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Case Report

A Case of Percutaneous Thrombectomy for Internal Carotid Artery Occlusion due to In-Stent Thrombosis Following Stent-Assisted Intra-Aneurysmal Embolization

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Objective: In-stent thrombosis (IST) is a known complication after stent-assisted coil (SAC) embolization. We report a case of mechanical thrombectomy using a stent retriever (SR) for IST and share our experience with this treatment to prevent a poor outcome in future cases.
Case Presentation: The patient was a 62-year-old man. SAC embolization for an unruptured left internal carotid artery (ICA) aneurysm was performed. Three weeks after discharge, right hemiparesis and aphasia developed. Magnetic resonance imaging (MRI) demonstrated cerebral infarction in the left middle cerebral artery (MCA) territory and the left ICA was occluded. His relatives told us that the patient discontinued taking antiplatelet drugs. IST was diagnosed and emergency thrombectomy was performed. First, we tried to introduce an aspiration catheter or balloon catheter into the occluded lesion, but they were unable to be sufficiently inserted to the distal site. Therefore, we used a SR even though it carried a risk of friction on the deployed stent. The occluded artery was finally recanalized using the SR, but the stent became shortened. For the treatment strategy, sufficient medication (antithrombogenic agents and edaravone) should be administered first, followed by mechanical treatment. In mechanical treatment, thrombus fragmentation with a guidewire or balloon and aspiration should be attempted first. New aspiration catheters to carry the devices to the far distal site easily are now available.
Conclusion: SRs cannot be utilized for thrombectomy with a stent. In emergency situations, careful consideration during troubleshooting rather than using a SR is needed.

Keywords ▶ in-stent thrombosis, stent-assisted coil embolization, thrombectomy, antiplatelets, medication adherence

Introduction

In-stent thrombosis (IST) is a known complication related to stent-assisted coil (SAC) embolization. In this study, we report a patient who underwent percutaneous thrombectomy with a stent retriever (SR) for IST related to the self-discontinuation of antiplatelet drug therapy.

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Case Presentation

The patient was a 62-year-old man who lived alone since retirement 2 years ago. Follow-up of a left internal carotid artery-superior hypophyseal artery aneurysm (IC-SHA AN) was continued, but the maximum diameter of the aneurysm increased from 5 to 8 mm during the 2 years; therefore, treatment was proposed (**Fig. 1**). We considered SAC to be indicated for the wide-necked aneurysm. After the necessity of postoperative antiplatelet drug therapy was explained, the patient understood the treatment and consented to it. The administration of aspirin at 100 mg and clopidogrel at 75 mg was started 2 weeks before treatment. The jail method with an LVIS 4.5 x 18 stent (Terumo, Tokyo, Japan) was adopted. The procedure was completed without complications. Stent crimping to the vascular wall was favorable (**Fig. 2**). There were no perioperative neurological complications. The oral administration of the two

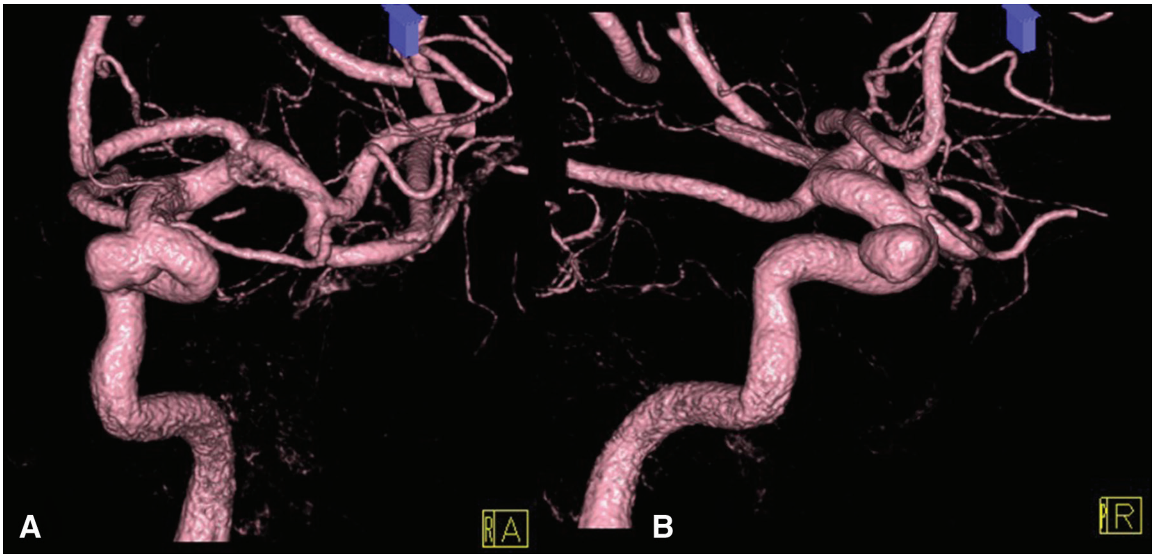

Fig. 1 (**A**) Frontal view on left internal carotid angiography (3D-DSA). (**B**) Lateral view. 3D DSA showed a wide-necked left para-sternal ICA aneurysm measuring 8 mm in diameter. ICA: internal carotid artery; 3D DSA: three-dimensional digital subtraction angiography

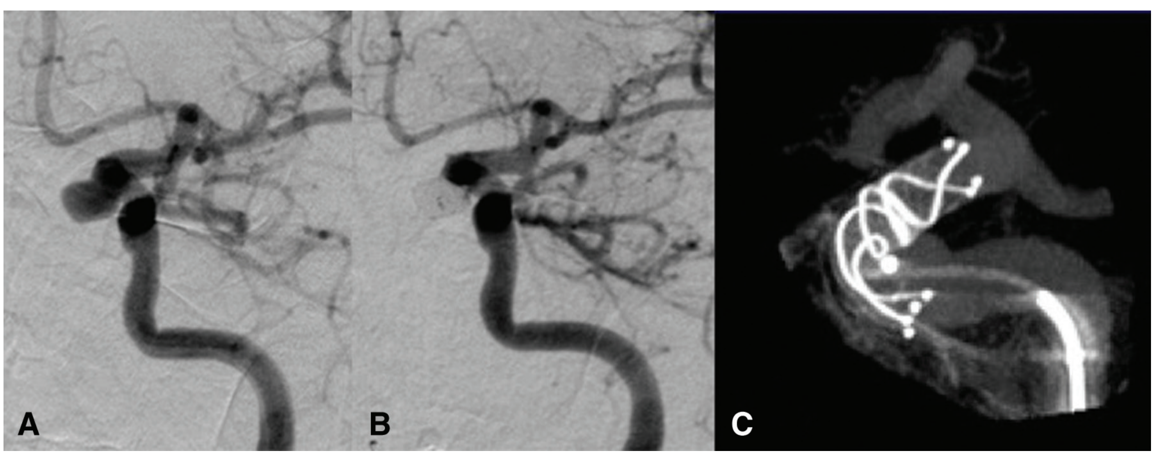

Fig. 2 (**A**) Preoperative left internal carotid angiography (angle at which the aneurysm was isolated from a maternal blood vessel) (**B**) After SAC embolization, complete occlusion was noted. The posterior communicating artery was maintained. (**C**) Cone-beam CT before coil insertion confirmed that there was no problem regarding stent deployment. CT: computed tomography; SAC: stent-assisted coil

antiplatelet drugs was continued and the patient was discharged 4 days after treatment with a modified Rankin Scale (mRS) score of 0.

However, aphasia and right hemiplegia developed 3 weeks after discharge, and the patient was brought to our hospital by ambulance. Magnetic resonance imaging (MRI) revealed an early ischemic focus in the left middle cerebral artery (MCA) region. Magnetic resonance angiography (MRA) demonstrated occlusion of the left internal carotid artery (ICA) (**Fig. 3**). At this point, we heard from his relatives that the patient drank alcohol during the day on an irregular diet and that he discontinued the two antiplatelet drugs by himself, although the timing of discontinuation was unclear. Left internal carotid angiography revealed IST-related occlusion of the left ICA (**Fig. 4A**) and emergency revascularization was performed. A 9Fr Optimo (Tokai Medical Products, Aichi, Japan) was guided into the left ICA. Initially, thrombectomy by aspiration was attempted at the proximal area of the stent to prevent interference with the aneurysmal stent. A Penumbra ACE 068 (Medicos Hirata, Osaka, Japan) was guided to the proximal area of the stent using a microcatheter (Marksman, Medtronic Japan Co., Ltd., Tokyo, Japan) and microguidewire (CHIKAI Black; ASAHI INTECC, Aichi, Japan), and aspiration was

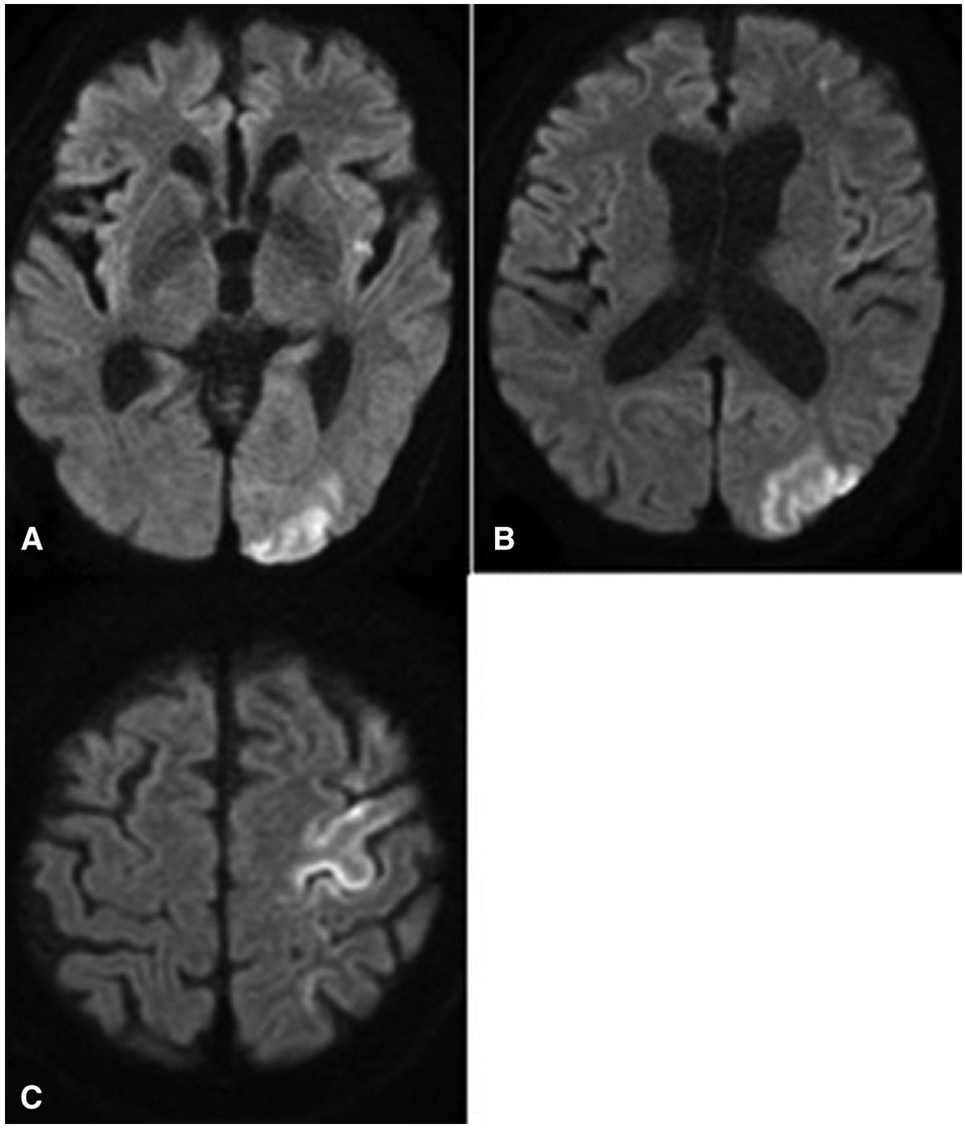

Fig. 3 Diffusion-weighted MRI on re-admission. Diffusion-weighted images showed high signal intensity involving the left occipital lobe (**A** and **B**) and left precentral gyrus (**C**). MRI: magnetic resonance imaging

conducted. However, the aspiration catheter end did not reach the thrombus and recanalization was not achieved. The end of the CHIKAI formed a J-shape. We attempted to guide the Marksman to the distal area of the stent, but the ICA was markedly flexed and the Marksman was unable to be guided beyond the posterior communicating artery branching from the distal area of the stent. Vasodilation with a balloon catheter (Gateway 2.0 × 9 mm; Stryker, Kalamazoo, MI, USA) was attempted, but it was impossible to guide the CHIKAI to a sufficiently distal area. The balloon catheter was caught in the siphon part and was unable to be guided to the lesion site; therefore, this was abandoned. After guiding the Marksman to the distal end of the stent, we decided to use a stent-type device. Considering its influence on the aneurysmal stent, a TrevoXp 4 × 40 (Stryker), which has a thin diameter, was selected, and recanalization was achieved. Based on angiography, the distal end of the LVIS had migrated to proximal through Trevo traction, resulting in shortening (**Fig. 5**). After recanalization, it became possible to guide a microguidewire into the MCA. Although imaging did not demonstrate poor crimping, there was a possibility that the stent was shortened while being partially flexed. Assuming that strut inversion may cause thrombus formation, angioplasty with a balloon catheter was performed at the site of stenting. Internal carotid angiography after 10 minutes confirmed the absence of re-occlusion and treatment was completed (Thrombolysis in Cerebral Infarction (TICI) grade: IIb)

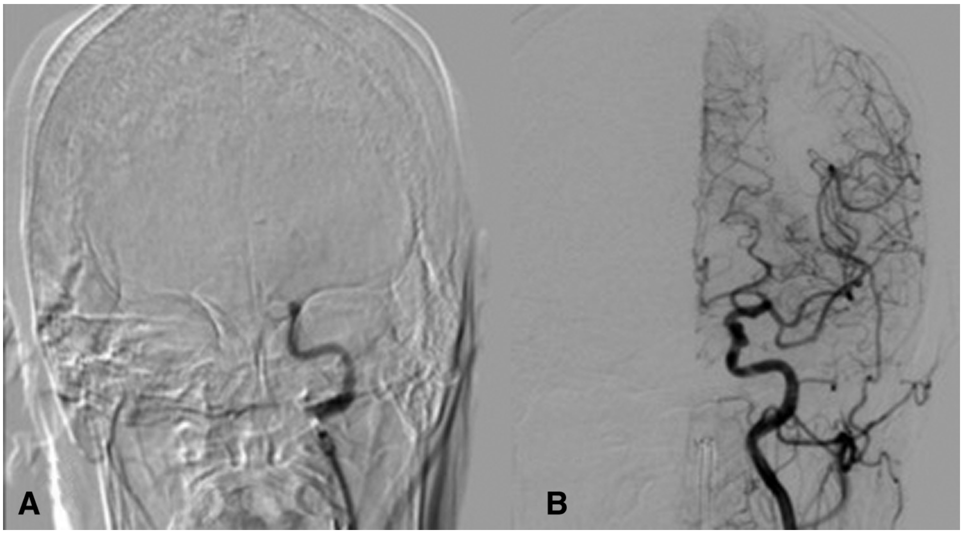

Fig. 4 (**A**) Left internal carotid angiography before recanalization. Occlusion was observed at the site of stent deployment on the lateral side of the coil-embolized aneurysm. (**B**) Left internal carotid angiography after recanalization. The procedure was completed with a Thrombolysis in Cerebral Infarction grade of 3.

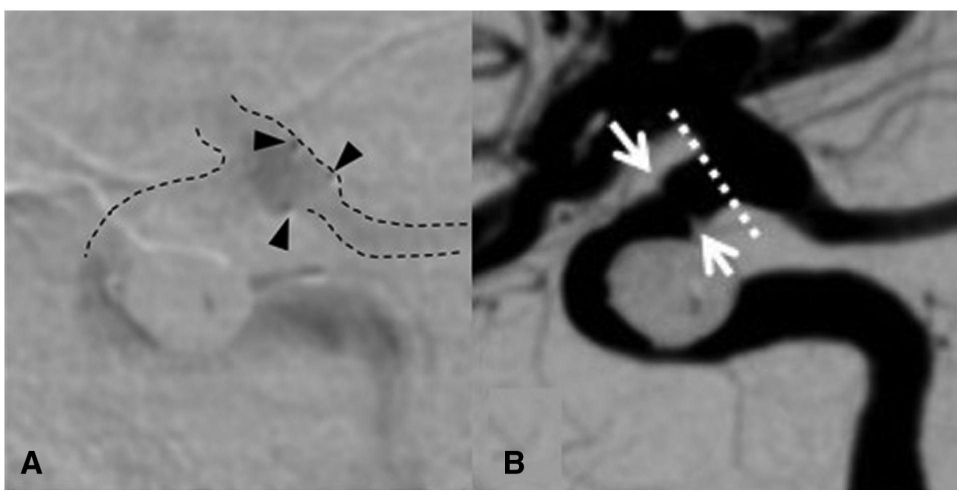

Fig. 5 (**A**) Trevo was partially deployed. The dotted line represents a blood vessel as an auxiliary line. The arrowhead represents the distal marker of the Trevo. It was deployed through the origin of the posterior communicating artery distal to an LVIS stent. (**B**) Left internal carotid angiography after thrombectomy. Due to interference from the LVIS stent, its distal end migrated to a proximal area (arrow). The dotted line indicates the distal end of the stent before shortening. There was no coil deviation.

(**Fig. 4B**). On MRI the day after surgery, slight enlargement of the ischemic focus detected before surgery was observed, but infarction involving an extensive penumbra area was avoided (**Fig. 6**). After surgery, consciousness disorder (Japan Coma Scale (JCS) score: 3), aphasia, and right hemiplegia (manual muscle testing (MMT): 2/5) remained. On the 41st postoperative day, the patient was referred to a recovery-phase rehabilitation hospital with a mRS score of 4.

Discussion

Coil embolization is increasingly indicated with the practical use of stent devices. Positive perioperative antiplatelet drug therapy has been standardized, but the incidence of ischemic complications has slightly increased, being the highest among perioperative complications.[1] The pathogenesis of IST involves a process of inflammatory responses: stent-related overdilation of the vascular wall

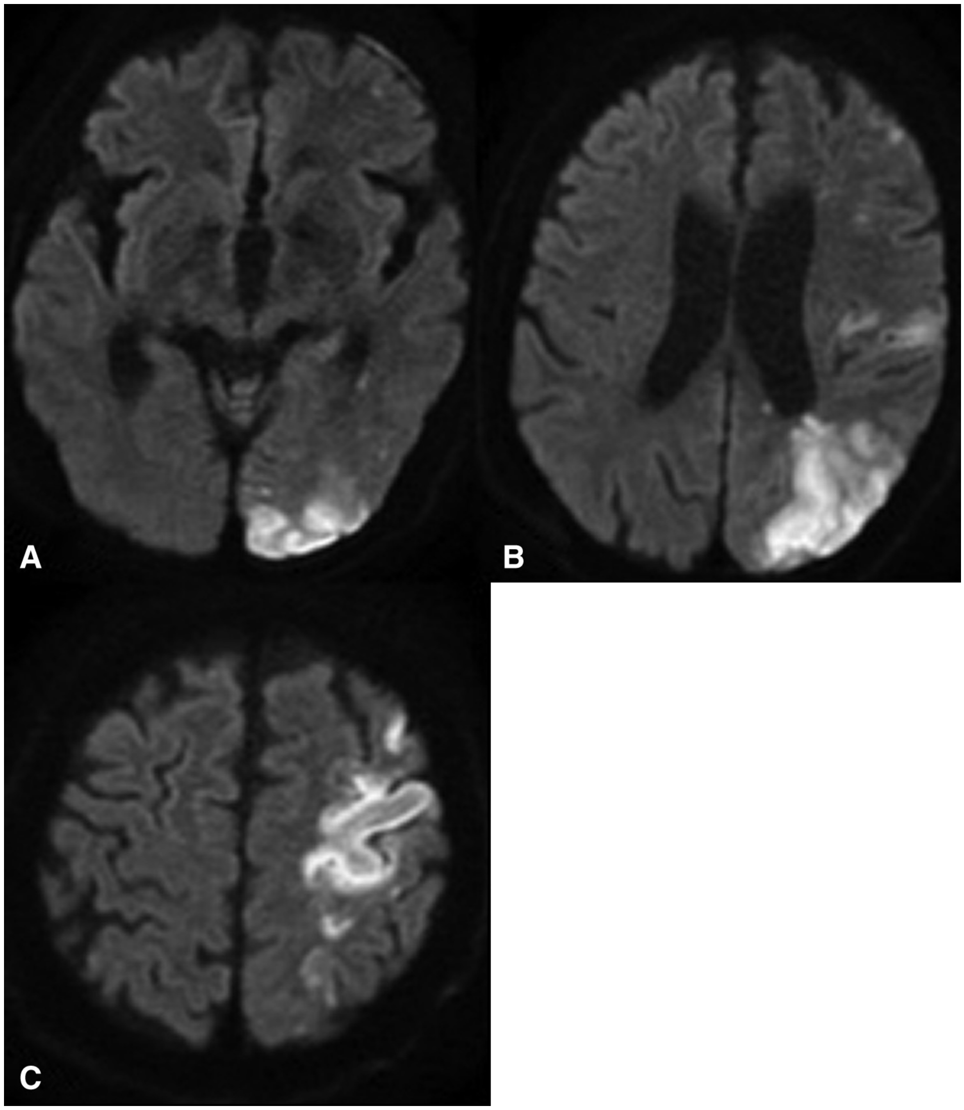

Fig. 6 Postoperative diffusion-weighted MRI. The infarcted focus before surgery increased in size (**A–C**), but extensive cerebral infarction in the left middle cerebral artery-dominated area was avoided. MRI: magnetic resonance imaging

may induce injury of the intima, internal elastic membrane, and media, promoting erythrocyte/fibrin aggregation through platelet activation on the stent surface prior to intimal neoplasia and leading to narrowing of the vascular lumen through remodeling mediated by the infiltration/migration of the vascular smooth muscle cells in aggregates and collagen synthesis.[2,3] As IST can be prevented by inhibiting platelet activation, the prophylactic administration of antiplatelet drugs is important. In Japan, when performing SAC, combination therapy with aspirin and clopidogrel is primarily selected, and this is also adopted at our hospital. Regarding postoperative antiplatelet drug therapy, dual antiplatelet therapy (DAPT) should be continued until stent covering by the endothelium prevents thrombus adhesion/enlargement. A study regarding intimal neoplasia of the coronary artery reported that the endothelium enlarged until ≤3 months after stent treatment, reaching a plateau and regressing ≥6 months after treatment.[3] At our hospital, DAPT is started 1–2 weeks before surgery and continued for at least 3 months after surgery. The timing of switching to subsequent monotherapy is regulated according to individual patients. Concerning unresponsiveness to antiplatelet drugs, unresponsiveness to aspirin accounts for approximately 5% and that to clopidogrel accounts for 20%–40%.[4,5] It is ideal to evaluate such unresponsiveness in each patient, but this is not realized at our hospital. In the present case, there was no ischemic complication during antiplatelet therapy and the antiplatelet drugs may have been effective. An etiological factor for occlusion in the present case was incompliance with antiplatelet drug therapy after discharge; it was the most concerning factor for SAC. As a background factor, the understanding of the patient's lifestyle was insufficient. To avoid incompliance with DAPT, sufficient explanation regarding possible complications due to incompliance and living environment are necessary. Attention should have been paid to resolve drug adherence problems before surgery.

As risk factors for IST, in-stent stenosis, antiplatelet drug reduction, bioactive coil usage, poor stent adhesion/flexion, radiotherapy, stent use for fusiform aneurysms, and complexly shaped stent (Y-stent) insertion have been reported.[6] According to Nii et al., the mean diameters of stents used for SAC were 3.0±0.9 mm in the intraoperative IST group and 4.5±0.7 mm in the non-IST group, demonstrating a significant difference.[7] Regarding the risk of IST for small-diameter stents, that for coronary artery stents has also been reported.[8] The diameter of the LVIS used in the present case was 4.5 mm, being relatively large; the stent was deployed without complication and there was no coil deviation. Concerning the structural characteristics of stents, a previous study found that braided stents induced thrombosis earlier than other stents due to a large metal coverage area and low-level wall shear stress, although there was no significant difference in the incidence of IST between braided and laser-cut stents.[9] In particular, early perioperative antiplatelet drug management must be continued more strictly. Furthermore, poor stent adhesion may delay stent endothelialization, causing IST. Therefore, when selecting closed-cell stents with a weak radial force, the above issue must be considered.[10]

The incidence of IST during SAC is 5.9%.[7] Many studies presented troubleshooting, but to our knowledge, no study has reported revascularization in patients with complete occlusion related to delayed IST. As the management of delayed IST, drug therapy (potentiation of systemic heparinization, antiplatelet drug loading, topical arterial injection of ozagrel sodium or urokinase, intravenous thrombolysis with tissue plasminogen activator (tPA), and neuroprotection by edaravone administration) and mechanical treatment (thrombus crushing with a guidewire or balloon and use of thrombus-aspirating devices) may be routinely selected in accordance with intraoperative IST management. Strict drug therapy should be prioritized rather than mechanical treatment. Concerning drug therapy in the present case, systemic heparinization and edaravone administration were conducted. As the time of onset was unclear, tPA was not administered. Considering re-occlusion after thrombectomy, antiplatelet drug loading through a nasogastric tube may have been necessary based on the above mechanism of IST. Regarding topical arterial injection, Nomura et al. reported a patient with incomplete occlusion associated with delayed IST related to drug incompliance and poor stent adhesion in whom the arterial injection of 40 mg of ozagrel sodium through the proximal site of incomplete occlusion led to ICA in-stent and MCA periphery thrombolysis.[6] In the present case, a Marksman was able to be guided to the distal site of occlusion once despite complete occlusion of the ICA; therefore, even if early recanalization is not achieved, the topical arterial injection of antiplatelet or thrombolytic drugs should have been performed prior to risky mechanical treatment using an SR. Understanding the procedure-related risks, we conducted thrombectomy using an SR. There were no serious complications related to surgery and recanalization was achieved, but the distal end of the stent migrated, resulting in shortening. If the SR became wrapped around the conventional stent, coil deviation may have occurred or it may have become impossible to collect the devices, leading to an unmanageable situation. Moreover, new complications, such as thrombus formation related to vascular endothelial disorder, dissection, or perforator withdrawal related to traction, may have developed. Therefore, thrombectomy with an SR for IST may be highly dangerous and may not be acceptable under any circumstances. In the present case, for thrombectomy, an aspiration-type catheter was unable to be guided to an area adjacent to the lesion site and a microguidewire was unable to be guided to a sufficiently distal area. Considering the risk of distal embolism, thrombus removal by aspiration is more appropriate than thrombus crushing; the former should be prioritized. Recently, aspiration-type catheters, characterized by high trackability, have also become available and they should be used preferentially. In addition, if a microcatheter whose diameter is greater than that of a Marksman had been used to reduce ledge effects, an aspiration-type catheter may have been guided to a more distal area. Shaping at the aspiration-type catheter end should have been arranged. We decided to adopt an SR, considering it difficult to guide a balloon catheter to the lesion site. However, lesion crossing with a microcatheter was accomplished and balloon-catheter guiding through wire exchange may also have been possible. Furthermore, if the buddy wire technique[11] or double wire technique with a thin-diameter microguidewire[12] had been applied to guide the Marksman to a more distal area, passage at the site of occlusion and operability at a distal area may have been improved. If it had been possible to guide the Marksman to a distal area, a balloon catheter may have reached the lesion site. Strategies to avoid the use of an SR should have been prepared.

In the present case, the use of an SR for IST 3–4 weeks after SAC resulted in stent migration. Although recanalization was achieved, we recognized that this treatment was highly dangerous. Concerning this procedure, the possibility of the stent moving depending on the frictional force between the SR and stent, even when the vascular endothelium covers the stent, cannot be excluded; therefore, even if the interval from stenting is long, an SR may not be available. It was optimistic to imagine stent covering by the endothelium at the point when IST developed following the progression of in-stent stenosis; this procedure is not acceptable under any circumstances. Even in emergencies, a treatment plan should be calmly arranged in such patients considering safety rather than urgency. In the future, similar events may increase with an increase in the number of SAC-indicated patients. Our report may provide information as a retrospective reference.

Conclusion

In a patient in whom incompliance with antiplatelet drugs led to ICA occlusion related to IST, we performed percutaneous thrombectomy with an SR. We recognized that the use of an SR for IST was not acceptable and physicians should therefore make efforts to prevent new complications by calmly troubleshooting even in emergencies. We reported the present case to provide information to prevent similar incidents.

Disclosure Statement

The authors declare no conflict of interest.

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