infarction (TICI) 3 revascularization of the occluded MCA through the aspiration catheter (Fig. 2C). The time to revascularization, defined as the time from femoral access to the achievement of revascularization, was 20 min.

Subsequently, additional intravenous heparin was administered as a 2000-IU bolus to achieve a peri-procedural activated clotting time of >275 seconds. Aspirin 100 mg and clopidogrel 300 mg were administered via the nasogastric tube. In order to prevent further vascular injury at the eICAD and intracranial embolism, an embolic protection device (FilterWire EZ, 300 cm; Boston Scientific, Marlborough, MA, USA) was placed away from the distal end of the eICAD through the aspiration catheter under proximal flow control (Fig. 2D). Then, the aspiration catheter was removed. We confirmed the exact location of the eICAD by intravascular ultrasonography (IVUS). IVUS showed an intimal flap dividing a true lumen and a pseudo lumen filled with an intramural hematoma as a low echoic lesion (Fig. 3A) at the level of the craniovertebral junction to C3. IVUS also showed a tear of intima and blood flow into a pseudo lumen (Fig. 3B). Subsequently, under distal filter protection and proximal flow control, an 8 × 29 mm self-expanding stent (Carotid wall stent, Boston Scientific) and a 10 × 31 mm self-expanding stent (Carotid wall stent, Boston Scientific) were deployed to overlap in place, which successfully treated the eICAD (Fig. 2E). IVUS after stenting confirmed the stents completely covered the eICAD.

The patient immediately experienced significant improvement in his neurological function. An MRI performed 1 day after the EVS demonstrated acute, small infarctions in the left basal ganglia and occipital lobe, without mass effect or hemorrhagic infarction (Fig. 4A), and successful recanalization of the left MCA was observed (Fig. 4B). At the time of discharge, 10 days after the late embolism, the patient’s NIHSS score was 2. The modified Rankin scale score at 90 days after discharge was 0. Dual antiplatelet therapy was maintained for 8 weeks after the procedure. Aspirin 100 mg once per day was then maintained for 1 year. Follow-up cervical echo showed patency of the ICA.

Discussion

Cervical artery dissection (CeAD) is characterized by a hematoma within a wall of the internal carotid or vertebral arteries. CeADs are classified as spontaneous or traumatic, but in reality, many patients with “spontaneous” dissections have sustained mild trauma. At least 5% of patients with CeAD have a hereditary connective tissue disorder, such as Ehlers–Danlos syndrome. The majority of CeADs are located in the extracranial ICA and may present with local symptoms, including neck pain and
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Horner’s syndrome, as well as cerebral ischemia. eICAD is a rare condition with an annual incidence of 2.6 cases per 100,000. eICAD is responsible for 20% of ischemic strokes in young adults under 45 years old and about 2% of ischemic strokes overall. The clinical course is mostly benign, and healing of the dissected artery can be expected with medical therapy alone. In some cases, however, eICAD may cause ICA occlusion, embolic iLAO, and/or hemodynamic impairment. The available evidence strongly supports embolism as the most common cause of ischemic stroke due to eICAD. In such cases, acute phase surgical intervention may be required. Milhaud et al. reported that 88 of 3502 patients with ischemic stroke, who were admitted to their population-based primary care center, were diagnosed with eICAD, and 73 had ICA occlusions. The mortality rate for eICAD with ICA occlusion was reported to be as high as 23%. DSA, which was the reference method for diagnosis before the advent of MRI, is no longer recommended for the diagnosis of CeAD, not only because it is invasive, but also because it does not enable visualization of the intramural hematoma. MRA is very sensitive, with up to 99% sensitivity for detecting dissection in some studies, especially if it is performed using a fat-suppression protocol. The most common finding on MRA is a crescent-shaped intramural hematoma on axial T1-weighted images, whereas the fat-suppressed T1 images allow the intramural hematoma to be distinguished from the fatty tissue around the vessel. Repeated MRIs show the evolution of the signal changes of the intramural hematoma. eICAD commonly occurs 2 cm distally from the carotid bulb, whereas stenosis due to atherosclerosis originates more proximally, at the carotid bulb. This case involved a young male patient with ICA occlusion that developed with mild neck pain. The ICA occlusion was detected at 1.4 cm distal from the ICA origin in MRA. Therefore, eICAD was suspected at the time of visit. There are no randomized trials comparing anticoagulants and antiplatelet drugs, thus there is no evidence to support their routine use for the treatment of eICAD. We chose a continuous infusion of argatroban to prevent recurrence of cerebral ischemia. To immediately identify the recurrence of brain ischemia due to late embolism, we conducted repeated MRI assessments and frequently checked neurological findings. Follow-up MRI revealed recanalization of the ICA with eccentric, smooth, and tapered stenosis, intimal flap, and pseudolumen at the cervical portion. These findings suggested that the patient’s ICA occlusion was caused by eICAD.

Unfortunately, 1 day after the recanalization, the patient developed a late embolism despite receiving a continuous infusion of argatroban. But, immediately before the neurological deterioration, the value of APTT did not reach 1.5 times baseline or over 40 seconds and the value of PT-INR did not also reach over 1.7. Therefore, we found our treatment was inadequate as an anticoagulation therapy, even if the value of APTT for this patient was 1.5 times the baseline or more at 1 day after admission. The late embolization might not have happened if we had increased the
and avoided the risk of losing the distal position within the true lumen during a treatment of a tandem occlusion caused by CeAD or high grade arteriosclerotic extracranial ICA stenosis.\(^5\) Cohen et al. used proximal flow control by temporary occlusion of proximal ICA by a balloon catheter, when the microcatheter crossed and pre-dilated the dissection to prevent further intracranial embolism.\(^4\)

We used proximal flow control and distal protection, as appropriate, in combination. We also used an aspiration catheter to avoid losing a true lumen and vascular injury. First, we performed proximal flow control by temporary occlusion of the proximal ICA to prevent further intracranial embolism of wall adherent thrombus at the ICA stenosis caused by eICAD, when a coaxial configuration of an aspiration catheter and a microcatheter for use in mechanical thrombectomy (MT) passed near the eICAD (\(\text{Fig. 5A}\)). Then, the stent retriever was withdrawn into the aspiration catheter under proximal flow control to prevent further vascular injury of the eICAD (\(\text{Fig. 5B}\)). After the recanalization of the left MCA occlusion, an embolic protection device was delivered at the distal site of the eICAD through the aspiration catheter prior to CAS to prevent further vascular injury of the eICAD and to definitively navigate it through the true lumen of ICA where the eICAD occurred (\(\text{Fig. 5C}\)). Then, the aspiration catheter was removed (\(\text{Fig. 5D}\)).

Finally, CAS was performed under a combination of a distal dose of argatroban or measured the value of APTT more frequently, or had administered heparin or warfarin from the beginning. Argatroban was continuously infused, but since there were no contraindications, including clotting ability, we started IV-tPA immediately after the CT scan. It has been reported that the combination of IV-tPA and argatroban is effective and safe against acute ischemic stroke (AIS).\(^18\) It has also been reported that IV-tPA was effective and safe against AIS caused by CeAD.\(^19\) Cohen et al. reported findings on EVS for iLAO caused by eICAD.\(^4\) They also used IV-tPA for patients they considered eligible for that treatment method, beginning immediately after the CT scan. They performed MT for iLAO following carotid artery stenting (CAS) for eICAD. However, we performed MT before CAS for eICAD because the patient had neurological symptoms, which were obviously caused by MCA occlusion, as the patient was asymptomatic owing to good collateral flow via the anterior communicating artery despite the ICA occlusion when he came to our hospital. For such patients, performing MT after CAS can be futile and may actually worsen the patient’s prognosis. At each step during the EVS for iLAO caused by eICAD, we have to pay attention to prevent further vascular injury of eICAD and intracranial embolization from a wall-adherent thrombus. Behme et al. reported a method in which a retriever wire supported carotid artery revascularization to quickly recanalize iLAO and avoided the risk of losing the distal position within the true lumen during a treatment of a tandem occlusion caused by CeAD or high grade arteriosclerotic extracranial ICA stenosis.\(^5\) Cohen et al. used proximal flow control by temporary occlusion of proximal ICA by a balloon catheter, when the microcatheter crossed and pre-dilated the dissection to prevent further intracranial embolism.\(^4\) We used proximal flow control and distal protection, as appropriate, in combination. We also used an aspiration catheter to avoid losing a true lumen and vascular injury. First, we performed proximal flow control by temporary occlusion of the proximal ICA to prevent further intracranial embolism of wall adherent thrombus at the ICA stenosis caused by eICAD, when a coaxial configuration of an aspiration catheter and a microcatheter for use in mechanical thrombectomy (MT) passed near the eICAD (\(\text{Fig. 5A}\)). Then, the stent retriever was withdrawn into the aspiration catheter under proximal flow control to prevent further vascular injury of the eICAD (\(\text{Fig. 5B}\)). After the recanalization of the left MCA occlusion, an embolic protection device was delivered at the distal site of the eICAD through the aspiration catheter prior to CAS to prevent further vascular injury of the eICAD and to definitively navigate it through the true lumen of ICA where the eICAD occurred (\(\text{Fig. 5C}\)). Then, the aspiration catheter was removed (\(\text{Fig. 5D}\)). Finally, CAS was performed under a combination of a distal...
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protection and proximal flow control to prevent further intracranial embolism. Our procedure is technically feasible and useful in tandem occlusions or iLAO caused by an eICAD or high grade arteriosclerotic extracranial ICA stenosis.

Conclusion
The clinical course of eICAD is usually benign with medical therapy alone, but late embolism may cause iLAO. When treating iLAO due to eICAD by MT and CAS, further vascular injury and intracranial embolism must be prevented. We used proximal and distal protection in combination. We used an aspiration catheter to withdraw the stent retriever and deliver a distal embolic protection device prior to CAS. As a result, our patient improved; as such, we present this new procedure to treat iLAO caused by eICAD.

Disclosure Statement
Neither the first author nor any of the coauthors have any conflicts of interest.

References