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Endovascular and interventional neurology – case report collection 2022

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CASE REPORT
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Case Report: Can Ruptured Aneurysms in the Hypoplastic and Plexiform Posterior Inferior Cerebellar Arteries Be Safely Occluded?

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Aneurysms arising from the posterior inferior cerebellar artery (PICA) are not rare and may originate from the proximal or peripheral segment of the PICA. However, when the affected PICA is hypoplastic and plexiform, it is difficult to occlude the aneurysm without sacrificing the parent vessel, the PICA. This type of aneurysm is rare, and whether it is safe to occlude the aneurysm and the parent artery, in cases of a ruptured aneurysm of the hypoplastic and plexiform PICA, has not been adequately studied and is still open to debate. In this report, two patients with ruptured aneurysms in the hypoplastic and plexiform PICA were presented. Both patients were admitted to our hospital for subarachnoid hemorrhage. After team discussions between the neurosurgeons and neurointerventionalists, the aneurysm and parent PICA had to be occluded *via* endovascular treatment under general anesthesia. One of the patients developed postprocedural brainstem infarction and exhibited favorable recovery. The other patient died of pulmonary infection, although improvement in the postoperative state was observed. Although rare, aneurysms can originate from the hypoplastic and plexiform PICA. Occluding the aneurysm and hypoplastic parent PICA *via* endovascular treatment might be a reasonable option.

Keywords: posterior inferior cerebellar artery, hypoplastic, plexiform, aneurysm, endovascular treatment, subarachnoid hemorrhage

INTRODUCTION

The posterior inferior cerebellar artery (PICA) is one of the three most important cerebellar arteries. Aneurysms arising from the PICA are not rare and may be located at its proximal or peripheral segment (1, 2). Generally, due to advancements in endovascular treatment (EVT), coiling the aneurysm while sparing the parent PICA is achievable because the involved PICA is often well-developed (3). However, when the affected PICA is hypoplastic and plexiform, it is difficult to occlude the aneurysm without sacrificing the parent PICA.

This type of aneurysm is rare, and whether it is safe to occlude the aneurysm and parent artery in cases of a ruptured aneurysm of the hypoplastic and plexiform PICA has not been adequately studied and is still open to debate (4, 5). In this report, we report 2 cases of ruptured aneurysms of a

hypoplastic and plexiform PICA. Endovascular occlusion of the aneurysms and parent PICAs was performed, and no severe brainstem complications were encountered.

CASE REPORTS

Case 1

A 53-year-old male suffered a sudden severe headache and vomited 4 h before admission. He was a Chinese patient of Han nationality who was healthy and denied having a history of chronic diseases. He had no history of drug abuse or surgical treatment of craniocerebral disease. Upon admission, a physical examination was performed, and the results were unremarkable, except for nuchal rigidity. Head CT showed subarachnoid hemorrhage (SAH) concentrated at the perimesencephalic cistern with involvement of the fourth ventricle (**Figure 1A**). CT angiography (CTA) revealed no underlying vascular lesions (**Figure 1B**). Catheter angiography revealed that the left PICA was hypoplastic and plexiform. Several small arteries originated from the left vertebral artery (VA) near the origin of the PICA. A pseudoaneurysm was located in the hypoplastic and plexiform PICA (**Figures 1C,D**). His family had no similar diseases.

Occlusion of the aneurysm and parent PICA *via* EVT was planned under general anesthesia. During the procedure, a Marathon microcatheter (Medtronic, Irvine, California, USA) was introduced into the PICA *via* the guidance of a microwire to access the aneurysm as much as possible. Then, the aneurysm and parent PICA were occluded with an Onyx liquid embolic system (Medtronic, Irvine, California, USA) (**Figure 1E**). Postoperatively, he showed no consciousness or movement disturbance. Mild hoarseness, dysphagia, and left central facial paralysis were noticed. The patient was discharged 1 week later. On follow-up one and a half years later, he recovered significantly, except for mild hoarseness. MRI only revealed the old brainstem infarction (**Figure 1F**).

Case 2

A 60-year-old female suffered a sudden onset of headache and vomited 3 h before admission. She was a Chinese patient of Han nationality and had a 10-year history of diabetes, but she had no history of drug abuse or surgical treatment of craniocerebral diseases. On physical examination, she was drowsy. The strength of the four limbs was normal. Head CT showed SAH concentrated at the cisterns around the brainstem and cerebellomedullary cistern (**Figure 2A**). CTA revealed no vascular abnormalities that might be responsible for the SAH (**Figure 2B**). Catheter angiography showed that the right PICA was hypoplastic and plexiform. Multiple slim arteries originated from the right VA near the hypoplastic PICA. A pseudoaneurysm was detected in the plexiform PICA (**Figures 2C,D**). Her family had no similar disease.

Occlusion of the aneurysm and parent PICA *via* EVT was planned under general anesthesia. A Marathon microcatheter was advanced to the parent artery of the aneurysm *via* the guidance of a microwire to access the aneurysm. Then, the Onyx liquid embolic system was cast, successfully occluding the aneurysm and parent PICA (**Figure 2E**). The patient was stable postoperatively and regained consciousness 1 week later. A head CT scan performed 8 days later showed partial resolution of the SAH (**Figure 2F**). She was discharged to a local hospital for rehabilitation. A telephone follow-up revealed that she died of pulmonary infection 1 month later at the local hospital.

DISCUSSION

The PICA is a complex cerebellar artery (6, 7). In 80–95% of the cases, the PICA arises from the intracranial intradural VA. In 5–20% of the cases, the PICA has an extradural origin from the VA; rarely, the PICA may originate from the basilar artery (8). The PICA often begins in a single trunk, and in 2.5–6% of the cases, it begins from the VA as duplicate trunks (9). The PICA may be hypoplastic in 10–32% of the cases and absent on one side in 15–26% of the cases and on both sides in 2% of cases (10).

In hypoplastic PICA, the PICA may be plexiform and arise from the VA, consisting of multiple perforating arteries along the PICA course (8). Among these multiple perforating arteries, the strongest branch can be considered the hypoplastic PICA. These hypoplastic and plexiform PICAs mainly should perforate the brainstem rather than supply the posterior inferior facet of the cerebellum (11).

Aneurysms in hypoplastic and plexiform PICAs are rare entities. These aneurysms are dissecting aneurysms and can transform into pseudoaneurysms after rupture (1). They share the same pathophysiological mechanism with other intracranial perforator aneurysms, including the loss of internal elastic lamina induced by arteriosclerotic, hemodynamic, or inflammatory stress, such as perforating aneurysms in moyamoya disease (12, 13).

The ruptured pseudoaneurysms in hypoplastic PICA should be given aggressive treatment to avoid repeated rupture, including open surgery and EVT. The treatment with open surgery is challenging in the following two aspects: (a) it is difficult to identify the aneurysm intraoperatively, and (b) it is very hard to spare a hypoplastic PICA while occluding the aneurysm (14). Hence, EVT is a reasonable option. However, due to the narrow diameter of the PICA, it is challenging to embolize the aneurysm while sparing the parent PICA.

Therefore, occluding an aneurysm and hypoplastic parent PICA had to be performed. Although occluding an aneurysm and hypoplastic parent PICA is not technically difficult, it is unclear whether it is safe to occlude the hypoplastic PICA (1, 2).

Trivelato et al. reported that 14 patients harboring isolated dissecting aneurysms in the PICA with normal development were assigned to EVT, eight to selective coiling vs. six to parent artery occlusion (PAO). Both techniques were proven effective in preventing rebleeding; however, PAO was significantly associated with a higher risk of ischemic events (15). Based on the experience of the above study, two cases of this report can be tried to perform the occlusion of the hypoplastic and plexiform PICA.

In performing the PAO with the aneurysm in the hypoplastic and plexiform PICA, coiling was difficult to perform because the

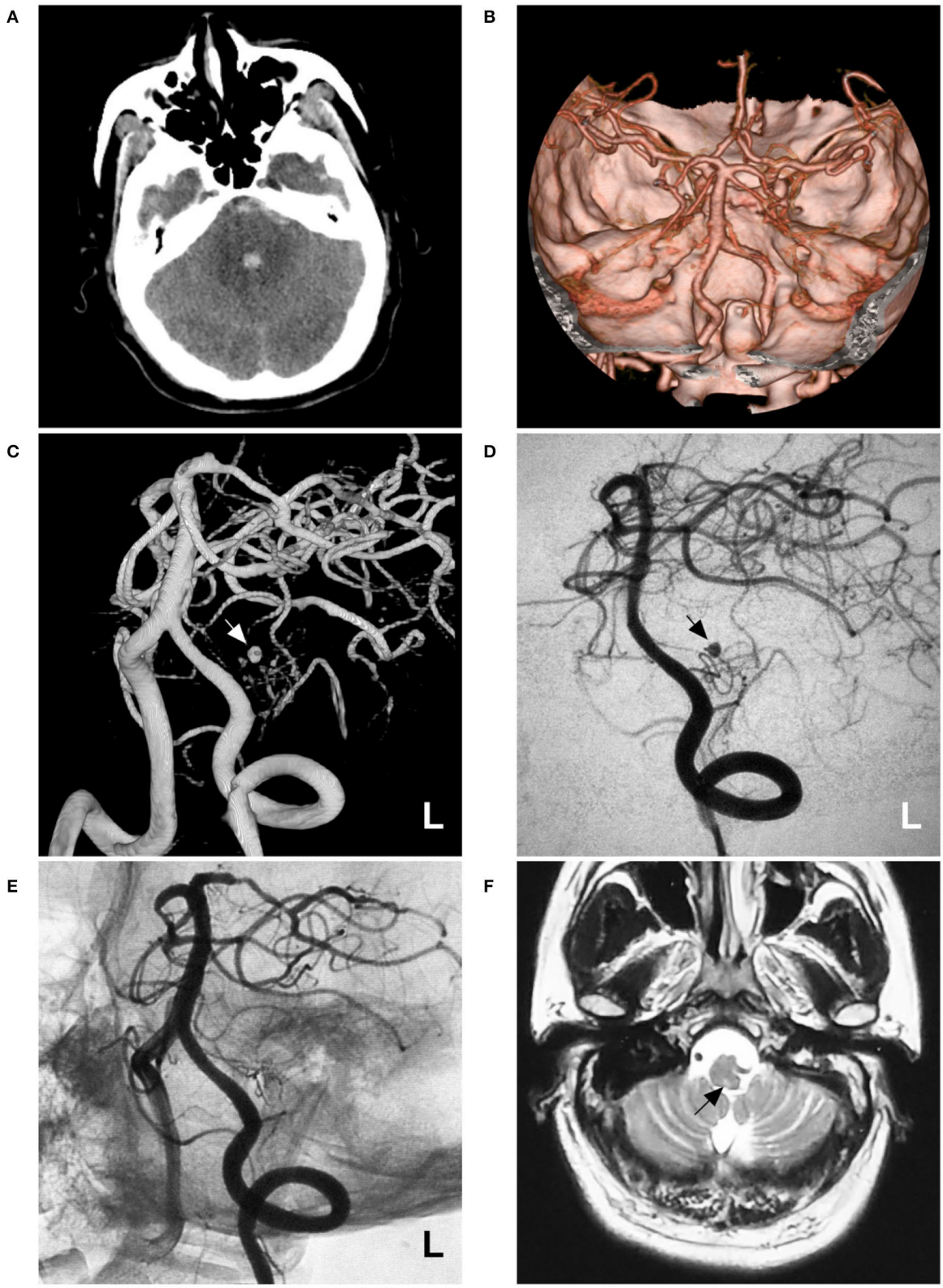

FIGURE 1 | Imaging of case 1. **(A)** CT shows subarachnoid hemorrhage concentrated at the perimesencephalic cistern with involvement of the fourth ventricle. **(B)** CTA reveals no underlying vascular lesions. **(C,D)** Angiograms of the left VA show a pseudoaneurysm (arrow) located in the hypoplastic and plexiform PICA. **(C)** shows a three-dimensional angiogram, and **(D)** shows a two-dimensional angiogram. **(E)** Angiogram of the left VA shows that the aneurysm and parent PICA are cast with Onyx, and other branches are visualized. **(F)** Follow-up MRI scan shows a minor brainstem infarction (arrow). CT, computed tomography; CTA, CT angiography; L, left; MRI, magnetic resonance imaging; PICA, posterior inferior cerebellar artery; VA, vertebral artery.

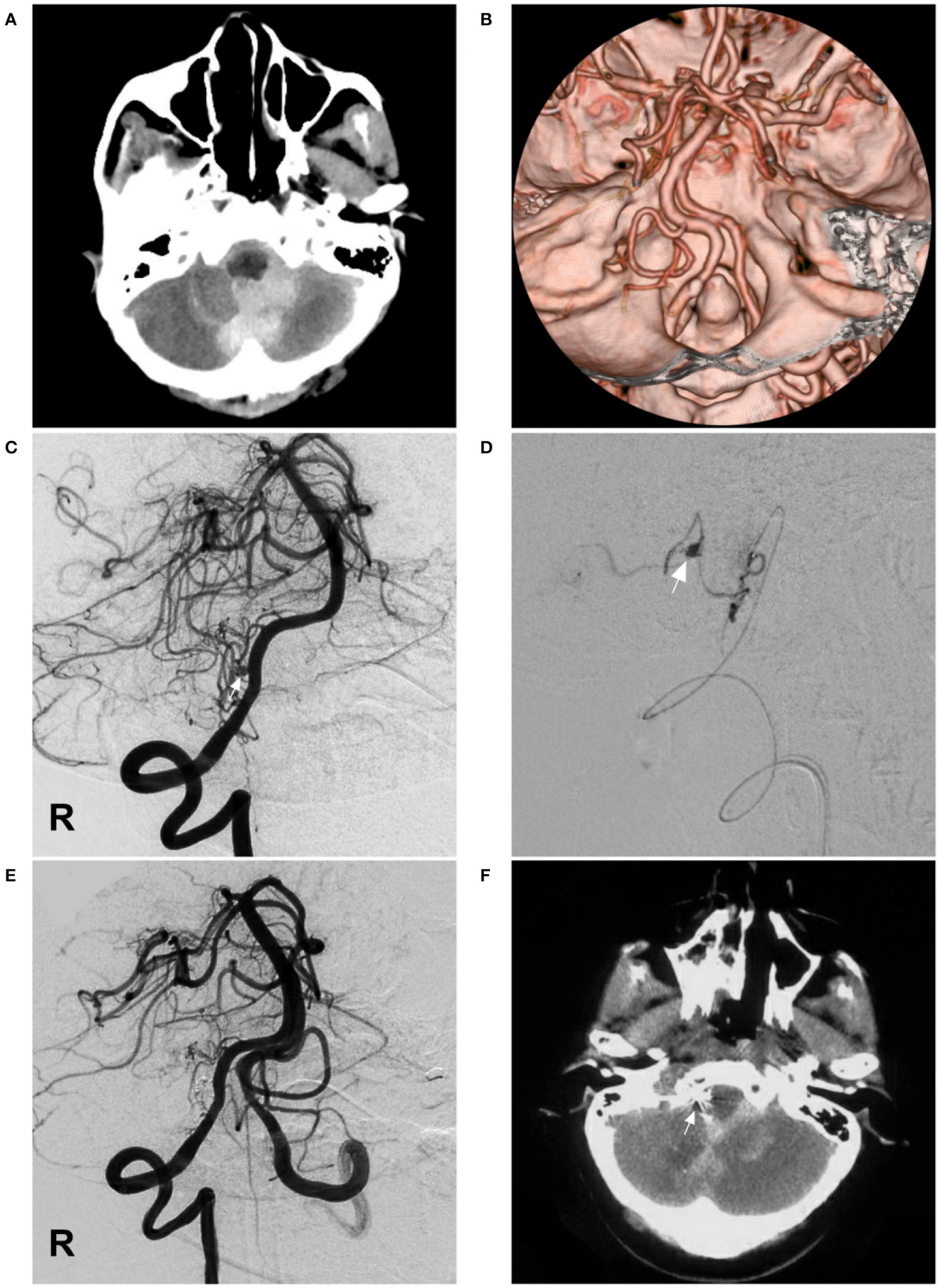

FIGURE 2 | Imaging of case 2. **(A)** CT shows SAH concentrated at the cisterns around the brainstem and cerebellomedullary cistern. **(B)** CTA reveals no vascular abnormalities. **(C)** Angiogram of the right VA shows a pseudoaneurysm (arrow) located in the hypoplastic and plexiform PICA. **(D)** Superselective angiogram of the right PICA showing the pseudoaneurysm (arrow). **(E)** Angiogram of the VA shows that the aneurysm and parent PICA were cast with Onyx, and other branches are visualized. **(F)** Postoperative CT scan shows the location of casting Onyx (arrow) and partial resolution of the SAH. CT, computed tomography; CTA, CT angiography; PICA, posterior inferior cerebellar artery; R, right; SAH, subarachnoid hemorrhage; VA, vertebral artery.

microcatheter of delivering coils was too thick and stiff, and it was difficult to go further in the hypoplastic PICA. In addition, the coil was too stiff and easily resulted in perforation of the vessel and aneurysm. Therefore, the Onyx liquid embolization system was a good choice. However, the drawback of Onyx is that it sacrifices too many normal vessels. In a previous report, for patients with basilar artery perforated aneurysms, occluding the parent vessel to the perforated aneurysm was acceptable, despite the risk of brainstem stroke in some patients (16).

However, the consequences of occluding a hypoplastic PICA have never been studied. Therefore, we tried to occlude the ruptured aneurysms in the hypoplastic and plexiform PICA because the supply region of the hypoplastic PICA might be compensated by the neighboring arteries and other cerebellar arteries. Although brainstem infarction can occur, we believe the benefits outweigh the risks. After informing the patients and families about surgical plans and risks, the occluding of ruptured aneurysms in hypoplastic and plexiform PICA was performed; fortunately, no severe complications occurred.

CONCLUSION

Aneurysms in hypoplastic and plexiform PICA were rare. Sometimes, occluding the aneurysm and the hypoplastic parent PICA *via* EVT had to be the last resort. Because the supply region of the hypoplastic PICA can be compensated by the neighboring arteries, occluding the ruptured aneurysms in the hypoplastic and plexiform PICA may be feasible.

LIMITATION

This is a report of two cases, and the conclusion of this study should be cautiously interpreted. In addition, no case of surgical treatment can be provided as a comparison with EVT, which was a limitation of the study.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

ETHICS STATEMENT

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

AUTHOR CONTRIBUTIONS

JY designed the study and drafted the manuscript. KH collected the data. JY and KH confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

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CASE REPORT
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Case Report: Trigeminocardiac Reflex in Endovascular Recanalization of Intracranial Internal Carotid Artery Occlusion

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Background: The trigeminocardiac reflex (TCR) is a unique brainstem reflex that manifests as sudden negative hemodynamic changes. Although rare, TCR may develop during interventional neuroradiology procedures. Intracranial internal carotid artery occlusion (ICAO) is a cause or risk factor of ischemic stroke. Endovascular recanalization is an effective treatment for intracranial ICAO. The occurrence of TCR during the endovascular treatment of intracranial ICAO has not been reported previously.

Methods: We identified and reviewed four intracranial ICAO cases who suffered a sudden negative hemodynamic change during endovascular therapy at our hospital between March 2019 and December 2020.

Results: There were five sudden heart rate and/or blood pressure drops in the four cases; all occurred just after contrast agents were injected. Some angioarchitectural characteristics were common among the four cases. First, the intracranial internal carotid artery distal to the ophthalmic artery was occluded, leaving the ophthalmic artery as the only outflow tract. Second, there were obstructive factors proximal to the end of the guiding catheter, including a vasospasm or dilated balloon. This type of angioarchitecture with a limited outflow tract creates a "blind alley." The five negative hemodynamic events all recovered: two spontaneously and three after drug administration. Postoperatively, two of the four patients developed ocular symptoms.

Conclusions: Intracranial ICAOs may produce a distinctive angioarchitecture, such as a blind alley, that predisposes patients to TCR. Surgeons should pay special attention to the possibility of TCR during the endovascular recanalization of intracranial ICAO. Low-pressure contrast injections should be attempted, and anticholinergics should be ready for use.

Keywords: trigeminocardiac reflex, internal carotid artery occlusion, interventional complications, endovascular recanalization, ischemic stroke

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INTRODUCTION

The trigeminocardiac reflex (TCR) is a unique brainstem reflex that manifests as sudden negative hemodynamic changes, including a sudden lowering of both the heart rate and mean arterial blood pressure, cardiac arrhythmias, asystole, and other autonomic reactions such as apnea and gastric hypermotility (1). TCR is thought to be associated with the stimulation of sensory branches of the

trigeminal nerve. The hemodynamic changes can often return after a stimulus has ceased, and the inadequate awareness or inappropriate treatment of TCR can lead to catastrophic consequences. TCR may occur in a variety of diseases as well as during or after surgery involving the trigeminal nerve (most commonly neurosurgery or ophthalmic surgery). Although rare, TCR can also be encountered during interventional neuroradiology procedures (2–5).

Intracranial internal carotid artery occlusion (ICAO) is a cause or risk factor of ischemic stroke (6). Endovascular therapy for selected patients with acute ICAO has definite benefits and has been widely accepted. Endovascular recanalization of non-acute ICAO has also been selectively performed, with promising results (6). Here, we report four cases of intracranial ICAO with sudden negative hemodynamic changes during endovascular therapy, which were probably TCRs. We suggest that intracranial ICAOs have distinctive angioarchitectural characteristics that are prone to TCR, and that particular attention should be paid to TCR in the endovascular recanalization of intracranial ICAOs.

METHODS

We identified and reviewed four patients with intracranial ICAO who suffered a sudden negative hemodynamic change during endovascular therapy at our hospital between March 2019 and December 2020. Ethical approval was obtained from the Human Research Ethics Committee of our hospital and written consent was obtained from all patients.

RESULTS

Case 1

A patient presented with transient weakness in both left limbs in the preceding 2 weeks. Six months previously, the patient suffered a stroke resulting in left limb weakness, which recovered after medical treatment. The patient had a 2-year history of hypertension but no history of diabetes or heart disease. Magnetic resonance imaging (MRI) showed some non-acute infarcts in the right basal ganglia and frontal lobe. Computed tomography angiography (CTA) showed an intracranial ICAO, which was confirmed by femoral digital subtraction angiography (DSA) with iohexol contrast agent (**Figure 1A**). Perfusion-weighted imaging (PWI) revealed hypoperfusion in the occluded intracranial carotid artery (ICA) territory. There were no obvious contraindications on preoperative examination. Endovascular treatment was performed using iohexol as a contrast agent. After general anesthesia, the patient's heart rate was maintained at ∼70 beats per minute (BPM) and their blood pressure around 130/90 mmHg. A Navien 6F, 115 cm, intermediate catheter (Medtronic; Irvine, CA, USA) was placed into the cavernous segment of the right ICA with the support of a 6F, 90 cm, guiding sheath. A roadmap was generated by manual injection through the Navien, whereupon the patient's heart rate suddenly dropped to 14 BPM (**Figure 1B**). After ∼8 s, the heart rate reverted to 55 BPM without medication and the blood pressure was 95/70 mmHg. The operation then continued. A 0.014-inch microwire and a 0.021-inch microcatheter were passed through the occluded site. Another manual injection was then performed, whereupon asystole suddenly occurred and the systolic pressure subsequently dropped to 30 mmHg (**Figure 1C**). After cardiac resuscitation for 5 min, including chest compressions and atropine, heart rate and blood pressure returned to normal; however, for fear of a catastrophic cardiac complication, the operation was aborted. Postoperatively, the patient suffered decreased vision in the right eye. No other neurological complications occurred and cardiac examinations revealed no cardiac abnormalities. The patient was transferred to an ophthalmic hospital for further treatment. We were unable to obtain the relevant ophthalmic examination data from that hospital, and follow-up data are not available for this patient.

Case 2

A patient presented with right limb weakness that had suddenly appeared 2 months previously. Imaging studies at onset indicated a watershed cerebral infarction and severe stenosis of the intracranial ICA. The patient's symptoms greatly improved after the initial event, but had worsened over the preceding week. The patient had experienced hypertension for 5 years but no diabetes or heart disease. PWI revealed hypoperfusion in the right middle cerebral artery territory. DSA with the contrast agent iopromide showed an intracranial ICAO (**Figure 2A**). Endovascular treatment was performed using iopromide. After general anesthesia, the patient's heart rate was maintained at ∼60 BPM and the blood pressure at ∼115/85 mmHg. A 6F guide catheter was placed into the petrous segment of the ICA and a diagnostic catheter was inserted into the left vertebral artery. A dual vascular roadmap was generated manually by injecting from both the ICA and the vertebral artery (7), whereupon a sudden drop in heart rate occurred (to 30 BPM), accompanied by a decrease in blood pressure to 65/40 mmHg (**Figure 2B**). After 2 min of intravenous administration of 2 mg atropine, the heart rate and blood pressure returned to normal. The operation then continued and the occluded ICA was successfully recanalized by the passage of a microwire/microcatheter, balloon dilatation, and stent release (**Figure 2C**). Postoperatively, the patient complained of right ocular and orbital pain, which completely resolved after 3 days. The patient had no visual impairment or other neurological dysfunction.

Case 3

This patient suffered an acute ischemic stroke. The patient was admitted having experienced speech impairment and right limb weakness for 11 h, with an NIHSS score of 12. He had a 6-year history of hypertension and a 4-year history of diabetes. Imaging studies indicated a left ICAO and an ipsilateral acute watershed infarction with a large penumbra. Emergent endovascular treatment was performed and a left ICAO was confirmed by diagnostic angiography with iodixanol contrast agent (**Figure 3A**). After general anesthesia, the patient's heart rate and blood pressure were normal. A balloon guide catheter was placed into the petrous segment of the ICA. A vascular roadmap was then manually generated, whereupon the patient's heart rate suddenly dropped to 40 BPM, although the blood pressure did not change substantially (**Figure 3B**). Two

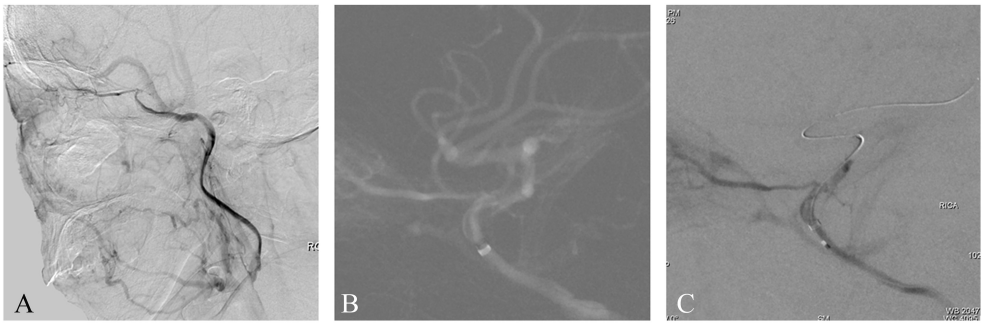

FIGURE 1 | (A) This is a non-acute ICAO. The intracranial ICA was occluded, and the ophthalmic artery was the only outflow tract. **(B)** A Navien 6F catheter was placed as close as possible to the occluded segment. A roadmap was generated by manual injection, whereupon the patient's heart rate and blood pressure suddenly dropped. **(C)** After a microwire and microcatheter were passed through the occluded site, another manual injection was performed, whereupon another serious drop in heart rate and blood pressure occurred. Finally, the operation was aborted.

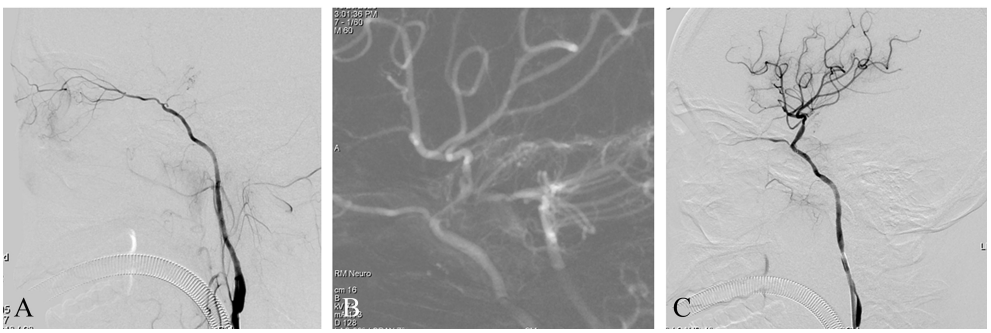

FIGURE 2 | (A) This is a non-acute ICAO. The intracranial ICA was occluded, and the ophthalmic artery was the only outflow tract. **(B)** A dual-roadmap was generated manually, whereupon a sudden drop in heart rate occurred, accompanied by a decrease in blood pressure. **(C)** Postoperative angiography showed severe vasospasm of the proximal ICA.

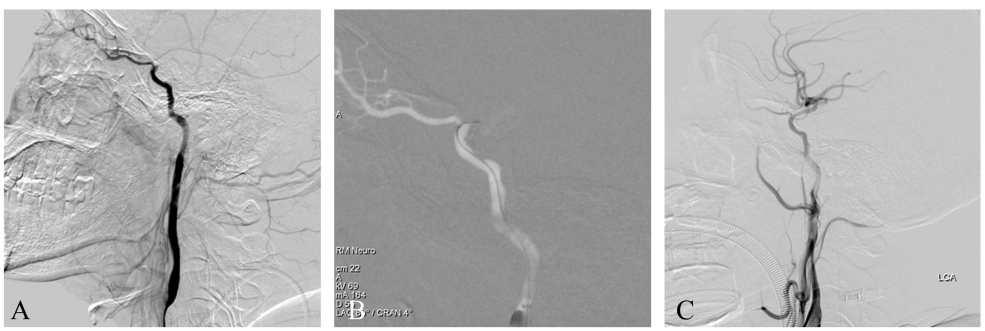

FIGURE 3 | (A) This is an acute ICAO. The intracranial ICA was occluded, and the ophthalmic artery was the only outflow tract. **(B)** A balloon guide catheter was used. After the balloon was dilated, a roadmap was manually generated, whereupon the patient's heart rate suddenly dropped, although the blood pressure did not change substantially. The heart rate returned to normal after atropine administration and the operation was continued. **(C)** Postoperative angiography showed that the occluded ICA was recanalized successfully.

milligrams of atropine was administered intravenously and the heart rate returned to normal in 1 min. The operation continued routinely, including a stent-retriever thrombectomy and rescue therapy with both balloon dilation and stent release. Finally, the occluded ICA was successfully recanalized and no negative hemodynamic changes recurred (**Figure 3C**). The postoperative course was uneventful.

Case 4

A patient presented with frequent transient left limb weaknesses lasting 1 month. MRI showed some non-acute infarcts in the right watershed area; PWI revealed hypoperfusion in the left middle cerebral artery territory. DSA with the contrast agent iopromide showed an intracranial ICAO (**Figure 4A**). Endovascular treatment was performed using iopromide. After

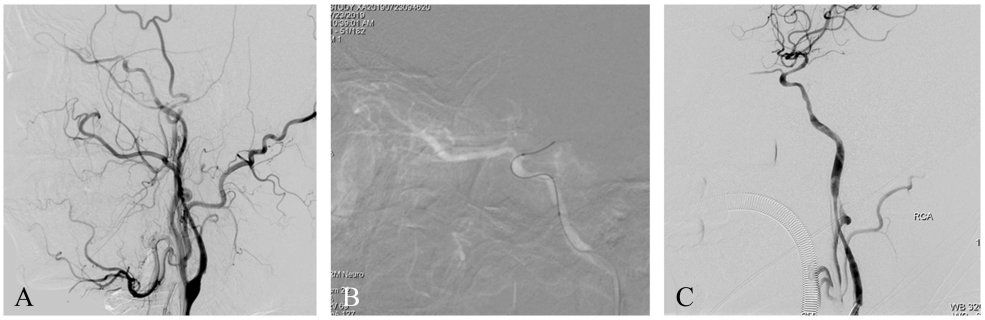

FIGURE 4 | (A) This is a non-acute ICAO. The intracranial ICA was occluded, and the ophthalmic artery was the only outflow tract. **(B)** A roadmap was generated manually, whereupon a sudden drop in heart rate and blood pressure occurred. After 1 min, the heart rate and blood pressure recovered spontaneously. The operation was then continued. **(C)** Postoperative angiography showed severe vasospasm of the proximal ICA.

general anesthesia, the patient's heart rate was maintained at ∼70 BPM and the blood pressure at ∼130/90 mmHg. A 6F guide catheter was placed into the petrous segment of the ICA. A vascular roadmap was generated manually, whereupon a sudden decrease in heart rate occurred (to 45 BPM), accompanied by a decrease in blood pressure to 90/40 mmHg (**Figure 4B**). After 1 min, the heart rate and blood pressure recovered spontaneously. The operation was then continued, and the occluded ICA was successfully recanalized by the passage of a microwire/microcatheter, balloon dilatation, and stent release (**Figure 4C**). The postoperative course was uneventful.

DISCUSSION

Although iatrogenically induced TCRs are common in neurosurgery and ophthalmology operations, they can also be encountered in interventional neuroradiology procedures. In the field of interventional neuroradiology, TCRs are mainly reported with embolization procedures for arteriovenous fistulas or nasopharyngeal tumors—especially those involving the internal maxillary artery, middle meningeal artery, or cavernous sinus (3–5, 8–10). To the best of our knowledge, a sudden drop in heart rate and/or blood pressure during the endovascular recanalization of ICAO, as in our cases, has not been reported previously.

There were five sudden heart rate and/or blood pressure drops in our four cases. They all happened just after the contrast agents were injected and there were no other possible inducements. We therefore consider that these events were TCRs. TCRs can be induced by a wide variety of mechanical or chemical stimulations of the sensory branches of the trigeminal nerve. Most TCRs in interventional neuroradiology are thought to be related to the toxicity of intravascularly injected drugs, such as dimethyl sulfoxide, Onyx liquid embolic agents, chemotherapeutic drugs, or contrast agents (3–5, 8–10). In the four cases reported here, three different contrast agents were used, and we therefore cannot conclude that they were responsible for the TCRs. TCR can also be caused by high pressure caused by the manual injection of contrast agents into selected arteries, which can stimulate branches of the trigeminal nerve (2). Some of the angioarchitectural characteristics were similar among the four cases. First, the intracranial ICA distal to the ophthalmic artery was occluded. Second, there were obstructive factors proximal to the end of the guiding catheter, including a vasospasm or dilated balloon. Thus, when injection was performed through the guiding catheter, the ophthalmic artery was the only outflow tract and the pressure in the artery and ocular structures would have suddenly risen beyond the normal tolerable range. This would have stimulated the ophthalmic branch of the trigeminal nerve, triggering an oculocardiac reflex, which is a peripheral variant of the TCR and a dysrhythmic physiological response to physical stimulation of the eye. This kind of angioarchitecture, with a limited outflow tract, can be referred to as a "blind alley." An enormous elevation of intraluminal pressure in the outflow artery by the injection of contrast has been shown by Sadayoshi and colleagues using a silicon vascular model (11). We therefore suggest that high pressure from the contrast injection was the factor that induced TCRs in our four cases. We believe that if the catheter is located in the extracranial carotid or more proximally in the cervical region, the aforementioned reflex will not occur because the contrast agent can reflux into the common carotid artery. Indeed, TCR did not occur during the process of diagnostic angiography in any of these patients. Patients with chronic intracranial ICAOs often experience natural atrophy of the proximal ICA. The narrowed vessel is prone to spasm during catheter placement, which leads to an occlusion proximal to the guiding catheter and a subsequent blind alley. The same mechanism applies to intracranial ICAOs with cervical ICA stenosis or the use of a balloon catheter. Intracranial ICAOs may therefore have a distinctive angioarchitecture that is prone to blind alleys and TCR. Thus, surgeons must be alert to the existence of a blind alley and not use too much pressure when injecting the contrast medium. For some special ICAOs, such as those with preoperative bradycardia, prophylactic medication may be considered.

In addition to TCR, the blind alley angioarchitecture and injection-induced high pressure in the ophthalmic artery may also damage ocular structures and visual function. Glaucoma can arise as a complication of superselective ophthalmic angiography (12). Two of our four patients developed ocular symptoms.

One patient suffered severely decreased vision and another had ocular and orbital pain with no visual impairment. These symptoms were probably related to injection-induced high intraocular pressure and/or orbital pressure, although the specific mechanism for these effects is not clear.

In most TCRs, when the stimulus stops, the patient's heart rate and blood pressure improve spontaneously. However, in some cases, medical intervention is necessary. The preferred drugs are anticholinergics, such as atropine, which is effective for most patients (4). However, if the stimulation is intense, the TCR may be refractory to this treatment modality. For some cases with severe bradycardia, adrenaline and a transcutaneous pacemaker may even be used. In three of the five sudden heart rate or blood pressure drops presented here, atropine was used, and all three negative hemodynamic changes returned to normal. We believe that both drug administration and stimulus cessation may help to prevent injection-/pressure-induced TCR in intracranial ICAO surgery.

CONCLUSIONS

These four cases highlight some important considerations. Intracranial ICAOs may have a distinctive angioarchitecture, such as a blind alley, which is prone to TCR. We suggest that surgeons pay special attention to TCR during the endovascular recanalization of intracranial ICAO. Low-pressure contrast injections should be attempted, and anticholinergics such as atropine should be ready for use. We recommend the gentle manual injection of contrast material during interventional procedures for patients with intracranial ICAO. For those with preoperative bradycardia, prophylactic medication may be considered.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

ETHICS STATEMENT

The studies involving human participants were reviewed and approved by Tianjin University Huanhu Hospital. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

AUTHOR CONTRIBUTIONS

HR, YW, and YH: study concept and design. HR, YW, and BL: data acquisition and operation. HR and YW: manuscript drafting. HR and YH: review and editing. YH: supervision. All authors contributed to the article and approved the submitted version.

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Case report: Endovascular treatment of two scalp arteriovenous malformation cases *via* direct percutaneous catheterization: A case series

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Background: Scalp arteriovenous malformations (AVM) are rare vascular malformations reported only in small case series. Scalp AVMs usually present with symptoms, including headache, tinnitus, epilepsy, cerebral ischemia, and necrosis of the scalp, which can cause functional, cosmetic, and psychological problems. There are many difficulties in the treatment of scalp AVM because of its complex characteristics of vascular anatomy, non-uniform structure, and intracranial-extracranial anastomosis.

Case description: To illustrate the endovascular treatment of scalp AVM *via* direct percutaneous puncture while traditional arterial and venous approaches were not available. In this report, access was obtained through a direct puncture of the enlarged frontal vein. Onyx-18 was injected through a microcatheter to occlude draining veins, fistulous connection, and the feeders. An 18-gauge indwelling needle was inserted into draining veins directly. Postembolization angiography demonstrated complete sAVM occlusion immediately and no non-targeted embolization. At a 1-year follow-up, no procedure-related complications and evidence of recurrence were observed.

Conclusion: The technique of endovascular embolization *via* direct percutaneous puncture approach is safe, rapid, and effective for specific sAVM. Treatment options should be made in terms of size, vascular anatomical characteristics of the lesions, patient's preference, cosmetic factors, and available expertise.

KEYWORDS

scalp arteriovenous malformation, scalp arteriovenous fistula, endovascular embolization, direct percutaneous puncture, case report

Introduction

Scalp arteriovenous malformations (sAVM), also known as cirsoid aneurysms or scalp arteriovenous fistulas (AFV), are anomalous connections between superficial arteries and veins without capillaries. The pathological mechanism of scalp AVMs is still unclear. These cases are relatively rare and most pediatric cases are congenital.

Many factors, such as trauma, craniotomy, hair implantation, infection, and inflammation, are involved with the etiology of scalp AVMs (1). The AVMs have been reported to account for 8.1% of all AVMs (2). These AVMs are pulsatile lesions with headache, tinnitus, vascular murmur, local bleeding, and necrosis of the scalp (3). In addition, epilepsy and cerebral ischemia could be caused by abnormal shunting of common carotid blood flow (4). The clinical symptoms could worsen while the lesions are enlarged. The mass developed from vascular abnormalities can cause functional, cosmetic, and psychological problems.

In this article, we reported a case series of scalp AVMs treated with Onyx *via* a direct percutaneous puncture approach.

Case description

This study was approved by the Institutional Review Board of Ethics of our hospital. Both patients agreed to be photographed and understood that their identity could be revealed on camera and in the content of the publication. CARE Checklist was implemented in this case report.

Case 1

History and examination

The first case is a 16-year-old male patient with complaints of progressive enlargement of forehead mass for 10 years. The lesion presented as a soft, pulsatile mass, and the border was not clear. Bowed head and physical exercises could increase the volume of mass. Other neurological symptoms are negative. The patient had no family history of vascular malformations, no history of head trauma, and febrile illness. Local hospital magnetic resonance imaging (MRI) demonstrated a subcutaneous flow void sign in the frontal region, which indicated abnormal vessel mass in the lesion.

Endovascular treatment

Cerebral diagnostic digital subtraction angiography (DSA)was performed under local anesthesia after the patient was admitted to our department. DSA confirmed the presence of frontal sAVM with feeding arteries from bilateral frontal branches of STAs and ophthalmic arteries and draining into orbital veins and facial veins (Figure 1A). We analyzed sAVM angio-architecture and a decision was made for treatment *via* endovascular embolization.

The embolization was performed under general anesthesia. A 5-Fr H1 catheter (Cook Medical, Bloomington, U.S.A) was targeted at the right external carotid artery (ECA) as a monitoring catheter through the sheath. In consideration of the location of the sAVM, access was obtained through direct puncture of the enlarged frontal vein with an 18-gauge needle and sutured in place (Figures 2A,B). Next, a microcatheter (Echelon 10; Covidien, Irvine, California, USA) was navigated through the 18-G venous indwelling needle. The contrast was injected to confirm the position of the microcatheter tip within the draining vein and was close to the fistulous connection (Figures 1Bi,ii). The microcatheter was flushed with dimethyl sulfoxide(DMSO) (0.3 ml). Onyx-18 (ev3 Endovascular; Medtronic, Minneapolis, Minnesota, USA) liquid embolic material (2.5 ml) was then carefully injected through the microcatheter under a road map and allowed to diffuse to fill the draining veins, fistulous connection, and the feeders successfully (Figures 1Biii,iv). Post-embolization angiography of bilateral internal carotid arteries (ICA) and ECAs demonstrated complete sAVM occlusion immediately after Onyx-18 injection (Figure 1C).

Postoperative course

The size of the mass decreased immediately after the embolization and did not present any more pulsation (Figures 3A,B). The lesion was pressurized bondage slightly after embolization for 12 h. One-year follow-up cerebral angiography demonstrated no evidence of the sAVM recurrence (Figure 3D). No skin necrosis was observed (Figure 3C).

Case 2

History and examination

A 23-year-old female patient presented with a 5-year-history of right occipital tender, pulsatile mass, and continued to enlarge recently. Neurological examination showed no pathological signs. The patient had no history of head trauma, hair transplantation, and other pertinent histories. MRI showed an abnormal vascular mass of the lesion.

Endovascular treatment

In our department, super-selective diagnostic DSA was performed. DSA confirmed the diagnosis of high-flow right occipital sAVM and revealed arterial supply from right OA, whereas the temporal and occipital tributaries of the external jugular vein were acting as drainers (Figure 4A). Then, we planned to perform treatment through a venous approach.

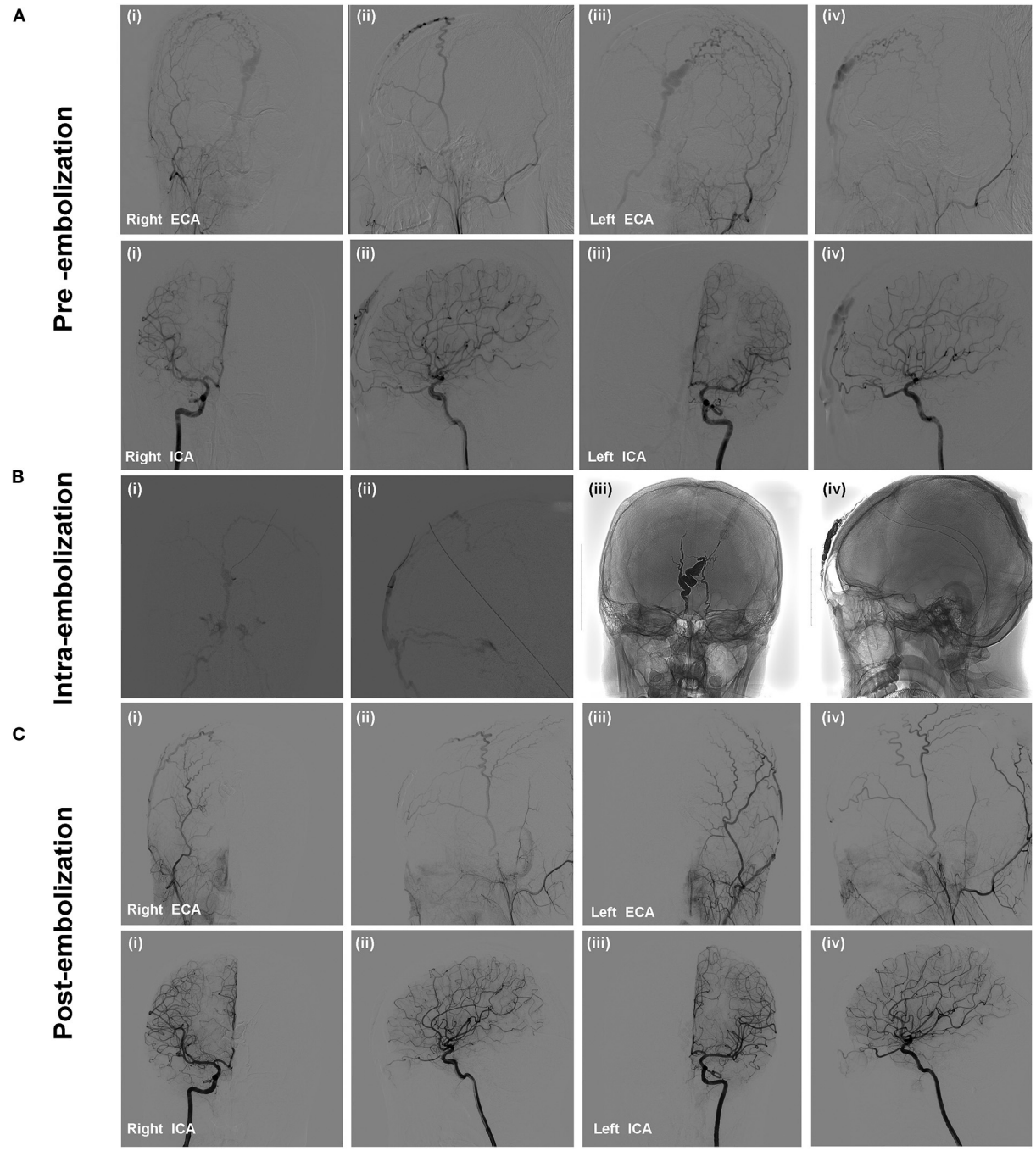

FIGURE 1
The patient presented with a pulsatile forehead mass without specific medical history. Selective cerebral DSA confirmed the presence of scalp AVM. Angiographic images showed that the feeding arteries of the lesion were bilateral frontal branches of STAs and ophthalmic arteries **(A)**. Onyx-18 liquid embolic material was injected to embolize the draining veins, fistulous connection, and feeding arteries. **(B)** Angiography was performed *via* microcatheter (i,ii); Penetration and solidification of Onyx after embolization (iii,iv); **(C)** Post-embolization angiography demonstrated the scalp AVM was occluded completely without non-targeted vessels embolization.

After cannulation into the right femoral vein was achieved using a 6-Fr guiding sheath, the 6-Fr Envoy guiding catheter (Codman, Miami Lakes, Florida, USA) was positioned within the right external jugular vein (EJV). Two microcatheter (Echelon 10) were advanced and placed in the distal primary targeted vessel assisted with microwire. Angiographic images

FIGURE 2
(A,B) Direct percutaneous catheterization of the draining veins was performed with an 18-gauge needle.

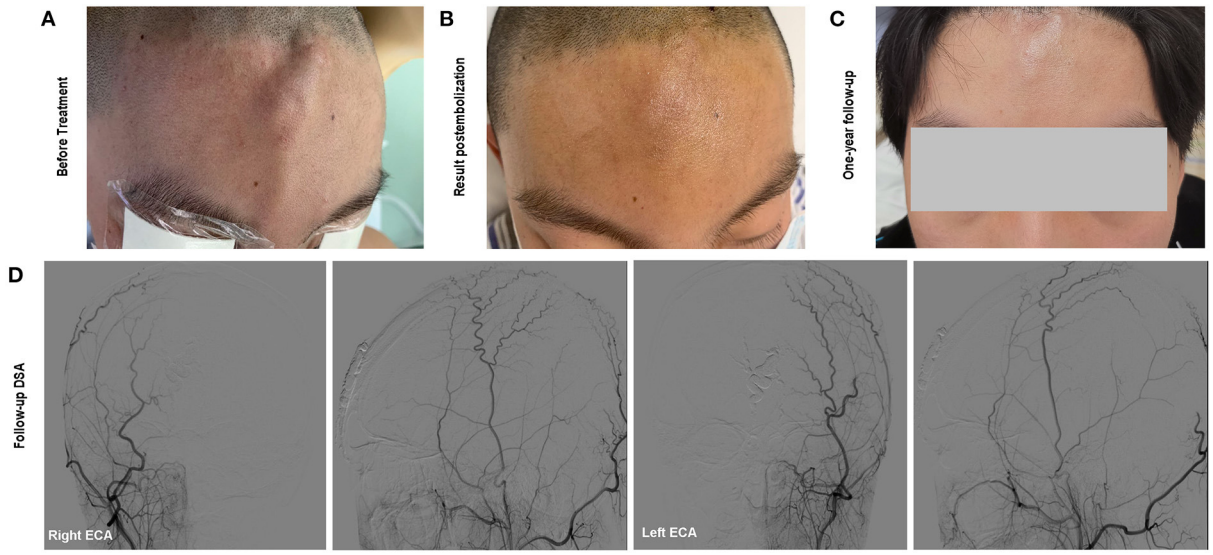

FIGURE 3
(A) The soft and pulsatile lesion with no clear border before treatment; **(B)** Immediate status of the lesion postembolization; **(C)** One-year follow-up showed no evidence of recurrence and scalp necrosis. Onyx was not visible beneath the skin; **(D)** Follow-up angiography showed complete occlusion of the scalp AVM.

demonstrated that the microcatheter tip was far from the malformation mass, which could lead to poor Onyx diffusion and microcatheter trapping. Thus, direct percutaneous catheterization under the guidance of the roadmap was performed after the occipital region was sterilized. Contrast injection confirmed an 18-gauge needle was placed in the draining vein. The 18-gauge needle system was flushed with DMSO, and Onyx-18 liquid embolic material (13 ml) was injected to completely occlude the nidus, partial feeding arteries, and draining veins, which was confirmed by post-embolization angiography. Post-embolization angiography showed that the fistula was occluded and no non-targeted embolization (Figure 4B), with preservation of the main intracranial branches of bilateral ICAs.

Postoperative course

The occipital lesion was wrapped with pressure dressing after the removal of the needle. At the 1-year follow-up visit, complete resolution of the pulsatile mass with no cutaneous necrosis was found.

Discussion

Scalp arteriovenous malformations (sAVM) is an abnormal fistulous connection between arteries and veins without an intervening capillary bed in the subcutaneous layer of the scalp (5). They used to be called aneurysm cirsoide, aneurysma serpentinum, plexiform angioma, and scalp AVF (6). The lesions

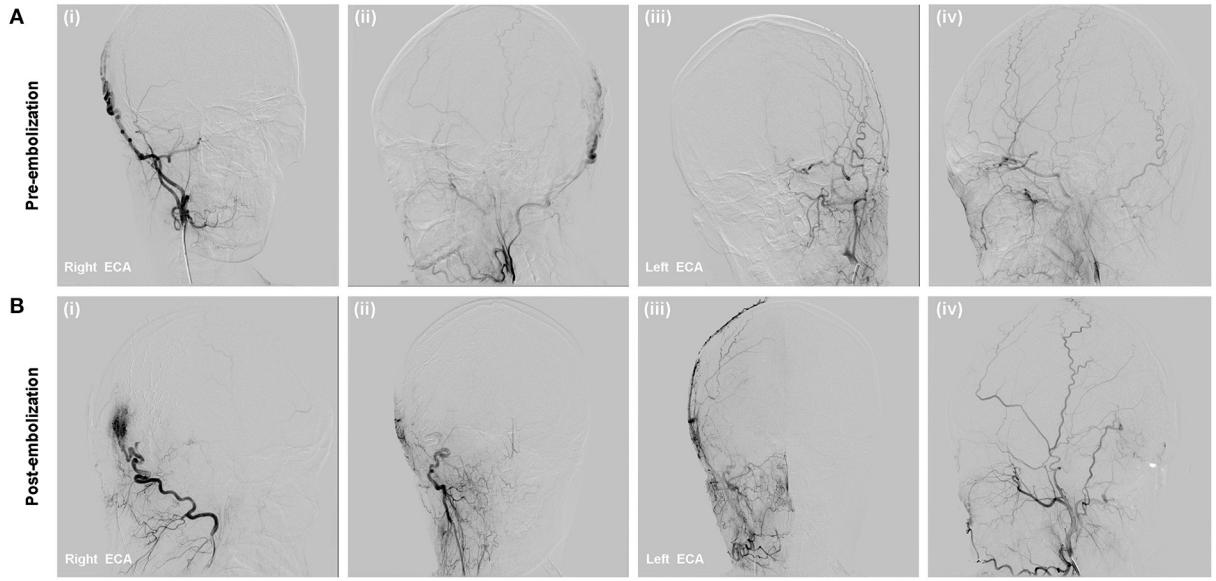

FIGURE 4
(A) DSA showed right occipital high flow scalp AVM fed from the right OA branches and drained to the external jugular vein; **(B)** Onyx-18 was injected *via* direct percutaneous puncture approach (i,ii); Immediate complete occlusion of the scalp AVM post-embolization (iii,iv).

are rare and little is known about their etiology and pathology. Most sAVM is spontaneous, however, it can be acquired after hair transplantation, head trauma, or craniotomy (1). sAVM often presents as progressively enlarged pulsatile mass (with 94.4% of patients) associated with headaches (25.3%), tinnitus (20.2%), bruits, local pain, epilepsy, hemorrhage, and scalp necrosis (7).

The sAVM is often detected by physical examination and the diagnosis is proven by computed tomography angiography (CTA) and magnetic resonance angiography (MRA) (8). Most sAVMs are located in frontal, temporal, and occipital regions, and their feeding arteries often arise from the superficial temporal artery (STA) or occipital artery (OA), and then, drain into the extracranial venous system. Statistics results indicate that there are more than one distinct feeding arteries in 54.2% of cases (7). The gold diagnostic standard is selective DSA. Catheter angiography is recommended to differentiate sAVM from other diseases, including venous malformation, hematoma, lipoma, cyst, abscess, lymphadenopathy, and tumor with abundant blood supply (5, 9, 10).

The sAVM is a kind of intractable vascular disease because of its specific characteristics, including heterogeneous vascular anatomy, high flow shunt, intracranial-extracranial anastomosis, and, probably, cosmetic demands. DSA can reveal whether there is a co-occurrence of intracranial vascular abnormalities and intracranial communication of sAVM, which affect treatment strategies. Besides, preoperative angiographic evaluation can be used for the assessment of feeders, draining pattern, amount of fistular connections, and abnormal shunt blood volume, which contribute to avoiding complications (11). Thus, DSA evaluation is essential before surgical and endovascular treatment.

Surgery used to be the first choice in the past years (12). However, endovascular embolization and surgery combined with embolization have been used more frequently with the development of endovascular technologies and a new type of liquid embolic agent (13). Some other treatments have also been reported, like simple fistular ligation and sclerotherapy with ethanol, which is suitable for small lesions with low blood volume and bleeding probability (14).

A previous literature review indicated that open surgery is preferred for large cases (>4 cm) with multiple feeding arteries (15, 16). The key steps of surgical resection include the design of flap incision, feeders controlling, and *en bloc* excision without scalp necrosis and massive blood loss (17). Possible complications are hematoma, seroma, alopecia, and flap necrosis. Surgical excision is limited by the risk of normal scalp vascularization impairment and severe blood loss, even though a better cosmetic result may be obtained (18).

Surgical resection of sAVM used to be the most common and successful method before the endovascular era. Recently, endovascular therapy has become the most extensively accepted as a single treatment or combined with open surgery for some complex cases. Endovascular embolization is preferred for small lesions (<4 cm) and fewer feeding/draining vessels (19, 20). It has also been used to reduce excessive hemorrhage

during surgical procedure. Previous work by Kawamata et al. showed that embolization of both feeders and nidus before surgery is more effective than embolization of the feeders alone to control the hemorrhage during excision (21). Coils and Onyx are most frequently used in the treatment of sAVM. The risks of endovascular therapy include scalp ulceration, non-targeted vessel embolization, systemic embolization, and local tattooing (22, 23). To minimize the above-mentioned risks, the method of "armored concrete" embolization (coils and Onyx are used) (24) and the balloon-protect technique *via* transvenous approach have been reported (25).

The most frequently used approach to embolization is femoral trans-arterial and transvenous routes. However, direct puncture of the fistular is recommended as an alternative option, while feeding/draining vessels are tortuous (26, 27). In the direct puncture technique, the venous pouch is targeted. During the embolization, external compression is performed, which causes the reflux of the Onyx into the nidus (28). Our experience showed direct puncture could reduce cost and operative time compared with the trans-arterial approach, especially for small and low-flow lesions.

In this paper, we reported two cases of sAVM embolization by direct percutaneous catheterization of the draining veins. A "plug" is usually made to prevent the regurgitation of embolic agents during the embolization of intracranial vascular malformations (brain AVM or brain AVF). In our cases, Onyx was injected under temporary compression of draining vein by fingers, which retrogradely allowed penetration of the agent into the feeding arteries, nidus, and venous drainage. Due to the short access distance, there was little difficulty in extubation, and the risk of bleeding during extubation was low. The two cases were superficial scalp AVMs with moderate blood flow. The onyx could be injected into nidus effectively. Besides, we did not make the plug-in consideration of cosmetic and economic factors. For cases with high blood flow, the double-lumen balloon catheter and cooker technology could be used (29). The interventional access of the patients through an artery or vein was not possible, which did not facilitate adhesion and solidification of Onyx or penetration of Onyx into the shunt. In our series, no procedure-related complications were recorded. At a 1-year follow-up, none of the symptoms had recurred.

Limitations

There are some limitations to this study. Scalp AVMs are rare lesions and this was a retrospective single-center study with a small number of patients. However, our experience demonstrated that endovascular treatment *via* direct puncture was safe and effective while traditional approaches were not available.

Conclusion

In our series of cases, we reported technical details of scalp AVM endovascular therapy *via* a direct percutaneous puncture approach, which indicates that scalp AVM embolization with Onyx is safe and effective. There is still no consensus on the treatment of the scalp AVM. Treatment options should be made in terms of size, vascular anatomical characteristics of the lesions, patient's preference, cosmetic factors, and available expertise.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the study was approved by the Huashan Hospital Institutional Review Board (HIRB), Fudan University, Shanghai, China. The patients/participants provided their written informed consent to participate in this study.

Author contributions

YS and PLiu: conception and design of study, collection and/or assembly of data, data analysis and interpretation, and manuscript writing. YT: conception and design of study and revision and final approval of manuscript. WZ: provision of study and revision and final approval of manuscript. PLi: manuscript writting. YL and ZL: data analysis and colleague. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Onyx embolization of tentorial dural arteriovenous fistula *via* the meningohypophyseal trunk and medial tentorial artery of Bernasconi-Cassinari

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For tentorial dural arteriovenous fistula (TDAVF), the meningohypophyseal trunk (MHT), and medial tentorial artery (MTA) of Bernasconi-Cassinari are rarely used as transarterial paths to perform the successful endovascular treatment (EVT). We reported a TDAVF mainly fed by the MHT. Onyx-18 casting in the MTA of Bernasconi-Cassinari under the assistance of coil embolization in proximal MHT was performed. The technique was reported in case 1. At the same time, case 2 with a similar TDAVF was chosen as a control. In case 1, a 52-year-old man suffered a cerebellar hemorrhage. A TDAVF was confirmed by computed tomography angiography and digital subtraction angiography. The feeding arteries included the MHT, middle meningeal artery (MMA), and the artery of Wollschlaeger and Wollschlaeger of the superior cerebellar artery. The MHT and MTA of Bernasconi-Cassinari were hypertrophied. First, a Marathon microcatheter was placed in the MTA to wait for Onyx casting, and then an Echelon-10 microcatheter was placed in the proximal MHT trunk with an aneurysmal dilation to perform coiling to prevent Onyx reflux. Then, Onyx casting obliterated the TDAVF. Case 2 was a 75-year-old woman with TDAVF, and the MTA of Bernasconi-Cassinari was the main feeder. First, the TDAVF experienced incomplete EVT with Onyx casting *via* the MTA under no assistance of coil embolization in the proximal MTA. The second EVT had to be performed *via* MMA. Then, Onyx casting obliterated the TDAVF. Therefore, for selected TDAVFs with hypertrophied MHT, under the assistance of coil embolization in proximal MHT, Onyx casting *via* MHT can finish the complete EVT.

KEYWORDS

tentorial dural arteriovenous fistula, meningohypophyseal trunk, medial tentorial artery of Bernasconi-Cassinari, Onyx, embolization

Introduction

Among all intracranial dural arteriovenous fistulas (DAVFs), tentorial DAVF (TDAVF) has a 4–8% prevalence (1). Due to high hemorrhagic risk, TDAVF requires appropriate treatments (2). Currently, endovascular treatment (EVT) with a liquid embolic agent is a valid, effective, and safe alternative for achieving complete occlusion in the majority of TDAVFs, in which the transarterial approach is still a first-line strategy, although the transvenous approach may be attempted (3, 4). However, EVT of TDAVF remains challenging (5).

Feeders of dural arterial origin of TDAVFs can include the middle meningeal artery (MMA), meningohypophyseal trunk (MHT), and medial tentorial artery (MTA) of Bernasconi-Cassinari, a meningeal branch of the occipital artery, a posterior meningeal artery from the vertebral artery, etc. (1). In addition, the meningeal branches of intracranial pial arteries can be involved as feeders, such as the artery of Davidoff and Schecter of the posterior cerebral artery, the artery of Wollschlaeger and Wollschlaeger of the superior cerebellar artery (SCA) (6, 7).

In theory, all feeding arteries can be used as transarterial paths, in which the MMA is commonly used to finish the complete obliteration of the TDAVF (8). However, when MMA is hypoplastic and too slim to act as a transarterial path, the MHT and MTA of Bernasconi-Cassinari can rarely be used as a transarterial path (3, 4). Here, we report a TDAVF with a dilated MHT as a feeder, casting Onyx-18 in the MTA of Bernasconi-Cassinari under the assistance of coil embolization in the proximal MHT with an aneurysmal dilation that finished the EVT. The technique was reported. At the same time, another similar TDAVF was chosen as a control.

Case reports

Case 1

A 52-year-old man with an unremarkable medical history presented with acute onset of headache and then became drowsy. He was a patient of the Mongol nationality who lived in China, was healthy, and denied having a history of chronic diseases. He had no history of drug abuse or surgical treatment of craniocerebral disease. On physical examination, the patient was weakened and could not answer the questions correctly. His limbs had grade V muscle strength. His neck was stiff. The Babinski sign was positive in both lower limbs. CT showed cerebellar hematoma, subarachnoid hemorrhage (SAH), and hydrocephalus (Figure 1A). CT angiography (CTA) indicated a suspected DAVF of the tentorial margin, and a tortuous draining vein with varix was shown clearly, draining to the torcular herophili (Figures 1B,C). Digital subtraction angiography (DSA) confirmed the TDAVF and that the feeding arteries included the MHT, MMA, and artery of Wollschlaeger and Wollschlaeger of the SCA, in which the MHT was the main feeder (Figures 1D–F). The DAVF was Cognard Type IV and ruptured.

Onyx-18 (Medtronic, Irvine, CA, USA) embolization *via* MHT was planned. Three-dimensional reconstruction of the internal carotid artery (ICA) showed the best projection degree of the MHT and MTA of Bernasconi-Cassinari (Figure 2A). First, a Marathon microcatheter (Medtronic, Irvine, CA, USA) was placed in the MTA, and then an Echelon-10 microcatheter (Medtronic, Irvine, CA, USA) was placed in the MHT. The proximal MHT trunk with an aneurysmal dilation was embolized with coils [Axium Prime 3.5 mm × 10 cm, 2 mm × 8 cm (Medtronic, Irvine, CA, USA)] to produce a mass effect to prevent Onyx reflux (Figure 2B). Then, the Onyx casting penetrated the fistula into the draining vein (Figures 2C,D). DSA of the carotid artery and vertebral artery confirmed that the TDAVF was completely obliterated (Figures 2E,F). Postoperatively, external ventricular drainage was performed, and the patient recovered gradually. One and a half months later, the patient could walk and answer the questions correctly.

Case 2

A 75-year-old woman with a history of hypertension presented with acute onset of headache and then fell into a coma. She was a patient of the Mongol nationality who lived in China. She had no history of drug abuse or surgical treatment of craniocerebral diseases. On physical examination. She was in a coma. Her limbs had grade II muscle strength. The Babinski sign was positive in both lower limbs. CT showed cerebellar hematoma, intraventricular hemorrhage, and hydrocephalus (Figure 3A). DSA confirmed the TDAVF and showed that double MTAs of Bernasconi-Cassinari were the main feeding arteries. Double MTAs shared the common trunk with the inferior lateral trunk (ILT) of the cavernous ICA (Figures 3B,C). The DAVF was Cognard Type IV and ruptured.

EVT was planned *via* the MTA of Bernasconi-Cassinari. First, a Marathon microcatheter tried to go into the distal MTA, but it could only be placed at the tortuous MTA beginning (Figure 3D). Then, Onyx-18 was cast (Figures 3E,F). EVT was incomplete, and DSA of the external carotid artery showed that the MMA and ascending pharyngeal artery still supplied the TDAVF (Figures 4A,B). The second Onyx casting was performed by a Marathon microcatheter *via* the MMA, and the TDAVF was cured (Figures 4C–F). Postoperatively, external ventricular drainage was performed, and she did not recover gradually. She was still in a coma 1 month later.

Discussion

Compared with DAVFs in other locations, 60–75% of TDAVFs are prone to hemorrhage due to venous hypertension

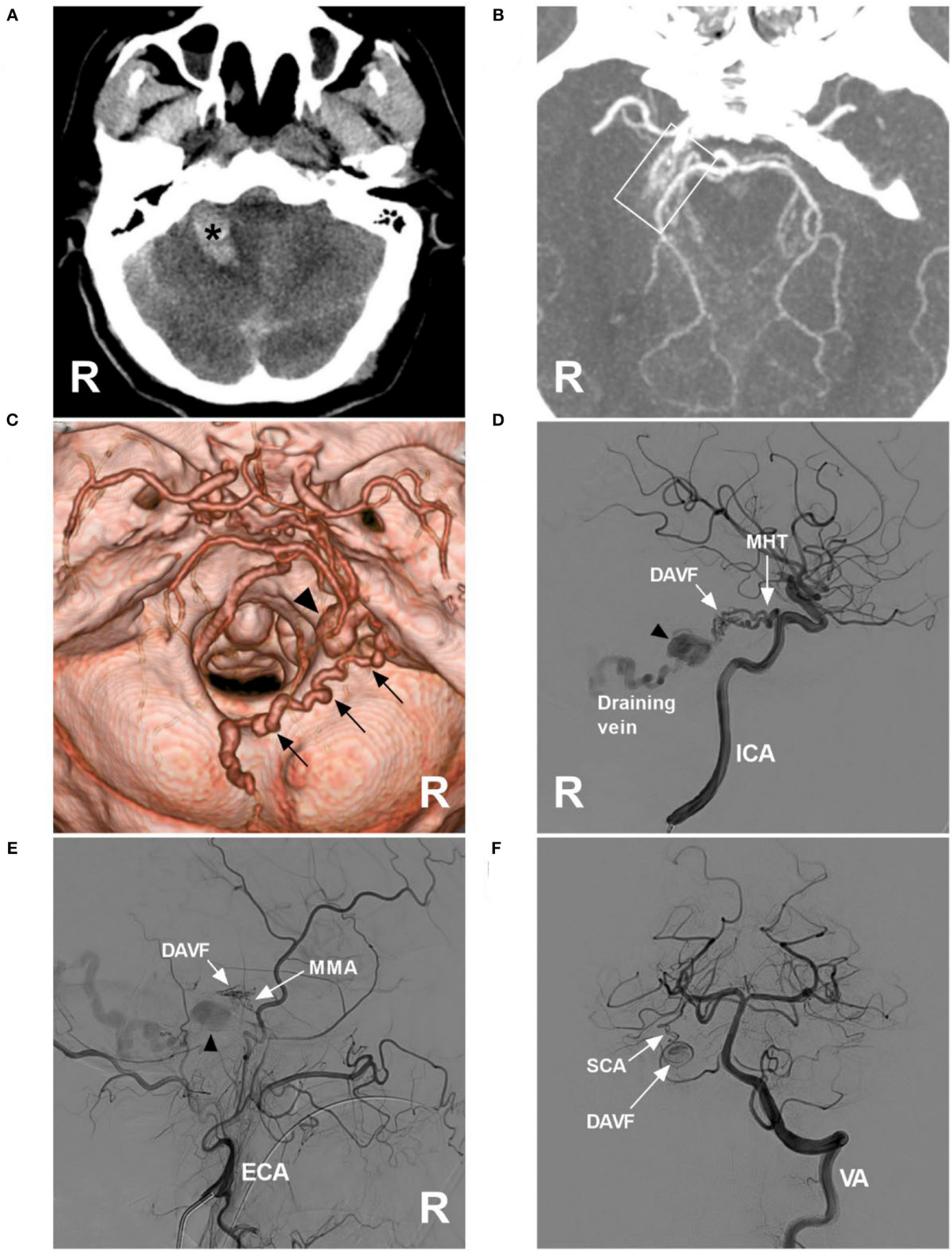

FIGURE 1
Preoperative images in case 1. **(A)** CT showing right cerebellar hemorrhage (asterisk). **(B)** Maximum intensity projection of CTA showing a tangle of abnormal vessels (frame) at the right margin of the tentorium; a DAVF was suspected. **(C)** Three-dimensional reconstruction of CTA showing

(Continued)

FIGURE 1
a tortuous draining vein (multiple arrows) along the cerebellopontine fissure, the surface of inferior cerebellar hemisphere, and inferior vermin, went into the torcular herophili, with varix (triangle) at the beginning. **(D)** DSA of the right ICA showing that the MHT was the main feeding artery, and there was varix on the draining vein (triangle). **(E)** DSA of the right ECA showing that the petrous branch of the MMA was a minor feeding artery, and varix (triangle) was indicated. **(F)** DSA of the VA showing that the artery of Wollschlaeger and Wollschlaeger of the SCA was the minor feeding artery. CT, computed tomography; CTA, CT angiography, DAVF, dural arteriovenous fistula; DSA, digital subtraction angiography; ECA, external carotid artery; ICA, internal carotid artery; MHT, meningohypophyseal trunk; MMA, middle meningeal artery; R, right; SCA, superior cerebellar artery; VA, vertebral artery.

caused by retrograde leptomeningeal drainage, including the supra- and infratentorial veins, as well as the deep veins of the brain stem (Cognard Type III or IV) (9–11). Thus, aggressive intervention is necessary (10). In a systematic review by Cannizzaro et al., over the past 35 years, TDAVFs have increasingly been treated with EVT, and the use of the Onyx liquid embolic system may continue to shift the balance increasingly toward EVT (12). Of all feeding arteries that can potentially be used as transarterial paths to perform EVT, the MMA is still the gold transarterial path to complete the obliteration of the TDAVF (7). The MHA and MTA of Bernasconi-Cassinari are challenging for TDAVF, and the success rate is low, such as in case 2.

Normally, the MHT originates in the posterior genu of the cavernous ICA, with a diameter of approximately 1 mm, and then trifurcates into the MTA of Bernasconi-Cassinari, dorsal meningeal artery (the dorsal or lateral clival artery), and inferior hypophyseal artery (13–15). Ninety percent of MTAs are usually the terminal branch of the MHT, and 10% of them can arise directly from the cavernous ICA; 80% of MTAs originate as a single branch and as a bifurcation and trifurcation in 20% (16). In this report, case 1 had an MTA that arose from MHT, case 2 had an MTA that directly arose from the cavernous ICA, and the MTA in two cases was the bifurcation pattern. The MTA travels along the tentorium just lateral to the tentorial incisure and contributes to the supply of the medial portion of the tentorium. A normal MTA is slim, and its diameter was 0.7 mm in the Banerjee et al. specimen (16) and 0.5 in the Peltier et al. specimen (17). The MTA had a length of 15 mm in the Banerjee et al. specimen (16) and 21.7 mm in the Peltier et al. specimen (17).

According to these normal anatomical parameters, the MHT and MTA of Bernasconi-Cassinari were not appropriate for use as the transarterial path of the current EVT. Under the increased blood flow in TDAVFs, the MHT and MTA can be hypertrophied to provide accessible catheterization. In case 1, the MHT reached 2.3 mm, and the MTA reached 1.1 mm in diameter. However, catheterization of the MHT and MTA of Bernasconi-Cassinari is still difficult due to tortuosity (18). In addition, the allowable reflux distance of Onyx was too short for them.

Therefore, EVT with the MHT and MTA of Bernasconi-Cassinari as the transarterial path is rarely performed. In Rezende et al.'s report with a large series of 45 TDAVFs treated with transarterial embolization, the MTA path was used only once (2.2%, 1/45) (4). Van Rooij et al. studied the feasibility of the MTA as a transarterial path to embolize TDAVFs, with a balloon temporarily deployed within the ICA in front of the MHT origin to stabilize the microcatheter and prevent reflux of embolic material into the ICA (19). However, the technique is still difficult to apply. Recently, the Scepter Mini dual-lumen balloon microcatheter (MicroVention, Aliso Viejo, CA, USA) with a 1.6 French distal profile and 2.2 mm balloon at its tip were introduced (20). It can avoid the Onyx reflex in embolizing DAVFs (21). However, the Scepter Mini balloon microcatheter is stiff and thick for the catheterization for MHT and MTA of Bernasconi-Cassinari.

In case 1, the MHT and MTA were hypertrophied, and the current softest and thinnest Marathon microcatheter had accessed the fistula. Therefore, during Onyx casting, if too much reflux can be prevented, the TDAVF can be cured. Due to an aneurysmal dilation at the proximal MHT, we planned to coil the aneurysmal dilation to produce a mass effect to prevent Onyx reflux. The technique was similar to that reported by Chapot et al.; it was designed to create a plug by trapping the Onyx-compatible microcatheter with coils to obtain wedge-flow conditions (22). With the assistance of the technique, the TDAVF was cured in case 1. Therefore, the technique is feasible only for highly selective TDAVFs. As a control of case 2, the MTA of Bernasconi-Cassinari was dilated, but the MTA was tortuous, the microcatheter did not access the fistula point, and without coiling to prevent Onyx reflux, complete EVT was not achieved.

In our report, we chose Onyx-18 as an embolic agent because Onyx-34 with a high viscosity was not appropriate (23). In case 1, the Onyx reflux reached the coils, but the reflex did not penetrate them. Therefore, this technique cannot typically be used because of the danger associated with possible reflux into the ICA, which should not be underestimated. Prior to this technique, all other paths should be exhausted, especially the MMA path, which has been attempted (24). In addition, microsurgery should be considered as a surgical approach, especially for TDAVF with a single draining vein into the posterior fossa (25).

In case 1, after finishing Onyx embolization, the Marathon microcatheter can be easily removed without difficulty, which was suggested in our previous reports (26, 27). When removing the Marathon microcatheter, backing mass coils toward the ICA should be considered. However, in case 1, the proximal MHT had an aneurysmal dilation, and the

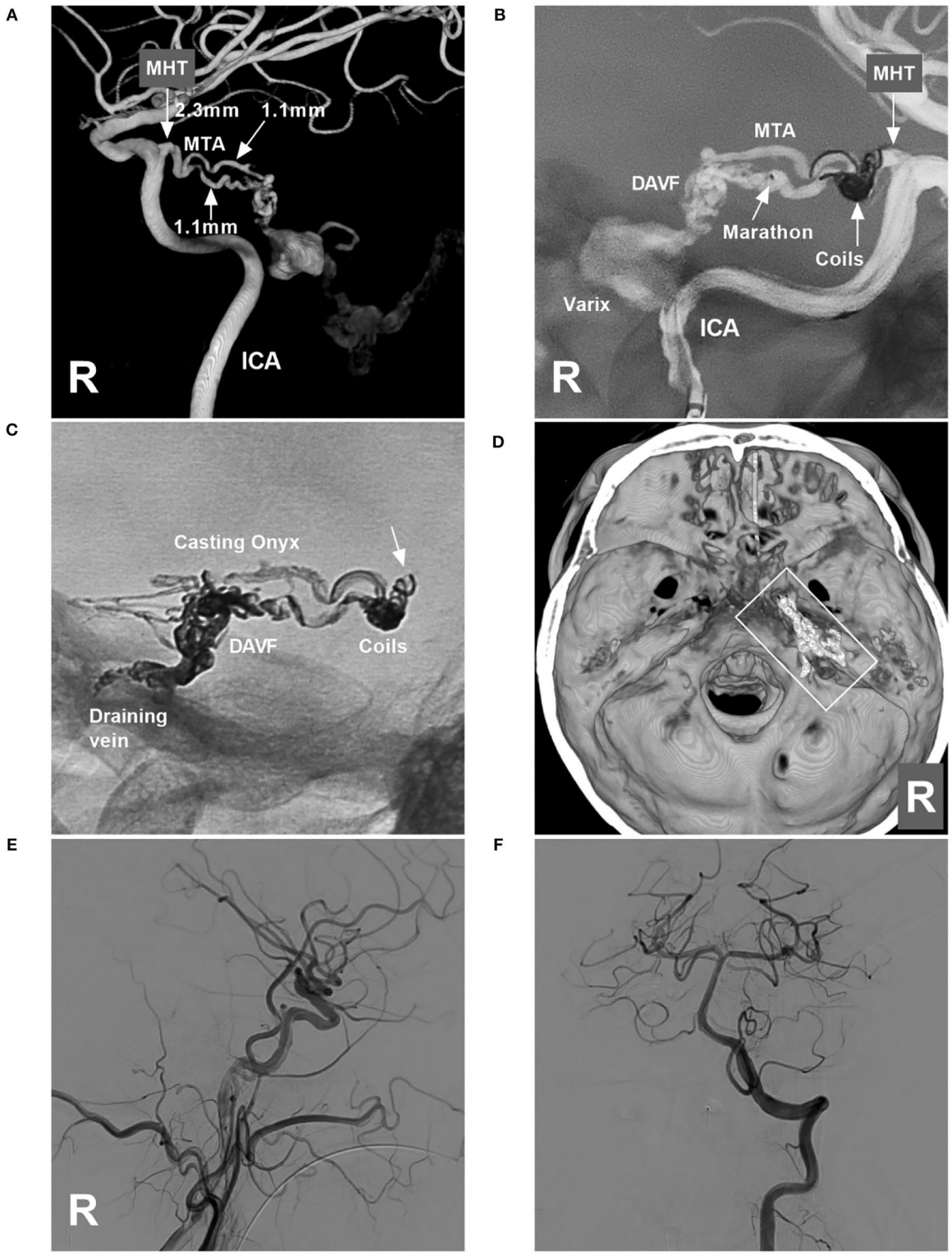

FIGURE 2
Operative images in case 1. **(A)** Three-dimensional reconstruction of DSA of the right ICA showing the diameters of the feeding artery to the TDAVF. The MHT origin was 2.3 mm, and the MTA of Bernasconi-Cassinari was 1.1 mm in diameter. **(B)** Road map of the ICA showing a Marathon microcatheter placed in the lower MTA. The MHT trunk with an aneurysmal dilation was coiled to produce the mass effect. **(C)** X-ray film showing the coils and casting Onyx. Onyx reflux reached the coils (arrow) but did not extend beyond the coils. **(D)** Three-dimensional reconstruction of Xper-CT showing the location of the Onyx casting (frame) at the margin of the tentorium. **(E,F)** DSAs of the right carotid artery **(E)** and VA **(F)** show complete obliteration of the DAVF. DAVF, dural arteriovenous fistula; DSA, digital subtraction angiography; ICA, internal carotid artery; MHT, meningohypophyseal trunk; R, right; MTA, medial tentorial artery; VA, vertebral artery.

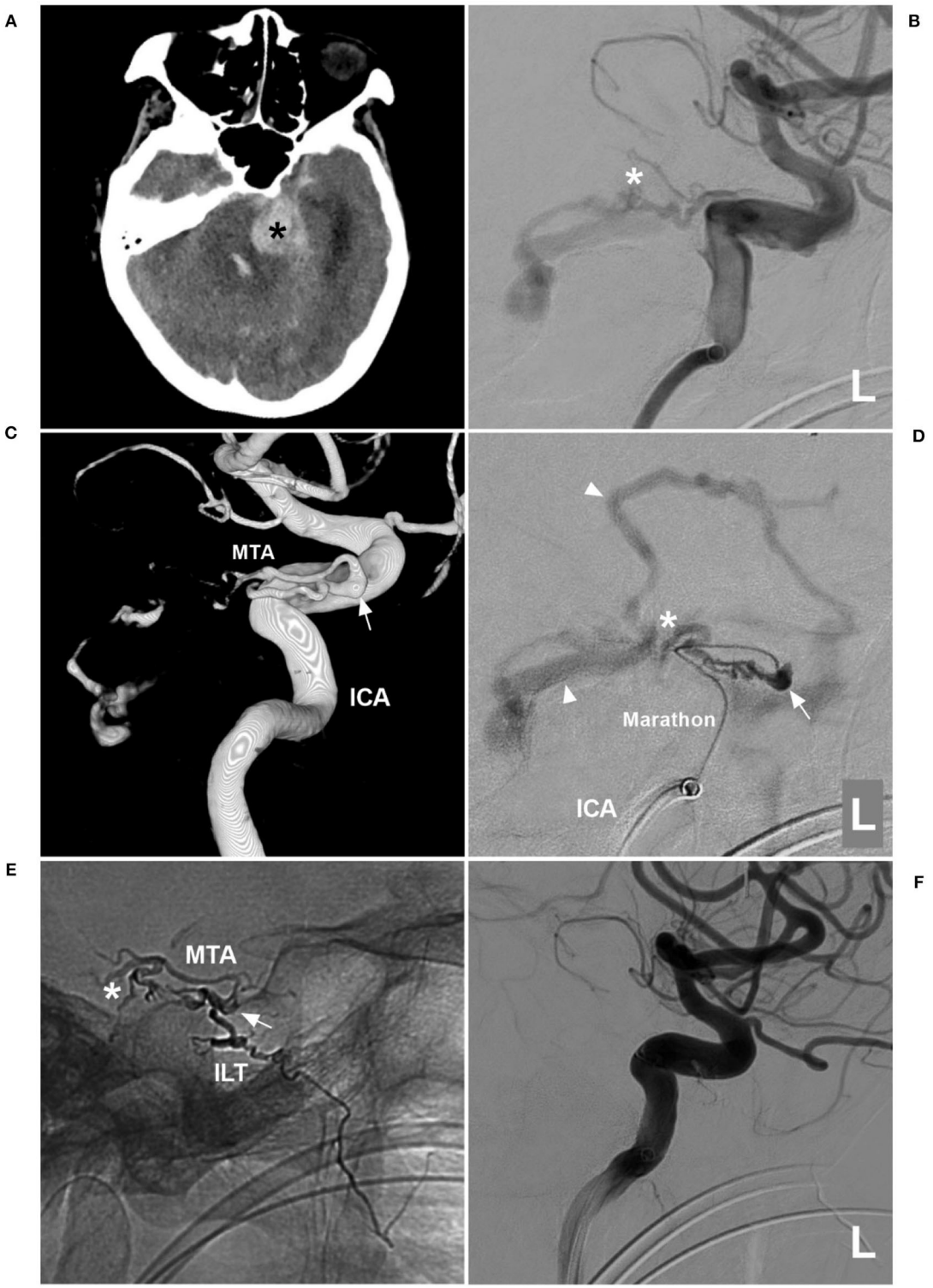

FIGURE 3
First EVT *via* MTA in case 2. **(A)** CT showing left cerebellar hemorrhage (asterisk). **(B)** DSA of the left ICA showing that the MTA of Bernasconi-Cassinari was the feeding artery to a DAVF (asterisk). **(C)** Three-dimensional DSA showing that double MTAs should share the common trunk with the ILT of the cavernous ICA; the arrow indicates the origin of these vessels. **(D)** Superselective angiogram *via* a Marathon microcatheter showing the TDAVF angioarchitecture. The arrow indicates the dilated beginning of the MTA, the asterisk indicates the fistula point, and the triangles indicate draining veins. **(E)** X-ray film showing Onyx casting. The arrow indicates the beginning of the MTA, the asterisk indicates that Onyx casting reached the fistula point *via* the MTA, and the Onyx also went into the ILT. **(F)** DSA of the left ICA showing that the DAVF was not seen. CT, computed tomography; DAVF, dural arteriovenous fistula; DSA, digital subtraction angiography; EVT, endovascular treatment; ICA, internal carotid artery; ILT, inferior lateral trunk; L, left; MTA, medial tentorial artery.

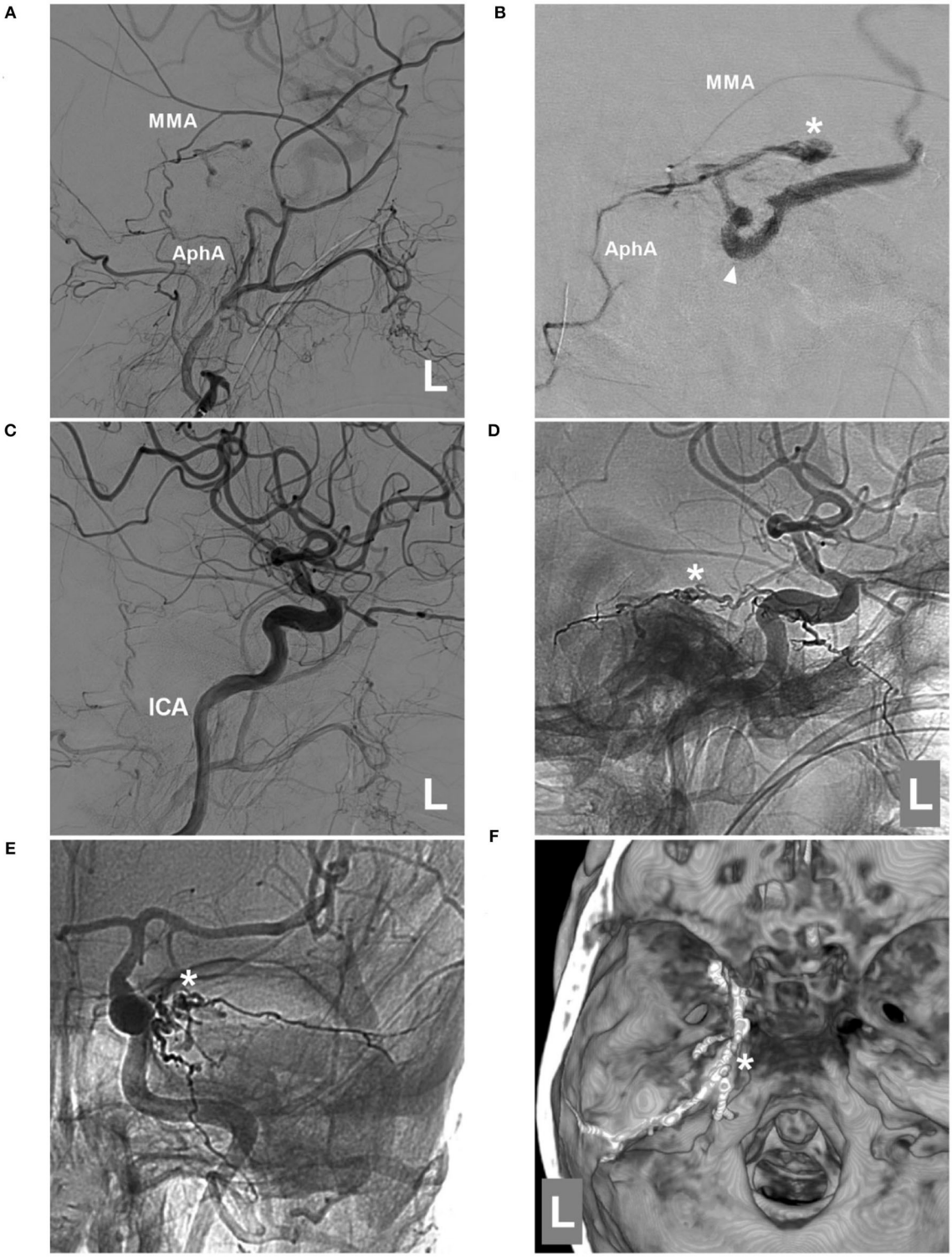

FIGURE 4
Second EVT *via* MMA in case 2. **(A)** DSA of the left external carotid artery showing that the MMA and AphA still supplied the DAVF. **(B)** Superselective angiogram of the MMA *via* a Marathon microcatheter showing the DAVF angioarchitecture. The asterisk indicates the fistula point, and the triangle indicates the draining vein. **(C)** DSA of the left carotid artery showing that the DAVF was completely embolized after Onyx casting *via* the MMA. D-E: Lateral view **(D)** and anteroposterior **(E)** unsubtracted DSA showing the casting Onyx; the asterisk indicates the fistula point. **(F)** Three-dimensional reconstruction of Xper-CT showing Onyx casting. The asterisk indicates the fistula point at the margin of the tentorium. AphA, ascending pharyngeal artery; DAVF, dural arteriovenous fistula; DSA, digital subtraction angiography; EVT, endovascular treatment; ICA, internal carotid artery; L, left; MMA, middle meningeal artery.

coils were stable. In addition, the Echelon-10 microcatheter should not be removed too early; it can support coils when removing the Marathon microcatheter. In addition to the Marathon microcatheter, the Apollo detachable tip microcatheter (Medtronic, Irvine, CA, USA) was an alternative for case 1 (28). However, the detachable tip lengths of 15 and 30 mm were too long, and the detachment zone may be located in the ICA. After detachment, the detachable tip in the ICA was detrimental.

Conclusion

Currently, for TDAVFs, if there is no blood supply from the MMA, the MHT and MTA of Bernasconi-Cassinari are highly hypertrophied. With the assistance of coil embolization in the proximal MHT, Onyx casting *via* the MHT and MTA can finish the complete EVT.

Limitation

This is a report, and the conclusion should be cautiously interpreted. In addition, no case of surgical treatment can be provided as a comparison with EVT, which was a limitation.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval were not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JY designed the study and drafted the manuscript. KH collected the data. JY and KH confirm the authenticity of all the raw data. Both authors have read and approved the final manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Spontaneous carotid-cavernous fistula associated with persistent primitive trigeminal artery aneurysm rupture

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Background: The incidence of carotid cavernous fistula (CCF) associated with persistent primitive trigeminal artery (PPTA) aneurysm rupture is extremely rare. We presented a case about a spontaneous CCF secondary to a ruptured PPTA aneurysm, which was successfully embolized with coils and onyx-18 by a trans-arterial approach.

Case presentation: A 55-year-old female suffered a sudden onset of headache, left orbital pain, and pulsatile exophthalmos for a month without any history of trauma. Angiography revealed a left-sided CCF associated with a ruptured PPTA aneurysm, with major drainage to the ipsilateral superior ophthalmic vein. Through a trans-arterial approach, the fistula and ruptured PPTA aneurysm were embolized with coils and onyx-18, while the cavernous sinus and PPTA were well-preserved. However, the preserved PPTA vanished at 4 month follow-up. The patient had no neurological deficit from hospitalization to 1 year follow-up period.

Conclusion: Trans-arterial approach was a reasonable choice for spontaneous CCF associated with ruptured PPTA aneurysm. The requirement for PPTA preservation depended on individual evaluation.

KEYWORDS

spontaneous carotid-cavernous fistula, persistent primitive trigeminal artery, aneurysm, interventional treatment, case report

Introduction

Persistent primitive trigeminal artery (PPTA) is the most common embryonic communication between vertebra-basilar and carotid systems in adulthood. It has been reported to occur in 0.1–1% of the population (1). The origin of PPTA is usually in the posterior or lateral surface of the intracavernous internal carotid artery (ICA), proximal to the origin of the meningo-hypophyseal trunk (MHT). The PPTA passes in sequence through the cavernous sinus (CS) and subarachnoid space, then enters into the basilar artery (BA) between the superior cerebellar artery (SCA) and anterior inferior cerebellar

TABLE 1 Timeline of clinical and procedural data.

Admission	Spontaneous headache, left orbital pain and pulsatile exophthalmos
Day 3	PE: Left orbital bruit, chemosis and abducens nerve paresis
Day 4	Cerebral angiography
Day 5	Embolized with coils and onyx-18 by trans-arterial approach
Day 10	Discharged without any neurological deficit during hospitalization
4 month	Clinical and angiographic follow up
1 year	Clinical follow up

PE, physical examination.

artery (AICA) (2). PPTA can be associated with many vascular anomalies and disorders, including aneurysm, arteriovenous malformation (AVM), and carotid cavernous fistula (CCF). Due to its anatomical features, a ruptured PPTA aneurysm may lead to CCF or subarachnoid hemorrhage (SAH) (3). The incidence of CCF associated with PPTA aneurysm rupture is extremely rare. We presented a case about a spontaneous CCF secondary to a ruptured PPTA aneurysm, which was successfully embolized with coils and onyx-18 by a trans-arterial approach.

Case presentation

A 55-year-old female of Chinese origin presented with sudden onset of headache and left orbital pain without any history of head trauma a month ago. She also suffered from progressive left-sided exophthalmos and diplopia since then. Physical examination on admission demonstrated left-sided pulsatile orbital bruit, chemosis, and abducens nerve paresis (Table 1). This patient had a history of surgery for femoral shaft fracture 3 years ago, but it was decided this was probably irrelevant to the present complaint. Computed tomography showed an enlarged left superior ophthalmic vein (SOV). Left ICA angiography revealed a left-sided CCF associated with a ruptured PPTA aneurysm, with major drainage to the ipsilateral SOV (Figure 1A). Vertebral angiography also revealed a retrograde blood flow of PPTA from BA to CS (Figure 1B).

Endovascular embolization with detachable coils and Onyx-18 liquid embolic system (Medtronic-ev3, Minneapolis, MN, USA) by a transarterial approach was planned. Under general anesthesia, 4,000 units of heparin were intravenously administered to the patient. A 6F Envoy guiding catheter (Codman & Shurtleff, Inc., Raynham, MA, USA) was introduced through a femoral sheath into the petrous segment of the left ICA. Under an optimal projection for PPTA emitting from left

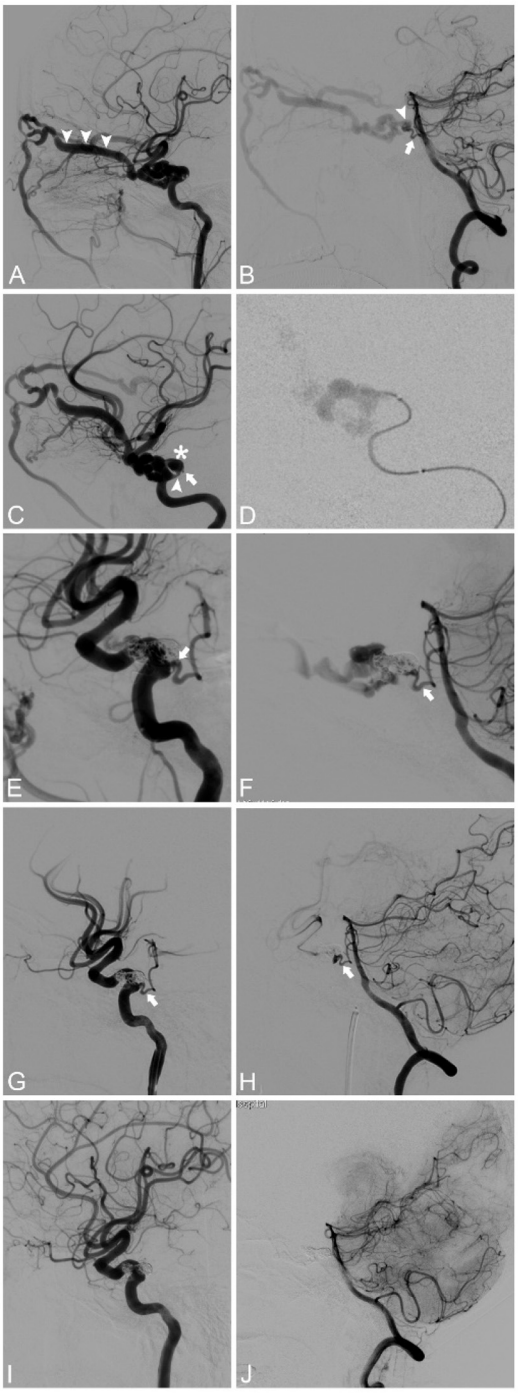

FIGURE 1
(A) Lateral view of the left ICA angiography showing a CCF with dilated SOV (arrowhead). **(B)** Lateral view of the right VA angiography showing the retrograde blood flow (arrow) from a ruptured PPTA aneurysm (arrowhead), projecting into the left CS. **(C)** The optimal projection for PPTA emitting (arrowhead) from left ICA, the PPTA aneurysm (asterisk), and the distal orifice (arrow) of PPTA connecting to BA. **(D)** The fistula was confirmed by super-selective angiography. **(E,F)** Partial embolization of the fistula and the adjacent PPTA aneurysm exhibited the PPTA
(Continued)

FIGURE 1 (Continued)
trajectory (arrow) more evident than untreated. **(G,H)** The fistula and aneurysm were completely embolized, while the CS and PPTA (arrow) were well-preserved. **(I,J)** Four-month follow-up angiography demonstrated complete obliteration of the fistula and PPTA aneurysm, while the preserved PPTA vanished. BA, Basal Artery; CCF, Carotid Cavernous Fistula; CS, Cavernous Sinus; ICA, Internal Carotid Artery; PPTA, Persistent Primitive Trigeminal Artery; SOV, Superior Ophthalmic Vein; VA, Vertebral Artery.

ICA (Figure 1C), an Echelon-10 microcatheter (Medtronic-ev3, Minneapolis, MN, USA) guided by a Synchro2 microguidewire (Stryker, Salt Lake, Utah, USA) was directed into the PPTA aneurysm which was confirmed by super-selective angiography (Figure 1D). Partial embolization of fistula and proximal ruptured PPTA aneurysm exhibited the PPTA trajectory more obviously than untreated (Figures 1E,F). Finally, the fistula and aneurysm were completely embolized with four Axium detachable coils (Medtronic-PLC, Dublin, Ireland) followed by a 1.6 ml Onyx-18 liquid embolic system, while the CS and PPTA were well-preserved (Figures 1G,H).

The left orbital bruit and chemosis of the patient subsided immediately after embolization, while residul mild abducens nerve paresis lasted for a month. There is no focal neurological deficit during hospitalization. Four-month follow-up angiography demonstrated complete obliteration of the fistula and PPTA aneurysm. However, the preserved PPTA vanished (Figures 1I,J), but the patient had no neurological deficit. No evidence of recurrence was observed during the 1-year clinical follow-up.

Discussion

Embryology

At 28–29 days of embryonic development (3 mm human embryonic stage), there are four special channels, including the proatlantal artery, hypoglossal artery, otic artery and trigeminal artery, which are connecting the carotid systems with the longitudinal neural arteries (4). At the 14 mm human embryonic stage, the posterior communicating artery (PComA) replaces the previous four vessel channels, which regress and are subsequently obliterated as the major blood supply to the posterior circulation (4). The PPTA is the largest and most common fetal carotid-basilar anastomotic artery that persists into adulthood, although the exact cause for its persistence remains unclear.

Etiology

Despite its extremely rare incidence, PPTA can be associated with aneurysms, AVMs, and CCF. Due to the trajectory of the PPTA, spontaneous ruptured PPTA aneurysm may cause CCF or SAH. The CCF associated with the PPTA may also be traumatic. When an external force acts on the head in trauma, the PPTA, as the most susceptible target, bears maximum shear stress during acceleration or deceleration injury (3, 5). The tear in the proximal segment of the PPTA results in traumatic CCF. However, owing to the structural vulnerability of the PPTA, formation and subsequent rupture of PPTA aneurysm often lead to spontaneous CCF (3). Furthermore, delayed rupture of the dissecting PPTA aneurysm resulting from trauma may also be the cause of spontaneous CCF (6).

In our case, a spontaneous CCF was identified by angiography in a patient without trauma history. The root of the PPTA (Figure 1C, arrowhead) emitted from the left cavernous ICA and then poured into an associated aneurysm (Figure 1C, asterisk) which was ruptured in the cavernous sinus to form a CCF. The orifice of the distal PPTA connecting to the BA was also noticed (Figure 1C, arrow). For hemodynamic reasons, the direction of blood flow in the distal PPTA reversed from the BA to the cavernous sinus during VA angiography (Figure 1B). Super-selective angiography confirmed the fistula and associated PPTA aneurysm (Figure 1D).

Classification

Based on its emitting site in the ICA and vascular course, the PPTA may be classified into lateral or medial subtype, both of which are equally common in the population (7). In the lateral subtype, the artery arose from the posterolateral portion of the intracavernous ICA. It courses adjacent to the lateral wall of the CS. When crossing the CS, the PPTA passes between the abducens nerve and the ophthalmic division of the trigeminal nerve. Conversely, when the PPTA arises from the posteromedial aspect of the cavernous segment of the ICA, it should be medial to the abducens nerve in the majority of cases (8). Along its intracavernous course, the PPTA may give rise to the branches to the trigeminal nerve and the pituitary (9).

In 1959, Saltzman reported eight cases about the PPTA, and proposed an angiographic classification (10, 11), In Saltzman type 1, the PPTA inserts into the BA, between SCA and AICA. The BA, proximal to the PPTA insertion, may be hypoplastic and the PComA may be absent or poorly developed. In other words, the main blood supply for the distal BA, PCA, and SCA comes from the PPTA, thus the PPTA must be well-preserved in order to avoid posterior circulation ischemia during treatment (10, 11). In Saltzman type 2, the PPTA inserts into the BA before the origin of SCA, but only supplies the bilateral SCAs, while the PCAs are supplied by the PComA (10, 11). Later, both Saltzman and Parkinson demonstrated cases as a combination variant of Saltzman type I and II (12, 13). This means the PPTA supplied the bilateral SCAs and contralateral PCA, while a fetal PComA supplies the ipsilateral PCA. Many Saltzman variants, referred to as Saltzman type 3, have been reported subsequently. The PPTA

variants terminated directly to the SCA (Saltzman Type 3a), AICA (Saltzman Type3b), or PICA (Saltzman Type3c) rather than inserting into the BA (4).

The PPTA in our case inserted into the BA between SCA and AICA, but the BA proximal to the PPTA insertion was well-developed and provided sufficient blood supply for bilateral PCAs and SCAs. Thus, the PPTA could be safely sacrificed when treating the PPTA aneurysm and the associated CCF.

Treatment

Treatment strategies for PPTA aneurysm associated with CCF involve the occlusion of the fistula pouch and adjacent ruptured PPTA aneurysm while minimizing the impact on normal arterial supply and venous drainage (3). In 1977, Enomoto et al. reported a spontaneous CCF induced by a ruptured PPTA aneurysm. The patient's ICA was then ligated without any signs of ischemia due to the inverted blood flow of the PPTA (14). Due to the low technique success rate and inevitable complications, microsurgery had been replaced by endovascular treatment. In 1982, Charlin and his colleagues treated a PPTA aneurysm-associated CCF with a detachable balloon (15). However, the detachable balloon could only be applied for selected cases because of its inherent material limitation (16).

In 1998, Bernstein et al. treated a spontaneous CCF associated with a ruptured PPTA aneurysm with coils for the first time (17). In 2008, Geibprasert et al. performed a staged treatment for the same disease. Firstly, they coiled the fistula with 19 coils through the right SOV by a trans-venous approach. Then, they embolized the remnant with N-butyl cyanoacrylate (NBCA) through the right PPTA by a trans-arterial approach. It was the first time that a liquid embolic agent had ever been used for such diseases (3). Since then, coiling with liquid embolic agent became the first choice for such types of CCF cases.

Both trans-arterial and trans-venous approaches could be applied for the treatment according to individual angioarchitecture. When the trans-arterial approach is too tortuous and a microcatheter could not be successfully guided into the targeted position, the trans-venous approach could then be adopted (18). However, trans-venous embolization was believed to require more coils or liquid embolic agent than trans-arterial embolization. The mass effect of excessive cavernous sinus packing might cause iatrogenic cranial nerve palsy and other complications. Moreover, unexpected obliteration of the anatomical drainage from the CS may lead to venous hypertension. Subsequently, the blood would reflux into the cortical or ophthalmic veins, which would increase the risk of hemorrhage or aggravate ocular symptoms (19). In 2018, Imrie et al. treated a spontaneous CCF secondary to a ruptured PPTA aneurysm with detachable coils in the CS through the inferior petrosal sinus (IPS). Eventually, the CS was completely occluded and the fistula vanished (20). In 2000, Oka et al. also used detachable coils to treat a similar CCF through the right IPS approach. Although, the fistula wasn't completely occluded immediately after treatment. Fourteen days later, follow-up angiography revealed the complete disappearance of the fistula probably due to thrombosis, which was presumably accelerated by the coils (19).

Compared with trans-venous embolization, trans-arterial embolization was believed to be a more reasonable choice for treating the PPTA aneurysm-associated CCF, due to the short access in distance and minor mass effect (21). Through the trans-arterial approach, a microcatheter could be navigated into the fistula pouch within the CS through the ruptured PPTA aneurysm. Thus, targeted embolization for the fistula pouch and ruptured aneurysm could be achieved, while the structure and function of the CS could be well-preserved (22). In 2011, Yoshida et al. treated a PPTA aneurysm associated CCF with coils. They failed to navigate the microcatheter into the fistula pouch by a transvenous approach because the fistula orifice was too small. Then they embolized the PPTA aneurysm with detachable coils by a trans-arterial approach. Finally, the fistula disappeared (23). In 2019, Fan et al. navigated a microcatheter into the CS through the PPTA aneurysm crevasse by a trans-arterial approach. The CS was firstly carefully embolized with detachable coils. After ipsilateral ICA protection with a Hyper-Glide balloon, the fistula and PPTA aneurysm was then embolized with Onyx-18 (18).

As for specific PPTA aneurysm-associated CCF cases, both trans-arterial and trans-venous approaches had to be used together for treatment. Taichi et al. successfully treated a spontaneous case of CCF secondary to a PPTA aneurysm with a multipronged embolization strategy, which meant a combination of trans-arterial with a trans-venous approach. Three microcatheters were guided into the fistula as follows: (1) through the PPTA to the CS from the left ICA, (2) through the PPTA to the CS from the BA, and (3) through the CS to the PPTA aneurysm from the internal jugular vein. The fistula was then completely occluded without any signs of recurrence during the follow-up period. They suggested that this multipronged approach was safe and effective for tortuous artery cases and was beneficial for avoiding incomplete fistula occlusion (24).

Whether the PPTA should be preserved or not is another concern for treatment strategies. In Saltzman type 1, the PPTA is a critical blood supply for the posterior circulation, thus PPTA must be retained (10, 11). In Saltzman type 2, the blood flow of the PCA mainly comes from the PComA. It seems that PPTA preservation is not so critical. However, as we have mentioned before, the PPTA may give off branches to the trigeminal nerve, pituitary, and brainstem (9–11). Thus, the sacrifice of the PPTA needs cautiously evaluation.

As to our case, because the PPTA was not too tortuous, there was no difficulty in navigating the microcatheter into the PPTA aneurysm and subsequent fistula pouch through a trans-arterial approach. Our concern focused on the following points: (1) maximizing the preservation of the CS structure

and function, (2) whether the PPTA could be sacrificed or not, and (3) the possibility of onyx-18 reflux into the ICA or BA. As we noticed that the bilateral VAs were well-developed and there was inverted blood flow in the PPTA from BA to the fistula. We were confident that it was quite safe to sacrifice the PPTA. Even so, we decided to try our best to preserve of the PPTA during treatment. On account of the enough PPTA reflux distance and unnecessary PPTA preservation, balloon protection for the ICA or BA was not needed. Firstly, we cautiously coiled the very regional fistula pouch and proximal PPTA aneurysm with proper size coils as a framework. Onyx-18 was then carefully injected within the coil framework as far as we possibly could until complete fistula occlusion. Finally the CS was minimally sacrificed and the PPTA was well-preserved. This patient recovered well without any ischemic neurological deficit during hospitalization. Four months later, follow-up angiography revealed the disappearance of the well-preserved PPTA, probably owing to the delayed PPTA occlusion, but the patient encountered no related symptom.

Conclusion

The incidence of spontaneous CCF secondary to the PPTA aneurysm rupture is extremely rare. Trans-arterial embolization by coils with a liquid embolic agent is a safe and effective treatment for selected cases. Preservation of the PPTA depends on the individual assessment.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author/s.

Ethics statement

Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article. The Ethics Committee of Tangdu Hospital of Fourth Military Medical University approved the research protocol in compliance with the Helsinki Declaration.

Author contributions

TZ and YC completed the operation. WF and HC assisted the operation. PS wrote the first draft of the manuscript. QL and ZZ reviewed the case and manuscript. TZ designed the treatment strategy and final revised the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Combined acute revascularization in early bilateral carotid stent occlusion

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Introduction: The introduction of a carotid stent involves the use of effective antiplatelet therapy to maintain stent patency. We present a case report of combined acute revascularization in a patient with occlusion in recently introduced stents of both carotid arteries.

Methods: The patient (male, 73 years) was admitted for stroke recurrence upon discontinuation of antiplatelet therapy. According to the CTA, the closure of implanted stents of both carotid arteries was confirmed. Intravenous thrombolysis and mechanical thrombectomy were performed with complete recanalization of the left carotid stent. At 3 days apart, clinical deterioration was found with progressive stent restenosis. Percutaneous transluminal stent angioplasty, mechanical embolectomy and prolonged low-dose intravenous thrombolysis have been used repeatedly.

Results: With the impossibility of maintaining the patency of carotid stents even on the maximum drug therapy and despite endovascular procedures, bilateral neurosurgical revascularization of the middle cerebral arteries using ECIC bypasses was successfully performed. Prolonged low-dose intravenous thrombolysis (20 mg recombinant plasminogen aktivator (rTPA)/10 h) has proven to be an acute bridging therapy until surgery.

Conclusion: Early occlusion of the carotid stent is a significant complication of endovascular treatment of stenotic arteries. ECIC bypass revascularization of the middle cerebral artery can be a highly effective therapeutic procedure.

KEYWORDS

ECIC bypass, prolonged low-dose intravenous thrombolysis, carotid stent occlusion, stroke, mechanical thrombectomy

Introduction

The introduction of a internal carotid artery (ICA) stent in the treatment of significant stenosis is a standard procedure. It involves the subsequent use of antiplatelet therapy to maintain stent patency. We present a case report of combined acute revascularization in a patient with occlusion in recently introduced stents of both carotid arteries.

Methods

The case report deals with a patient (male, 73 years). The patient's medical history included arterial hypertension, ischemic heart disease, diabetes mellitus of the second type with insulin therapy, and hyperlipidemia. In August 2017, he suffered a acute ischemic stroke (AIS) during preocclusive stenosis of the right ICA. Intravenous thrombolysis (IVT, 70 mg rTPA-10 bolus and 90% by hourly infusion) was performed and acute carotid endarterectomy was performed the same day. The patient was completely free of clinical deficits the next day. In the following months, there is a gradual asymptomatic stenotization of both ICA. Endovascular treatment (stent) was considered, however, laboratory testing of the effectiveness of antiplatelet therapy repeatedly proved to be completely insufficient (acetylsalicylic acid, clopidogrel, ticlopidine, effient, prasugrel were gradually used - all were laboratory ineffective). In April 2021 he was brought with a severe AIS during occlusion of the right ICA. IVT was administered (70 mg rTPA −10 bolus and 90% by hourly infusion). The ICA was partially recanalized and ticagrelol was added to secondary prevention. The patient's clinical condition was very good (very mild left-sided hemiparesis). A stent was inserted into the ICA 8 days apart with laboratory-proven effectiveness antiplatelet therapy. One month later, due to the presumed effective antiplatelet therapy, a stent was inserted into the left asymptomatic critically stenotic ICA. At an interval of 8 days, the patient was brought in with very severe left lateralization when occlusion of both carotid stents was found (Figure 1). According to an angiographic finding, the right ICA has already been chronically occluded for many days. The etiology of a left hemisyndrome was hypoperfusion of the right hemisphere with a sudden insufficiency of collateral supply due to occlusion of the already solitary left ICA at that time. We find out at a glance that the patient has stopped the antiplatelet therapy himself. IVT was performed (70mg rTPA −10% bolus and 90% by hourly infusion) and mechanical embolectomy [MT, a large number of massive thromboemboli were repeatedly obtained by aspiration technique from the area of the stent in the left ICA and from the distal embolization in the middle cerebral artery (MCA)] was performed with complete recanalization of the left carotid stent closure, followed by continuous antithrombotic therapy with ebtifibatide. There was a significant clinical improvement in the patient.

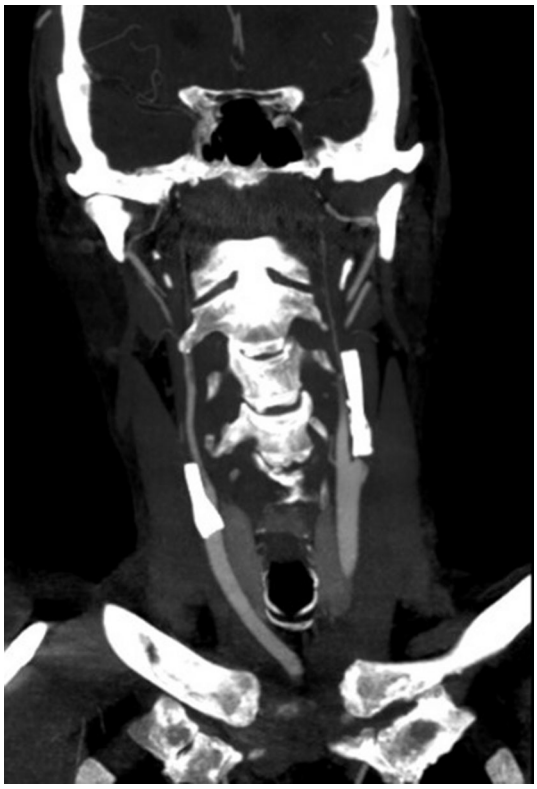

FIGURE 1
Occlusion of both carotid stents.

Results

At intervals of 3 days, plegia of the right limbs and aphasia suddenly develop, according to the CTA, progressive thrombosis in the stent was detected. Prolonged low-dose IVT was administered (20 mg rTPA for 10 h). Percutaneous transluminal stent angioplasty was performed simultaneously. Around 4 h after the end of IVT, the arteries are occluded, prolonged low dose IVT is administered again and the MT of the left carotid stent and middle cerebral artery is performed again (20 mg rTPA for 10 h, aspiration technique of mechanical embolectomy). Left ICA stent occlusion and its subsequent recanalization is shown in the figure (Figures 2, 3). The clinical condition was strongly dependent on blood pressure values. Transcranial Doppler ultrasonography shows signs of hypoperfusion of both cerebral hemispheres. Thus, neurosurgical revascularization—extra-intracranial anastomosis (ECIC) of the temporal artery into the middle cerebral artery basin—was performed acutely in one operation with a very good graphical result and reflection in the patient's clinical condition (Figures 4, 5). The mobility of all limbs and speech were restored and targeted rehabilitation was started for a patient with great rehabilitation potential. However, the patient subsequently refused to fully rehabilitate. Even after

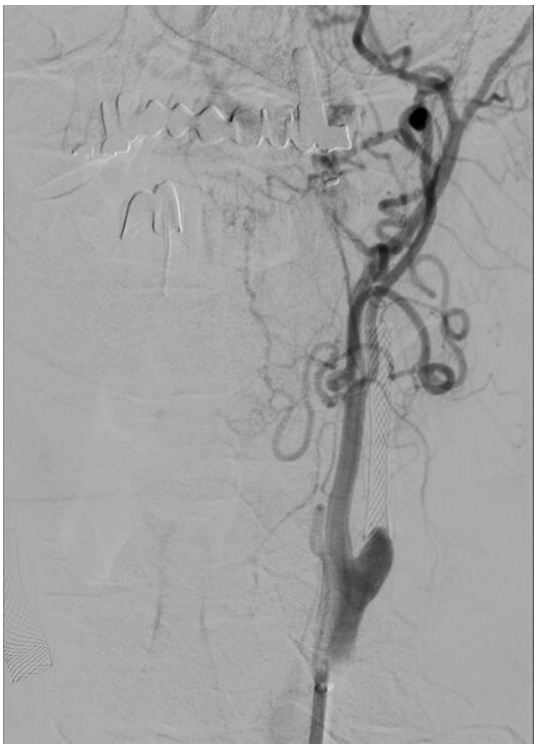

FIGURE 2
Occlusion of left carotid stent on digital subtraction angiography.

the intervention of the family, the cooperation does not improve and the patient died 2 months later.

Discussion

The risk of early occlusion of the inserted carotid stent is very high. Pop et al. report early stent restenosis in 19% of cases in AIS (1). Jost et al. reported 14% reocclusions with co-infusion of eptifibatide at an early stage to prevent acute reocclusion (2). Acute stent placement is comparable to elective in ineffective antiplatelet therapy. The need for efficacy testing is presented by Collette et al. (3). The use of prolonged low-dose IVT in AIS is reported sporadically, and the results of a large randomized study are not available. The available data indicate a relatively good safety profile and efficacy of this treatment (4, 5). Acute ECIC bypass in very well-selected patients with ICA occlusion improves the chance of a good clinical outcome (6).

Among other things, our case report shows the need for patient cooperation in the rehabilitation process. The patient needs to be motivated for rehabilitation. If this is not successful despite all efforts, the hope for a good clinical result and a technically successful resolution of the brain revascularization is minimal. Our collection of patients with acute revascularization

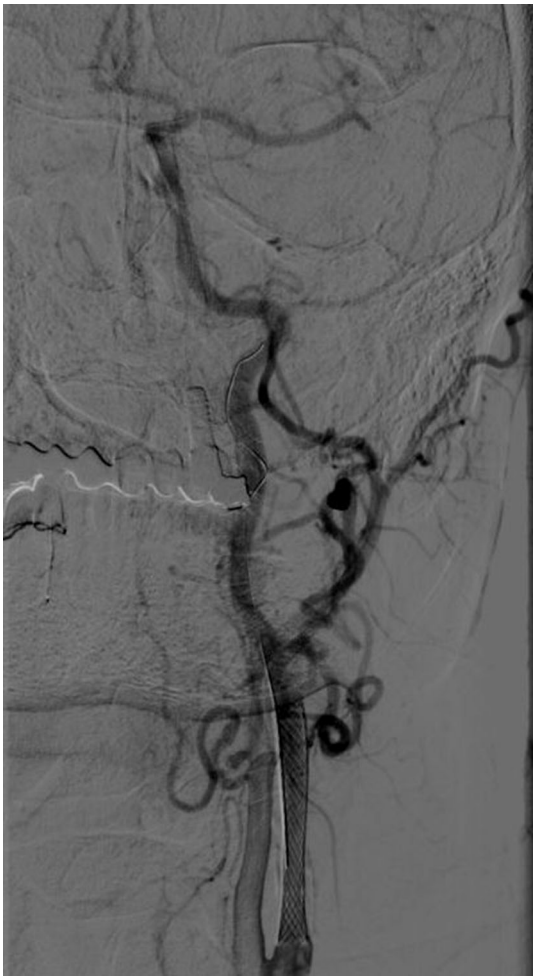

FIGURE 3
Recanalization of left carotid stent on digital subtraction angiography.

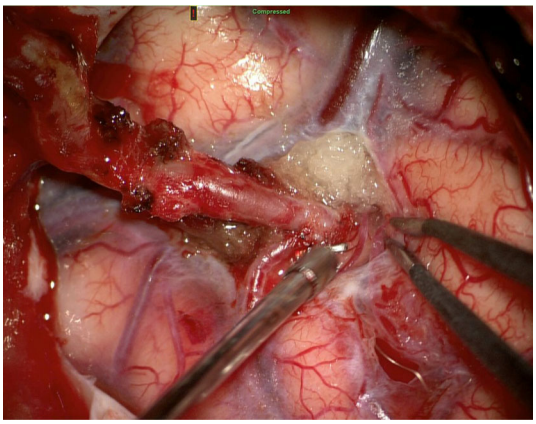

FIGURE 4
Extra-intracranial anastomosis (ECIC) of the superficialis temporalis artery—middle cerebral artery.

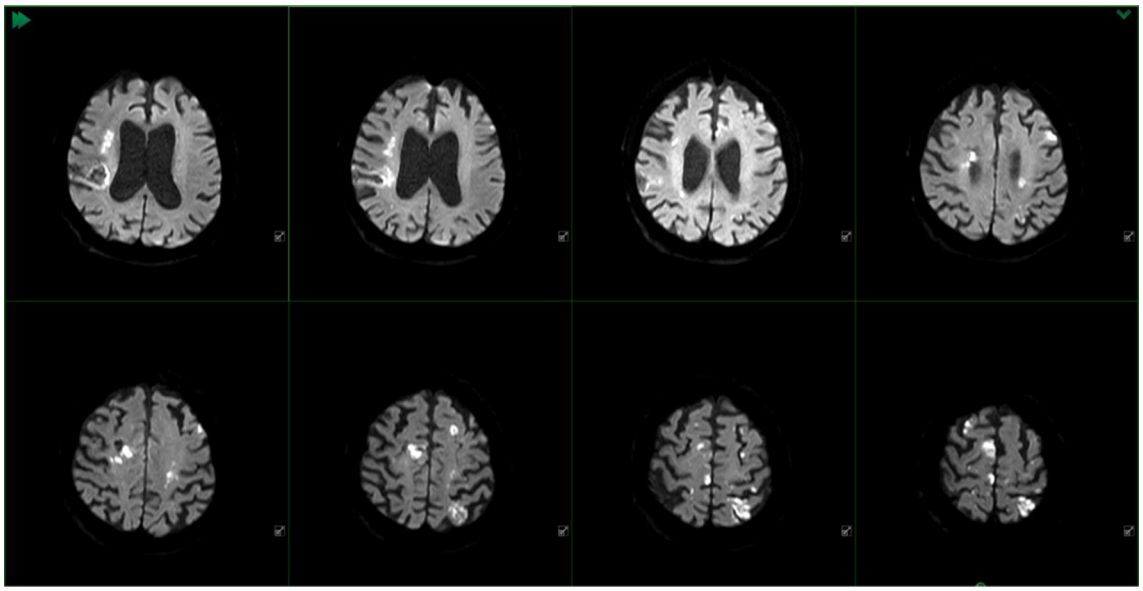

FIGURE 5
MR DWI of the patient before surgery with documentation of hemodynamic ischemia districts in both hemispheres.

using ECIC bypass indicates a good long-term perspective for patients with a similar technical result as in this case report.

One of the reasons for the ineffectiveness of antiaggregant therapy may be the patient's non-use of medication. We should always think about this possibility, especially if resistance to several different antiplatelet drugs is detected.

In our case, there was no search for hematological abnormalities in the patient. However, with a high probability, none would have been detected—the patient admitted to not using anti-aggregation medication during hospitalization. Acute restenosis in a stent without premedication with antiaggregation therapy is known as discussed above. In the acute phase, however, even knowing the cause of thrombosis would not help us. Before stent implantation, this information would certainly be beneficial—it would disqualify the patient from elective stent implantation.

This is a case report, so a larger randomized study would be needed to draw more significant conclusions. However, the case report draws attention to the possibilities of combined therapy in a specific situation with the potential for a good clinical outcome. In our case, we can evaluate this only in the short term for the patient's death (which, however, was not caused by a recurrence of stroke).

In conclusion, early occlusion of the carotid stent is a significant complication of endovascular treatment of stenotic arteries. The use of antiplatelet therapy is careful to prevent this complication. Preventive laboratory testing of the effectiveness of antiplatelet therapy is appropriate. ECIC bypass revascularization can be a highly effective therapeutic procedure. Prolonged low-dose IVT has proven to be an acute bridging therapy until surgery. However, the absolute most important thing is to persuade the patient to follow the treatment regimen—to use regularly prescribed medication.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

Author contributions

DČ: manuscript writing. RB and MS: critical revision of the manuscript content (neurosurgery). JN and NF: manuscript writing, critical revision of the manuscript content and revision of english. FC: critical revision of the manuscript content (radiology). ŠB: critical revision of the manuscript content

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Endovascular embolization of a cerebral pseudoaneurysm caused by SARS-CoV2 infection

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Background: Severe COVID-19 has been shown to produce convulsions, encephalitis, Guillain-Barré syndrome, or cerebrovascular disease. However, only 4 case reports described subarachnoid or brain hemorrhage caused by ruptured cerebral aneurysms or pseudoaneurysms in patients with COVID-19. Cerebral pseudoaneurysms represent <1% of all intracranial aneurysms and have been related to radiation therapy, vasculitis, rupture of true saccular aneurysms, arteriovenous malformations, and infections by bacteria and viruses, such as Epstein-Bar and Herpes virus.

Case presentation: A 28-year-old Caucasian woman, with no medical history of interest and completely vaccinated against SARS-CoV-2, was admitted to Neurology due to progressive tetraparesis with areflexia, a cough, and a fever of 38°C. SARS-CoV2 PCR was positive while lumbar puncture, blood tests, and electromyogram showed criteria for Guillain-Barré syndrome. Despite the treatment, the patient developed dyspnea and tetraplegia requiring invasive mechanical ventilation. There was motor neurological improvement but a decreased level of consciousness was observed on day 13. A brain CT scan demonstrated an acute haematoma and cerebral arteriography showed a 4-mm pseudoaneurysm located in a branch of the left middle cerebral artery. Given the high risk of rebleeding, endovascular treatment was decided upon. Therefore, complete embolization of the pseudoaneurysm was carried out by using the synthetic glue N-butyl-cyanocrylate. Two days later, the patient was clinically and neurologically recovered and was discharged. Lastly, a new angiography showed no evidence of the pseudoaneurysm 3-weeks later.

Conclusions: We report, for the first time, a patient suffering a severe immune reaction caused by SARS-CoV2 infection and developing a cerebral pseudoaneurysm treated with endovascular embolization without complications.

KEYWORDS

COVID-19, pseudoaneurysm, subarachnoid hemorrhage, embolization (therapeutic), CLOCCs, Guillain-Barre syndrome

Introduction

The SARS-CoV-2 infection is well-known for causing common symptoms such as fever, cough, fatigue, pneumonia, and severe acute respiratory distress syndrome (SARS), leading to multi-organ failure and death. Furthermore, severe COVID-19 has been related to the impairment of the nervous system in hospitalized patients producing convulsions, encephalitis, and Guillain-Barré syndrome (1). Finally, haemostatic function represents a complex interaction between the coagulation and fibrinolytic systems, platelets, and the vascular wall (2). This haemostatic function is impaired by the SARS-CoV2 infection (3), causing cerebrovascular disease (1).

Cerebrovascular disease occurs in 1–2% of hospitalized patients suffering from COVID-19 and it has been extensively reported as ischemic stroke, while a few cases of brain hemorrhage have been reported (4). Three case reports published subarachnoid hemorrhage caused by ruptured cerebral aneurysms with COVID-19 (5) and another case was reported in an adolescent suffering an intracerebral haematoma due to cerebral distal pseudoaneurysm rupture (6).

Cerebral pseudoaneurysms represent <1% of all intracranial aneurysms (7) and their treatment and management is a challenge. Pseudoaneurysms are characterized by complete disruption of the artery wall, resulting in an extravascular hematoma contained by just a thin layer of connective tissue (8). Thus, these lesions have been shown to cause intracranial hemorrhage in up to 60% of patients and 31–54% mortality (7, 8). Several causes have been related to the formation of intracranial pseudoaneurysms including radiation therapy, vasculitis, rupture of true saccular aneurysms, arteriovenous malformations, and infections (8). Infectious pseudoaneurysms have a slight preference for younger people, most of them are located in the anterior circulation and often multiple (8). They are known to be caused by bacteria, mainly *streptococcus* and *staphylococcus*, fungi, tuberculosis, and by viruses, such as the Epstein-Bar and Herpes viruses (7, 8).

Here, we report a case of an adult Caucasian woman suffering from COVID-19 with progressive respiratory symptoms, who developed a Guillain-Barré syndrome and a brain hemorrhage caused by a pseudoaneurysm.

Case description

A 28-year-old Caucasian woman, with no medical history of interest and completely vaccinated against SARS-CoV-2 4 months ago, was admitted to Neurology due to a fever of 38°C and simultaneous progressive distal onset tetraparesis with areflexia. She also suffered mild respiratory symptoms, asthenia, and a cough from 1 week before (see Figure 1 for timeline scheme). No previous family history of autoimmune diseases, aneurysms, or stroke.

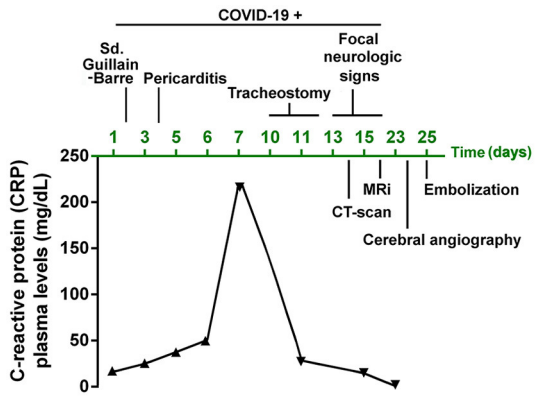

FIGURE 1
Timeline of the case report scheme summarizing the disease, complications and progression of the patient. Study follow-up of the C-reactive protein (CRP) plasma levels.

A chest X-ray showed bilateral pulmonary infiltrates and SARS-CoV2 PCR was positive. A lumbar puncture, blood tests, and an electromyogram (see Table 1 for details) were performed showing criteria for idiopathic acute demyelinating polyneuropathy or Guillain-Barré syndrome with positive IgG antiganglioside (GM1, aGM1, and GD1b) antibodies in relation to COVID-19 (day 2). Nonetheless, SARS-CoV2 subtype genotyping and PCR in cerebrospinal fluid (CSF) were not available. No other risk factors were identified underlying or related to Guillain-Barré syndrome (other viral or bacterial infections, recent surgery, hematological malignant diseases, or immune diseases such as lupus). Despite the patient being treated with immunoglobulins and corticosteroids she developed pericarditis on day 4 and progressed the polyneuropathy until she developed dyspnea and tetraplegia. No cranial nerve palsy was observed and neither was bowel or bladder dysfunction. Thus, she was transferred to the Intensive Care Unit (ICU), requiring invasive mechanical ventilation. As shown in Figure 1, neurological and respiratory worsening was in parallel with an increase in C-reactive protein (CRP) which peaked (>200 mg/dL) on day 7. As observed in a new chest X-ray, acute respiratory failure was probably secondary to a mucus plug causing airway obstruction and left lung atelectasis.

On day 10, an elective tracheostomy was performed and sedation was suspended. Then, motor neurological improvement was observed on examination. Strikingly, a decreased level of consciousness and an absence of spontaneous language was observed on day 13. A brain CT scan (day 14) demonstrated an acute left parietal lobar haematoma (Figure 2A). It is worth noting that the patient was previously treated with a non-anticoagulant dose of enoxaparin 40 mg once/day (normal INR range in blood tests). A body CT and echography of the carotid, renal arteries, and heart were

TABLE 1 Patient's demographic and clinical data.

Age and sex	28 y.o., woman
Ethnicity	Caucasian, Mediterranean European
Symptom prompting first neurological examination	Tetraparesis of distal onset (day 1)
Vital signs at admission	SBP/DBP 115/80 mmHg; HR 90 bpm; O2sat 95%
Sequence of findings	- COVID-19 pneumonia (day 1) - Guillain-Barre syndrome evidence (day 2) - Pericarditis (day 4) - Brain haematoma (day 14) - Pseudoaneurysm (day 15)
CSF biochemical, cytology and microbiologic test by PCR, culture and gram test	- Protein 26 g/dL, 3 cells, glucose 61 mg/dL - Cytology negative for malignant cells, isolated inflammatory cells - PCR NEGATIVE for *E. coli K1*, *Haemophilus influenzae*, Listeria monocytogenes, *Neisseria meningitidis*, *Streptococcus agalactiae and pneumoniae*, *Cryptococcus neoformans and gattii*, Citomegalovirus, Epstein-Barr Virus Enterovirus, Herpes simple virus 1, 2, 6, Parechovirusand Varicela-Zoster Virus. - Gram and long-term cultive for micobacteria and anaerobes negative
Antiganglioside antibodies	Antimonosialogangliosides GM1 = 1/8,907, GM2 and GM3 negative; antiaisialogangliosides GM1 = 1/18,189; antidisialogangliosides GD1b = 1/1,546, GD1a and GD3 negative; antitri- and tetrasialogangliosides GT1a, GT1b, GQ1b negative; antisulfatids negative.
EMG/ENG findings	Prolonged distal motor latencies and temporal dispersion of CMAP of bilateral peroneal and median nerves, complex A-waves of tibial nerves. Sensory nerves conduction studies were normal. No denervation signs were found. An acute inflammatory demyelinating polyradiculoneuropathy was diagnosed (AIDP).
Treatments	- Guillain-Barre syndrome: 0.4 g/kg/day intravenous immunoglobulin for 5-consecutive days - Pericarditis: colchicine 1 mg/day (for 3 months), Prednisone 0.5 mg/kg/day progressively decreased. - Pseudoaneurysm: endovascular embolization with N-butyl-cyanoacrylate
Recovery	- Guillain-Barre syndrome: 6 weeks - Pericarditis: 3 weeks - SARS-CoV2 pneumonia: 2 weeks

SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate in beats per minute; O2sat, oxygen saturation; CMAP, compound muscle action potentials; ASA, acetylsalicylic acid.

performed, finding no other aneurysms or pseudoaneurysms. Given these findings (and the arteriography results below), the absence of clinical features, and the lack of family history, other causes of aneurysms were reasonably discarded such as polycystic kidney disease, hereditary haemorrhagic telangiectasia, Ehlers-Danlos syndrome IV, Marfan syndrome, and neurofibromatosis I (7).

On day 18, an MRI confirmed the haematoma and showed a striking image of an irregular artery (Figures 2C,D). Interestingly, the MRI also revealed a non-specific focus of increased signal in the splenium of the *corpus callosum* (Figure 2B) on DWI sequences suggesting a cytotoxic lesion of the *corpus callosum* (CLOCC).

After treatment and stabilization in the ICU, the patient presented clinical-neurological improvement (day 19). Then, diagnostic cerebral arteriography (day 24) showed a 4-mm distal pseudoaneurysm located in a branch of the temporo-occipital artery of the left middle cerebral artery (MCA), at the M4 level (Figure 3A). The parental artery of the pseudoaneurysm was a very thin caliber with irregular morphology, such as mycotic or vasculitic angiographic appearance (Figure 3B). Moreover, a hypoperfused left parietal lobe was observed, due to the mass effect of the haematoma, and a parieto-occipital artery from the left posterior cerebral artery (PCA) was compensating for the blood flow (Figure 3E). Given the high risk of rebleeding, endovascular treatment was decided upon. Therefore, complete embolization of the pseudoaneurysm (day 25) was carried out by sacrificing the parental artery by using the synthetic glue N-butyl-cyanocrylate (Glubran®, GME, Italy) through a 1.2F microcatheter (Magic®, Balt group, France) (Figures 3C,D). As expected, following the procedure, blood circulation was compensated by a parieto-occipital artery from the left PCA (Figure 3E). Two days later, the patient was clinically and neurologically recovered (excepting mild distal weakness in

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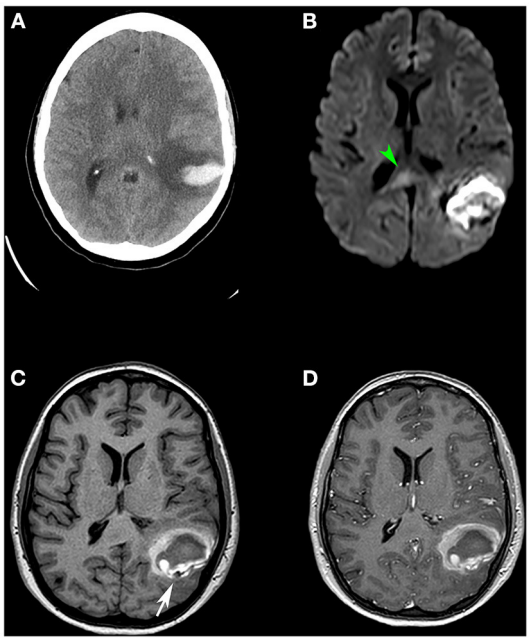

FIGURE 2
(A) Cranial CT scan showing left temporo-occipital intraparenchymal haematoma. **(B)** Diffusion-weighted MR image showing increased signal (diffusion restriction) and thickening of the splenium of the corpus callosum (green arrowhead), suggestive of a cytotoxic lesion of the corpus callosum (CLOCC). **(C,D)** 3D T1-weighted volumetric sequence without contrast **(C)** and with contrast **(D)** demonstrating the existence of a nodular image adjacent to the haematoma (white arrow). It presents as a signal void and after contrast administration, it enhances in an analogous way to vascular structures, compatible with a pseudoaneurysmal lesion.

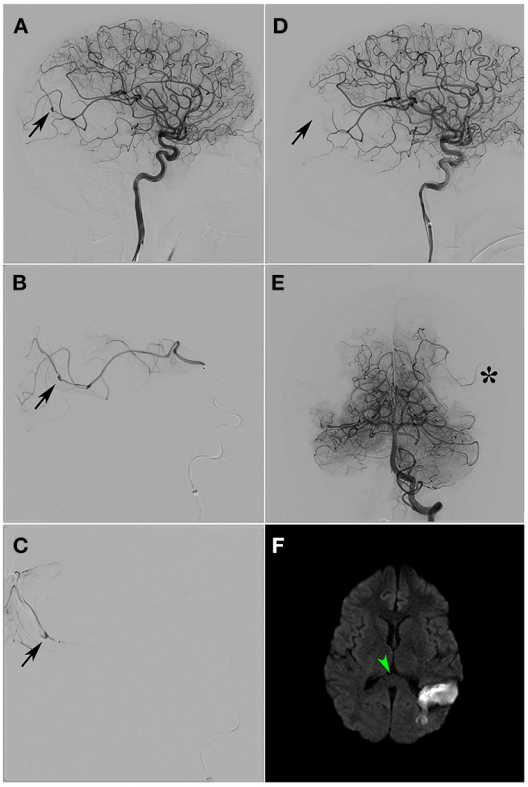

FIGURE 3
(A) Selective arteriography of RICA. The presence of a pseudoaneurysm is detected at the level of the distal temporo-occipital vasculature (black arrow). **(B)** Angular artery supraselective arteriography. The branch presenting the pseudoaneurysm shows an irregularity of the arterial wall suggesting arteritis (black arrow). **(C)** Glue cast after embolization (black arrow). **(D)** Selective arteriography of RICA after branch embolisation. Absence of pseudoaneurysm (black arrow). **(E)** Selective arteriography of LVA. Compensation of the left temporo-occipital territory through temporal branches of the left vertebral artery (black asterisk) is demonstrated. **(F)** Diffusion weighted MR image 1 month after treatment. Morphological and signal normalization of the splenium of the corpus callosum (green arrowhead). Absence of additional ischemic lesion after embolisation. RICA, Right internal carotid artery; LVA, Left vertebral artery.

both hands) and was discharged from the hospital. A new MRI (Figure 3F) showed no ischemia, the CLOCC lesion had disappeared and the haematoma was reduced. Finally, a new angiography performed 3-weeks later showed no evidence of the pseudoaneurysm. At this point, motor function was completely recovered.

Discussion

As previously reported, infectious pseudoaneurysms are often caused by bacteria or fungi and less frequently by viruses (8). COVID-19 has been reported as causing aneurysms and pseudoaneurysms in the heart and peripheral arteries (9–11). Nonetheless, only one case of cerebral pseudoaneurysm has been reported in an adolescent suffering from COVID-19 (6). This patient was diagnosed with a brain haematoma and a pseudoaneurysm in the left M2 segment. At this point, the patient had no respiratory symptoms caused by COVID-19 and the severe inflammatory or immune dysregulation took place 10 days after the treatment of the pseudoaneurysm by surgery.

In contrast, our patient suffered a severe immune reaction causing pericarditis and a severe Guillain-Barre syndrome with positive antiganglioside antibodies. Research on COVID-19 shows a prevalence of pericarditis of ∼1.5% and it has been associated with increased odds of cardiac arrest, heart failure, and new-onset cardiovascular sequelae (12). Nonetheless, to the best of our knowledge, this is the first report of a patient suffering pericarditis and an intracranial pseudoaneurysm as COVID-19 complications. Moreover, in recent systematic reviews and meta-analyses, Guillain-Barre

syndrome has been described in 1 per 10,000 cases of COVID-19 and antiganglioside antibodies have been reported in 0.8% of patients with Guillain-Barre and COVID-19 (13, 14). While few cases of Guillain-Barre and peripheral aneurysms have been reported, this is the first case reporting Guillain-Barre syndrome and an intracranial pseudoaneurysm related to COVID-19. No research has been conducted on antigangliosde antibodies and pseudoaneurysm formation. Furthermore, following the peak of the immune reaction, as suggested by the respiratory distress and the CRP plasma levels, our patient suffered a cerebral haematoma, and simultaneously, imaging tests demonstrated the presence of a CLOCC lesion and a pseudoaneurysm. CLOCCs have been described in a wide variety of conditions, including immune diseases, seizures, toxins, nutritional deficiencies, and infections such as the SARS-CoV2 as previously reported (15).

The SARS-CoV2 entry to the endothelial cell is facilitated by the binding of a spike protein to the angiotensin-converting enzyme-2 (ACE2) receptor leading to the inflammation and lesion of the artery wall through various mechanisms (16). Briefly, cell ACE2 internalization following SARS-CoV-2 entry impairs angiotensin 2 degradation and angiotensin 1–7 formation. Further, infected endothelial cells secrete cytokines and interferons which are recognized by their myeloid cell receptors mediating their migration and inflammatory activity. Moreover, spike protein exposure increases interleukins, MHC II, and costimulatory molecule (CD80 and CD86) expression by macrophages and dendritic cells, increasing the inflammatory and T cell-stimulatory activity (16). Finally, brain injury creates hypoxaemia, increasing proaneurysmal hypoxia-inducible factor (HIF)-1 levels. In this regard, previous studies have demonstrated that smooth muscle within the tunica media responds to localized hypoxia first by increasing HIF-1, resulting in the stabilization of the HIF-1α subunit, nuclear transcription, and binding to the hypoxia response element of VEGF and ets-1 transcription factor. The up-regulation of these genes induces the up-regulation of the matrix metalloproteinase (MMP)-2 and 9 and their increased protein levels. MMP-2 and 9 induce extensive artery matrix remodeling from tissue hypoxia (17). Therefore, we hypothesized that, through these mechanisms, SARS-CoV2 could cause aneurysms and pseudoaneurysms. Interestingly, evidence suggests that vascular dysfunction caused by COVID-19 manifests as deep venous thrombosis, embolism, and large arterial thrombosis. These manifestations are caused by hypoxaemia, viral sepsis, immobility, and vasculitis or vasculitis mimics (18, 19). Other cases of peripheral aneurysms and pseudoaneurysms have been reported (20, 21). These pseudoaneurysms secondary to COVID-19 are supposed to be secondary to inflammatory and vasculitis processes linked to viral multisystem inflammatory syndrome (18). Despite our radiological findings, the body CT scan and arteriography not being compatible with large/medium artery vasculitis means we cannot rule out that the formation of the pseudoaneurysm was caused by a multisystem inflammatory syndrome.

Several cases of endovascular treatment in pseudoaneurysms have been reported by using different approaches such as stents (22, 23), stent-assisted coils (24), embolic liquids/glues (25), and a case was even treated with a flow diverter device (26). In our case, we discarded the use of coils, stents, and flow diverter device because of the poor quality of the wall, thin artery caliber, and because the risk of haemorrhagic event was higher with the need for dual antiplatelet therapy. The reported case of pseudoaneurysm with simultaneous COVID-19 was treated with surgery (6). Nonetheless, we discarded that option to avoid significant periprocedural complications or poor outcomes as described (6).

In the present report, given the distal localization and the small caliber of the parental artery of the pseudoaneurysm, the evident collateral circulation from a parietal branch from the PCA, and the diminished parenchymal irrigation from the parental artery, we decided to sacrifice it by using embolic agents such as adhesive liquids and were successful.

Conclusion

To the best of our knowledge, here we report for the first time, a patient suffering a severe immune reaction caused by SARS-CoV2 infection and developing a cerebral pseudoaneurysm treated with endovascular embolization without complications.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Comité de Ética de la Investigación con Medicamentos de la Gerencia de Atención integrada de Albacete. The patients/participants provided their written informed consent to participate in this study.

Author contributions

FH-F, JG-C, and EQ conceived the study and drafted the manuscript. FH-F, JG-C, EQ, JM-N, JG-G, MP, and TS acquired the data and critically reviewed the manuscript.

All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Cerebral venous sinus thrombosis with an acute subdural hematoma treated with endovascular intervention: A case report

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We report two cases of endovascular intervention for management of cerebral venous sinus thrombosis complicated by an acute intracranial hemorrhage during treatment with therapeutic anticoagulation. The first patient developed an acute subdural hematoma with progressive enlargement and was subsequently managed with venous sinus thrombectomy. The second patient developed an intraparenchymal and subdural hematoma and was treated with middle meningeal embolization. Anticoagulation is the primary treatment for cerebral venous sinus thrombosis but also contraindicated in an acute intracranial hemorrhage. In these cases, after endovascular intervention both patients resumed therapeutic anticoagulation without further hematoma expansion or additional invasive interventions. Both patients made an excellent neurological recovery and returned to their baseline functional independent status. Given the need for anticoagulation, endovascular intervention in the form of thrombectomy or middle meningeal artery embolization may be a viable adjuvant to anticoagulation in select patients.

KEYWORDS

sinus thrombosis, subdural hematoma, thrombectomy, coagulopathies, COVID-19

Introduction

Cerebral venous sinus thrombosis (CVST) is a rare cause of stroke, which is one of the leading causes of long-term morbidity and mortality (1). CVST frequently affects young adults and pre-menopausal females three times more than males, occurs more frequently in prothrombotic states such as Factor V Leiden mutation, antithrombin III deficiency, oral contraceptive, trauma, malignancy, and manipulation in operative procedures (1, 2). The cornerstone treatment for CVST is prompt initiation of anticoagulation therapy (3, 4). CVST can propagate into large cortical veins resulting in a physiological increased venous and intracranial pressure (ICP) leading to cerebral edema, hemorrhage, or a venous infarct (1, 2).

There have been a few cases reported in which patients have developed an acute subdural hematoma (aSDH) secondary to CVST (5–7). As a result, anticoagulation is a relative contraindication in these patients leaving limited treatment options for the management of CVST complicated by aSDH. Various studies have reported middle meningeal artery (MMA) embolization as a means to prevent recurrent rupture of the neovasculature supplying the SDH (8, 9).

We present two cases where endovascular interventions, venous sinus thrombectomy and MMA embolization, were utilized to manage hemorrhagic complications in patients with CVST requiring anticoagulation.

Case reports

Case 1

A 69-year-old female presented with COVID-19 pneumonia, altered mental status, atrial fibrillation with rapid ventricular response and severe diarrhea. A head computed tomography (CT) was obtained which showed the initial mixed density acute subdural hematoma (Figure 1A). An additional axial head CT demonstrated multifocal hyperdensities throughout the dural sinuses, highly concerning for multifocal acute dural sinus thrombosis (Figure 1B). She was admitted to the medical intensive care unit (MICU) COVID unit, resuscitated and started on a heparin infusion. Her neurologic course was also complicated by status epilepticus which required intubation, burst suppression and multiple anti-epileptics agents. A CT venogram (CTV) was obtained which confirmed the diagnosis of multi-focal sinus thrombosis. Occlusions were identified in the superior sagittal sinus (SSS), torcula, bilateral transverse sinuses/sigmoid to the jugular bulb and straight sinus along with generalized venous congestion (Figure 1C). While in burst suppression a surveillance head CT was obtained which demonstrated interval development of bilateral hemispheric and posterior fossa mixed density subdural hematomas and generalized sulcus effacement. An optic nerve sheath diameter was obtained, which measured 6 mm, suggestive of intracranial hypertension. The heparin infusion was paused briefly until a definitive treatment plan could be developed.

A multi-disciplinary team discussed multiple treatment options, and ultimately decided with family to resume therapeutic anticoagulation and proceed with endovascular mechanical thrombectomy of the venous sinuses. She was taken for mechanical thrombectomy of SSS and transverse sinuses thrombus with thrombo-aspiration and stent-retriever techniques. Three thrombectomy passes were made using the Solumbra technique with a Trevo 4 × 40 mm stent retriever device, polyvinyl alcohol particles 150–250 microns, and an aspiration catheter. After the third pass, she developed acute desaturations which were concerning for clot mobilization and a pulmonary embolism. The microcatheter was left in the SSS and recombinant tissue plasminogen activator (tPA) was infused for 10 h. The patient's respiratory status quickly improved but several hours after the procedure she developed anisocoria. A head CT was obtained which demonstrated interval expansion of the hemispheric mixed density SDH, global effacement of the sulci and 4th ventricle. The tPA infusion was discontinued. A decision was made to return to the endovascular suite for further attempts at thrombectomy. A total of five thrombectomy passes were completed with removal of large thrombus fragments after each pass.

The final angiogram showed significant improvement in antegrade venous drainage in the SSS, bilateral transverse and sigmoid sinuses with residual multifocal non-occlusive thrombi (Figures 1D,E). After a prolonged hospital course she was discharged to a long term acute care facility. On clinic follow up 10 months later, she had returned living at home independently with a modified ranking score of 2. A head CT obtained during the clinic follow up showed near complete resolution of the SDH (Figure 1F).

Case 2

A 41-year-old female with history of polysubstance abuse and factor V Leiden mutation who presented with several days of worsening headaches. A head CT was obtained which demonstrated a left temporal intraparenchymal hemorrhage (Figure 2A). She was admitted to the Neuroscience Intensive Care Unit (NSICU) and started on a heparin infusion and then transitioned to dabigatran. A CTV was obtained which demonstrated a thrombosis extending from the straight sinus through the right transverse sinus to the jugular vein (Figure 2B). She was discharged home 7 days after presentation at her neurological baseline. Three days after discharge she presented to the Emergency Department with an acute severe headache and new onset seizures. A head CT demonstrated a new left frontal acute subdural hematoma. The dabigatran was reversed with idarucizumab and she was readmitted to the NSICU. Her neurologic exam remained stable and she was restarted on a heparin infusion.

A surveillance head CT was obtained, which demonstrated a slight interval enlargement of the subdural hematoma (Figure 2C). After discussing the treatment options and need for continued anticoagulation, a decision was reached to proceed with particle embolization of the left middle meningeal artery (MMA). A 5fr Envoy guide catheter, Excelsior 1018 microcatheter and Asahi 14 microwire were used to embolize the left MMA using polyvinyl alcohol 150–250 μm particles. The embolization was uneventful and she tolerated the procedure well. A surveillance head CT obtained 2 days after the embolization demonstrated stable size of the SDH (Figure 2D).

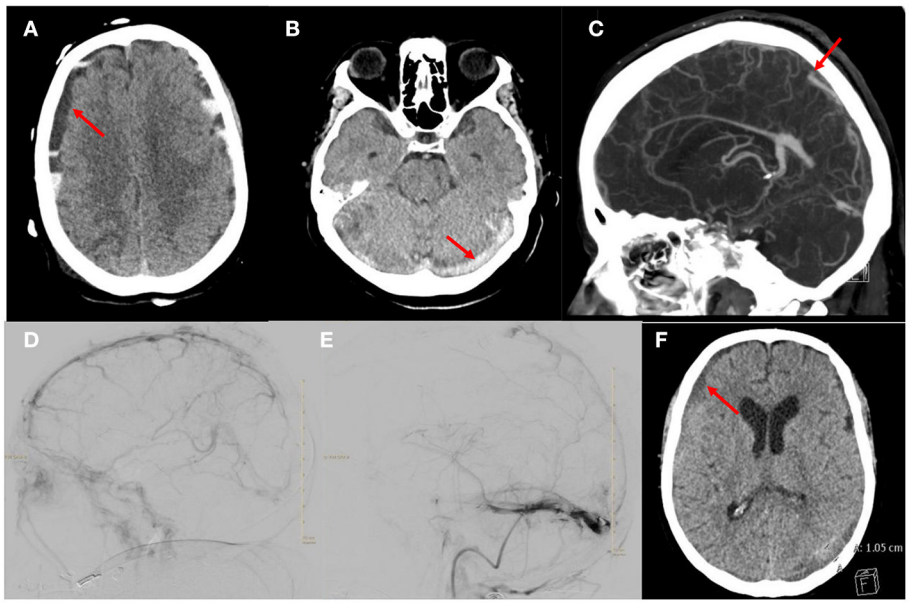

FIGURE 1
Images from the patient who received mechanical thrombectomy and anticoagulation for aSDH with CVST. **(A)** Axial head CT demonstrating the mixed density acute subdural hematoma. **(B)** Axial head CT demonstrating hyperdensity in the torcula and transverse sinuses suggestive of acute thrombosis. **(C)** Sagittal CTV demonstrating occlusion of the SSS, straight sinus and torcula along with generalized venous congestion. **(D)** Right ICA injection, lateral projection of late venous phase demonstrating thrombus in the SSS and partial occlusion of the straight sinus and occlusion of the transverse sinuses. **(E)** Venogram of right sigmoid sinus, lateral projection after thrombectomy and tPA infusion showing improvement in drainage of the SSS and transverse sinus. Note there is a persistent non-occlusive thrombus of the transverse sinus. **(F)** Axial head CT demonstrating decreased size of the subdural hematoma.

She was transitioned from a heparin infusion to dabigatran. She was discharged home 11 days after presentation with no new neurological deficits. At her last clinic follow up 6 months after admission she had returned to living completely independent with a modified ranking score of 0. She is being followed by the hematology department for management of long term anticoagulation.

Discussion

Cerebral Venous Sinus Thrombosis is a rare cause of stroke accounting for roughly 0.5% of all strokes. CVST frequently affects young adults and pre-menopausal females three times more than males and occurs more often in prothrombotic states such as Factor V Leiden mutation, antithrombin III deficiency, oral contraceptive, trauma, malignancy, and manipulation in operative procedures (1, 2). CVST results in the formation of a thrombus in the cerebral veins, as the thrombus extends, it can occlude draining venous sinuses resulting in a global increased pressure of the venous system. This increased venous pressure can lead to cerebral edema, hemorrhage due to rupture of capillary beds, and a venous infarct (1–3). As a result, the clinical presentation of CVST can be thought of as three separate categories including symptoms of elevated ICP, a focal deficit or a combination of both (1). Generally, headache is the most common presenting symptom and can range from mild to severe. Papilledema can be observed and serves as a surrogate marker for intracranial hypertension. More severe symptoms include altered consciousness, seizures, and focal neurological deficits. Currently, the mainstay treatment for symptomatic CVST is anticoagulation to prevent thrombus extension even in the setting of intraparenchymal hemorrhage (4). However, in severe cases of CVST unresponsive to anticoagulation or in instances where anticoagulation is contraindicated, endovascular thrombolysis or mechanical thrombectomy has been proposed as a possible alternative treatment (1).

Rarely, patients with CVST can develop an aSDH, however, the mechanism of hemorrhage is unclear. Takahashi et al., proposed that a sudden rise in ICP in addition to hemodynamic stress of a CVST can result in the tearing of bridging veins and subsequent formation of aSDH (5). In addition, therapeutic anti-coagulation in CVST, venous hypertension, and the development of spontaneous intracranial hypotension have also been proposed as possible mechanisms for developing an aSDH secondary to CVST (6). Few cases have been reported in the literature that have addressed management approaches to treating aSDH secondary to CVST. Notably, Bansal et al., presented a case of a 40-year-old female on oral contraceptive with an aSDH and subarachnoid hemorrhage secondary to

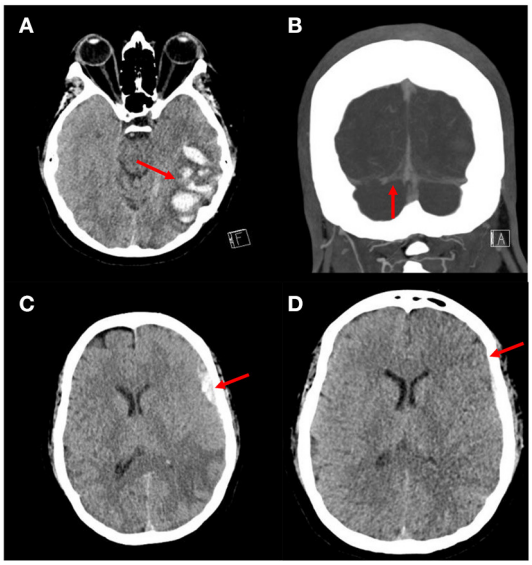

FIGURE 2
Images from patient who underwent MMA embolization followed by anticoagulation for management of aSDH with CVST. **(A)** Axial head CT demonstrating an ill-defined intraparenchymal hemorrhage in the left temporal lobe concerning for a venous infarct. **(B)** Coronal CTV showing occlusion of the right transverse sinus. **(C)** Axial head CT demonstrating an acute left frontal subdural hematoma. **(D)** Axial head CT demonstrating decreased size of the left frontal subdural hematoma.

CVST who required a decompressive hemicraniectomy with evacuation of the aSDH. However, as anticoagulation was contraindicated, the patient continued to deteriorate and perished on post-op day one (6). Akins et al. presented a case series of three patients with CVST who developed an aSDH. One patient, a 38-year-old female on oral contraceptive was treated with an intravenous heparin infusion and transitioned to warfarin upon discharge. The second patient was a 68-year-old woman with polycythemia vera who was treated conservatively with hydroxyurea, hydration, and aspirin. The third patient was a 60-year-old male who underwent thrombectomy for CVST that developed 7 days after undergoing burr hole evacuation of an aSDH (2).

Given the complexity of starting or resuming anticoagulation in patients who develop aSDH secondary to CVST, management decisions are difficult. Though it is standard practice to initiate anticoagulation for hemorrhagic venous strokes, this is not well-studied or reported in the literature. Sahoo et al. reported a patient with CVST and aSDH that was successfully managed conservatively with warfarin (7). Furthering management complexity, the pathophysiology of concurrent aSDH and CVST is not well-elucidated and could also be due to different unrelated mechanisms, such as concurrent trauma. In this case report, we present two contrasting cases of management strategies of CVST complicated by development of an aSDH. One patient underwent a mechanical thrombectomy to reduce the overall thrombosis burden and was then managed with anticoagulation and close monitoring. We propose that the thrombectomy was effective in preventing subdural expansion by reducing the global venous pressure and back pressure on the small and fragile bridging veins. In contrast, the second patient was treated with middle meningeal artery (MMA) embolization to prevent subdural hematoma expansion and resumed long-term anticoagulation. Since neither patient had progression or recurrence of the aSDH we propose that MMA embolization or thrombectomy can be considered as a treatment option for CVST complicated by aSDH in the appropriate situation. Further research is necessary to identify appropriate patients and the most efficacious endovascular intervention.

In recent years, embolization of the middle meningeal artery (MMA) has been recognized as an alternative or adjuvant treatment to surgical evacuation for recurrent and primary chronic subdural hematoma (cSDH) (8–12). Notably, peripheral branches of the MMA directly provide the blood supply for fragile sinusoidal neovessels that compose the outer neomembrane of cSDH (9, 10). Embolization of the MMA prevents the recurrent rupture of this neovasculature, which averts hematoma recurrence. This was demonstrated by Onyinzo et al. who analyzed 132 patients who were diagnosed with cSDH and underwent MMA embolization and/or surgical treatment. Patients who were treated with MMA embolization alone received fewer repeat surgeries when compared to those who underwent surgical evacuation. In addition, patients who were treated with MMA embolization were found to have complete hematoma resolution (11). Details regarding the technique of MMA embolization are limited; however, injection of polyvinyl alcohol particles was utilized in our technique and reported by other studies as well (8, 10, 12). Notably, Aronov et al. employed the non-adhesive SQUID-18 embolic agent as a treatment for recurrent cSDH warranting further research to determine the most effective agent (13).

While MMA embolization continues to be a safe and efficacious minimally invasive treatment for cSDH, less is known regarding its efficacy in treating patients who develop aSDH or those who develop aSDH secondary to CVST. Ding et al. successfully performed MMA embolization on a 56-year-old woman with a right hemispheric aSDH 2 days after undergoing a craniotomy for evacuation. The patient did not develop recurrent hemorrhage upon follow-up (12). This was the only study to our knowledge to have explored MMA embolization as a treatment for aSDH in our literature search.

In conclusion, MMA embolization may be a novel approach for management of a patient with aSDH secondary to CVST when anticoagulation is contraindicated. Many unknowns

regarding the natural history and pathophysiology of CVST complicated by aSDH are still prevalent. Thus, further research is needed to better establish and understand these mechanisms and to determine whether more aggressive interventional therapies may be beneficial compared to anticoagulation and monitoring alone.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. Written informed consent was not obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

NQ, EY, and WL provided direct patient care while the patients were admitted and contributed to the conception and design of the study and wrote sections of the manuscript. MC and NQ reviewed the patient charts and collected the data. MC wrote the first draft of the manuscript. All authors contributed to the manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Endovascular treatment of an aneurysm associated with fenestration of the supraclinoid internal carotid artery: Case report and review of the literature

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Background: Fenestrations or divisions of the vascular lumen into separate channels appear to be common anatomical variations in patients with intracranial aneurysms. The most frequent sites of occurrence are the anterior communicating artery (ACom), followed by vertebrobasilar and middle cerebral artery (MCA) locations.

Case presentation: A 61-year-old female was brought to the emergency department after experiencing severe headache with abrupt onset, nausea, and vomiting. Clinical examination on arrival showed a drowsy patient (GCS 14), with neck stiffness, but no cranial nerve palsies or other neurological deficits (Hunt-Hess 2). Non-contrast head CT and CT angiography revealed subarachnoid and intraventricular hemorrhage (modified Fisher 4) and two saccular aneurysms, one located on the right supraclinoid ICA with peripheral calcifications, measuring 20 × 12 mm, the second on the left MCA bifurcation, 6 × 4 mm. 3D rotational angiography revealed a right ICA fenestration located between the ophthalmic (OA) and posterior communicating artery (PCom). The proximal part of the fenestration harbored a large saccular aneurysm projecting superiorly with the neck engulfing the origin of the fenestration; due to the favorable neck and geometry of the aneurysm, endovascular coil occlusion was chosen as a treatment option without balloon or stent assistance. The decision was taken to clip the MCA aneurysm.

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Conclusion: Supraclinoid ICA fenestrations are rare anatomical variations. Endovascular treatment of supraclinoid ICA fenestration-related aneurysms is feasible and safe, with the notable concern of perforators originating from the limbs.

KEYWORDS

fenestration, intracranial aneurysms, endovascular, neuroradiology, internal carotid artery

Introduction

Fenestrations or divisions of the vascular lumen into separate channels appear to be common anatomical variations in patients suspected with intracranial aneurysms. The most frequent sites of occurrence are: the anterior communicating artery (ACom), followed by vertebrobasilar and middle cerebral artery (MCA) locations (1). The internal carotid artery (ICA) is an extremely rare location for this anomaly, only 23 cases being reported in the medical literature so far.

We present the case of an acutely ruptured saccular aneurysm developed on the proximal part of a supraclinoid ICA fenestration, treated by endovascular coil embolization; a review of the literature regarding supraclinoid ICA fenestrations was also conducted.

Case report

A 61-year-old female was brought to the emergency department after experiencing severe headache with abrupt onset, nausea, and vomiting. Clinical examination on arrival showed a drowsy patient (GCS 14), with neck stiffness, but no cranial nerve palsies or other neurological deficits (Hunt-Hess 2); her blood pressure was 190/110 mmHg. Other laboratory blood tests were within normal ranges.

Non-contrast head CT and CT angiography revealed subarachnoid and intraventricular hemorrhage (modified Fisher 4) and two saccular aneurysms, one located on the right supraclinoid ICA with peripheral calcifications, measuring 20 × 12 mm, the second on the left MCA bifurcation, 6 × 4 mm (Figure 1). Due to its displacement by the aneurysm, only retrospectively was the fenestration identified on the CTA (not shown). Due to a larger maximal diameter, a higher aspect ratio, and the presence of a bleb, the ICA aneurysm was considered the most likely culprit of the subarachnoid hemorrhage.

Catheter angiography was performed the next day on a biplane Siemens Artis Zee machine (Siemens, Erlangen, Germany); 3D rotational angiography revealed a right ICA fenestration located between the ophthalmic (OA) and posterior communicating artery (PCom). The proximal part of the fenestration harbored a large saccular aneurysm projecting superiorly with the neck engulfing the origin of the fenestration (Figure 2A); due to the favorable neck and geometry of the aneurysm, endovascular coil occlusion was chosen as a treatment option without balloon or stent assistance. The decision was taken to clip the MCA aneurysm at a later stage because of its wide neck and the necessity to perform stent-assisted coiling, requiring dual antiplatelet therapy.

With the patient under general anesthesia, a right femoral approach *via* a 6F sheath (Cordis Corporation, California, USA) was used to navigate a 6F Chaperon guiding-catheter (Microvention, Tustin, California) in the distal part of the cervical ICA, through which a straight-tipped PxSlim (Penumbra, Alameda, California) microcatheter was introduced into the aneurysm sac, followed by packing with 8 Penumbra 400 coils (Penumbra, Alameda, California) until almost complete obliteration was achieved assessed by Raymond-Roy occlusion classification as IIIb (Figures 2B,C). All catheters were continuously flushed with saline and unfractioned heparin throughout the procedure. After introduction of the first coil, a bolus of 5,000 IU of unfractioned heparin was administered intravenously to prevent thromboembolic complications. An Angio-Seal (Terumo, Tokyo, Japan) closure device was used for hemostasis.

There were no intraprocedural complications. The patient received 10 ml/h i.v. nimodipine during hospitalization and her clinical condition and neurological status improved in the following days. Follow-up CT at 24 h did not show additional complications. The patient was discharged 15 days later with mRS 1, with a slight disorientation.

Methods and materials

A MEDLINE search (PubMed) was performed, using the following terms: "Internal Carotid Artery" (all fields) AND "Fenestration" (all fields) sorted by "Best match". The search generated 145 results. The inclusion criteria were imaging and/or surgical confirmation of a fenestration located on the ICA segments distal to the anterior clinoid process or ophthalmic artery. The authors independently read the titles,

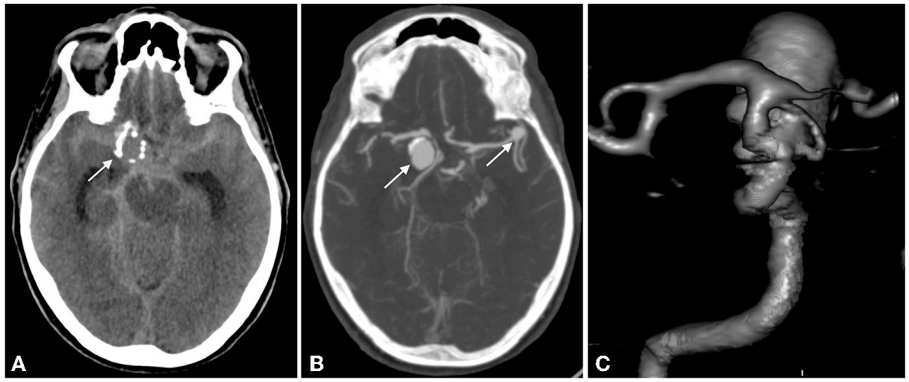

FIGURE 1
NCCT: subarachnoid hemorrhage in the basal and sylvian cistern >1 mm thick and in the 4th ventricle; a round mass with peripheral calcification is seen (white arrow) **(A)**; CTA and VRT display 2 aneurysms, one on the right supraclinoid ICA, the second on the left MCA bifurcation (white arrows) **(B,C)**.

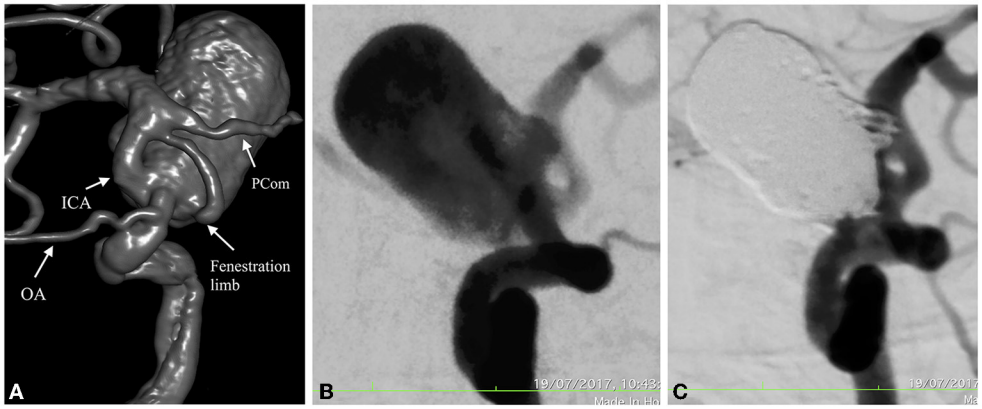

FIGURE 2
3D Angio in oblique views show the fenestration arising distal to the OA and ending proximal to a fetal type PCom **(A)**; DSA in working projection depicts the aneurysm before and after endovascular coil embolization with near complete obliteration of the sac (Raymond-Roy Occlusion Classification IIIb) **(B,C)**.

abstract, full text and relevant references. Out of the 145 results, 21 met the inclusion criteria and no relevant study was found in the references.

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Târgu-Mureș Emergency County Hospital, Romania (Protocol Code 30418, on December 7, 2021) and written informed consent has been obtained from the patient to publish this paper.

Results

A total of 23 cases with supraclinoid ICA fenestration were published between 1983 and 2018 in the 21 articles which met the inclusion criteria (2–22); in all of them the fenestration began at or above the OA, and 18 had at least one associated aneurysm at the proximal and/or distal part (2, 6, 8, 10–17, 19–22). Only 3 out of the 23 cases had no intracranial aneurysms (4, 9, 18). Endovascular treatment was undertaken in 8 aneurysms (8, 14–16, 20–22), the rest being treated surgically. All cases are included in Table 1.

Discussion

A fenestration is defined as a division of the vascular lumen in two separate channels, each with its own tunica intima, media and adventitia, although the adventitia can be shared (23). In a recent prospective angiographic study, intracranial artery fenestrations were found in 24% of patients with ruptured aneurysms. The ACom was the most frequent site of occurrence (69%), followed by the A1 segment of the anterior cerebral artery

TABLE 1 Literature review of all published cases with supraclinoid ICA fenestrations.

References	Age (years)	Sex	SAH	Associated aneurysm	Treatment	Aneurysms in other location
Yock (2)	41	F	Yes	Yes	Wrapping	No
Findlay et al. (3)	28	F	Yes	No	No	ACom
Takano et al. (4)	51	F	No	No	No	No
Hattori and Kobayashi (5)	38	F	Yes	No	No	ICA bifurcation
Katsuta et al. (7)	46	F	Yes	No	No	SCA
Banach and Flamm (6)	37	F	Yes	Yes	Clipping	PCom
Ng et al. (8)	34	F	No	Yes, 2	Clipping/coiling	No
Bharatha et al. (9)	73	M	No	No	No	No
Chen et al. (10)	31	M	Yes	Yes	Wrapping	No
Onoda et al. (11)	42	F	No	Yes	Wrapping	n/a
Plumb et al. (12)	48	F	Yes	Yes	Clipping	No
Ichikawa et al. (14)	47	F	No	Yes	Coiling	ACho
Dey and Awad (13)	39	F	No	Yes	Clipping	n/a
	32	F	Yes	Yes	Clipping	n/a
Nakiri et al. (16)	47	F	No	Yes	Coiling	n/a
	44	M	Yes	Yes	Coiling	n/a
Park and Lee (15)	44	M	Yes	Yes	Coiling	MCA
Rennert et al. (17)	52	F	No	Yes	Clipping	ACho
Orru et al. (18)	26	F	No	No	No	No
Uchino and Tanaka (19)	73	F	No	Yes	No	No
Lee et al. (20)	65	F	No	Yes	Coiling	No
Sgreccia et al. (21)	55	M	No	Yes	Coiling + FD	MCA
Jha et al. (22)	60	F	No	Yes	Coiling + FD	No

SAH, subarachnoid hemorrhage; ACom, anterior communicating artery; ICA, internal carotid artery; SCA, superior cerebellar artery; PCom, posterior communicating artery; ACho, anterior choroidal artery; MCA, middle cerebral artery.

(ACA) (9%), MCA (9%), basilar artery (9%) and the vertebral artery (2%) (1). Intracranial ICA segments seem to be extremely rare locations affected by fenestrations, to our knowledge only 23 cases being reported in the literature so far (2–22).

The primitive ICA develops from the dorsal aorta during the first 3 stages of embryologic development [4–12 mm crown-rump length (CRL)] (6). In the first stage (4–5 mm CRL), both ICA's are connected by a network of plexiform anastomoses, which fuse to form the main ICA channels; it is during this stage also that the primitive ICA divides distally into a posterior trunk, the precursor of the PCom and an anterior trunk, the ACA with its branches (anterior choroidal artery, MCA); the division point is just distal to the ophthalmic artery.

Although not clearly understood, two main theories emerged as possible explanations for the development of supraclinoid ICA fenestrations:

- *Bifurcation failure* of the ICA into the anterior and posterior trunks;
- *Fusion failure* of the plexiform anastomoses between the two ICA's.

In our opinion, the second theory is more plausible because of the numerous reports of ICA fenestrations occurring in all segments, including cervical, petrous and cavernous (24, 25) suggesting that the ICA develops through fusion of numerous plexiform channels. An additional argument supporting the fusion failure theory is that intracranial vessels like the ACA, MCA and the vertebrobasilar system also develop through fusion of numerous vascular channels.

The association between fenestrations and aneurysms is not clearly understood. In their prospective angiographic study, van Rooij et al. (1) didn't find a significant relationship between them; on the contrary, out of the 24 cases with supraclinoid ICA fenestrations, including our own, 17 (74%) harbored one or more aneurysms at the fenestration site (Table 1) suggesting that a causative association is plausible; moreover, 7 patients including our own had additional aneurysms at other sites, while 3 had only in other locations. Only 3 patients had no intracranial aneurysms.

Each end of the fenestration is a potential place for aneurysm formation. Histologic specimens of a fenestrated basilar artery revealed thinning and even disappearance of the muscularis layer at both ends of the fenestration (26) pointing to structural

wall weaknesses in fenestrated segments that can lead to aneurysm formation. Furthermore, the observation that in 20 cases (87%) intracranial aneurysms were present, may reflect a lack of vascular immaturity and vulnerability to developing aneurysms at the fenestration site or elsewhere. Fenestrations can be mistaken for aneurysms as reported by Weil et al. (27).

Treatment of supraclinoid ICA fenestration related aneurysms was performed for 19 aneurysms (Table 1): 9 open surgery, 8 endovascular, either by coiling alone, balloon/stent assistance or flow-diversion, and in one case with 2 aneurysms treatment was performed by a combined surgical and endovascular approach. No procedural complications were encountered during endovascular treatment; interestingly one limb of the fenestration was sacrificed in two cases (14, 16) with no clinical consequences. Moreover, in two cases (21, 22) flow-diverters were successfully deployed inside one limb of the fenestration without intra- or postprocedural complications. Flow-diverting stents can be a promising therapeutic option, if recanalization of fenestration-associated aneurysms occurs. Despite this, one should be cautious because perforators can emerge from either limb as noticed by Onoda et al. (11) during craniotomy. Due to the "friendly" dome-to-neck ratio (i.e., ∼2), we were able to treat our patient by simple coiling, without procedural complications and an uneventful postoperative course.

To our knowledge, we presented the 9th case of a supraclinoid ICA fenestration associated aneurysm treated by endovascular coil occlusion, providing further evidence that in such cases this therapeutic option is safe and effective, without significant procedural complications.

Conclusion

Supraclinoid ICA fenestrations are rare anatomical variations. There appears to be a causative relationship between them and associated aneurysms suggesting the need for careful analysis of imaging and angiographic studies related to these patients. Endovascular treatment of supraclinoid ICA fenestration-related aneurysms is feasible and safe, with the notable concern of perforators originating from the limbs.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of Târgu-Mureș Emergency County Hospital, Romania. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

Conceptualization, writing—original draft preparation and methodology: RF and LM. Software and data curation: EA. Validation: All authors. Formal analysis, investigation, and resources: ER, AM, and CC. Writing—review and editing and visualization: RF. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Preliminary experience with recanalization of large vessel occlusion due to underlying long-segment dissection using a standby microwire technique

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Purpose: This study aimed at investigating a novel standby microwire technique to facilitate revascularization of large vessel occlusion due to underlying long-segment dissection.

Methods: Patients with acute ischemic stroke with emergent large vessel occlusion (ELVO) due to underlying long-segment dissection were screened from the prospectively established database between January 2021 and May 2022. The clinical and radiological data of eligible patients who underwent endovascular treatment by using a standby microwire technique were investigated.

Results: Of the 165 acute ischemic stroke patients who underwent mechanical thrombectomy, the standby microwire technique was used in five patients aged 33–55 years old with occlusion due to underlying long-segment dissection. Of them, three patients were diagnosed with tandem lesions and three were located at the anterior circulation. A 300 cm exchange microwire was used as the standby microwire. Stent deployment was performed in all five patients. Groin puncture to reperfusion time ranged from 10–68 min. Technical success and favorable clinical outcomes were achieved in all five patients (100%). No technique-related complication was observed.

Conclusion: Our preliminary experience showed that the standby microwire technique was a useful ancillary approach to facilitate the revascularization of large vessel occlusion due to underlying long-segment dissection.

KEYWORDS

stroke, thrombectomy, technique, dissection, experience

Introduction

Mechanical thrombectomy (MT) has been accepted as first-line treatment for emergent large vessel occlusion (ELVO) due to internal carotid artery (ICA) or vertebral artery (VA) dissection as an infrequent entity. However, it may potentially lead to severe and catastrophic acute ischemic stroke (AIS) (1). Vascular dissection accounts for ∼2% of AIS in the general population (2) and 10–25% in patients under the age of 50 years (3). MT for LVO caused by dissection remains a clinical challenge (4). One of the reasons is that ICA or vertebral dissection is commonly accompanied with long-segment vessel injury and massive thrombus burden, making it difficult to be revascularized in a short time. In addition, intracranial mechanical thrombectomy is difficult and time consuming due to difficult access and the need for revascularization of the long and complex lesions (1).

The subsequent development of the technique of preserving the true lumen for repeated thrombectomy makes the procedure safer and less time-saving. In this article, we present a novel technique of "standby microwire technique" using an exchange microwire to ensure the patency of the dissection lumen during the endovascular procedure.

Methods

Patients diagnosed with AIS due to long-segment dissection who underwent endovascular treatment were enrolled from Jan 1, 2021 to May 30, 2022. Clinical and radiological data were obtained from the prospectively collected database. Written and signed informed consent was obtained from all participating patients.

Long-segment dissection was defined as dissection extending over at least two artery segments on the first angiogram. The study was approved by the institutional review board. According to local regulations, patient consent was not required for this study which involved strictly anonymized data. The data supporting the findings of the present study were available from the corresponding author on reasonable request. The following procedural outcomes were prospectively assessed. Successful recanalization was defined as extended Thrombolysis in Cerebral Infarction (eTICI) 2b/3. Technical success was defined as eTICI 2c/3 after using the standby microwire technique without the use of rescue therapy. Procedure-associated complications included arterial perforation, new arterial dissection, embolization in a new territory, or subarachnoid hemorrhage. Technique-related complications included tanglement of the devices, difficulty with stent retrieval, and arterial perforation due to the exchange microwire and bounce of the exchange microwire. The favorable clinical outcome rate was defined as a modified Rankin Scale (mRS) score at 90 days of 0–2 or equal to pre-stroke mRS. Symptomatic intracranial hemorrhage was defined as any intracranial hemorrhage visualized in follow-up imaging study and associated with a worsening of 4 or more points on the NIHSS score or death.

Technique details

The key step of standby microwire technique is illustrated in Figure 1. Three key steps are as follows.

Super-selection of true lumen

Intermediate catheter (5F or 6F Catalyst, Stryker, USA) was advanced with the tri-axial technique, afterward, a microwire (synchro 0.014/150, Stryker, USA) supported by the microcatheter was manipulated gently to cross the occluded segment. If needed, contralateral access was established to provide the roadmap of the distal lumen, especially for VA occlusion with underlying long-segment dissection. After passing through the dissection, angiography was performed *via* the microcatheter to verify the entrance of the true lumen.

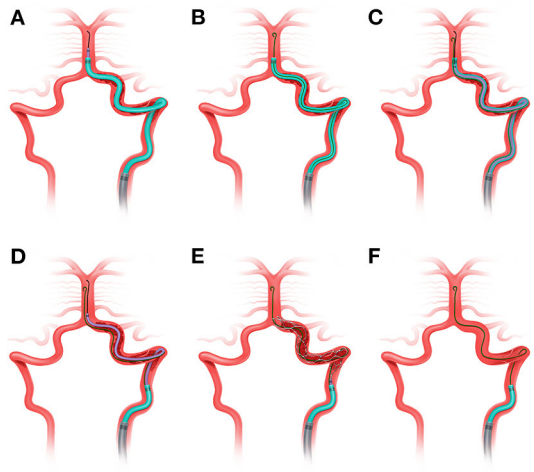

FIGURE 1
Illustration of "standby microwire technique". **(A)** The guiding catheter (gray) was advanced to V1 segment, the aspiration catheter (light green) and microcatheter (purple) were advanced to the basilar artery with the assistance of Synchro microwire (black). **(B)** A Floppy 300 microwire (dark green) was then exchanged with Synchro microwire and stayed in the basilar artery. The tip was shaped into protective "J" (black arrow). **(C)** The microcatheter was then advanced through the dissection to the basilar artery. **(D)** The aspiration catheter was retrieved to proximal part of dissection under continuous aspiration. **(E)** Synchro microwire was withdrawn and the self-expandable stent retriever was advanced to the distal part of dissection and was then delivered. **(F)** The thrombus was removed with the stent through the aspiration catheter, without affecting the position of the exchange microwire.

Then, an intermediate catheter was advanced to the distal normal lumen.

Preservation of true lumen with exchange microwire

Afterward, the tip of exchange microwire, with 300 cm length and 0.014 inch diameter, would be shaped into a "J" shape and stayed in the true lumen. After retrieval of the microcatheter, the microcatheter supported by the microwire would be re-advanced through the intermediate catheter to perform mechanical thrombectomy. When the stent retriever was in position, the intermediate catheter was pulled back to the proximal normal lumen.

Thrombectomy

Then, thrombectomy was performed. If second thrombectomy needed, the intermediate catheter was re-advanced to the distal normal lumen along with the standby microwire. Afterwards, angioplasty with balloon dilation or stent implantation could be performed with the assistance of the standby microwire if necessary. Unnecessary angiography should be avoided to reduce the risk of thrombus migration. The whole system was retrieved after successful revascularization. Tirofiban was initiated during MT if stenting was performed, and maintained for 36 h. Thrombo-elastography with platelet mapping (TEG) was performed after MT.

Results

Of the five patients included in the analysis, the mean age was 46.2 ± 8.9 years, the median NIHSS score was 9 (5–20), the median initial NCCT ASPECTS or pc-ASPECTS (5) was 9 (6–10), and the median time from symptom onset to revascularization was 277 (123–795) min (Table 1). Two patients had tandem lesions, with proximal occlusion of the ICA and distal occlusion of the MCA. The successful reperfusion status, defined as Thrombolysis In Cerebral Infarction (TICI) 2b-3, was achieved in all 5 cases (Table 1).

Thrombolysis was performed in three patients prior to endovascular treatment. Endovascular treatment was performed under conscious sedation in two patients, and under general anesthesia in the other three patients. Thrombectomy was performed even in case of low NIHSS, knowing that symptom fluctuation in this patient was due to involvement of a very eloquent area. A floppy microwire and a synchro 0.014 inch microwire with length of 300 cm were used as the exchange microwire during the procedures. Extra stent implantation was required in all patients (Table 1). No bounce or tanglement was observed. Four out of the five patients resulted in a favorable clinical outcome in terms of modified Rankin Scale (mRS) ≤ 2 at 3 months. There were neither intra- nor peri-interventional complications.

Illustrative case

A 33-year-old male patient complained of sudden aphasia and numbness of the left extremities for 5 h. The patient complaint of neck pain upon neck massage, which progressively extended from the neck to occipital region, face and left extremities. He also reported aphasia, choking and even loss of consciousness on one occasion. The patient was suspected with cerebral infarction in a local hospital, but ineligible for thrombolysis. Then, he was quickly transferred to our hospital. At admission, the NIHSS score was 9. CT showed no hypo-intensity or brain edema. CT perfusion showed penumbra volume = 5 ml. No special previous medical and disease history was recorded.

Mechanical thrombectomy was performed under general anesthesia (Figure 2). The femoral route was established with a long sheath (Infinity, Stryker, USA). Afterward, a thorough angiography was performed to evaluate the collaterals and dissection profiles. The first angiogram showed left VA occlusion (Figure 2A arrow), potentially caused by dissection; a synchro microwire was super-selected to the basilar tip after several attempts. Gentle angiography from the guiding catheter showed a long segmental dissection in the left VA (Figure 2B) and then the 300 cm microwire (black arrow) was shaped into a "J" and exchanged with the synchro microwire as a standby microwire. The 300cm microwire remained at the basilar tip (Figure 2C). Meanwhile, a Solitaire platinum stent (4 × 40 mm) was delivered to the dissection and expanded. After first thrombectomy with the stent retriever, the anterior inferior cerebellar artery was not recanalized and intermediate catheter was repositioned at the distal true lune along the standby microwire. Then microcatheter supported by microwire was advanced to distal true lumen and second thrombectomy was performed and PICA (black arrow) could be partially observed (Figure 2D). Balloon was advanced to the dissection segment along the standby microwire and dilation was subsequently performed (Figure 2E). Blood flow of the VA (white arrow) and PICA was further improved (Figure 2F). An Enterprise 2 stent (4 × 39 mm) was then implanted, followed by a Leo stent (4.5 × 75 mm) (Figure 2G). Finally, eTICI 3 grade recanalization was achieved (Figures 2H,I). Six months later, angiography showed excellent recovery of the VA and PICA (Figure 2J).

TABLE 1 Characteristics of enrolled patients.

	Age/sex	Medical history	Occlusion site	NIHSS	ASPECTS	Thrombolysis	General anesthesia
Case 1	33/M	Neck massage	L-VA	9	10	N	Y
Case 2	44/M	/	Tandem R-ICA & R-M1	9	10	Y	N
Case 3	55/M	DM/HTN	R-ICA	20	7	Y	Y
Case 4	45/M	DM	Tandem L-ICA & L-M2	5	9	Y	N
Case 5	54/M	/	L-VA	9	6	N	Y

	Exchange microwire	SR/AC/AP	Stent implanted	TICI	Complications	Time from onset to recanalization	Prior mRS	m mRS
Case 1	Floppy 300	2/1/3	Enterprise/Leo	3	None	4 h 37 min	0	0
Case 2	Floppy 300	1/0/1	Wallstent	3	None	2 h 56 min	0	0
Case 3	Synchro 300	0/0/1	Xpert	3	None	10 h 35 min	0	1
Case 4	Floppy 300	0/1/1	Xpert	3	None	2 h 3 min	0	0
Case 5	Floppy 300	2/3/2	Enterprise*2	2b	None	13 h 15 min	0	3

ASPECTS: Alberta stroke program early CT score; DM: diabetes mellitus; HTN: hypertension; ICA: internal carotid artery; NIHSS: National Institute of Health stroke scale; VA: vertebral artery. SR/AC/AP: times of stent retriever, aspiration and angioplasty used. Complications included hemorrhagic complications including perforator bleeding, intracranial hemorrhage, subarachnoid hemorrhage, puncture hematoma and ischemic complications including new territory stroke, perforator occlusion, re-occlusion and intra-stent occlusion.

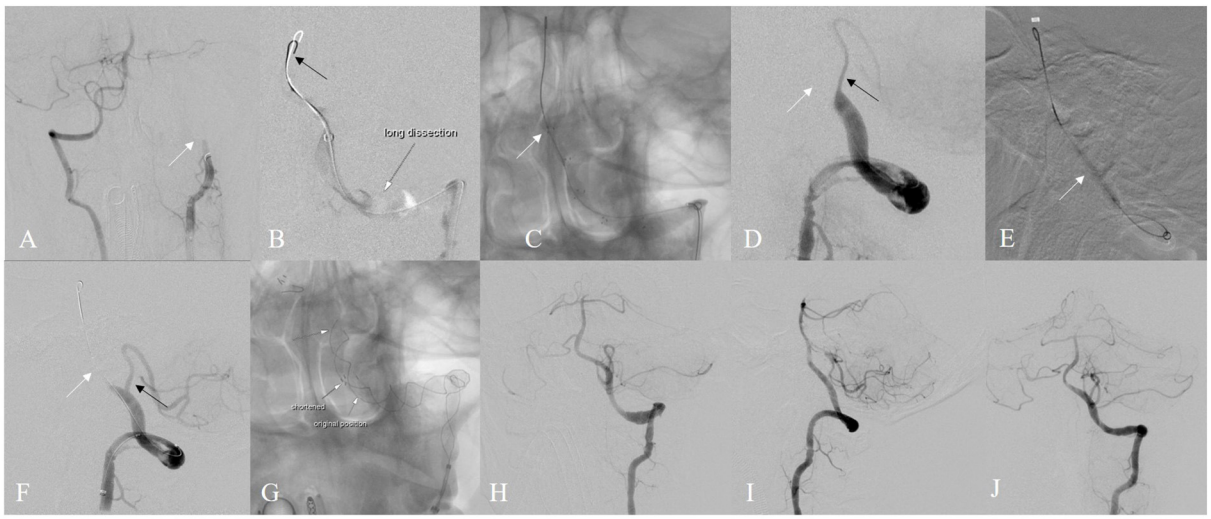

FIGURE 2
Illustrative case of "standby microwire technique" **(A)** left VA was occluded **(B)** superselection of exchange catheter through long segmental dissection **(C)** "J" sahpe microwire remained in the dissection **(D)** after 1st thrombectomy **(E)** balloon dilation was then used **(F)** partial recanalization **(G)** stent implantation was performed **(H,I)** eTICI 3 grade recanalization was achieved **(J)** excellent recovery after 6 months.

Discussion

In this study, we reported recanalization of large vessel occlusion due to underlying long-segment dissection using a standby microwire technique in five cases. In this technique involves the use of an exchange microwire in performing mechanical thrombectomy or angioplasty. The standby microwire embedded in the dissection was used to preserve the lumen of dissection. The technique was successfully performed in all cases, without technique-related complications or affecting thrombectomy and angioplasty.

Dissection is an infrequent, albeit catastrophic form of stroke in the young (6). Given the long-segment and complex injury of the ICA and VA, identification of the true lumen is quite difficult in endovascular treatment (1). In clinical practice, the true lumen is commonly identified after several attempts. Thereafter, preservation of the true lumen is quite essential for the following steps (7). Our experience demonstrates that the

standby microwire technique can provide a potential method for stable and safe preservation of the true lumen. In addition, the standby microwire does not interfere with the thrombectomy and angioplasty processes.

There are several challenges in managing dissection of ICA and VA (8). First, identification of the true lumen is the priority but most difficult step before performing the subsequent treatment steps. Before identification of the true lumen, angiography should be avoided to prevent the enlargement of the false lumen and extrusion of the true lumen, leading to failure of super-selection. Once proceeding the catheter and microwire through the false lumen, the true lumen might be thinner by rude manipulation. This is a one-way door decision, namely we might only have one chance to pass through the true lumen. Thereafter, the preservation of the true lumen is the key step. Second, after thrombectomy with the stent retriever or aspiration, the thrombectomy system including the microcatheter and stent was totally retrieved from the dissected lumen. If not successfully revascularized, the true lumen would disappear and become more difficult to pass for the second time than the first. Thirdly, dissection is commonly complex and involves a long segmental lesion, leading to long puncture-to-revascularization time. If thrombectomy fails, balloon dilation and stent implantation are alternative techniques. A standardized anti-platelet regimen is required.

Spontaneous cervical artery dissection has been associated with violent, sudden neck movements including neck massage and golf (9). A young man who complained of neck pain, blurred speech and limb numbness during neck massage was diagnosed with left VA dissection (Figure 2). In this case, the true lumen was identified after over 20 min of attempt. The large internal lumen and smooth drug-eluting inner membrane of guiding catheter facilitates the conduction of standby microwire technique during thrombectomy in this patient.

Take-home message of the technique is as follows. First, the tip of the microwire should always stay on the screen and the tension should be noted during the procedure, preventing potential perforator bleeding by bouncing of the microwire. Second, tangling of the exchange microwire and stent retriever should be noted by the standardized procedure protocol. Also, this study has some limitations. First, the sample size was small due to rare occurrence of long-segment dissection. In addition, statistical analysis was not performed due to the small sample size.

Conclusion

We described a modified standby microwire technique assisted by a long exchange microwire revascularize large vessel occlusion due to underlying long-segment dissection, with satisfactory clinical outcomes. As our experience is preliminary and the sample size is relatively small, further studies with larger series are required to evaluate the safety and efficacy of this technique for the treatment of emergent large vessel occlusion with underlying long-segment dissection.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Changhai Ethics Committee. The patients/participants provided their written informed consent to participate in this study.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Case report: Treatment of anterior cerebral artery aneurysms with combined remodeling technique and flow diverter deployment through a dual lumen balloon catheter

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We present the technical aspects of embolization for two unruptured medium-sized aneurysms of the anterior cerebral artery treated with balloon-remodeling technique and loose coiling of the sac with the final deployment of a 0. 017-compatible flow diverter. Both procedures were performed with dual antiplatelet therapy premedication and under general anesthesia. The anatomy of the two aneurysms was similar with a wide neck and the presence of a collateral artery branching off it, which required the additional use of a compliant balloon in order to retain patency and avoid coil protrusion. After initial coiling, a nitinol flow-diverter was deployed through a coaxial dual lumen balloon microcatheter. Both these interventions encountered no complications, and the patient was discharged on day 2. At 6-month clinical and radiological follow-up, neither patient had neurological deficits, the aneurysms were both completely occluded, nor the stented arteries were patent along with their collateral branches.

KEYWORDS

distal aneurysms, flow diverter (FD), remodeling technique, endovascular treatment (EVT), difficult aneurysms

Background

Flow diverters (FDs) have gained wide acceptance for the treatment of unruptured intracranial aneurysms due to their proven efficacy and safety with high occlusion rates on long-term follow-up. Nevertheless, their profile and stiffness originally limited their use for distal locations.

The Derivo 2 Embolization Device (Acandis, Germany) and Silk Vista Baby (Balt, France) are two of the newest FDs and represent a dramatic improvement in ease of use distally as they accommodate a 0.017 microcatheter ensuring a safe option for aneurysms of small vessels. Their low profile also makes them compatible with dual lumen balloon catheters, representing a safe alternative to braided stents after balloon-assisted coiling.

Case presentation

Written informed consent was obtained from the individuals for the publication of any potentially identifiable images or data included in this article.

Case 1

An adult patient with subarachnoid hemorrhage and multiple aneurysms was admitted to our institution and treated endovascularly for the right middle cerebral artery and posterior communicating artery aneurysms.

After 6-months and a full recovery, the patient was initiated on dual antiplatelet therapy and called back for treatment of a 6 × 5 mm aneurysm of the A3 segment of the right anterior cerebral artery. The aneurysm had an irregular shape, a wide neck, and the internal middle frontal cerebral artery arose directly from the sac.

Under general anesthesia, *via* right femoral access, a Neuron Max (Penumbra, USA) and a Navien 0.072 (Medtronic, Ireland) were parked in the right internal carotid artery (ICA). A Scepter C 4 × 10 (MicroVention, USA) balloon was then positioned at the neck of the aneurysm over a Synchro 0.014 guidewire (Stryker, USA). An Echelon 10 (Medtronic, Ireland) microcatheter was then navigated into the aneurysm and a single coil (Stryker 360 Ultra 5 × 10) was deployed while the balloon was inflated. At the end of coiling, a Derivo 2 2.5 × 10 was deployed covering the neck of the aneurysm through the Scepter. No complications occurred and the patient was discharged on post-procedure day 2.

Six-month DSA follow-up demonstrated complete occlusion of the aneurysm with patency of the middle internal frontal artery (Figure 1).

Case 2

A patient in their 60s' underwent magnetic resonance angiography (MRA) as part of a vertigo workup and an aneurysm was detected on the A3 segment of the left anterior cerebral artery. Pre-treatment digital subtraction angiography (DSA) showed a 7.5 × 4 mm aneurysm at the pericallosal-callosomarginal bifurcation. The neck of the aneurysm was wide and a tiny pericallosal branch arose directly from the lesion.

Under general anesthesia and with dual antiplatelet premedication, the same materials were employed as in the previous case and a single coil was detached (Stryker 360 Soft

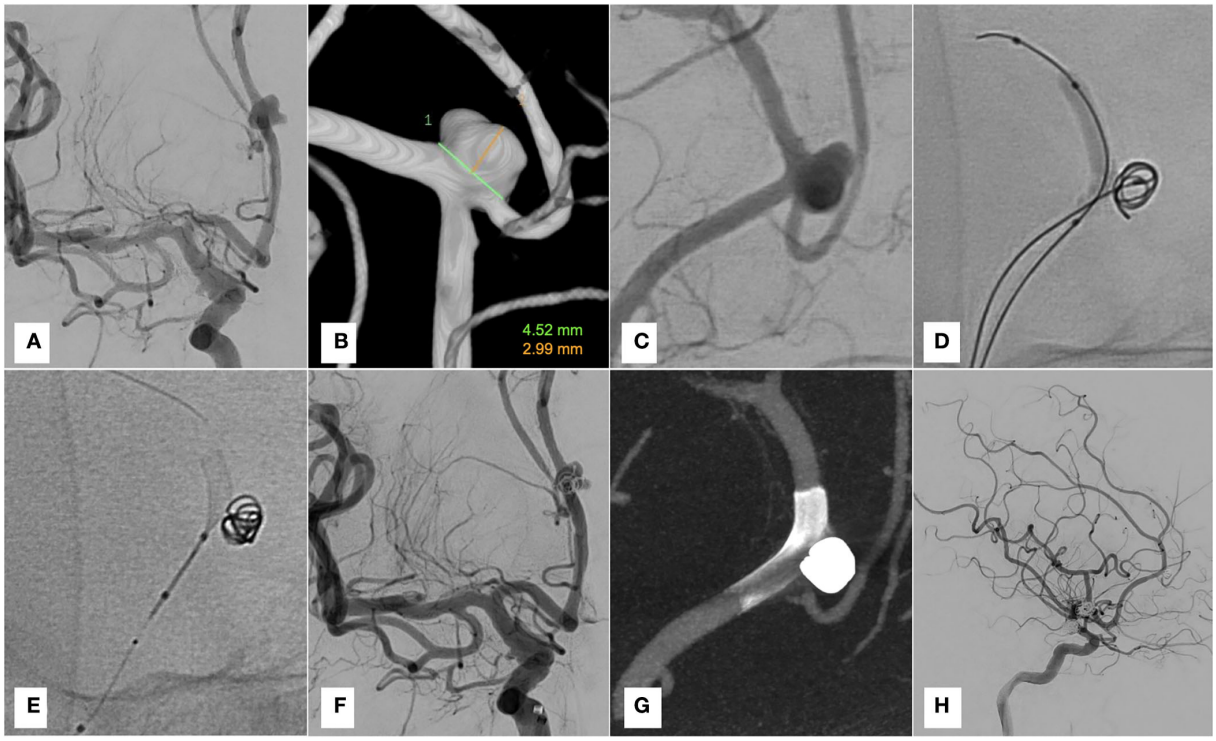

FIGURE 1
Case 1. **(A–C)** Pre-treatment DSA and 3D reconstruction. **(D)** Coiling with Scepter C inflated. **(E)** Deployment of Derivo 2 through the dual lumen balloon. **(F,G)** Final run and Vaso-CT. **(H)** Six-month-DSA follow-up.

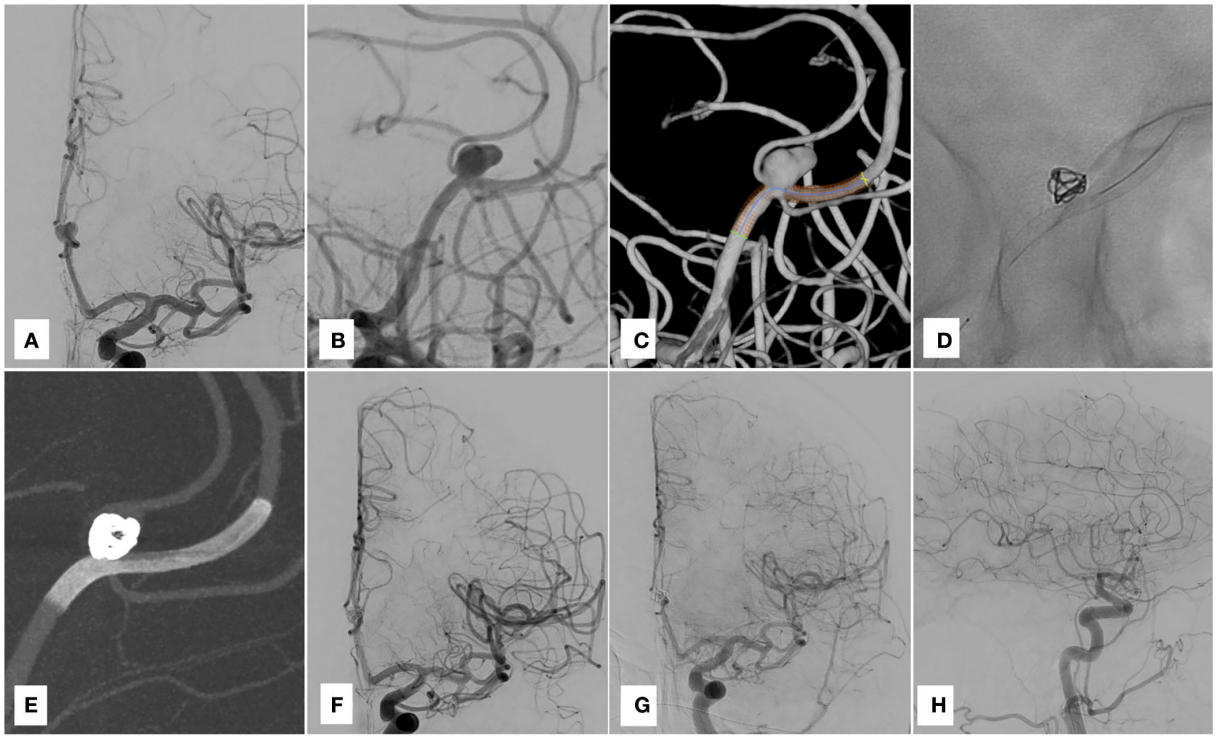

FIGURE 2
Case 2. **(A–C)** Pre-treatment DSA and 3D reconstruction. **(D)** Derivo 2 deployed. **(E,F)** Post-treatment run and Vaso-CT. **(G,H)** Six-month-DSA follow-up.

5 × 10) while inflating the balloon. A Derivo 2 2.5 × 15 was then deployed into the calloso-marginal artery with some difficulties related to the trackability of the stent. On the final angiogram, contrast stagnation within the aneurysm was noted. The patient was discharged home on day 2 with no deficits. The 6-month DSA follow-up demonstrated complete occlusion of the aneurysm and patency of the pericallosal artery (Figure 2).

Discussion

Elective treatment of distal aneurysms with FDs has become feasible due to new generation low-profile stents (1, 2). In most cases, the stent itself is enough to guarantee occlusion of the sac and any conventional microcatheter may be used to deploy it. In bifurcation aneurysms in which the shunted branch has no direct collateral supply, coiling of the sac should be considered and sometimes a compliant balloon might be useful to achieve a good cast of the coils preserving the branching artery (3). Until now, if balloon-assisted coiling had to be performed, either an exchange maneuver or a second catheterization had to be carried out as FDs were not compatible with dual lumen balloon catheters.

However, Silk Vista Baby and Derivo 2 are now available and accommodate a dual lumen balloon. Derivo 2 is a 48-nitinol composite wire construct with a high platinum core stent. Its construction is designed to make the stent open smoothly and adapt to the vessel walls. In both of these cases, we encountered significant friction of the stent inside the microcatheter due to poor trackability. As a result, not only did the intermediate catheter need to be parked quite distally (i.e., at the origin of A1), but in the second case, the balloon had also to be navigated into the A4 segment, to allow the stent to take the A1–A2 curve despite otherwise straightforward anatomy with little tortuosity.

We acknowledge that simple coiling could have been considered for the two cases, nevertheless, the use of remodeling technique in experienced centers has proven not to increase procedural risks and we prefer using the balloon also because it can be inflated if an aneurysmal rupture occurs (4).

The technique we illustrate has only been published for the treatment of proximal aneurysms with 21 inch compatible FDs and it merges the advantages of balloon assisted coiling and flow-diversion (5). Low-profile FDs might therefore replace braided stents in the so-called "balloon-then-stent" technique, especially in cases of bifurcation aneurysms (6).

Stent deployment following balloon-assisted coiling is a well-described technique, but there are no reports on this technique using low-profile flow-diverters to our knowledge (7).

Learning points/take home messages

- Flow diverters deployment following balloon-remodeling is a promising technique for challenging bifurcation aneurysms.
- Large diameter flow diverter stents still do not fit 0.017 microcatheters.
- The Derivo 2 can be deployed through a Scepter C balloon, but trackability is poor and tortuous anatomy may present a major obstacle.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individuals for the publication of any potentially identifiable images or data included in this article.

Author contributions

LR and FC performed the cases and wrote the draft. SN, AL, and CC reviewed the literature and reviewed the manuscript. NL wrote the draft and reviewed the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Mechanical thrombectomy for acute multivessel occlusions with duplicated middle cerebral artery: A case report

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Acute multivessel occlusions generally have multisite clot burden with lower successful reperfusion rates, and cerebrovascular anatomical variants increase the challenge of endovascular clot retrieval. We report a case of acute anterior multivessel occlusions patient with duplicated middle cerebral artery. Combined balloon guide catheter with stent retriever and aspiration approach has gained complete revascularization and good functional outcomes at 3 months follow-up.

KEYWORDS

acute ischemic stroke, duplicated middle cerebral artery, mechanical thrombectomy, multivessel occlusions, large vessel occlusion

Introduction

Acute ischemic stroke (AIS) with multivessel occlusions (MVOs), usual involvement of more than one territory in the ipsilateral or bilateral anterior circulation or the anterior circulation plus the posterior circulation, accounts for 10–15% of AIS admission (1, 2). Simultaneous occlusions of two or more large or medium vessels have a poorer prognosis because of the multisite clot burden and lower successful reperfusion rates associated with a higher incidence of downstream flow disruption (3, 4). Duplicated middle cerebral artery (DMCA) is a rare intracranial vascular variant, and angiography may confuse operators and lead to missed diagnoses because one branch of the DMCA is occluded while the other branch shows a normal middle cerebral artery, which requires careful screening (5). Simultaneous occlusions of the middle cerebral artery (MCA) with the anterior cerebral artery (ACA) and DMCA decrease the rates of first-pass effect and successful recanalization. The results of using the combined balloon guide catheter (BGC) with stent retriever (SR) and distal access catheter (DAC) technique for mechanical thrombectomy (MT) showed a higher rate of the first-pass and overall complete reperfusions and shorter procedure times in patients with the internal carotid artery (ICA) or the proximal MCA occlusions (6). We describe a patient presenting acute anterior MVOs with DMCA who underwent MT using a combined technique.

Case report

A female patient in her late 70s presented to the emergency department with left-sided MCA syndrome. The patient had a history of ischemic stroke without residual deficits, persistent atrial fibrillation, and rheumatic heart disease, which successfully underwent mitral valve replacement and aortic valve replacement in 1996 and 2001, respectively. She is taking a daily warfarin dose of 3 mg to prevent thromboembolism but has not monitored the international normalized ratio (INR) for the last month. Her baseline modified Rankin score (mRS) was 0 and the well-known last time was 7 h. National Institutes of Health Stroke Scale (NIHSS) score at admission was 17 for left-sided gaze, right-sided facial palsy, right-sided upper and lower extremity motor deficits, and diminished sensation and aphasia.

Non-contrast CT of the brain showed evidence of acute infarction in the left parietal lobe with an Alberta Stroke Program Early CT Score (ASPECTS) of 8 (Figures 1A, B). CT angiography (CTA) demonstrated occlusion of the left distal MCA (Figure 1C). CT perfusion (CTP) showed massive hypoperfusion with reduced cerebral blood flow (CBF) and cerebral blood volume (CBV), the left cerebral hemisphere had increased mean transit time (MTT) and time to peak (TTP), and a CBF/CBV mismatch that may be a good candidate for reperfusion therapy (Figures 1D–G). CTP data were processed using Siemens syngo *via* CT Neuroperfusion (version VB20A; Siemens Healthcare, Erlangen, Germany). Given the perfusion mismatch, the patient was subjected to mechanical thrombectomy.

Under ICA sedation, right femoral artery access was achieved within 7 h and 45 min after symptom onset using an 8-French sheath. Using a coaxial technique, a 0.087-inch SeparGate balloon guide catheter (BGC) (Ruikangtong Technology Development Co., Hunan, China) was advanced from the 5-French select catheter to the left ICA. Digital subtraction angiography (DSA) showed that the patient had MCA duplication on the left side, with proximal occlusion of the left A1 segment of ACA, superior M1 proximal, and inferior Sylvian M2 (Figures 2A, B), explaining the patient's symptoms and the perfusion deficit seen on CTP.

The BGC was positioned in the extracranial segment of the occluded ICA, and then the 6FDAC (Ruikangtong Technology Development Co., Hunan, China) was introduced, and the Rebar 18 microcatheter (ev3 Covidien, Irvine, CA, USA) was first placed on the 0.014-in Traxcess microguide wire (Microvention, Aliso Viejo, CA, USA) in the M1 segment of the occluded MCA. Based on the roadmap, a 6 × 30 mm Solitaire AB stent (ev3, Irvine, California, USA) was advanced into the occluded segment, the microcatheter was withdrawn, and the stent was deployed for 5 min. Subsequently, the stent was partially retrieved with the microcatheter and the DAC was pushed proximal to the stent. Prior to stent retrieval, the

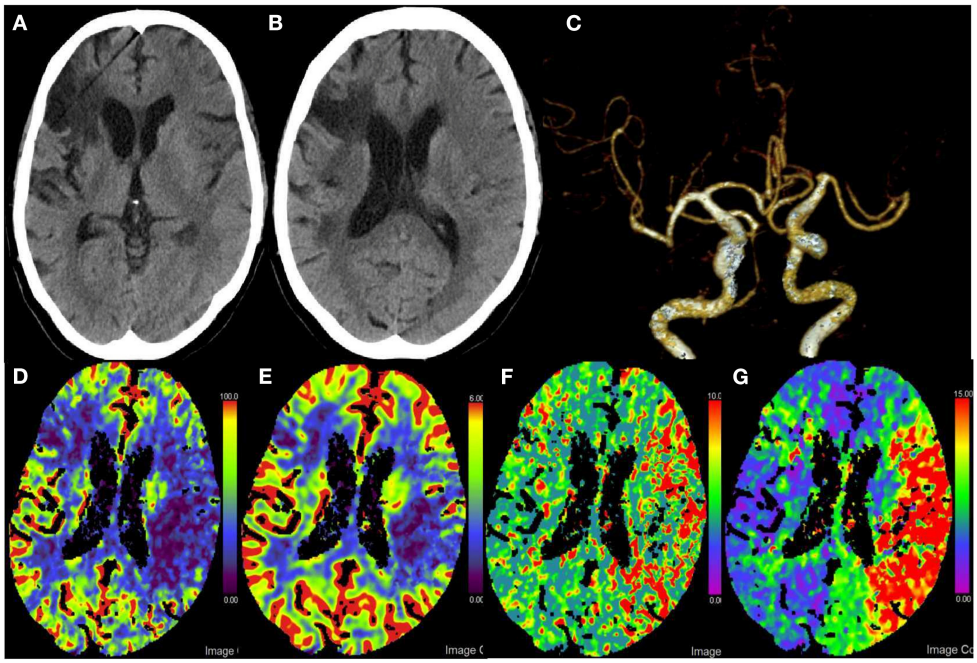

FIGURE 1
Pre-procedural imaging. **(A,B)** Axial pre-procedural CT of the head non-contrast shows the blurring of the gray-white border in the middle third and fourth of the left middle cerebral artery (MCA) territory. **(C)** Pre-procedural CT angiography demonstrating occlusion of the M1 terminus. **(D–G)** Pre-procedural CT perfusion shows decreased CBF and CBV and increased MTT and TTP in the left MCA territory. CBF suggests a large area of hypoperfusion in the left cerebral hemisphere; CBV suggests an infarct core that is smaller in extent than CBF, suggesting a mismatch in CBF/CBV, which may be good candidates for reperfusion therapy.

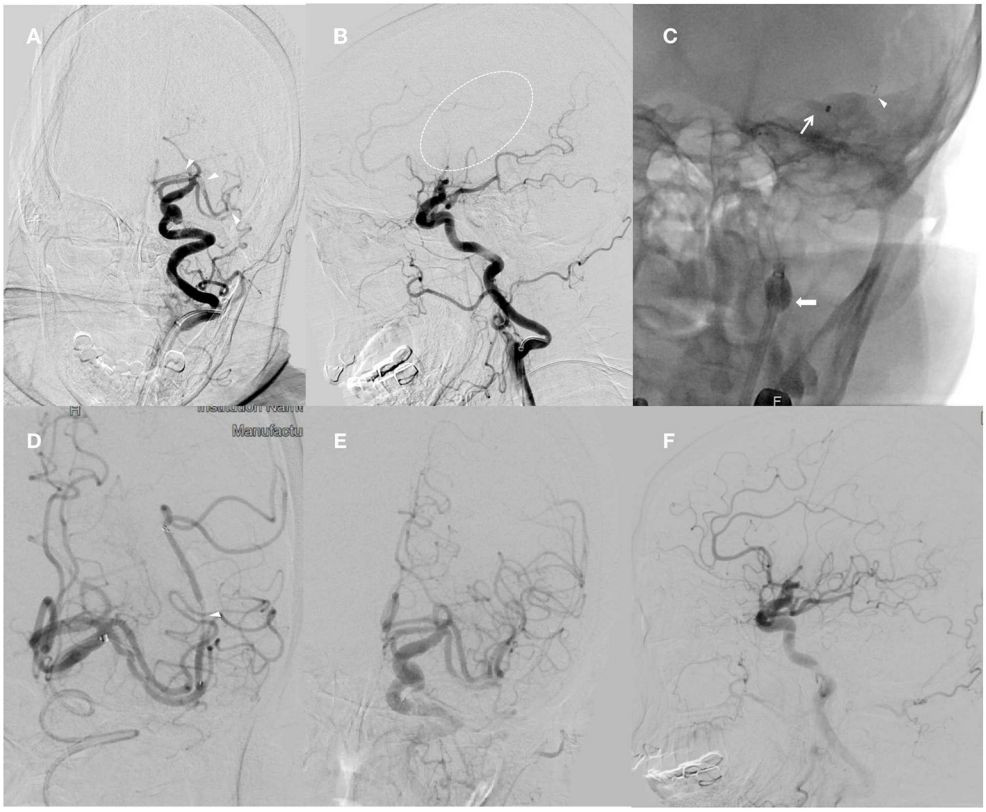

FIGURE 2
Angiographic acquisitions, left internal carotid artery injection, and anteroposterior and lateral view obtained during thrombectomy. **(A)** Demonstration of the left A1 segment of ACA, superior M1 proximal, and inferior Sylvian M2 occlusions (arrow). **(B)** Lateral view displaying abrupt cutoff of the M1 branch of the left MCA (dashed arrow). **(C)** Combined balloon guide catheter with stent retriever and distal access catheter technique used in mechanical thrombectomy procedure. The balloon of the BGC is inflated to arrest the antegrade ICA flow (thick arrow). The tip of the DAC indicates placement within the M1 segment (thin arrow). The stent retriever is placed from M1 into the terminal ICA (arrowhead). **(D)** The same procedure is repeated for the inferior Sylvian M2 occlusion (arrow). **(E, F)** Full recanalization of the MCA and ACA territory following the second pass.

balloon of the BGC was inflated to stop the retrograde flow of the ICA (Figure 2C). The stent and microcatheter as a unit were gently pulled back into the DAC. During the aspiration process, the DAC was slowly pulled back until free blood was obtained through the aspiration syringe. After stent retraction, the balloon was immediately released to allow recirculation of the ICA. Follow-up angiography showed complete recanalization of the ACA and supra-MCA regions, consistent with a modified Thrombolysis in Cerebral Infarction (mTICI) score of 2b. The repeated treatment of the thrombus in the inferior Sylvian M2 was performed using a 4 × 20 mm Solitaire AB stent (Figure 2D), which showed complete recanalization with an mTICI score of 2b (Figures 2E, F). There was no evidence of any untoward events in either procedure.

Follow-up brain CT was performed immediately and 24 h after MT and demonstrated stable subacute left MCA distribution infarction with no evidence of acute hemorrhagic complications. Five days later, follow-up of CTA and CTP showed patency of ACA and DMCA complete normalization of perfusion in the left cerebral hemisphere (Figure 3). The patient was discharged 10 days after the thrombectomy with an NIHSS score of 1 for right facial palsy. At the 3-month follow-up, the mRS of the patient was 0.

Discussion

Simultaneous MVOs are rare conditions but devastating diseases, which may be encountered during MT for AIS (7). The prevalence of MVOs is 0.34–2.0% in patients with AIS who underwent MT (2, 7). Most simultaneous MVOs are caused by cardioembolic origin or artery-to-artery embolism (2, 4). Kim et al. reported 12 patients with simultaneous ACA and MCA occlusion and found that all patients were diagnosed with atrial fibrillation (4). In our study, the patient had a history of persistent atrial fibrillation and rheumatic heart disease. Hence, it is important to evaluate cardioembolism for simultaneous MVO (4).

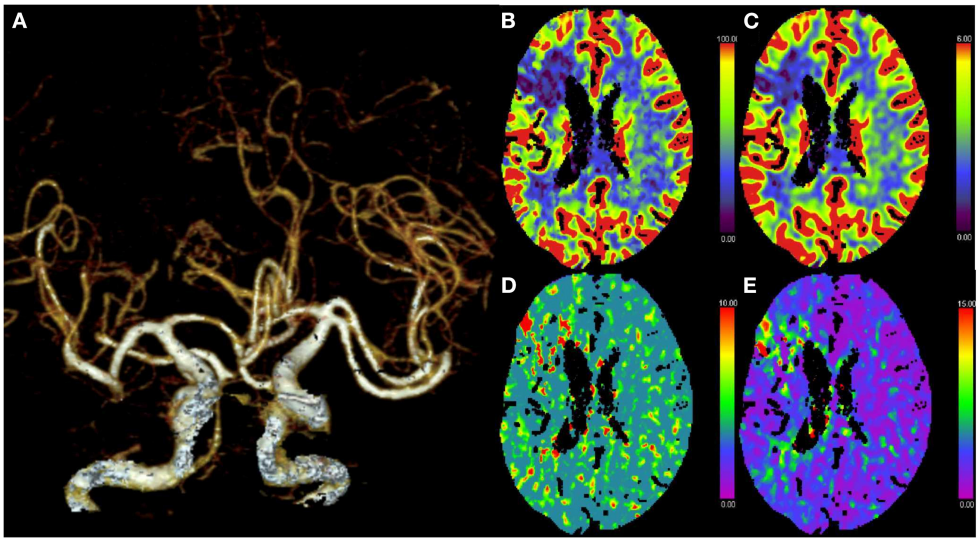

FIGURE 3
Post-treatment CT angiography (CTA) and perfusion (CTP) at 5 days. **(A)** CTA demonstrates no occlusion of the ACA and DMCA. **(B–E)** CTP shows normalization of perfusion in the left cerebral hemisphere.

Cerebrovascular anatomical variants increase the challenge of endovascular clot retrieval in patients with MVOs. We report a case of acute anterior MVOs in a patient with DMCA. In 1962, Crompton first used the term accessory middle cerebral artery (AMCA) to describe the vessels that enter the Sylvian fissure with the MCA, including the AMCA and DMCA (8). Teal et al. proposed in 1973 that the term AMCA should be strictly limited to the anomalous arteries arising from the ACA, whereas branches arising from the ICA should be referred to as the DMCA (9). When one branch of the DMCA is occluded, the angiogram may confuse the operator and lead to a missed diagnosis because one branch of the DMCA is occluded while the other may show a normal middle cerebral artery, which requires careful screening. In the present case, there was no malignant middle cerebral artery occlusion syndrome, such as coma and cerebral edema. Considering the acute occlusion of the MCA, the DMCA can compensate for the blood supply to a certain extent and avoid the occurrence of large cerebral infarction (5). CTA was initially interpreted as no proximal MCA occlusion since the DMCA showed a distal M1 occlusion. However, a CTP scan showed a large ischemic penumbra, which was then suspected to be due to an emergent large vessel occlusion (LVO) not shown on CTA. This was then diagnosed by DSA as an occlusion of one of the two left MCAs proximal to the MCA, as well as segment A1 of the ACA. Therefore, in acute stroke patients with a high clinical suspicion of LVO, continued CTP is necessary even if the CTA is negative to avoid missing strokes in patients with DMCA or other similar vascular variants (5, 9).

Acute MVO frequently leads to adverse neurological outcomes, which may be partly due to the multisite thrombus burden precluding sufficient recanalization. How to perform MT in patients with MVO remains a technical challenge. Since occlusions occur at multiple sites at the same time, it is a challenge to decide how to prioritize the target vessels. A recent case series (treated with BGC, catheter aspiration, and stent retrievers) showed that the successful recanalization rates of MCA and ACA were 83.3 and 83.3%, respectively (4). Numerous clinical studies also have found that first-pass complete reperfusion of acute internal carotid artery occlusions, usually simultaneous involvement of MCA and ACA, is best achieved by combining a BGC with both DAC and stent retriever (10, 11).

To the best of our knowledge, the present case is the first reported case of an acute embolic occlusion of the multivessel with DMCA who underwent a thrombectomy where we used the combined BGC, SR, and DAC technique. We initially targeted the M1 segment for thrombus removal because the occluded segment was located proximal to the M1 segment. BGC was used to block the antegrade flow of ICA and SR combined with DAC for thrombus removal. Fortunately, the superior proximal M1 and A1 segments were removed simultaneously, and we found a thrombus on the stent and in the DAC. The BGC vacuum-assisted aspiration of DAC removed the thrombus from the A1 segment. The same procedure was repeated for the occlusion of the M2 segment of the DMCA and demonstrated complete recanalization with an mTICI score of 2b. To date, two cases of thrombectomy associated with DMCA have been reported. Koge et al. described vessel wall injury by a stent retriever device that caused failed recanalization in a case of ICA occlusion with concomitant MCA and DMCA occlusions (12). They reported that if MCA duplication was suspected from a lateral

view microangiography, they might use a contact aspiration technique in the first-pass. There are several advantages to the use of combined techniques compared with single device techniques. First, SR allows distal capture of the thrombus while vacuum-assisted aspiration reaches the proximal side, allowing capture of the thrombus on both sides, thereby reducing the risk of thrombus fragmentation during thrombectomy (13). In addition, by capturing a portion of the SR through DAC, there is less contact between the SR and the artery wall, reducing radial and traction forces, and thus reducing the risk of vascular injury (13). The proximal block of the BGC further reduces the risk of thrombus escape to the distal ACA and MCA. At the same time, the vacuum state improves the aspiration of the DAC. Pressman et al. reported another case and showed that it was difficult to diagnose a proximal MCA stroke in a patient with DMCA, which missed the obstruction given the patency of the second MCA (5). Prompt diagnosis of this LVO is essential so that mechanical thrombectomy can be performed on the patient as soon as possible to restore perfusion to the penumbra before the temporary defect becomes permanent (5).

In conclusion, this case suggested that the DMCA may play a role in collateral flow around the main MCA occlusion and could confuse our decision-making. Owing to the anatomical characteristics of the DMCA, we should pay attention to the endovascular treatment strategy in case of concomitant ACA and DMCA occlusions.

Take-away lessons

Identification of duplication MCA is challenging because, in these patients with acute ischemic stroke, CTA appears to show patency of all intracranial vessels and compensates to some extent for the blood supply, avoiding the development of a large cerebral infarction.

Combined balloon guide catheter with stent retriever and aspiration technique can increase the likelihood of first-pass recanalization in multivessel occlusions.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Institutional Review Board of the Nanjing Medical University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

H-JH and Y-FW drafted the manuscript. QS, X-MW, and Y-FW added clinical data and revised the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.1089255/full#supplementary-material

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Case report: Utilization and efficacy of large-bore catheters in mechanical thrombectomies

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Thrombotic strokes are caused by occlusion of flow in a blood vessel by a clot or thrombus, resulting in disruption of oxygen and nutrients to the brain that can result in neurological deficits. There are many devices now available for safe and effective removal of thrombi from large blood vessels. This report focuses on the Zoom 0.088" large-bore catheter, which has the potential to be navigated into a large vessel for thrombus removal *via* aspiration, and weigh the risks and benefits of its utilization in thrombectomy patients. In this case, we discuss the use of this device for thrombectomy of a left M1 middle cerebral artery occlusion that resulted in a distal left MCA dissection and eventual loss of access to the site of the thrombus. Ultimately, the patient died from a large stroke in the left MCA territory. In light of this occurrence, we seek to explore the utility and feasibility of large-bore catheters and their risks in thrombectomy candidates.

KEYWORDS

mechanical thrombectomy, large-bore catheters, safety, efficacy, stroke

Background

Thrombotic strokes account for approximately one-half to two-thirds of strokes across the U.S. Commonly seen in the elderly population, notable risk factors include severe atherosclerosis and cardiac arrhythmias, such as atrial fibrillation, which predisposes patients to formation of thrombi that break off and travel into small vessels. While blood flow can be salvaged with the administration of Tenecteplase and other thrombolytic agents, they can only be done so within a 4.5-h time span from the patient's last known normal time. Mechanical thrombectomy, however, offers another opportunity for clot removal within a longer 24-h period and has been proven to be safe and efficacious for patients in which thrombolytic therapy is contraindicated (1).

According to the current literature, mechanical thrombectomy is safe in patients with intracranial large-artery occlusions and by employing a standardized rescue therapy (i.e., stenting and/or angioplasty), patients could benefit from this procedure (2). In fact, mechanical thrombectomy with stent retrievers has been shown to be effective in acute ischemic stroke of the anterior circulation caused by intracranial large artery occlusion (ILAO) in several randomized controlled trials (2). However, it should be noted that the techniques used during catheterization and clot mechanics can play a major role in the outcome as there is the possibility of clot reformation (3).

As of more recently, there have been multiple reports and studies done supporting the use of larger catheters during thrombectomies. In the majority of cases, thrombus aspiration resulted in successful recanalization after a short procedure time. With the additional use of stent retrievers, a high recanalization rate can be achieved (96.5%) (4). Moreover, catheter selection is not an independent predictor of a successful first-pass, final reperfusion, or clinical outcome (5).

The Zoom 0.088"catheter has shown to be quite effective in thrombus retrieval as it gets as close to the blockage as possible. The beveled tip allows for better suction force and there is smooth 1:1 advancement, offering a more supportive access platform. Essentially, intracranial navigation of 0.088"large-bore catheters in mechanical thrombectomies appears technically feasible and safe (6). This catheter itself comes in four sizes (0.071", 0.055", 0.045", and 0.035"Internal Diameter) and is designed to enable seamless tracking through challenging vasculature. Coupled with access catheters, navigating the brain's highly complex and tortuous vascular system becomes a much less daunting task.

At Cooper University Hospital, strokes are treated based on a clinical finding of a disabling deficit along with an ASPECT score > 7 and visually seen blockage on CTA of the head. This institution uses aspiration thrombectomy as its first line with large-bore catheters. In this case, the patient had a left M1 MCA occlusion along with an ASPECT score of 10 and a disabling stroke with an initial NIHSS of 17. The procedure was initiated with an 8-French sheath placed in the right groin. Through that, a Zoom 088/Simmons-2 construct was utilized to access the left common carotid artery. After this, the Simmons-2 was removed and a Zoom 71/velocity microcatheter construct was navigated into the left M1 MCA. The Zoom 088 was then navigated over the Zoom 71 into the left M1 MCA. However, the Zoom 088 inadvertently overshot the thrombus while removing the Zoom 71.

Pure manual aspiration thrombectomy (MAT) was performed resulting in recanalization of the ICA with the M1 occlusion. However, post treatment angiography demonstrated a non-flow limiting dissection of the left M1 MCA.

How effective and efficient large-bore catheters can be exactly must be studied further as methods for improvement continue to be tested with trial and error. While reperfusion catheter failures resulting in injury or death are rare and FDA surveillance of any outliers has proven effective, here, we present a case of an unfavorable post-operative outcome after use of a 0.088"Zoom catheter (7).

Case presentation

A 71-year-old male with a past medical history significant for alcohol abuse presented to the emergency department with right hemiparesis and aphasia from an outside hospital. He was performing his usual activities of daily living when he slumped over. Upon admission, he was not following commands and was found to be in atrial fibrillation with hemoflash imaging indicative of a left M1 hyperdensity, as shown in Figure 1, and diffusion-weighted imaging demonstrating the extent of the stroke in Figure 2. He had an ASPECT score of 10 and an NIHSS of 17. The patient was subsequently administered 0.25 mg/kg of Tenecteplase, approximately 1.5 h after his last known normal time, at which point his NIHSS increased to 19. He was unable to protect his airway and was intubated, after which he was taken directly to the catheterization lab for a left ICA thrombectomy, TICI 0 to 2B. While the immediate outcome after the operation was uncomplicated, the catheter was inadvertently overshot past the thrombus, which resulted in an M1 MCA dissection during the procedure, pictured in Figures 3A, B.

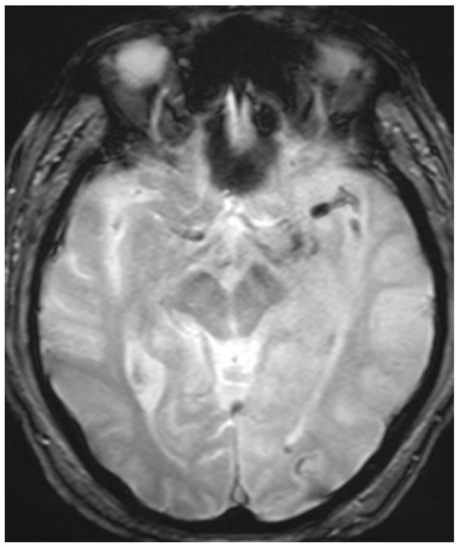

FIGURE 1
Initial hemoflash image demonstrating a thrombus in the left M1 branch of the left MCA prior to MAT.

Treatment

After informed consent the patient was brought into the angiography suite and placed supine on the angiographic table. The right groin was prepped and draped using sterile techniques. The skin overlying the right femoral artery was locally anesthetized with 1% Lidocaine. Using Standard Micropuncture with fluoroscopic guidance, the right femoral artery was accessed, a small skin incision was made, and an 8-French 65-cm sheath was placed. A Zoom 088 was advanced over a Zoom 71 over a velocity microcatheter into the left ICA occlusion. Pure MAT was performed resulting in recanalization of the

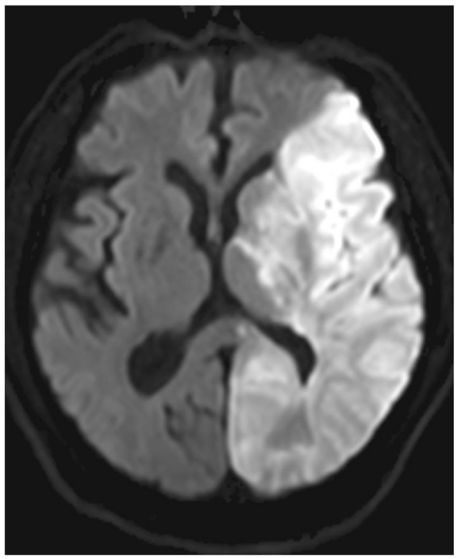

FIGURE 2
Diffusion-weighted imaging demonstrating the topographical distribution of the left MCA stroke.

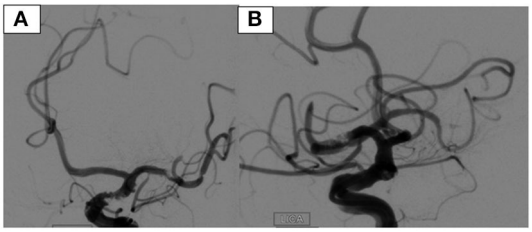

FIGURE 3
AP **(A)** and lateral **(B)** views of a left ICA dissection after MAT was performed.

ICA with continued M1 occlusion. Next, the Zoom 71/velocity construct was navigated into the left M1 MCA and the Zoom 088 was then navigated over the Zoom 71 into the left M1 thrombus. The Zoom 71/velocity construct was removed, at which point the Zoom 088 moved further past the clot into the distal M1/proximal M2 segment interface. Repeat manual aspiration with the Solitaire 4 × 40 stent retriever was performed for further clot retrieval, resulting in TICI 2B flow with a grade 2 dissection of the M1 MCA division. Multiple attempts were made to re-catheterize the MCA, but were unsuccessful due to progressive narrowing from the dissection. At the completion of the procedure, the catheter and sheath were removed and hemostasis in the right groin was obtained by placement of an 8-French Angioseal arteriotomy closure device. The device was deployed without complication. No new neurological deficits or complications were encountered during or immediately

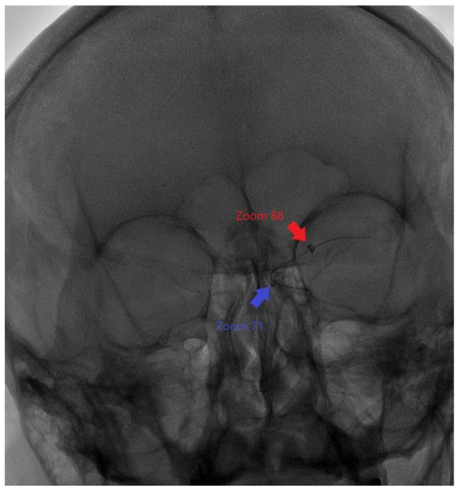

FIGURE 4
Relative positions of Zoom 88 and Zoom 71 catheters to each other during the mechanical thrombectomy procedure.

following the procedure. The patient was then transferred to the neurological ICU intubated and sedated.

Outcome and follow-up

After it was found the patient had a dissection, neurosurgery discussed the possibility of a decompressive hemicraniectomy with the patient's wife due to significant swelling on imaging. She declined at the time due to the patient's poor prognosis. On repeat MRI, there was a large left hemispheric infarct within the vascular distributions of the middle and posterior cerebral arteries with no evidence of parenchymal hemorrhage. Additionally, a left-to-right midline shift of approximately 4.5 mm on post-operative day one was appreciated. An intra-arterial thrombus within the M1 branch of the left middle cerebral artery and M2 branches was found. The patient remained intubated due to neurological deficits and lack of improvement of mental status. He was ventilator-dependent until he was transitioned to comfort care and was palliatively extubated on post-operative day two. The patient passed on post-operative day three.

Discussion

Traditionally, the treatment of intracranial occlusions involves medical therapy in the form of thrombolytics. However, not every patient is a candidate for the usual standard of treatment and first-line treatment may not always be successful. Moreover, if the patient's last known normal time exceeds

more than 4.5 h, they are generally just given aspirin and managed medically.

As an alternative, mechanical thrombectomies have shown to be quite successful. For the procedure to show promising results, neurointerventional surgeons lean heavily on their equipment, i.e., the use of catheters. In general, these catheters have a proximal outer diameter of approximately 0.08 inches and a proximal inner diameter of approximately 0.07 inches. They are advanced into the vascular system using the Seldinger technique, which is modified accordingly depending on the target site of interest. In this case, the Zoom 0.088"catheter was utilized. It is the first stroke-specific 0.088"access catheter designed to get closer to the clot. Consistently reaching intracranial anatomy, it minimizes the distance to retrieve the clot, while providing flow control with an outer diameter closely matched to the vessel size. Maximizing the catheter-to-vessel size facilitates near flow-arrest on catheter insertion, potentially negating the need for a balloon-guide catheter. For instance, a 0.088 inch aspiration catheter enables significant flow reversal in the distal MCA during aspiration (8). According to some recent studies, catheters with an inner diameter of 0.040 inch and 0.064 inch, respectively, are needed to be effective in the middle cerebral artery (2.5-mm diameter) or in the internal carotid artery (4 mm) in an average patient (9). The solo use of large-bore catheters resulted in better recanalization outcomes and significantly reduced distal emboli for internal carotid artery and MCA occlusions compared with all other devices and combinations *in vitro* (8). With the goal of TICI 3 in 10 min, Zoom Aspiration Catheters are designed for optimized clot engagement, effortless navigation and uncompromised structural integrity.

Here, the Zoom 088 catheter was advanced over the Zoom 71/velocity construct to prevent injury to arteries and ensure a smooth transition to the site of interest as pictured in Figure 4. While designed to get as close to the face of the clot as possible, it was advanced further past the clot into distal segments of the MCA in order to aspirate secondary emboli coming from disturbance of the primary clot. Given the large bore catheter size, it is important to be careful with how quickly it is advanced and how distal it travels when the inner catheters that facilitate its transition are removed as the vessels in the brain are small and therefore easily prone to damage. Sometimes the stored potential energy from the multiple loops in the head and neck can allow the large-bore catheters to travel further into the brain than warranted, leading to complications, such as what happened in this case. Based on this information, it can possibly be surmised that there may have been a technical error in the way the catheter had been handled during the case, but not because of any defects of the catheter itself. On a different note, it can also be argued that the unique shape of the beveled tip of the catheter may cause complications, such as dissections, but it has been shown by Vargas et al. that patients who underwent mechanical thrombectomy with the beveled tip catheter have a higher proportion of TICI 2C or better and a significantly lower mRS score on discharge and at 90 days, though this does not rule out the possibility of dissection (10). There is also the likelihood of introducing infections into the cerebrovascular system or damaging the vasculature. Additionally, there are the issues of limited access to trained neurointerventionalists, technical difficulty with the navigating wire in delicate intracranial vessels, trauma to vessels, distal embolization, vessel dissection and vasospasm leading to worsening of stroke (11). The need for greater efficacy and efficiency still remains and larger prospective studies are warranted (6). Despite the drawbacks, both small- and large-scale studies have consistently shown how beneficial large-bore catheters are.

According to one study, five patients (ages 50–85 years; baseline NIHSS 17–23) were treated. The 0.088"catheters were used as the primary tool for contact aspiration in two patients (distal basilar artery and proximal MCA occlusions) with complete thrombus ingestion (eTICI3) during the first pass. Out of the five patients, the 0.088"catheter was used for flow control in two of them. As the first patient presented with an M2 occlusion, the catheter was placed in the distal M1 segment and treated with a combination of a stent-retriever and 0.070"aspiration catheter; the second patient came in with a distal M1 occlusion, so the catheter was placed in the proximal M1 segment and treated with a 0.071"aspiration catheter. In the end, both patients had an eTICI3 reperfusion score. Additionally, it should be noted that the fifth patient in the same study had the 0.088"catheter navigated into the cavernous ICA to support 0.071"aspiration catheter treatment of an M2 occlusion resulting in eTCI2B67 reperfusion. Procedural duration ranged between 14 and 33 min. There were no adverse events, further substantiating the use of large-bore catheters during mechanical thrombectomies (6).

In another study by Tonetti et al. (5) 464 cases of large-vessel thrombectomies using multiple large-bore catheters were scrutinized, 180 of which were done *via* MAT using various large-bore catheters. The findings of this study concluded that the choice of the catheter had no influence on clinical outcomes, first-pass aspiration, or final reperfusion (5). Out of the four catheters this study looked at, it was found the first-pass success rate did not differ significant between the Sofia, CAT6, 0.072-inch Navien, and ACE68, falling between 36 and 50% with a $p = 0.67$ (5). Additionally, TICI reperfusion scores of 2B or higher was achieved in 94% of cases overall, $p = 0.70$. Lastly, there was no significant difference between 90-day good outcome and 90-day mortality in patients treated with different catheters, suggesting that large-bore catheters in general can prove quite useful in mechanical thrombectomy procedures.

Conclusion

Strokes can be treated both medically and by interventional means. As far as the interventional means are concerned,

mechanical thrombectomy appears to be an increasingly popular option for patients who qualify. On the other hand, it should be noted that there are disadvantages, such as clot reformation or instrumental error. In our case, the patient passed away on the third post-operative day secondary to non-hemorrhagic left hemispheric infarction involving both the middle cerebral and posterior communicating arteries from an overshot catheter. While unfortunate, large-bore catheters have still proven to be highly successful in the retrieval of clots. Both small-scale and large-scale have demonstrated their usefulness, and while more studies are always encouraged, so far, the benefits outweigh the risks and the safety and efficacy of their use is fruitful.

Data availability statement

The datasets presented in this article are not readily available because of ethical and privacy restrictions. Requests to access the datasets should be directed to the corresponding author.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements. Written informed consent was not obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

MB and CB wrote and edited the manuscript. HS and BJ edited the manuscript. All authors contributed to the article and approved the submitted version.

Conflict of interest

BJ reports that he is a paid consultant for Medtronic and Stryker.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2022.1035959/full#supplementary-material

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A case report of multi-step management of extracranial carotid artery aneurysm and carotid-cavernous fistula combination in patients

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Extracranial carotid artery aneurysms (ECAA) and carotid-cavernous fistulas (CCF) are rare arterial pathologies with severe complications and increased risk of mortality. The optimal treatment approach for this combined condition is a topic of debate among neurosurgeons and neuroradiologists, and a standardized treatment protocol has yet to be established. The aim of this case report was to demonstrate the management of a rare combination of ECAA and CCF in patients. The treatment strategy included a two-step procedure of endovascular embolization of CCF followed by dual antiplatelet therapy and endovascular stenting of an aneurysm. Control angiograms showed the exclusion of an aneurysm from the blood circulation and CCF symptoms were resolved.

KEYWORDS

case report, fistula, aneurysm, endovascular embolization, stenting

1. Introduction

Extracranial carotid artery aneurysm (thereafter – ECAA) is a rare vascular disease that constitutes 1.5–4% of all cerebral aneurysms (1, 2). Early diagnosis and treatment of ECAA are important as many cases remain asymptomatic until thromboembolic events, cranial nerve compression, or a rupture of an aneurysm. Treatments for this condition represent 0.2–5% of carotid procedures according to the institutional reports (3). Carotid cavernous fistulas (thereafter – CCF) are abnormal communication of the cavernous sinus and the previously normal carotid arterial system (4). The combination of CCF and ECAA is an extremely rare condition that often requires neurosurgical intervention. In this report, we present two clinical cases of this rare combination of pathologies in patients, highlighting the challenges involved in diagnosing and treating this complex condition.

2. Case reports

2.1. Case 1

A 21-year-old man was admitted to the hospital with left eye redness and swelling, mild blurred, and double vision. He experienced nausea and visual deterioration after head trauma

a month earlier. He denied a history of diabetes and hypertension. There was no history of any infectious diseases and no history of fever, sickness, or any surgery. He was a non-smoker without allergies to any medications. An ophthalmic examination showed left eye proptosis, severe chemosis, lateral rectus palsy, and high intraocular pressure (thereafter – IOP; Figures 1A,B). Visual acuity (thereafter – VA) was 10/10 in the right eye and 1/10 in the left eye.

2.2. Case 2

A 27-year-old man was admitted to the hospital with head trauma resulting from a 3-meter fall. After 5 days, he developed redness in his right eye with diplopia. He had no history of diabetes or hypertension, but he was a smoker. An ophthalmic examination showed proptosis, chemosis, and lateral rectus palsy in the right eye. His visual acuity was 10/10 in the left eye and 3/10 in the right eye.

2.3. Diagnostic procedures

In both cases, magnetic resonance imaging (thereafter – MRI) revealed enlarged cavernous sinuses and enlarged superior and inferior ophthalmic veins (Figures 1C, 2A). Angiograms confirmed the direct left (first case) and right (second case) CCF between the internal carotid artery (thereafter – ICA) and the cavernous sinus by demonstrating rapid filling of the cavernous sinus. Cavernous sinus drained anteriorly through both ophthalmic veins, and posteriorly through the inferior petrosal sinus. Moreover, dissecting aneurysms at the extracranial part of the left (first case) and right (second case) ICAs were detected (Figures 1D, 2B).

2.4. Treatment

Procedures for both cases were identical. First, embolization of CCF with balloon-assisted coiling was performed under general endotracheal anesthesia. Right femoral access was obtained using a 7-Fr sheath on the arterial side. A 7-Fr guide catheter was placed at the ICA, and the AV fistula was catheterized using an Echelon 10 (ev3, Inc.) as a conduit to the cavernous sinus. An angiogram was performed to ascertain that the microcatheter was positioned proximally to the origin of the SOV. The patient was administered heparin intravenously (5,000 U). At this point, a Hyperglide balloon (ev3, Inc.) was navigated on the arterial side and was left in the position spanning the fistulous site. The balloon was subsequently

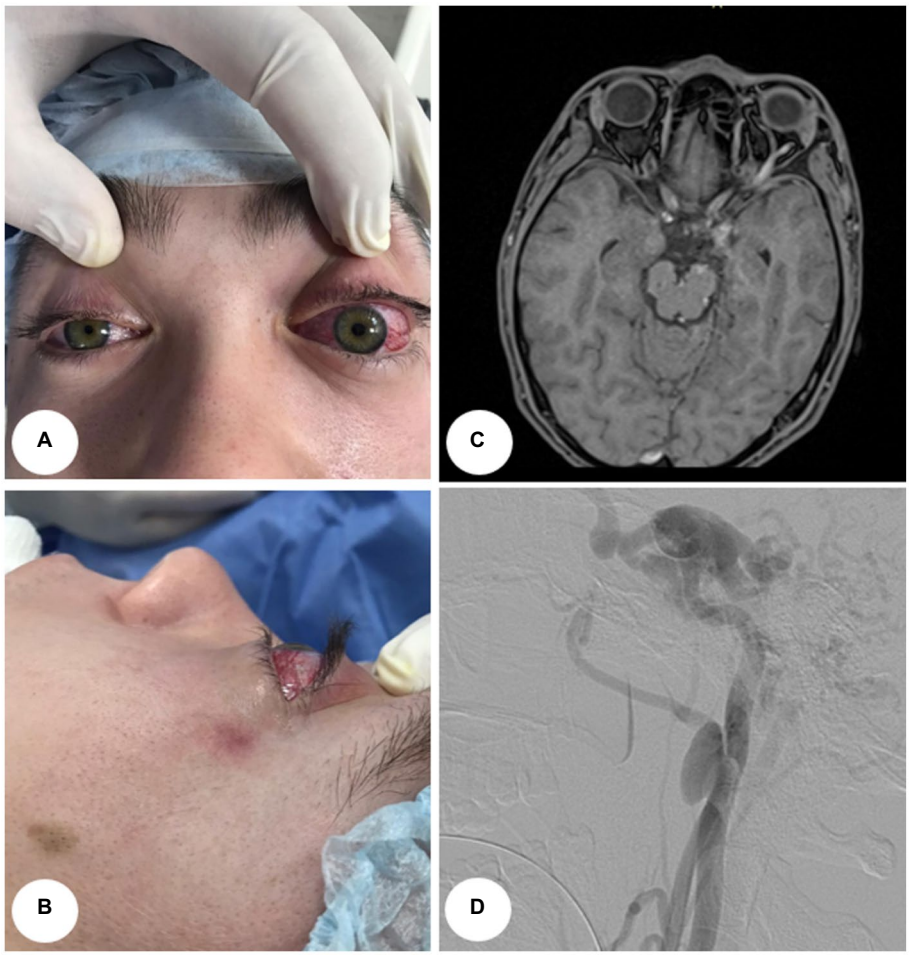

FIGURE 1
A visual manifestation and instrumental examinations of Case 1. **(A)** Anterior view. **(B)** Lateral view. **(C)** Axial MRI shows dilatation of the superior ophthalmic vein in a patient with left side carotid-cavernous fistula. **(D)** Digital subtraction angiogram (lateral view) shows a dural carotid-cavernous fistula drained anteriorly and posteriorly with a combination of extra cranial internal carotid aneurysm.

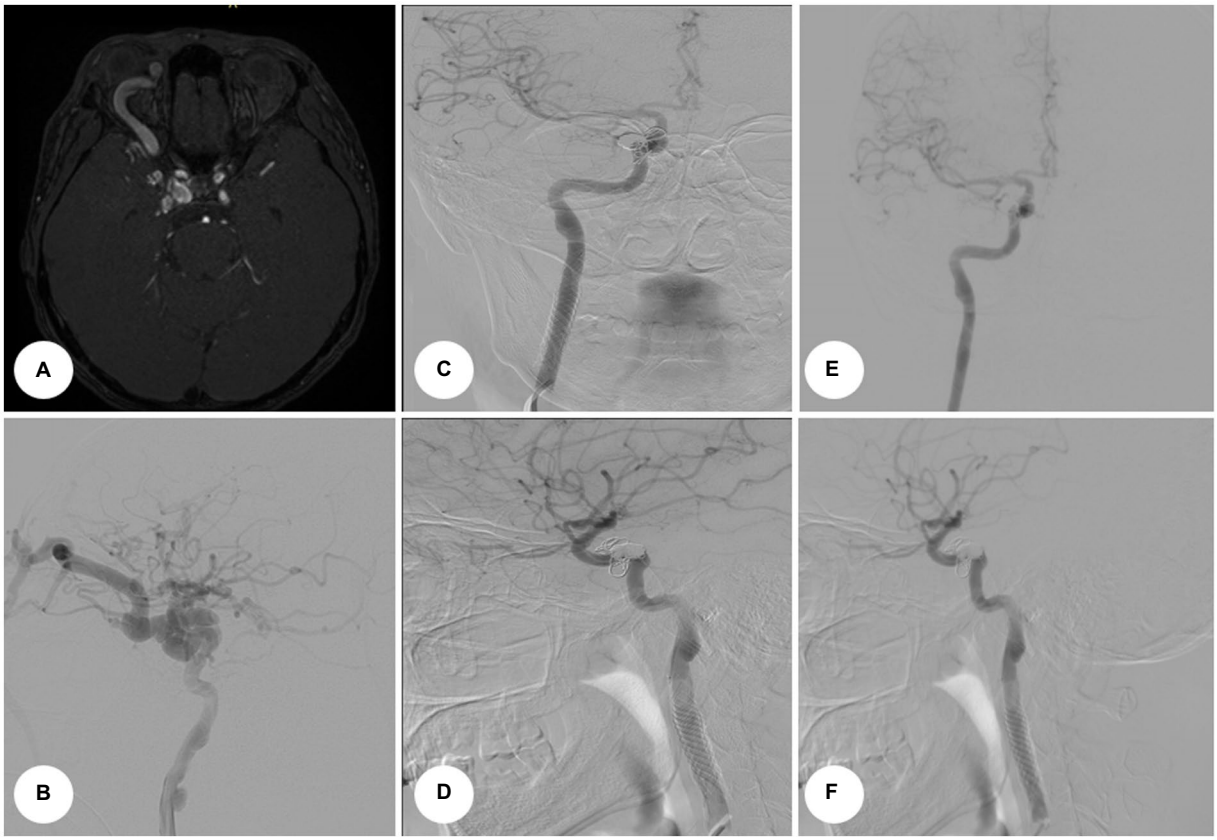

FIGURE 2
An instrumental examination of Case 2. **(A)** Axial MRI revealed enlargement of the superior ophthalmic vein and expansion of the right cavernous sinus in a patient with right side carotid-cavernous fistula. **(B)** Preoperative angiogram. **(C)** Postoperative control angiograms reveal stent deployment and aneurysm exclusion from the blood circulation. Anterior–posterior projection. **(D)** Lateral view. **(E)** Post-procedural angiograms (follow-up after 6months). Anterior view. **(F)** Post-procedural angiograms (follow-up after 6months). Lateral view.

inflated and coils were deployed in the cavernous sinus point to prevent coil herniation into the ICA. The balloon was deflated and the angiogram showed no early venous drainage from the arterial injection. The microcatheter was removed, and a control angiogram was obtained. It was compared with the initial angiogram to rule out embolic events and confirm complete fistula obliteration (Figure 3). Proptosis and chemosis resolved the next day in both patients (Figures 4A,B).

The second procedure was performed 3 months later. The patient was under dual antiplatelet therapy [clopidogrel 300 mg, acetylsalicylic acid (thereafter – ASA) 500 mg]. The endovascular procedure was performed under local anesthesia with continuous hemodynamic monitoring. The ICA access was obtained through the right femoral artery. After the femoral artery was accessed 5,000 U of heparin was administered. A guide catheter using a 0.035-inch stiff guidewire was placed in the common carotid artery (thereafter – CCA). After the placement of the soft guidewire past the lesion, a self-expanding bare stent Casper 7 × 30 mm (Terumo Co., Tokyo, Japan) was placed. The stent was expanded 1 cm proximal and distal to the aneurysm and was used for the landing zones of the stent-grafts. In the case of the first patient, the aneurysm was embolized by stent-assisted coiling (2 coils). Multiple control angiograms showed the exclusion of the aneurysm from the blood circulation (Figures 2C,D, 4C,D). Clopidogrel was discontinued after 6 months, while ASA was administered continuously. Control angiography was performed 6 months later on one patient (Figures 2E,F) and revealed complete occlusion of ECAA and CCF. The second patient was unable to undergo control angiography due to financial restraints. However, the patient reported no complaints during the telephone interview.

3. Discussion

Although some reports about ICA aneurysms with CCF exist (5), and literature on CCF and ECAA separately (6, 7), to our knowledge, this is the first study to present cases of CCF and ECAA combination occurring in a patient. Trauma is the most common cause of direct CCF and dissecting aneurysm. In two cases presented here, patients reported a history of trauma, confirming the recommendation to ask cases of single-hole dural fistula about trauma in case of suspicion of direct CCF (8). A treatment protocol for the two pathologies combination is not established.

In the presented cases, CCF was treated first. It reduced the risk of CCF resulting in hemorrhage from dual antiplatelet therapy. The resulting blood thinning could make the occlusion of CCF slower and

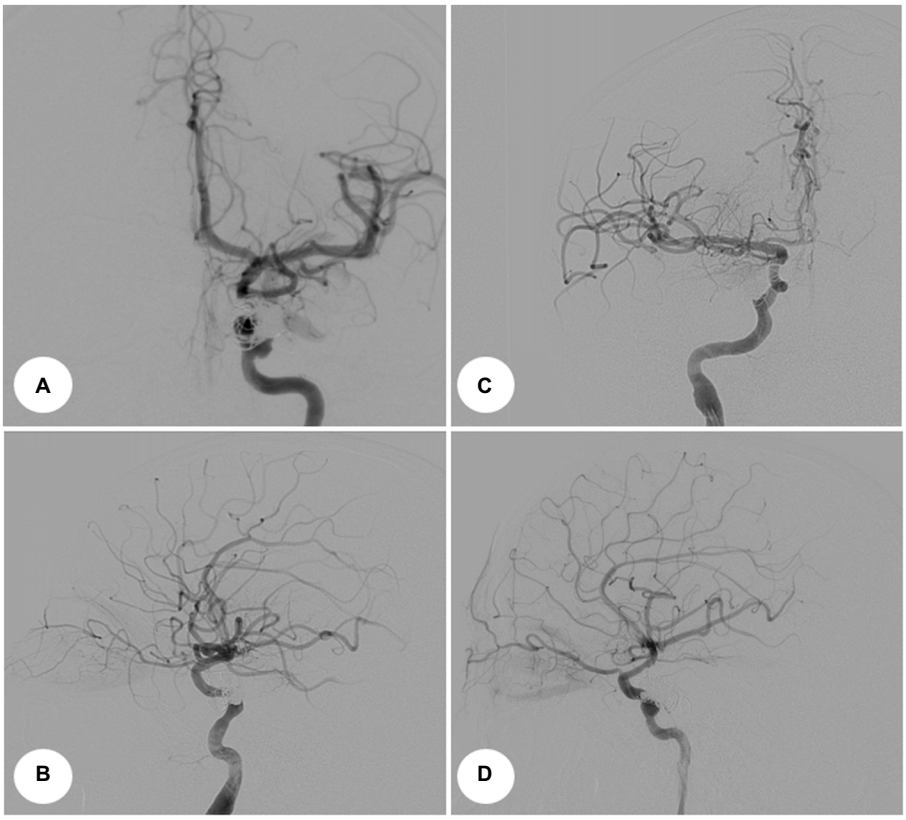

FIGURE 3
Intraoperative angiograms. Digital subtraction angiograms from internal carotid artery. **(A)** Anterior–posterior projection view, Case 1. **(B)** Lateral view, Case 1. **(C)** Anterior–posterior projection view, Case 2. **(D)** Lateral view, Case 2.

more difficult with more materials used due to slow thrombosis. CCF treatment would relieve patients' acute symptoms.

Different options for CCFs treatment are available, such as conservative management and embolization. Conservative management can be effective in approximately 30% of indirect CCF and 17% of direct CCF cases, but most of these cases had mild clinical presentations (9).

Detachable balloon occlusion is a cost-effective and straightforward option for treating CCFs, but it can lead to complications such as cerebral infarction or CCF recurrence (10). Embolization with the ethylene-vinyl alcohol copolymer Onyx is another treatment option for CCFs. However, using a combination of dimethyl sulfoxide and Onyx can be toxic and pose a potential risk for trigeminocardiac reflex-induced bradycardia (11).

Placement-covered or flow-diverting stents are also used as an alternative method for the treatment of CCFs. Despite dramatic initial improvement, delayed thrombosis remains a problem with the use of currently available covered stents in the cerebral circulation. In the cases presented, balloon-assisted embolization was chosen as the treatment method due to its advantages, such as the lack of complications, practicality, and ability to keep the ICA unobstructed.

The second surgical intervention was ECAA treatment. Surgical approaches include microsurgical resection of the aneurysm, with arterial reconstruction, and endovascular stenting (12, 13). In presented cases, the basis for choosing the latter was the prevention of cranial nerve injuries, which can occur during open surgical repair. Aneurysms near the neck often form from dissection, therefore; stent placement is optimal for the increase of vessel endothelialization. From the self-expandable carotid stent and flow diverter, the former was chosen due to its higher stent cell density, and cost-effectiveness, and demonstrated equal outcomes to the flow diverter (14).

4. Limitation

The main limitation of this study is the lack of enough cases. We cannot provide controlled clinical research to demonstrate the availability and efficacy of our strategy. However, follow-up results show a good outcome after 6 months.

5. Conclusion

The presented cases showed that aneurysm-associated CCF is a complex and risky pathology. Evaluation of the fistula and aneurysm angioarchitecture and digital subtraction angiography is essential. This case report suggests a treatment plan, and multi-step endovascular surgery when encountering CCF and ECAA combination in a patient.

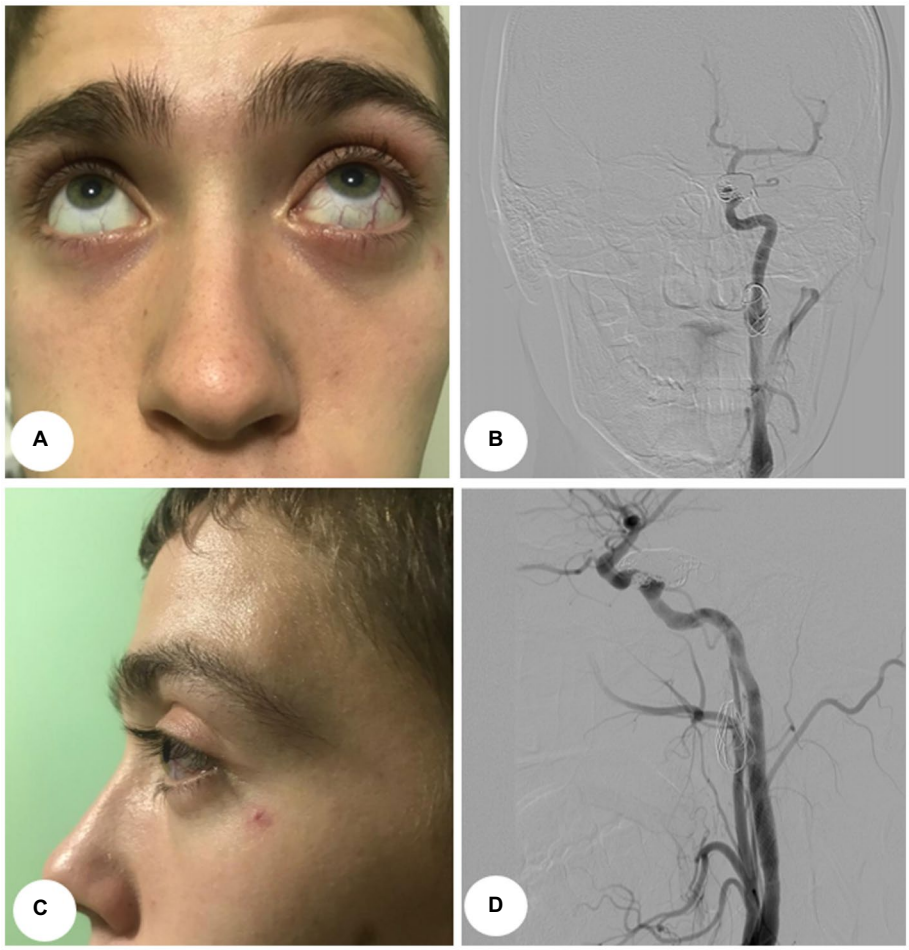

FIGURE 4
Postoperative images, Case 1. **(A)** Anterior view. **(B)** Lateral view. **(C)** Postoperative control angiograms show complete occlusion of the CCFs with coil mass. Anterior–posterior projection view. **(D)** Lateral view.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by The Institutional Review Board of the National Centre for Neurosurgery. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

All authors contributed to the study's conception and design. Material preparation and data collection were performed by CN and YM. CN and AK wrote the first draft of the manuscript. SA wrote the final version of the manuscript. All authors commented on previous versions of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Transvenous coil embolization of a high-grade Galenic dural arteriovenous fistula

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Introduction: Galenic dural arteriovenous fistulas (dAVFs) are a rare form of dAVF and rarely described in the literature. Their distinct location requires different surgical approaches than dAVFs occurring at the nearby sites of the straight sinus and torcular Herophili, and their high risk of hemorrhage makes these dAVFs very challenging to approach surgically. In this report, we present a unique case of Galenic dAVF.

Case description: The patient is a 54-year-old female who presented with a 2-year history of progressive headaches, cognitive decline, and papilledema. A cerebral angiogram demonstrated a complex dAVF to the vein of Galen (VoG). She underwent transarterial embolization with Onyx-18 which resulted in minimal reduction in arterial venous shunting. She subsequently underwent a successful transvenous coil embolization resulting in complete occlusion of dAVF. The patient's postoperative course was complicated by interventricular hemorrhage; however, she had a remarkable clinical recovery with resolution of headaches and improvement in cognitive function. A follow-up angiogram completed 6 months post-embolization demonstrated very mild residual shunting.

Conclusion: In the unique case presented here, we demonstrate the efficacy of transvenous embolization *via* an occluded straight sinus as an alternative therapeutic option to eliminate cortical venous reflux.

KEYWORDS

dural arteriovenous fistula, vein of Galen, transvenous embolization, occluded straight sinus, endovascular coiling

Introduction

Cerebral dural arteriovenous fistulas (dAVFs) are formed by the abnormal drainage of meningeal arteries directly into the dural venous sinuses or cortical veins (meningeal, subarachnoid) (1). Most are thought to be idiopathic in nature; however, associations with dural sinus thrombosis, venous hypertension, previous craniotomy, trauma, and infection have been reported (1, 2). They commonly present in the region of the transverse-sigmoid sinus, though several other locations have been identified (3, 4). Cerebral dAVF symptom severity is largely determined by venous drainage patterns, severity of shunting, and location. Cortical venous and pial venous reflux are known risk factors for hemorrhage, the most serious sequela in dAVF (5).

Dural AVFs at the vein of Galen (VoG) are a rare form of falco-tentorial dAVF and tend to have an aggressive course with a high risk of hemorrhage (2, 3). The deep midline location and fistulous connection at the VoG categorize them as Type 1, on the proposed classification of tentorial dAVFs by Lawton et al. (6). Given the location, VoG dAVF's presenting with hemorrhage can have devastating outcomes. Their distinct location at the anterior falco-tentorial junction and complex venous drainage (often earning a Borden Type III classification), make them among the most difficult fistulas to approach surgically (2, 5, 7). Transvenous approach around the tentorium to deeper locations of the brain, particularly for tentorial dAVFs that drain directly in the subarachnoid veins, is challenging (6). In this report, we present a case of dAVF with fistula point at the VoG that was successfully treated by transvenous embolization.

Case description

Our patient is a 54-year-old female with a history of chronic back pain, obstructive sleep apnea (OSA), depression, hypertension and hyperlipidemia, visual impairment requiring corrective lenses, and worsening headaches who was found to have papilledema on a routine ophthalmologic exam. She additionally has a family history of stroke in both maternal grandparents and aneurysms in both paternal grandparents. On presentation she reported 2 years of progressive headaches and subjective cognitive decline. Physical examination revealed no neurologic deficits except for mild give away weakness in bilateral lower extremities secondary to back pain. A brain MRI was obtained which demonstrated diffusely engorged cortical veins and a severely dilated left superior ophthalmic vein which was concerning for a dAVF or cavernous carotid fistula. A timeline of events from initial presentation through treatment and follow-up can be found in Figure 1.

A cerebral angiogram (Figures 2A–D) was obtained which demonstrated a complex dAVF with the fistulous connections at the vein of Galen (Lawton et al. Type 1). The arterial supply of the dAVF came from several arteries including bilateral superficial temporal arteries, bilateral occipital arteries, bilateral tentorial branches of the meningohypophyseal trunk, and bilateral branches of the posterior cerebral artery. There was a complex deep venous drainage pattern with retrograde venous drainage from the vein of Galen anteriorly to the left superior ophthalmic vein through a severely dilated basal vein of Rosenthal, and corticovenous reflux through the internal cerebral veins to several dilated medullary veins. The straight sinus was occluded and there was partial occlusion of the left transverse sinus. It is possible that the occluded straight sinus was the inciting event leading to this complex dAVF.

The treatment options were discussed including: transarterial embolization, transvenous embolization, open surgical ligation, radiosurgery, and continued observation. After a thorough discussion with the patient and her family, we decided to proceed with transarterial embolization, knowing that this dAVF would likely require multiple embolizations or a different approach for complete treatment.

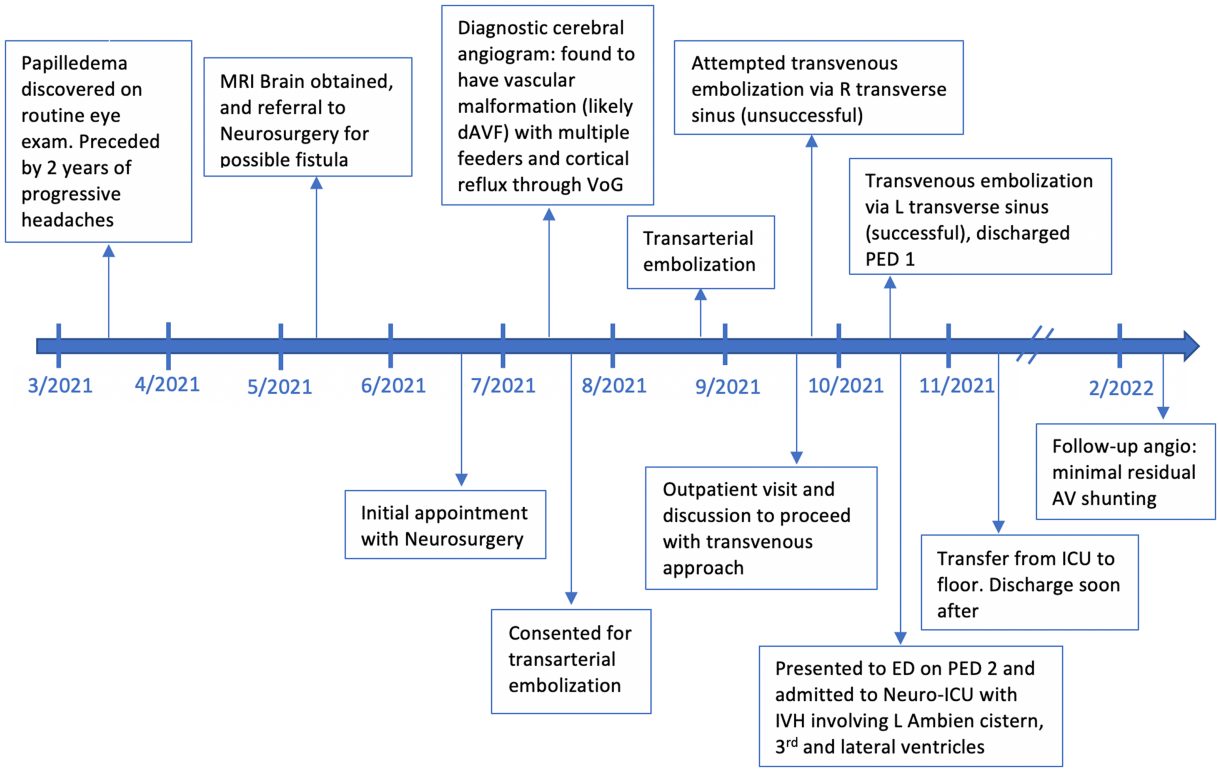

FIGURE 1
A timeline of events beginning with initial discovery of papilledema, outpatient visits related to the dAVF, angiography, embolization events, adverse events, and follow-up.

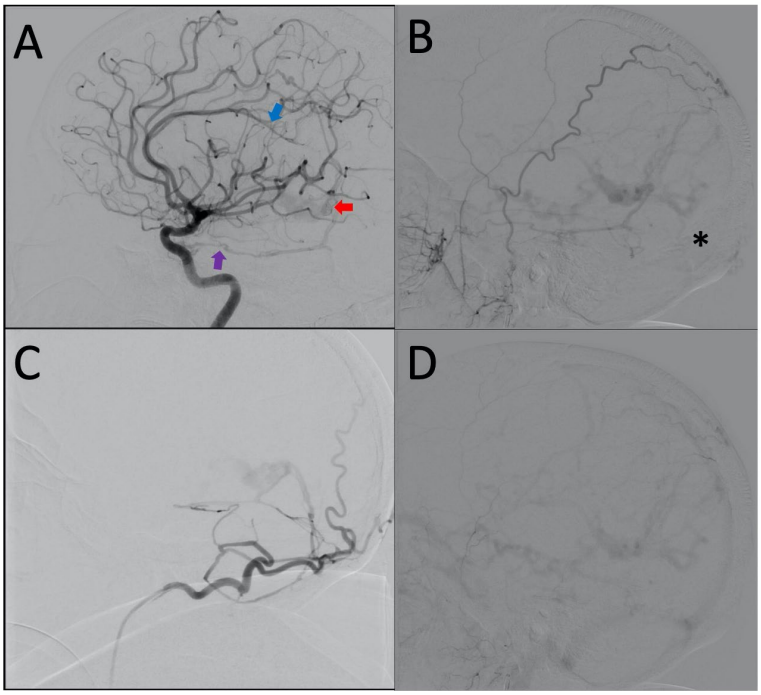

FIGURE 2
(A) Lateral projection of the right ICA demonstrating early shunting from the tentorial branch of the MHT (purple arrow) and distal ACA (blue arrow) filling the dilated vein of Galen (red arrow). **(B)** Lateral projection of the right ECA showing retrograde venous drainage and occlusion of the straight sinus (black asterisk). **(C)** Lateral projection of the right occipital artery. **(D)** Lateral projection of right ECA, late venous phase, demonstrating generalized venous congestion.

We began the transarterial embolization with superselective angiograms of the superficial temporal and occipital arteries. The most significant arterial supply to the fistula was from the left occipital artery. We were able to pass the transosseous point of the left occipital artery with the microcatheter but unable to achieve advance distally to fistulous point. Using Onyx-18 we were able to achieve partial penetration of the fistulous connection before significant reflux and cessation of antegrade Onyx penetration prevented further embolization. Follow-up superselective and external carotid angiograms demonstrated a minor reduction in arterial venous shunting (Figures 3A–D). At this point, we decided that further transarterial embolization would not be successful. She tolerated the procedure well and was discharged home the following day.

We again discussed the treatment options and ultimately recommended a transvenous approach given the diffuse arterial supply, complexity of venous drainage, largely unsuccessful transarterial embolization, morbidity of surgery, rupture risk, and delayed occlusion time with radiosurgery. Various transvenous access routes were discussed, including *via* the superior ophthalmic vein, but the navigation to the vein of Galen was thought to be challenging with a high risk for complications. We decided that access to the vein of Galen through the occluded straight sinus would carry a lower intra-operative risk if we could navigate a catheter through the occlusion.

Approaching the VoG *via* the right transverse sinus was attempted using a Navien 058 guide microcatheter over a headway duo 156 and Asahi 14. However, despite several attempts, the microcatheter could not be advanced into the VoG to the level of dAVF. Further attempts were made using a headway duo 167 advanced over an Asahi 008 microguidewire, and then with a Marathon microcatheter over the Asahi 008 microguidewire. However, each time the microcatheter could not track over the wire through the occluded straight sinus to reach the VoG. At this time, with no immediate complications, the procedure was aborted.

Two weeks later, transvenous embolization was attempted again *via* the contralateral (left) transverse sinus. A 6-French × 80 cm long shuttle sheath (Cook Medical LLC, Bloomington IN) was placed in the left Internal Jugular vein *via* a transfemoral approach. A 5F Glidecath (Terumo, Somerset NJ) was placed in the right external carotid artery through a transfemoral approach for roadmap guidance. We felt that the configuration of the left transverse sinus into the straight sinus had a more favorable angle for catheterization. A Navien 058 intermediate catheter was advanced *via* the shuttle into the left transverse sinus over an Excelsior SL-10 microcatheter and Asahi 14 microwire. The microcatheter and wire were advanced through the occluded straight sinus to the level of the vein of Galen (Figures 3B,C). Superselective venograms were obtained *via* the microcatheter to determine the level of the vein of Galen. Once through the occluded straight sinus, we were able to find an opening in the occluded connection between the vein of Galen and the straight sinus. The microcatheter and wire were then advanced distally to the level of the fistula (Figures 3D,E). Superselective venograms and right external carotid arteriograms were obtained confirming the appropriate positioning of the microcatheter just distal to the level of the fistula. Embolization was then performed in a retrograde fashion using Microplex Coils (MicroVention, Aliso Viejo CA) and Axium Coils (Medtronic, Minneapolis MN).

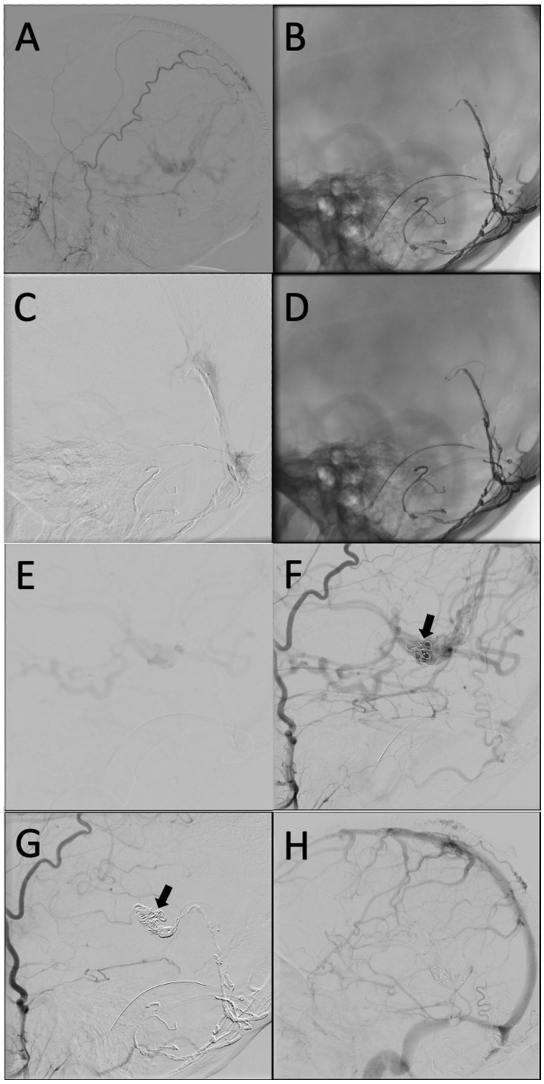

FIGURE 3
(A) Lateral projection of the right ECA again demonstrating an occluded straight sinus with retrograde deep drainage. **(B)** Un-subtracted lateral view showing the microcatheter in the straight sinus. **(C)** Venogram from the straight sinus showing that the vein of Galen had not been catheterized yet with delayed antegrade venous drainage through the channel created by the microcatheter. **(D)** Un-subtracted lateral view showing the microcatheter in the vein of Galen. **(E)** Venogram from the vein of Galen. **(F)** Lateral projection of the R ECA after the first coil placement (black arrow). **(G)** Lateral projection of the R ECA after the last coil (black arrow) in the late arterial phase. **(H)** Lateral projection of the R ECA after final coil placement and preservation of the internal cerebral veins with no residual shunting.

Intermittent angiograms were obtained to evaluate for occlusion of the fistula (Figures 3F,G). Final follow-up arteriograms were obtained from the right external carotid artery (Figure 3H), left vertebral artery and left common carotid artery which demonstrated no residual arteriovenous shunting. Intravenous heparin boluses were given throughout the procedure. Given the significant reduction of overall flow through the venous system and the history of venous thrombosis, we decided to maintain a heparin infusion out of concern for cortical vein thrombosis.

The patient tolerated the procedure well and was observed in the Neuro-ICU for 24 h. We elected to convert the heparin infusion to Eliquis for 30 days. She was able to be discharged home on post-embolization day 1. Unfortunately, she presented to the emergency department on post-embolization day 2 with complaints of severe headache, nausea, and vomiting and was found to have a moderate volume intraventricular hemorrhage involving predominately the left ambient cistern, third and lateral ventricles. She was admitted to the Neuro-ICU, the Eliquis was reversed, and an external ventricular drain was placed due to progressive lethargy with an opening pressure of 28 mmHg. After a prolonged ICU course due to intracranial hypertension, the external ventricular drain was able to be removed and she was discharged to acute inpatient rehabilitation. She has since returned home and has no new neurologic deficits.

A follow-up angiogram was obtained 6 months after the transvenous embolization which demonstrated significantly improved venous drainage pattern with greatly reduced venous congestion (Figures 4A–C). There was minimal residual arteriovenous shunting from the falcine artery and posterior choroidal artery with venous drainage through the basal vein of Rosenthal and left superior ophthalmic vein (Figure 4D). Clinically, she is doing remarkably well. The severe progressive headaches have resolved, and her cognitive function has improved. She is no longer experiencing "brain fog." Given the significant angiographic and clinical improvement, we plan to repeat an angiogram in 1 year to follow the residual fistula.

Discussion

Galenic dAVF is a rare form of falco-tentorial dAVF. Despite being the type of dAVF most associated with aggressive clinical presentation, Galenic dAVFs are infrequently described in the literature due to their overall rarity. They account for only 23% of tentorial dAVFs, with tentorial dAVFs accounting for less than 4% of all intracranial dAVFs (6, 8, 9).

Galenic dAVFs are distinct in their location at the anterior falco-tentorial junction, a location that is often obscured from surgical visualization, requiring complex operative approaches. In addition to their difficult location, their vast arterial supply and complex venous drainage, as in this patient, make them difficult to obliterate *via* endovascular approaches alone without microsurgical or radiosurgical interruption (6, 7, 10). Recent literature suggests an increase in the utilization of transarterial embolization approach in Galenic dAVFs. However, a recent report has shown that select cases can successfully be treated by the transvenous approach (8).

In our case, the absence of antegrade drainage of the VoG to the straight sinus with cortical venous reflux placed this patient at high risk for intracerebral hemorrhage. Given the hemorrhage risk and progressive symptoms, we believed that treatment was strongly indicated. Transarterial embolization was initially attempted due to promising targets at the left occipital arterial feeders, its preferred utilization in high-risk dAVFs, and an overall lower risk of intra and post-procedural hemorrhage (11). However, no significant reduction of the shunting was achieved due to the inability to reach the venous side of the fistula. In the setting of diffuse arterial supply, complexity, and lack of other safe and effective transarterial approaches, it was determined that a transvenous approach would be necessary to reach and completely occlude the fistula.

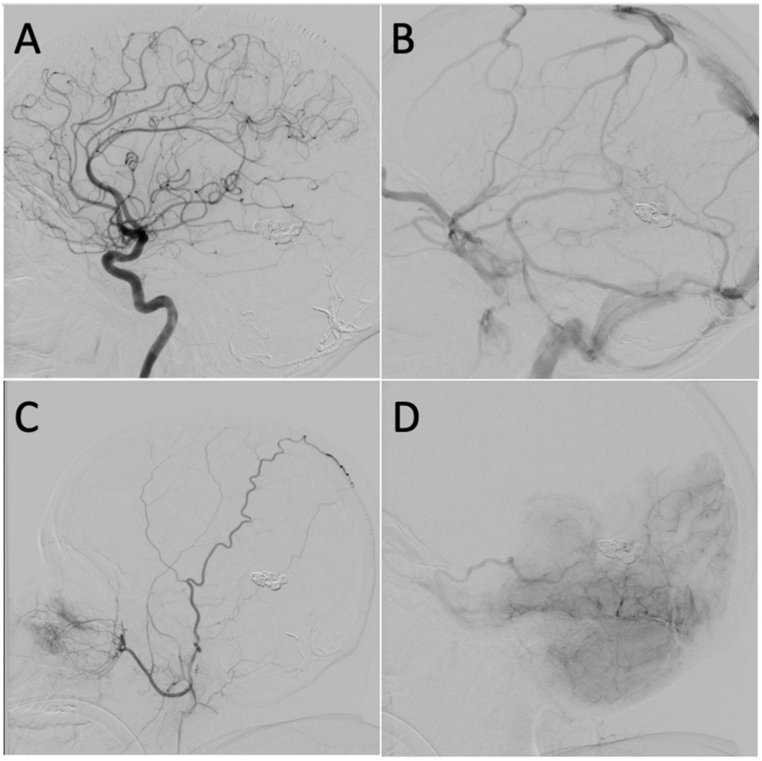

FIGURE 4
(A) Lateral projection of the left ICA, arterial phase, showing no shunting. **(B)** Lateral projection of the left ICA, venous phase, showing improvement in the overall venous congestion. **(C)** Lateral projection of the right ECA showing mild shunting from the falcine artery. **(D)** Lateral projection of the right vertebral artery, early venous phase, showing mild shunting from the posterior choroidal artery with venous drainage through the basal vein of Rosenthal and left superior ophthalmic vein.

However, several veins converge into the VoG and anatomical variation can create difficulty in distinguishing them from one another, making the transvenous approach more challenging (12). The venous drainage pattern must be assessed thoroughly to find the best venous route. Venous embolization can be performed with acceptable safety if the target veins no longer contribute to normal venous drainage (8). Utilization of angiography to confirm appropriate positioning of the coils is critical in limiting the risk of unintended distal venous occlusion and residual shunting. In the case presented here, the transvenous approach permitted complete occlusion of the dAVF in a single coiling session, with significant angiographic and clinical improvement at 6 months.

Conclusion

Galenic dAVFs are generally accepted as being one of the most difficult fistulas to approach surgically. While the transarterial embolization is typically the initial route chosen for treatment, the diffuse arterial supply of Galenic dAVFs can make this approach largely unsuccessful. Our case demonstrates the feasibility of transvenous endovascular coiling *via* an occluded straight sinus and its efficacy in treating high-grade Galenic dAVFs with retrograde venous drainage and corticovenous reflux.

Patient perspective

"In the spring of 2021 I went to my eye Dr. to get my eyes checked. My Dr. noticed that both of my optic nerves were swollen. I was then scheduled for an MRI where it showed a vein was enlarged and was scheduled for an angiogram of the brain. It showed I had a fistula and that I had problems with back flow of those veins. I then had two veins glued on the left side of my brain. After that procedure, I was scheduled for another angiogram, but it was unsuccessful. I was then scheduled for another angiogram where they put in seven coils in my brain. I stayed overnight and was sent home. The next day, I was very sick and had a really bad headache. My husband called 911 and I was taken to UNC Hospital's emergency room. I had bilateral bleeds. I do not know what all happened except I was put in a medically induced coma. The first day I was coherent I was talking to my husband and sister about what had happened to me. I went from ICU to a step-down unit then to rehab. I came home with the only thing wrong with me is a drop foot on the left side."

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

CC and NQ wrote the original draft of the manuscript. CC, NQ, EY, and SS conceptualized, analyzed, reviewed, edited, and approved the published version of this manuscript. NQ, EY, and SS were treating physicians of the patient. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that this report was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Late in-stent thrombosis in a patient with vertebrobasilar dolichoectasia after stent-assisted coil embolization due to the discontinuation of antiplatelet therapy

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Vertebrobasilar dolichoectasia (VBD) is a rare type of cerebrovascular disorder with high rates of morbidity and mortality. Due to the distinct pathological characteristics that fragmented internal elastic lamina and multiple dissections, VBD is difficult to treat and cured. Stent-assisted coil embolization is one of the main treatment modalities for such lesions. However, the duration of healing remained questionable, and there were no effective measures for evaluating endothelial coverage. Before complete endothelial coverage, the discontinuation of antiplatelet therapy may lead to fatal in-stent thrombosis; however, continued antiplatelet therapy could also result in bleeding complications. Thus, we present an autopsy case of late in-stent thrombosis due to the discontinuation of antiplatelet therapy and systematically review the literature to provide a reference for endovascular treatment and antiplatelet regimen of VBD.

KEYWORDS

aneurysm—dissecting, stent assisted coil embolization, thrombosis, case report, autopsy

Introduction

Vertebrobasilar dolichoectasia (VBD) is a rare type of cerebrovascular disorder resulting in ectasia, elongation, and tortuosity of the vertebrobasilar artery. However, there are no current data on the exact incidence of VBD in the general population. Flemming et al. (1) assumed that the incidence was <0.05%, while Ince et al. (2) revealed that VBD was detected in ∼2.06% of the first-ever stroke population. Patientswith VBD commonly present with ischemic stroke, intracranial hemorrhage, and compression of the brainstem and/or cranial nerves (3–9), which could lead to high rates of morbidity and mortality (10). Among endovascular treatments, stent-assisted coil embolization is one of the main treatment modalities for VBD.

In-stent thrombosis is one of the most common complications after stent-assisted coil embolization, the rate of which is ∼1.5% (1). Postoperative antiplatelet therapy is routinely administered to prevent the occurrence of in-stent thrombosis. However, the

duration of post-procedure antiplatelet therapy remains questionable. Some studies provide recommendations for the optimal duration according to clinical experience, but there is no definite evidence of timing for the discontinuation of antiplatelet therapy (2, 3). Thus, we present an autopsy case of late in-stent thrombosis due to the discontinuation of antiplatelet therapy and systematically review the literature.

Case report

A 66-year-old man presented with hemifacial spasm on the left side and hemiplegic paralysis on the right side, as well as lower extremity weakness. CTA revealed ectasia, elongation, and tortuosity of the vertebrobasilar artery, which indicated VBD. T2-weighted MRI showed that the aberrant vertebrobasilar artery contributed to facial nerve compression, which corresponded to the clinical symptoms (Figure 1A). Digital subtraction angiography (DSA) was also performed, and the diagnosis of VBD was confirmed. Meanwhile, severe stenosis of the basilar artery was detected according to the 3D volume rending reconstructed image. 2D angiography of optimal view demonstrated the stenosis, but the degree of stenosis was less severe. Balloon angioplasty along with stent implantation was performed to treat the stenosis. Postoperative angiography showed that the stenosis was partly improved (Figures 1B–E). Daily dual antiplatelet therapy (DAPT) including aspirin 100 mg and clopidogrel 75 mg was administrated postoperatively since then. Follow-up angiography was conducted 6 months later, which showed that the stenosis was improved while the existence of aneurysm remained. Stent-assisted coil embolization was performed to reduce the bleeding risk (Figures 1F, G). At 15 months after the endovascular treatment, follow-up angiography was performed and showed that an aneurysm-like protrusion of the VBD was occluded, but MRI indicated that facial nerve compression remained (Figures 1H, I). Furthermore, the patient complained of suffering from hemifacial spasms and desired further treatment. The surgical plan of microvascular decompression was then formulated. Because near-complete occlusion was observed in the recent angiography while DAPT was administrated continuously for ∼2 years, DAPT was discontinued for 1 week before the operation to avoid the risk of perioperative bleeding without alternative short-term anticoagulation therapy. Adhesions between the tortious vertebral artery and the facial nerve were confirmed and dissected, and the operation was uneventful. Unfortunately, the patient presented with unconsciousness 8 h post-operation. A mobile bedside computed tomography (CT) scan was immediately performed and revealed cerebral infarction, while cerebrovascular ultrasound indicated the occlusion of the basilar artery, which highly indicated in-stent thrombosis.

An autopsy was performed with the agreement of relatives. Gross specimens of the vertebrobasilar system showed VBD with obvious protrusion located at the middle of the basilar artery, where stent-assisted coil embolization was performed. Brain stem compression caused by VBD could also be observed (Figure 2A). The specimen of the vertebrobasilar system was dissected separately, which was then chemically fixed and embedded in resin. Three specified regions of VBD, the proximal region, the distal region, and the apparent dilatated region were cut into sections, and microscopic observation was performed (Figure 2B). The section of the apparent dilatated region showed that the stent was suspended, and there was no vascular endothelium coverage on the surface (Figures 2C, D), which was evident and likely contributed to the in-stent thrombosis after the discontinuation of antiplatelet therapy. For the proximal region, the stent was relatively adherent, and vascular endothelium or connective tissue coverage appeared above the stent (Figure 2E). For the distal region, even, smooth muscle coverage could be observed on the surface of the stent (Figure 2F).

Discussion

In contrast to saccular aneurysms and regular dissecting aneurysms, VBD presents a fragmented internal elastic lamina combined with multiple dissections in pathology (4). The distinct pathological characteristics may account for why VBD is difficult to treat and takes longer to cure. In the past, conventional stent-assisted coil embolization or conventional stent implantation was used to treat VBD, but the efficacy was limited. LEO stents were proven to be an effective endovascular treatment modality in a previous study, which showed that most patients had good reconstruction of the target vessels and improvement of symptoms shortly after treatment (5). However, the results with long-term follow-up suggested that the clinical outcome was poor despite a good radiological outcome (6). Patients who presented with compressive symptoms had an even worse prognosis after endovascular treatment, which may not be beneficial for such patients (7). Recently, a flow diverter was used to treat VBD. Nevertheless, a systematic review and meta-analysis suggested that there were no statistically significant differences in favorable clinical outcomes, complete/near-complete occlusion, or complications between stent-assisted coiling and flow diverter groups in treating posterior circulation non-saccular aneurysms, which are similar to VBD (8). Furthermore, the morbidity and mortality rates of VBD patients who receive surgical treatment are also extremely high (9). Overall, the optimal treatment modality for VBD remains controversial.

In-stent thrombosis is one of the most common complications after stent-assisted coil embolization. A systematic review and meta-analysis revealed that ischemic/thromboembolic events and in-stent thrombosis were the most common complications, and the rate of in-stent thrombosis was ∼1.5% (1). Postoperative antiplatelet therapy is routinely administered to prevent the occurrence of in-stent thrombosis. However, the duration of post-procedure antiplatelet therapy remains questionable. Early discontinuation of antiplatelet therapy may result in ischemic complications, while continuous antiplatelet therapy could increase the risk of hemorrhagic complications. For conventional stents, one retrospective study including 395 patients with 403 aneurysms treated with stent-assisted coil placement concluded that DAPT for more than 9 months and late switching to monotherapy are recommended for its prevention (2). Kim et al. suggested that longer-term DAPT (>9 months) should be considered after stent-assisted coil embolization for unruptured intracranial aneurysms, although its efficacy remains to be clarified (10). Noah Hong et al. (3) suggested that the optimal time to discontinue might

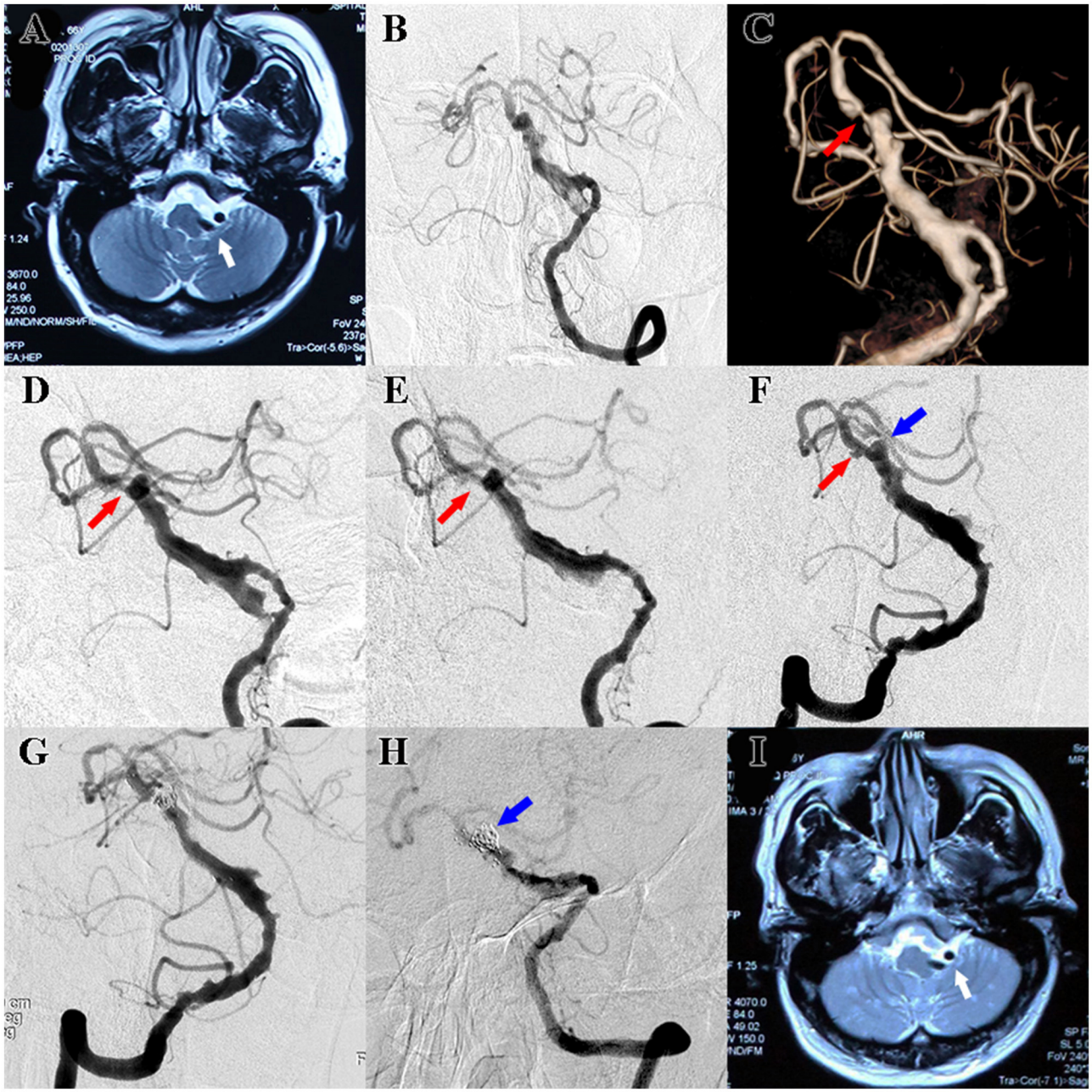

FIGURE 1
(A) Preoperative T2-weighted MRI showed facial nerve compression resulting from VBD (white arrow). **(B)** Standard frontal view of preoperative DSA also revealed ectasia, elongation, and tortuosity of the vertebrobasilar artery, and the diagnosis of VBD was confirmed. **(C)** 3D volume rending reconstructed image of preoperative DSA showed severe stenosis of the basilar artery (red arrow). **(D)** 2D angiography of optimal view of preoperative DSA demonstrated stenosis of the basilar artery, but the degree of stenosis was less severe (red arrow). **(E)** Postoperative angiography after balloon angioplasty along with stent implantation showed that the stenosis was partly improved (red arrow). **(F)** 6-month follow-up angiography showed that the stenosis of the basilar was improved (red arrow) while the aneurysm seemed enlarged (blue arrow). **(G)** Postoperative angiography after stent-assisted coils embolization showed that the aneurysm was occluded (blue arrow). **(H)** Follow-up angiography after stent-assisted coils embolization showed that an aneurysm-like protrusion of the VBD was occluded (blue arrow). **(I)** Follow-up MRI indicated facial nerve compression remained (white arrow).

be ~18–36 months after stent-assisted coil embolization. Large cohort-based studies or randomized clinical trials are warranted to confirm these results. However, the earlier three studies had limitations because none of them provided data on the rates of major bleeding for patients treated with antiplatelet therapy. A prospective randomized multicenter trial was conducted to compare the effect of short-term (6 months) and long-term (12 months) DAPT on UIAs in patients undergoing stent-assisted coil embolization to find the optimal duration, and the results were highly anticipated (11). For flow diverters, a systematic review and pooled analysis indicated that a duration of post-procedure clopidogrel therapy <6 months was associated with greater rates of

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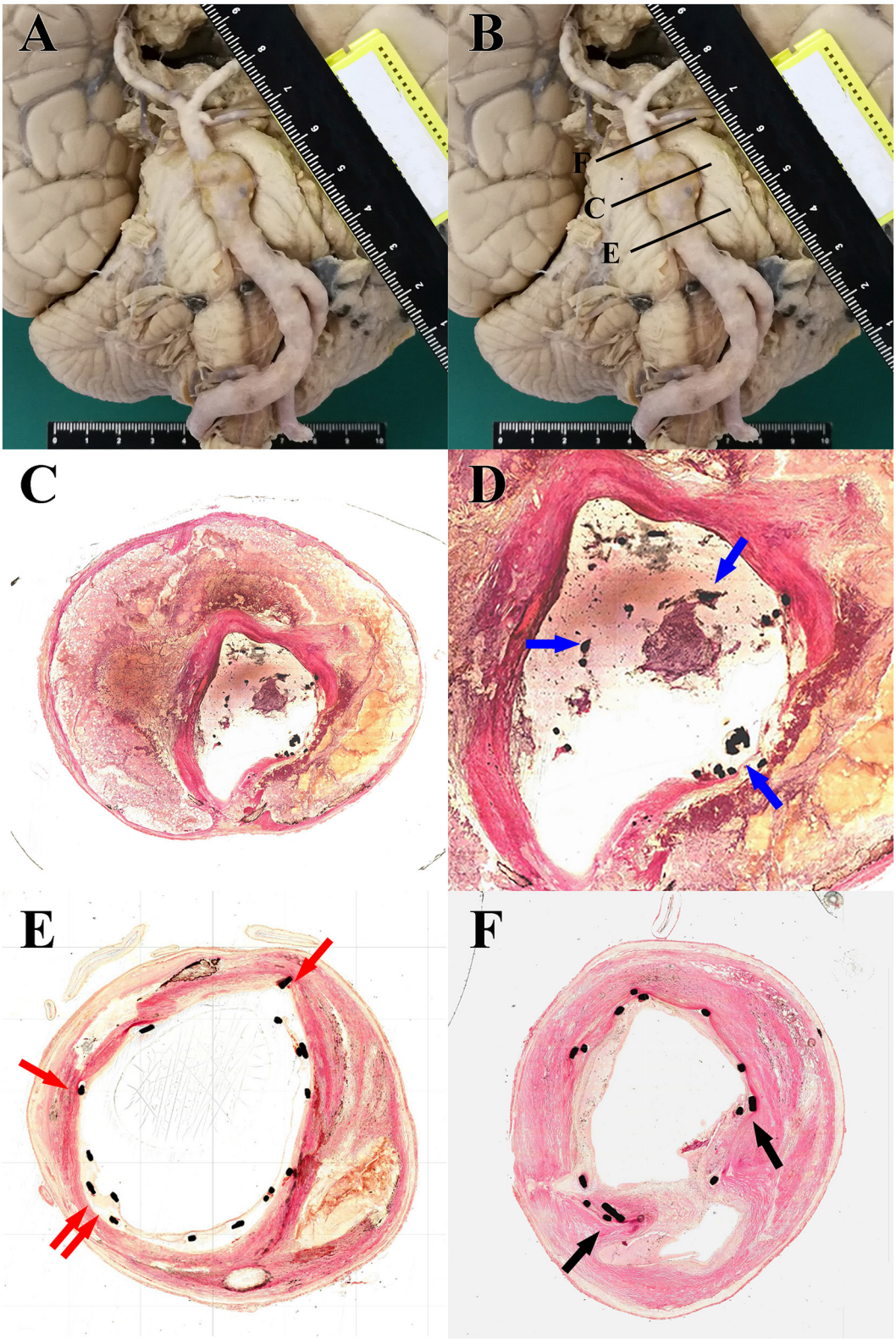

FIGURE 2
(A) Gross specimens of the vertebrobasilar system showed ectasia, elongation, and tortuosity of the vertebrobasilar artery accompanied by brain stem compression caused by VBD. **(B)** Schematic diagram of tissue slice position: the proximal region (E), distal region (F), and apparent dilatated region (C). **(C)** Light microscopy images from H–E staining (20×) of tissue slice of the apparent dilatated region: irregular intravascular lumen, loss of smooth muscle, and multiple thromboses among the dissection. **(D)** Locally magnified images (40×) focusing on the intravascular lumen of the section of the apparent dilatated region showed that the stent was suspended, and there was no vascular endothelium coverage on the surface (blue arrow). **(E)** Light microscopy images from H-E staining (40×) of tissue slice of the proximal region: the stent was relatively adherent, and vascular endothelium or connective tissue coverage appeared above the stent (red arrow). **(F)** Light microscopy images from H–E staining (40×) of tissue slice of the distal region: smooth muscle coverage could be observed above the stent (black arrow).

ischemic complications than a clopidogrel regimen of ≥6 months for pipeline embolization of cerebral aneurysms, while the duration of postprocedural high-dose ASA therapy was also not associated with ischemic complications (12). Another meta-analysis indicated that clopidogrel therapy ≤6 months is associated with higher rates of thrombotic events, but high-dose ASA >6 months is associated with fewer permanent thrombotic and hemorrhagic events (13). DAPT had been continuously administered for ∼2 years for the case presented, which was much longer than the so-called long-term DAPT in previous studies. However, the fatal basilar thrombo-ischemic event still occurred. All the studies mentioned earlier only provide recommendations for the optimal duration based on clinical experience, but there is no definite evidence or guidelines for the timing of DAPT discontinuation.

None of the routine imaging examinations, such as CT, MR, or DSA, could evaluate the situation of endothelial coverage above the stent, so the evidence provided by these imaging examinations for the timing of DAPT discontinuation is limited. Currently, another imaging method is being used to evaluate cerebral vascular disease: optical coherence tomography (OCT). OCT images can show more features at the pathological level, especially stent apposition and neointima formation (14). A study of coronary stenting demonstrated that incomplete apposition led to a delay in neointimal coverage of the stent struts, activation of platelet function, and late stent thrombosis (15). The study by Rouchaud et al. (16) demonstrated that good wall apposition was a key factor for aneurysm occlusion after flow diverter treatment in a histological evaluation of rabbits. Guerrero et al. (17) described the assessment of the endothelial healing of recurrent intracranial aneurysms after treatment with a PED shield at 8 weeks post-implantation by using OCT. These findings corresponded to our pathological results, which provided valuable support for the perspective that the better the stent adherence is, the easier it is to be covered by the intima or even the muscular layer. When complete endothelial coverage was confirmed in OCT, antiplatelet therapy could be confidently discontinued, whereas for those patients with incomplete intimal coverage, longer or even lifelong medication may be necessary (18). Nevertheless, there were still some limitations to using OCT in the neurovascular field. Stiff catheters and tortuous intracranial arteries may result in iatrogenic dissection and poor imaging quality (19, 20).

Conclusion

This case indicated that the discontinuation of long-term antiplatelet therapy for VBD patients treated with stent-assisted coil embolization could be a cause of late in-stent thrombosis and subsequent cerebral infarction, which may result in poor clinical outcomes. In regard to patients with VBD, the safety of discontinuation of long-term DAPT after endovascular treatment should be carefully considered.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual's legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

Author contributions

ZJ, WY, and YM drafted and revised the manuscript and were involved in the acquisition of data. ZJ and WY contributed equally to the manuscript. LB was involved in the acquisition of data. YF and YP performed the autopsy. GL and HZ supervised and revised the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: emergent endovascular treatment for carotid cavernous fistulas presenting as intracranial hemorrhage

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Objectives: This study aimed to discuss the clinical characteristics and emergent endovascular treatment of carotid cavernous fistulas presenting as intracranial hemorrhage.

Methods: The clinical data of five patients with carotid cavernous fistulas, who presented with intracranial hemorrhage and who were admitted from January 2010 to April 2017, were analyzed retrospectively, and the diagnoses were confirmed by head computed tomography. Digital subtraction angiography was carried out in all the patients for the diagnosis and further emergent endovascular procedures. All patients were followed up to assess the clinical outcomes.

Results: In total, five patients harbored five mono-lateral lesions; two of them were obliterated by detachable balloons, two by detachable coils, and one by detachable coils and Onyx glue. Only one patient was cured by another detachable balloon in the second session, and the other four patients were cured in the first session. At the 3- to 10-year follow-up, there was no intracranial re-hemorrhage in any of the patients; there was no recurrence of symptoms; and delayed occlusion of the parent artery was noted in one case.

Conclusion: Emergent endovascular therapy is indicated for carotid cavernous fistulas presenting as intracranial hemorrhage. Individualized treatment according to the characteristics of different lesions is safe and effective.

KEYWORDS

carotid cavernous fistula, treatment, endovascular, intracranial hemorrhage, case report

1. Introduction

Carotid cavernous fistula (CCF) is a pathological shunt that originates between a high-pressure internal carotid artery and a low-pressure cavernous venous system. The clinical presentation depends on hyperemia in the veins around the cavernous sinus (1). The most common clinical manifestations are pulsating exophthalmos, conjunctival edema, and cranial nerve palsy. Consequently, intracranial hemorrhage (ICH) is relatively rare, but it is a critical event and can result in a worse prognosis (2). Since January 2010, five cases of CCF presenting as intracranial hemorrhage have been treated in our department. All of these patients were treated endovascularly with an emergent procedure and had a good prognosis.

2. Case report

2.1. Clinical data

From January 2010 to April 2017, five adult patients who harbored CCF presented with ICH and were admitted to our hospital; all of them had a history of head trauma. ICH was found in one patient after surgery for traumatic brain contusion, in two patients after embolization by detachable balloons (Goldbal2, Balt, France), and in another two patients who did not have any medical intervention. The duration from head trauma to ICH varied from 1 month to 20 years. All patients suffered from headaches on admission, where three of them had additional pulsatile exophthalmos, and two of them had conjunctival edema as well. No cranial nerve palsy was noted (Table 1).

2.2. Imaging data

All patients were diagnosed with ICH by emergency head computed tomography (CT), and there were two patients with intraparenchymal hemorrhage (IPH), one patient with subarachnoid hemorrhage (SAH), and two patients with IPH with SAH. All of the patients underwent emergency digital subtraction angiography (DSA) for the diagnosis of CCF. In the study, five mono-lateral direct CCFs with high flow (Barrow type A) were noted, and all fistulas were located in the cavernous segment (C4) of the internal carotid artery; two of them showed signs of total flow steal. Reflux drainage of cortical vein reflux was detected in all patients, including three patients that had reflux drainage to the straight sinus and four patients who had it to the superior sagittal sinus. Three of them had bulbous dilation of the drainage vein (s).

2.3. Endovascular therapy

Endovascular treatment by detachable balloon: The patients were placed in the supine position, and local anesthesia was given. The femoral artery approach was established by an 8F (French) sheath followed by the introduction of an 8F guiding catheter into the lesional ICA. Subsequently, a Goldbal2 balloon equipped at the tip of a MABDTE microcatheter (Balt, France) was navigated into the cavernous sinus through the fistula by the arterial flow. Then, the balloon was gradually dilated by filling it with diluting contrast agent (normal saline: ousu [iohyanol 300 mL, Yangzijiang Pharmaceutical Group Co., LTD., China] =1:1) until the fistula had disappeared angiographically. Finally, the balloon was detached *in situ* after control angiography, by which the abnormal shunt disappeared. If the cavernous sinus cavity was too large, an additional balloon was used.

Endovascular treatment by a detachable coil. The patients were placed in the supine position with general anesthesia. The femoral artery approach was established by a 6F sheath, followed by an introduction of a 6F guiding catheter into the lesional ICA. Under fluoroscopic monitoring in the roadmap mode, two Echelon 10 microcatheters (eV3, USA) were navigated by a Traxcess 14 microguidewire (MicroVention, USA) into the cavernous sinus through the fistula successively. Thereafter, a series of detachable coils (Axium, eV3, USA) was introduced to occlude the fistulae. After confirmation of the obliteration of the abnormal shunt, the coils were detached, followed by retreatment with a microcatheter. If necessary, a HyperGlide 4 × 20 balloon (eV3, USA) was navigated to cover the fistula in the ICA by an X-pedion 10 microguidewire (eV3, USA). Based on the complete occlusion of the ICA by dilation of the undetachable balloon, Onyx 18 glue (eV3, USA) was injected slowly under fluoroscopy monitoring. Serial control angiography was carried out after the deflation of the balloon until the abnormal shunt had disappeared. Thereafter, the balloon and microcatheters were removed.

2.4. Follow-up

Scheduled head CT was performed immediately after the endovascular procedure, on the 2nd day after treatment, and on the day of discharge. The modified Rankin Scale (mRS) score for each of the patients was evaluated when they were discharged. All patients were followed up in the outpatient setting to detect any novel neurological deficits. The patients underwent follow-up CTs at 1 month, 3 months, 6 months, and 1 year after the endovascular procedure, and follow-up DSAs were performed at 6 months and 1 year after the procedure.

3. Results

A total of five patients (harboring 5 CCFs) underwent six endovascular procedures; two of them were cured by detachable balloons (one patient by two balloons and another by three balloons), two patients by detachable coils, and one patient by Onyx glue and detachable coils. Among them, only one patient was cured in a second session by detachable balloons, and the other four patients were cured in one session; two patients who were treated with detachable balloons experienced transient headaches after the procedure, which were spontaneously alleviated by medication. There were no novel neurological deficits immediately after the endovascular procedures. The mRS score at discharge was 0 in four patients and 1 in one patient.

All patients were followed up for 3–10 years (average 75.0 months), and no recurrence of intracranial hemorrhage or CCF-related symptoms was noted. One patient who was treated with detachable balloons was found to have delayed spontaneous occlusion of the lesional ICA after 6 months, but the good compensation of the Willis circle resulted in an asymptomatic course (Figure 1). The lesional ICAs of the other four patients were intact. A pseudoaneurysm was noted by head CT angiography (CTA) in one patient who was treated with detachable balloons 3 months after the endovascular procedure, and the patient did not receive any further therapy. At the 3-year follow-up, a slight shrinkage of the pseudoaneurysm was noted in the patient's CTA image (Figure 2).

TABLE 1 Clinical characteristics of patients.

	Case 1	Case 2	Case 3	Case 4	Case 5
Gender	Male	Female	Female	Male	Female
Age	33	39	65	48	64
Symptoms	Headache pulsatile exophthalmos	Headache pulsatile exophthalmos	Headache conjunctival edema	Headache pulsatile exophthalmos	Headache conjunctival edema
Time lag between presentation to intervention (hours)	1	1.5	1	0.5	2
Past history	Head trauma	Head trauma	Head trauma; Surgery for traumatic brain contusion	Head trauma	Head trauma
Reoperation		Endovascular embolization by detachable balloons		Endovascular embolization by detachable balloons	
Postoperative length of hospital stay(days)	6	7	12	14	5

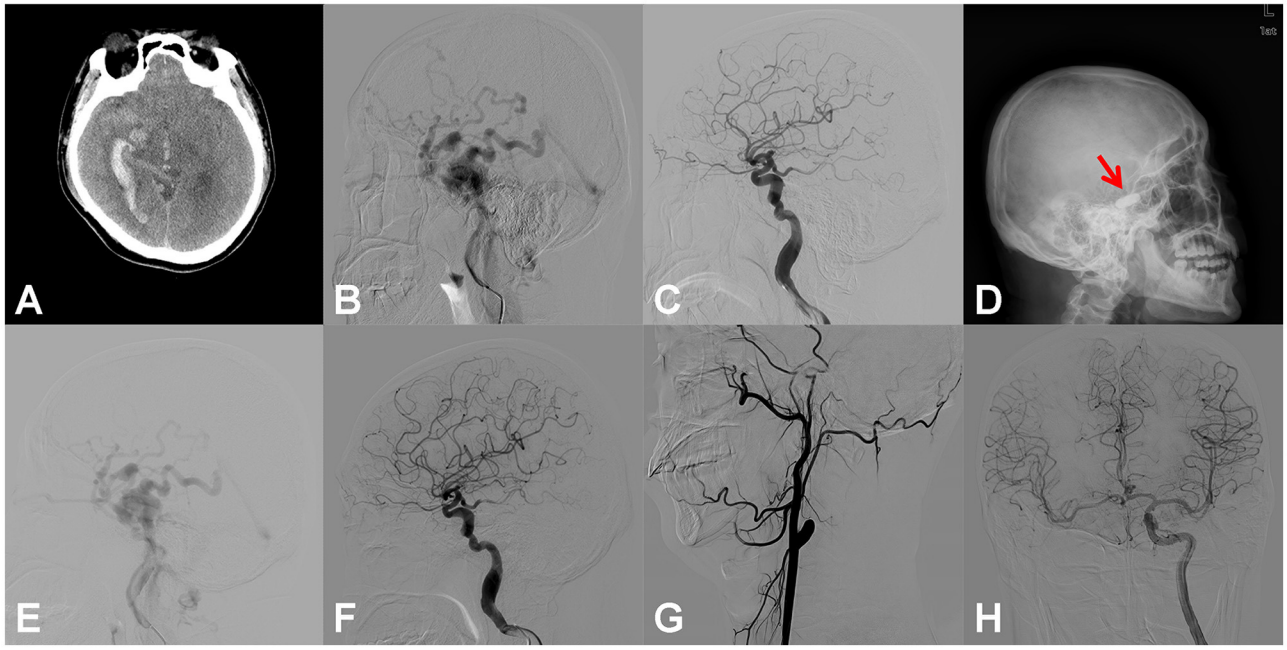

FIGURE 1
Right carotid cavernous fistula (CCF). An adult patient presented to the emergency room with an onset of severe headache for 6 h. Right temporal auscultation had a blowing murmur that was consistent with a heartbeat. **(A)** Emergency head computed tomography (CT) showed subarachnoid hemorrhage, right temporal lobe, and ventricular hematoma. **(B)** Digital subtraction angiography (DSA) of the right internal carotid artery (ICA) showed the CCF, with reflux drainage of cortical veins. **(C)** After the dilation of two detachable balloons (Goldbal2), the pathological shunt disappeared, and the cerebral blood flow recovered. **(D)** The patient suffered from sudden throbbing tinnitus on the left side 2 days after the endovascular procedure, and the head X-ray radiography revealed that only one balloon developed (red arrow). **(E)** Emergency DSA showed the recurrence of CCF. **(F)** With the introduction of another detachable balloon (Goldbal2) in the cavernous sinus, the pathological shunt disappeared angiographically and the patient recovered well without any neurological deficits. **(G)** DSA follow-up 6 months after the procedure showed complete occlusion of the lesional ICA. **(H)** DSA of the left ICA showed that the perfusion of the right hemisphere was compensated adequately by the anterior communicating artery.

4. Discussion

4.1. Causes of ICH originating from CCF

CCF was first reported by Travers et al. in 1809. It can be divided into traumatic CCF and spontaneous CCF, according to the etiology. The former type is more common, accounting for ~75% of the cases (3). Barrow et al. classified CCFs into direct (Barrow A) and indirect types (Barrow B–D). The former has a direct shunt between the ICA and cavernous sinus, usually with high blood flow (4). All five patients in this study had a clear history of head trauma attributed to Barrow type A. The

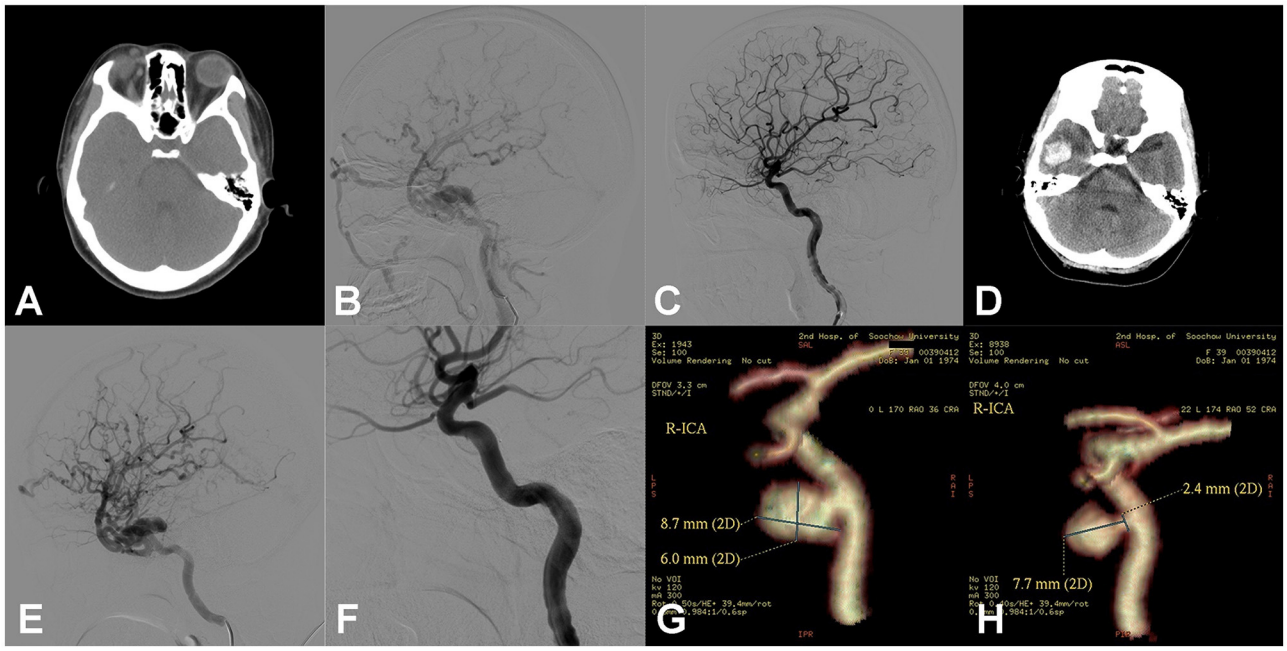

FIGURE 2
Right carotid cavernous fistula (CCF). An adult patient presented with right pulsing tinnitus after head trauma 1 month ago. Physical examination revealed a blowing murmur consistent with the heartbeat on the right temporal scalp, as well as a mild chemosis of the right side. **(A)** Head computed tomography (CT) showed the dilation of the right superior ophthalmic vein (SOV). **(B)** Digital subtraction angiography (DSA) of the right ICA showed the CCF with reflux drainage of cortical veins. **(C)** After dilation of one detachable balloon (Goldbal2), the pathological shunt disappeared and the cerebral blood flow recovered. The patient recovered well, and the symptoms of right chemosis and intracranial murmurs disappeared. **(D)** After 2 weeks, the patient presented to emergency with a sudden headache, and the head CT showed intracerebral hematoma of the right temporal lobe. The right temporal auscultation noted the recurrence of the blowing murmur. **(E)** Emergency DSA of the right ICA showed the recurrence of CCF and the reflux drainage of the cortical veins aggravated compared to previous images besides the undevelopment of SOV. **(F)** Another detachable balloon (Goldbal2) was introduced in the cavernous sinus, and the pathological shunt disappeared angiographically. The patient recovered well after the endovascular procedure with no neurological deficits. **(G)** After 3 months, CT angiography (CTA) showed the balloon had deflated and there was a consequent pseudoaneurysm in the cavernous sinus. The patient hesitated to receive another endovascular treatment. **(H)** In the 3-year follow-up, CTA showed the pseudoaneurysm was still present but smaller than before.

symptoms of CCF depend on the direction of venous drainage, and the most common symptom is caused by drainage into the superior ophthalmic vein (SOV), named the Dandy triple sign, which presents as pulsating exophthalmos, a murmur, and bulbar conjunctival edema (5). Drainage to the posterior superior and inferior petrosal sinuses is relatively rare and may cause cranial nerve palsy and hemiplegia. Directed upward drainage via cortical veins into the sagittal sinus and deep venous system is more dangerous (6). In ∼9% of cases, increased venous pressure can generate reflux drainage of the cortical veins, which are prone to various forms of ICH and even fatal brain stem hemorrhage. If bulbous dilation of the draining veins is noted, the risk of ICH will be higher (7). In this study, all five patients had reflux drainage of the cortical veins, including the superior sagittal sinus in one patient, the straight sinus in one patient, and the superior sagittal and straight sinus in three patients. Three of them were complicated with a venous bulbous dilation. All of this evidence supports that cortical venous hypertension is a risk factor for CCF resulting in ICH. It has been reported that if anterior drainage through the SOV or posterior drainage through the superior and inferior petrosal sinuses is poor or absent, arterial hypertension will drain to the cerebral venous system through the sphenoid sinus or other channels, eventually causing ICH (8). Interestingly, one patient in this study had this extremely rare circumstance. This patient was diagnosed with CCF due to ocular symptoms, and half a month after the first endovascular procedure with detachable balloons, she was hospitalized again due to ICH. Comparing the DSA images of the two procedures, the anterior venous drainage disappeared due to SOV obstruction by a premature deflated balloon, but the cortical venous drainage caused by venous hypertension was much more obvious than before, which resulted in ICH of the right temporal lobe.

4.2. Selection of endovascular strategy

Generally, life-threatening CCF requires emergent management, and some of the high-risk factors for ICH include severe epistaxis, cortical venous reflux, and angiographic venous bulbous dilation. With the development of endovascular technology, the open surgical strategy for CCF has been almost eliminated. The choice of endovascular strategy should depend on the feeding artery, the draining vein, the blood flow velocity of the fistula, and the integrity of the Willis circle (9). Malan et al. classified traumatic CCFs into small, medium, and large CCFs based on the vascular structure, and this classification is helpful for the selection of different endovascular strategies (10).

Although there are increasing reports of the transvenous approach for the treatment of CCF, the transarterial approach is safer and simpler and is still suitable for the majority of such lesions. Many materials, including detachable balloons, detachable coils, Onyx glue, and covered stents, are available (11). From the perspective of economy and convenience, the detachable balloon is the preferred method, which can be completed under local anesthesia, and the operation is simple. Compared with detachable coil and Onyx glue embolization, detachable balloon embolization can be performed under local anesthesia, and the operation process is simpler (12). However, as in two of the patients in this study, after the first balloon embolization of case 2, the patient's right eye visual acuity decreased on the 10th day after the operation, and the CT examination showed bleeding. Further improvement of DSA showed that the ophthalmic vein pathway was blocked by the deflated balloon, the direction of venous drainage was changed, and a large number of cortical veins were countercurrent, resulting in bleeding. Therefore, detachable balloon embolization of the right internal carotid cavernous fistula was performed again at the same time. Postoperative cerebral angiography showed fistula occlusion. In case 4 after the first balloon embolization, on the 3rd day after the operation, the examination of the anterior and lateral cranial radiographs showed that only one of the two balloons remained. Combined with clinical practice, considering the possibility of balloon leakage, the leakage is broken again, and secondary interventional surgery is needed to re-block the leakage. DSA examination showed that the original embolization balloon disappeared, the fistula reopened, and the cortical vein drainage was obvious, so the detachable balloon embolization of the right internal carotid cavernous fistula was performed at the same time. Postoperative cerebral angiography showed fistula occlusion. Herein, we think recurrence caused by premature deflation is a major problem that needs to be considered. In addition, detachable balloons may eventually cause ICA occlusion and/or a cavernous sinus pseudoaneurysm, and these balloons have been less commonly used in the treatment of CCF (13). The detachable coil has good control ability, but there have been reports that mass stuffing in the cavernous sinus can cause compression of the cranial nerves and the possibility of aseptic inflammation, in addition to the high medical cost (14). In this study, two patients treated with a detachable coil had a small, cavernous sinus cavity that was adjacent to the fistula and were regarded as having cavernous aneurysms during the procedure. Some neurosurgeons advocated using Onyx glue, not only for its low cost but also to improve the safety of patients who had a higher risk of vascular injury due to their connective tissue disease (15). Another advantage of using Onyx glue is that collateral feeders, which are not visible on angiography, can be revealed during the progressive injection, and the use of Onyx glue results in improved cure rates. Therefore, the combination of Onyx glue with a detachable coil can not only retard shunt flow but also limit the diffusion of the Onyx glue, which ensures the therapeutic effect and reduces the filling degree of the Onyx glue in the cavernous sinus, and this is the preferred treatment at present (16). Covered stents and flow diverters (FDs) are also options for the treatment of CCF, but their use in patients with ICH remains controversial due to the need for subsequent dual antiplatelet therapy (17, 18).

5. Conclusion

The overall disability and mortality rate of CCF is low, and consequent ICH is relatively rare. However, it is a serious complication that may cause irreversible neurological deficits or a life-threatening prognosis. The recovery rate of endovascular procedures is 90–100%, the complication rate is low, and the mortality rate is <1% (19–21). Therefore, individualized endovascular strategies should be carried out actively and in a timely manner for such patients.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

Written informed consent was obtained from the individual(s) and/or minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

Author contributions

Conceptualization, supervision, and project administration: QZ. Methodology: QZ, A-LC, and C-GD. Software and visualization: Z-LL, A-LC, C-GD, D-HY, Y-HW, and YW. Validation and writing: Z-LL, A-LC, and YC. Investigation: A-LC and QZ. Resources and data curation: Z-LL and A-LC. All authors have read and agreed to the published version of the manuscript.

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Conflict of interest

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Case report: Endovascular coil embolization of an aneurysm at the origin of the accessory middle cerebral artery from the A1 segment as the collateral artery to twigs

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An aneurysm at the origin of the accessory middle cerebral artery (AccMCA) from the A1 segment of the anterior cerebral artery (ACA) as the supplying artery of a twig-like MCA is exceptional. In this study, we reported on such a case and presented a review of the relevant literature. A 56-year-old male suffered a subarachnoid hemorrhage. Digital subtraction angiography confirmed a twig-like MCA and a ruptured aneurysm at the origin of the AccMCA. Endovascular coil embolization of the aneurysm was performed. After the microcatheter was positioned in the aneurysm, soft coils were delivered to complete the embolization. Postoperatively, the patient recovered uneventfully. One month later, the patient returned to his job without any neurological deficits. Postoperative computed tomography at the 3-month follow-up showed that the brain tissue was normal. By reporting our case and reviewing the relevant literature, we found that endovascular coil embolization for such aneurysms at the AccMCA origin is feasible in certain cases.

KEYWORDS

twig-like middle cerebral artery, accessory middle cerebral artery, anterior cerebral artery, aneurysm, embolization

Introduction

A twig-like middle cerebral artery (MCA) or MCA twig is an uncommon lesion in which a plexiform network of small vessels replaces the M1 segment. The embryological interruption of MCA trunk genesis may be the cause of these lesions (1, 2). Twig-like MCAs can cause a hemorrhagic or ischemic event (3, 4). A twig-like MCA has a complex angioarchitecture, and the accessory MCA (AccMCA) from the A1 segment of the anterior cerebral artery (ACA) can serve as an important collateral artery for MCA twigs (5, 6). In cases of twig-like MCAs, due to hemodynamic stress, aneurysms can occur at the origin of the AccMCA from the ACA (5–11).

Treatment is mandatory for ruptured aneurysms at the origin of the AccMCA; however, clipping may carry a risk of neurological complications because of the deep location and destruction of the collateral circulation (12). The International Subarachnoid Aneurysm Trial (ISAT) and its follow-up study confirmed the effect of endovascular coil embolization for ruptured aneurysms (13, 14). Therefore, endovascular coil embolization can be applied for aneurysms at the origin of the AccMCA (15).

However, endovascular coiling for an aneurysm at the origin of the AccMCA as the supplying artery of a twig-like MCA is exceptional. In this study, we reported on the application of endovascular coiling for such an aneurysm and reviewed the relevant literature.

Case report

A 56-year-old male with an unremarkable medical history presented with an acute onset of headache. The patient was of Chinese Han nationality and had no history of drug abuse or surgical treatment of craniocerebral diseases. The computed tomography (CT) obtained at the local hospital showed a grade 1 subarachnoid hemorrhage (SAH) on the modified Fisher scale (Figure 1A). After 6 days of conservative treatment, the patient was admitted to our hospital. CT was repeated and showed that the SAH had been absorbed (Figure 1B). CT angiography showed the arterial network of the right proximal MCA and an aneurysm on the A1 segment of the ACA (Figures 1C, D). The patient could correctly obey commands during the physical examination, and his condition was classified as grade I on the Hunt-Hess scale. The limb muscle strength was grade V, and the Babinski sign was positive in both lower limbs.

Then, endovascular coil embolization for the aneurysm was planned. During the treatment, digital subtraction angiography (DSA) confirmed that the right MCA was twig-like, an aneurysm with a diameter of 4 mm was located at the origin of the AccMCA from the A1 segment of the ACA, and the AccMCA was a collateral artery for the MCA twig (Figure 2). After the three-dimensional reconstruction of the DSA data, the best projection degree showed the aneurysm sac and its neck. An Echemon-10 microcatheter (Medtronic, Irvine, CA, USA) was used to perform the coiling [Axium Prime coils: 3.5 mm × 10 cm, 2 mm × 6 cm, 1.5 mm × 3 cm (Medtronic, Irvine, CA, USA)], and the aneurysm was completely embolized (Figures 3A, B).

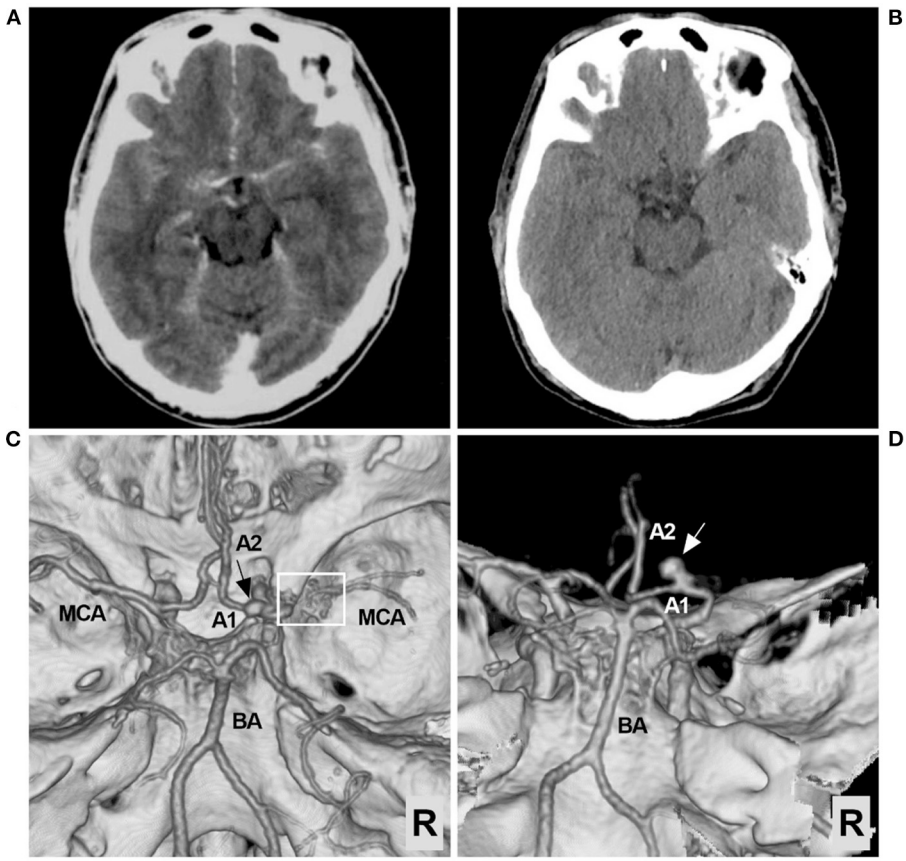

FIGURE 1
Preoperative CT and CTA images. **(A)** CT showing the extensive SAH, focusing on the left suprasellar cistern and the base of the Sylvian fissure. **(B)** Six days later, repeat CT showing absorption of the SAH. **(C)** CTA of the superior-inferior view showing the arterial network of the right proximal MCA (frame) and an aneurysm (arrow). **(D)** CTA of the posterior-anterior view showing the aneurysm in detail; the aneurysm (arrow) was located in the A1 segment of the ACA. ACA, anterior cerebral artery; A1, first segment of the ACA; A2, second segment of the ACA; BA, basilar artery; CT, computed tomography; CTA, CT angiography; MCA, middle cerebral artery; R, right; SAH, subarachnoid hemorrhage.

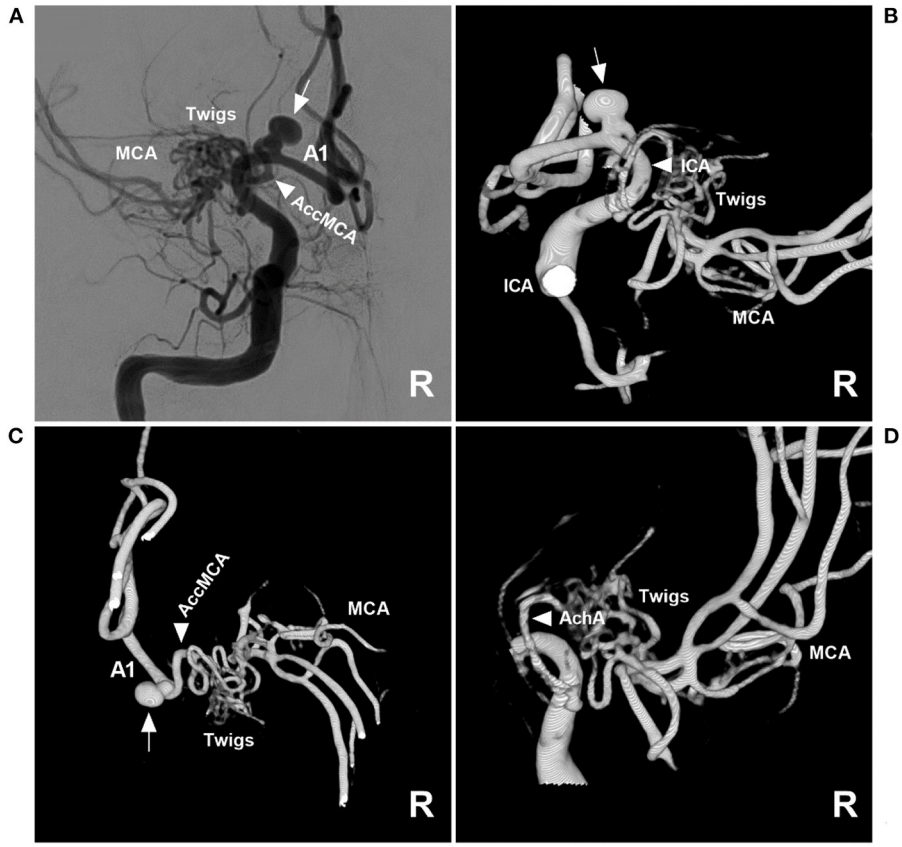

FIGURE 2
Angioarchitecture of twig-like MCA. **(A)** Two-dimensional DSA of the right ICA showing a right twig-like MCA and an aneurysm (arrow) at the origin of the AccMCA from the A1 segment. **(B)** Three-dimensional DSA showing that the ICA (arrowhead) did not give off the branch supplying the twig-like MCA; the arrow indicates the aneurysm. **(C)** Three-dimensional DSA showing the AccMCA (arrowhead) as a collateral artery from the A1 segment supplying the twig-like MCA; the arrow indicates the aneurysm. **(D)** Three-dimensional DSA showing that the AchA (arrowhead) supplies the twig-like MCA. A1, first segment; AccMCA, accessory middle cerebral artery; ACA, anterior cerebral artery; AchA, anterior choroidal artery; DSA, digital subtraction angiography; ICA, internal carotid artery; MCA, middle cerebral artery.

Postoperatively, the patient recovered uneventfully. One month later, the patient returned to his job without any neurological deficits. A postoperative CT at the 3-month follow-up showed that the brain tissue was normal (Figures 3C, D).

Discussion

MCA anomalies mainly included fenestration, duplication, AccMCA, and twig-like MCA, which occur less frequently than those of other major intracranial arteries (Figure 4) (6, 16–19). An MCA fenestration is defined as segmental duplication, presenting as a vessel with two distinct endothelium-lined channels (Figure 4A) (20). A duplicate MCA is a direct bifurcation near the internal carotid artery (ICA), lacking the essential bifurcation or trifurcation at the distal end of the M1 portion (Figure 4B) (21). AccMCAs are probably residual congenital arteries that can arise from the ACA at different locations, with an angiographic incidence of 0.3–0.4% (Figures 4C, D) (22–24).

AccMCAs are essential collateral arteries that supply the MCA territory. They can be classified into three types according to the original site, as follows: the ICA trunk (type 1), the proximal A1 segment (type 2), and the distal A1 segment or junction of the anterior communicating artery itself (type 3) (25). In our case, the AccMCA arose from the proximal A1 and was therefore classified as type 2 (Figure 2). Due to the hemodynamic stress of the collateral artery, aneurysms can occur at the origin of the AccMCA (26–29). Although they have rarely been reported, we found 20 cases of aneurysms at the origin of the AccMCA in our previous review (16).

Twig-like MCAs, as a rare anomaly, have a prevalence ranging from only 0.11 to 1.17% (30) and exhibit the following radiological features on DSA: an abnormal, plexiform, multiple-channel arterial network replacing the M1 segment; a nearly normal distal MCA caliber with anterograde blood flow; permissive collateral circulation from the ACA and posterior cerebral artery; lenticulostriate arteries arising from the twigs; and the absence of transdural collaterals (1, 30). The case presented in this report confirmed the angiographic diagnostic criteria of twig-like MCAs (Figure 2).

Twig-like MCAs can be supplied by many anomalous arteries, including the steno-occlusive MCA, anomalous branches originating from the A1 and A2 segments of the ACA, the

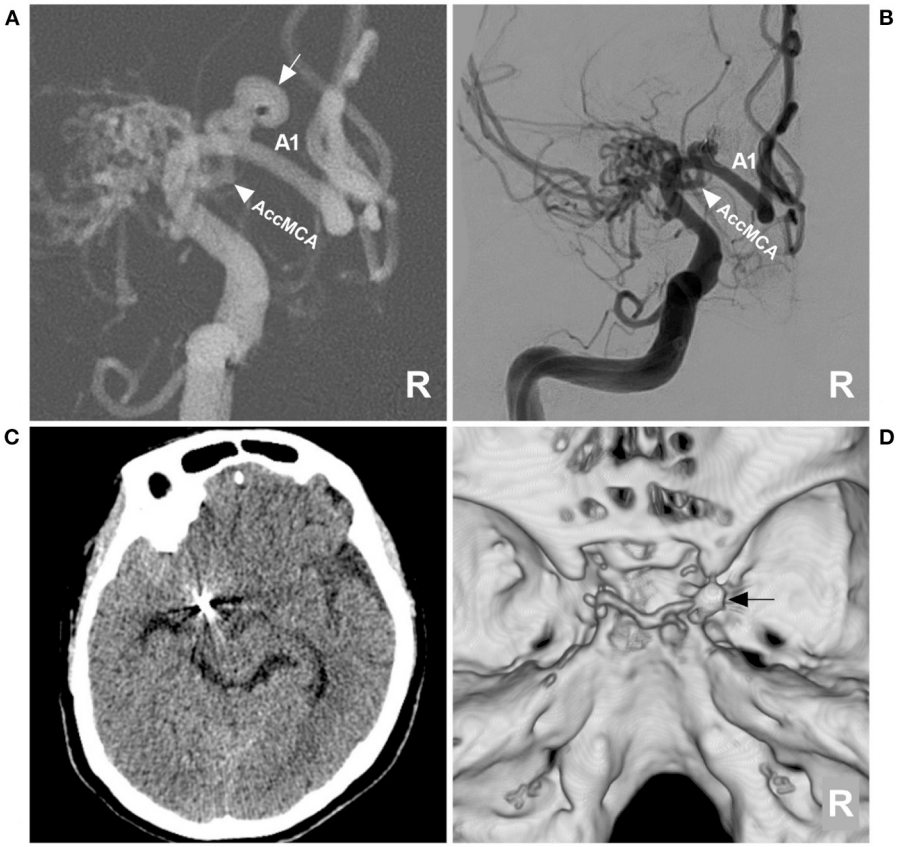

FIGURE 3
Aneurysm coiling and follow-up CT. **(A)** DSA roadmap navigation of the right ICA showing that the microcatheter was positioned into the aneurysm sac (arrow); the arrowhead indicates the AccMCA. **(B)** Postoperative DSA of the right ICA showing that the aneurysm was completely coiled and that the AccMCA (arrowhead) was preserved. **(C)** Follow-up CT showing normal brain tissue. **(D)** CT reconstruction showing the coils (arrow). A1, first segment; AccMCA, accessory middle cerebral artery; CT, computed tomography; DSA, digital subtraction angiography; ICA, internal carotid artery; MCA, middle cerebral artery; R, right.

AccMCA, the anterior choroidal artery (AchA), or the ICA terminus (Figures 4E, F) (3, 30). In our case, the main suppliers included AccMCA and AchA (Figure 2). With the AccMCA as a collateral artery of the twig-like MCA, an aneurysm can occur at its origin (31). Associated aneurysms are reported in nearly 40% of cases of twig-like MCAs, suggesting hemodynamic stress and structural vulnerability, and the aneurysms can be inside or outside the twig (3, 30, 32). In our case, the aneurysm at the AccMCA origin was outside the twig.

In the Serrano-Rubio et al. review in 2022, there were 42 cases in the international literature of aneurysms associated with twig-like MCAs, most of which were ruptured (31). In this report, although cases of aneurysms at the origin of the AccMCA were collected, the review was not as extensive. Due to the rarity of aneurysms at the AccMCA origin on the A1 segment, after updating the search data, seven cases, including ours, were collected and summarized in Table 1. These cases are as follows. In 1994, Han et al. reported a first case in which a concomitant twig-like MCA was combined with an aneurysm at the AccMCA originating from the ACA (5). Later, Cekirge et al. (6), Kim et al. (7), Sakai et al. (8), Fukuda et al. (9), and Soejima et al. (10) also reported similar cases in which the associated aneurysms were clipped or coiled, with good outcomes.

Treatment is necessary for aneurysms at the origin of the AccMCA, especially ruptured aneurysms. According to the International Subarachnoid Aneurysm Trial (ISAT) in 2005, clipping has shown superiority compared with coiling in preventing rebleeding in both the short and long term (13). However, at the 18-year follow-up of the UK cohort of the ISAT in 2015, although rebleeding was more likely after coiling than after clipping, the risk was low, and the probability of disability-free survival was significantly greater in the coiling group than in the clipping group at 10 years (14).

For aneurysms associated with twig-like MCAs, clipping may carry a risk of neurological complications because of the deep location and destruction of the collateral circulation. Therefore, considering the effect of the ISAT and its follow-up study (13, 14), when we found a saccular aneurysm of the neck that was not too wide, with a diameter of 4 mm, we determined endovascular coil embolization to be feasible and applied this strategy.

Although the endovascular coil embolization in our case was successful, we believed that the sharp upturning of the microcatheter from the ICA into the A1 aneurysm was still difficult and that the stabilization of the microcatheter was poor (15). Therefore, during coiling, soft coils, such as Axium Prime coils,

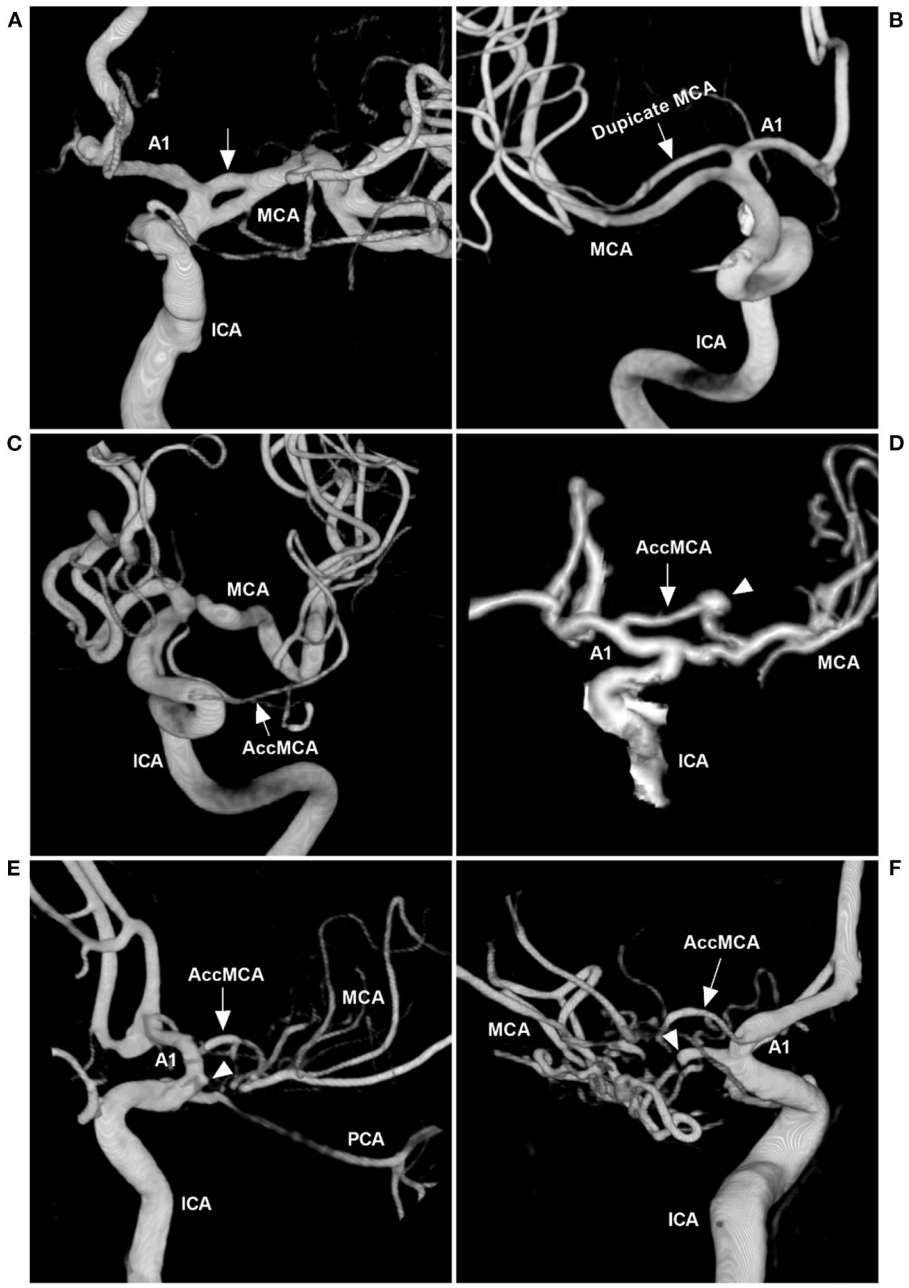

FIGURE 4
MCA anomalies on angiography. **(A)** Three-dimensional DSA of the ICA showing a fenestration (arrow) at the beginning of the MCA. **(B)** Three-dimensional DSA showing a duplicate MCA (arrow). **(C)** Three-dimensional DSA showing a type 1 AccMCA (arrow) from the ICA trunk. **(D)** Three-dimensional DSA showing a type 2 AccMCA (arrow) with complete anastomosis between the A1 middle segment and MCA forming a large fenestration; the arrowhead indicates an aneurysm. **(E)** Three-dimensional DSA showing a twig-like MCA supplied by the AccMCA (arrow) from the A1 end; the MCA did not supply the twig-like MCA, and the MCA origin presented with a protrusion (arrowhead). **(F)** Three-dimensional DSA showing that the twig-like MCA was supplied by the AccMCA from the A1 origin (arrow); the MCA supplied the twig-like MCA (arrowhead). A1, first segment; AccMCA, accessory middle cerebral artery; CT, computed tomography; DSA, digital subtraction angiography; ICA, internal carotid artery; MCA, middle cerebral artery; PCA, posterior cerebral artery.

are recommended to prevent the microcatheter from exiting the aneurysm too early, which would result in incomplete embolization and recurrence. For instance, in the report by Sakai et al. clipping had to be performed after coiling recurrence (8).

Therefore, in certain cases, the coiling of an aneurysm at the origin of the AccMCA as the collateral artery to a twig is feasible.

Limitations

As a result of the economic status in rural areas in China, after repeated requests, the patient only agreed to undergo a follow-up CT and refused to undergo an angiographic examination. Therefore, follow-up aneurysm embolization data could not be

TABLE 1 Clinical data from the literature review.

No.	References	Age/sex	Onset	AccMCA origin	Aneurysm location	Aneurysm size	Coiling or clipping	Other associated anomaly
1	Han et al. (5)	34/F	SAH	Close to A1 origin	Junction of AccMCA and A1 segment	4.5 mm	Clipping	No
2	Cekirge et al. (6)	32/M	SAH/IVH	Close to A1 origin	Junction of AccMCA and A1 segment	<5 mm	Coiling	No
3	Kim et al. (7)	64/F	SAH	Close to AcomA	Junction of AccMCA and A1 segment	<5 mm	Clipping	AcomA aneurysm
4	Sakai et al. (8)	65/F	SAH	Close to A1 origin	Junction of AccMCA and A1 segment	<5 mm	Clipping after coiling recurrence	Aneurysm in MCA twigs
5	Fukuda et al. (9)	60/F	SAH/IH	Middle A1	Junction of AccMCA and A1 segment	3.5 mm	Coiling	No
6	Soejima et al. (10)	63/F	Unruptured	Close to A1 origin	Junction of AccMCA and A1 segment	1.7 mm	Clipping and bypass	AcomA aneurysm
7	Present case	56/M	SAH	Close to A1 origin	Junction of AccMCA and A1 segment	4 mm	Coiling	No

AccMCA, accessory middle cerebral artery; AcomA, anterior communicating artery; A1, first segment of anterior cerebral artery; F, female; IH, intracerebral hemorrhage; IVH, intraventricular hemorrhage; M, male; MCA, middle cerebral artery; SAH, subarachnoid hemorrhage.

obtained. However, the aneurysm was saccular, and recanalization and regrowth were uncommon after complete initial coiling.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

JY contributed to the conception and design of the study. LZ and HS collected the data. JY and HS contributed to drafting the manuscript text and preparing the figures. LZ revised the manuscript. All authors have read and approved the final version of the manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Case report: Medulla oblongata and cervical cord reperfusion injury after intracranial vertebral artery angioplasty and stenting

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Background: White cord syndrome is an uncommon complication characterized by delayed neurologic deterioration with no other identified cause after spinal decompression surgery. Its etiology is attributed to spinal cord reperfusion injury. Here, we present the first case of an extended version of white cord syndrome, with concomitant involvement of the medulla oblongata and cervical cord reperfusion injury after intracranial vertebral artery angioplasty and stenting.

Case presentation: A 56-year-old male suffered an ischemic stroke in the right anteromedial medulla oblongata. Angiography revealed bilateral vertebral artery stenosis in the intracranial segment. We performed elective left vertebral artery angioplasty and stenting. An intraoperative flow arrest in the left VA occurred and was stopped after the withdrawal of the catheter. Several hours after the operation, the patient developed occipital headache, back neck pain, dysarthria, and worsening left-sided hemiplegia. Magnetic resonance imaging revealed hyperintensity and swelling in the medulla oblongata and cervical cord, in addition to small medullary infarction. A digital subtraction angiography revealed intact vertebrobasilar arteries and patency of the left vertebral artery, left posterior inferior cerebellar artery, and implanted stent. We considered that the reperfusion injury had caused the complication. After treatment, the patient's symptoms and neurologic deficits greatly improved. He achieved a favorable outcome at the 1-year follow-up, with normal intensity restored in the medulla oblongata and cervical cord on magnetic resonance imaging.

Conclusion: Concomitant reperfusion injury in the medulla oblongata and cervical cord secondary to vertebral artery angioplasty and stenting is extremely rare. However, this potentially devastating complication requires early recognition and prompt treatment. Maintaining the antegrade flow during vertebral artery endovascular treatment is a precaution against reperfusion injury.

KEYWORDS

medulla oblongata, cervical cord, reperfusion injury, white cord syndrome, vertebral artery, angioplasty, stenting, stroke

1. Introduction

White cord syndrome (WCS) is defined as an acute neurologic deterioration after spinal decompression surgery, mostly after cervical spine surgery. Typical magnetic resonance imaging (MRI) features include intramedullary hyperintensity on T2-weighted images representing cord edema, ischemia, swelling, and/or hemorrhage without any other extrinsic pathology (1). While reperfusion injury is its probable cause, WCS identification remains a diagnosis of exclusion (1, 2). Only one WCS case involving the medulla oblongata has been reported (3), and no report connecting WCS and endovascular treatment of the vertebral artery (VA) exists. Here, we report a case of delayed-onset medulla oblongata and cervical cord reperfusion injury in a patient exhibiting newly developed occipital headache, back neck pain, dysarthria, and worsening left-sided hemiplegia hours after successful left intracranial VA angioplasty and stenting. To our knowledge, this is the first report of simultaneous reperfusion injuries in the medulla oblongata and cervical cord related to VA endovascular treatment. This is also the first extended version of WCS, which is no longer limited to spinal cord lesions or spinal decompression surgery.

2. Case presentation

A 56-year-old male presented with worsening dizziness and left-sided hemiplegia overnight. The patient's medical history included 10-year-long hypertension and type 2 diabetes. The physical examination on admission revealed grade 0 muscle strength in the upper left extremity, grade 3 muscle strength in the lower left extremity, and left-sided hypoesthesia (Table 1). MRI demonstrated a new-onset ischemic stroke in the right anteromedial medulla oblongata (Figure 1A) and an old hemorrhage in the right medial pons. Computed tomography angiography (CTA) revealed bilateral VA stenosis in the intracranial segment (Figure 1B). Later digital subtraction angiography (DSA) confirmed this result, demonstrating a preocclusive (> 90%) narrowing of the left intracranial VA and tortuosity of the left VA (Figures 1C,D). We also found marked hypoperfusion in the brain stem and cerebella by computed tomography perfusion (Figure 1E). High-resolution MRI revealed atheromatous plaques in the stenotic segment of the left VA (Figure 1F). The patient's state had remarkably improved at discharge after treatment and rehabilitation.

After 50 days of rehabilitation, he was brought in for endovascular treatment. Physical examination on the second admission showed grade 4+ muscle strength in left extremities. Preoperative MRI revealed no new ischemic stroke. Five days after admission, the patient's left intracranial VA was recanalized under general anesthesia. A 90 cm 6F Neuronmax088 long sheath (Penumbra, Inc., Alameda, CA, USA) was introduced into the initial segment of the left subclavian artery. Angiography with a 115 cm 5F AXS Catalyst 5 distal access catheter (DAC) (Stryker Neurovascular, Michigan, USA) in the distal V2 segment revealed severe stenosis, dysplasia in the left posterior inferior cerebellar artery (PICA), and anastomosis supplying blood flow from the left VA to the cervical cord (Figure 2A). A concomitant clear visualization of the left VA and venous phase of the intracranial anatomy suggested that the DAC incompletely blocked blood flow (Figure 2B). A 2.25×9 mm Gateway balloon catheter (Stryker Neurovascular, Fremont, CA, USA) was delivered over a 300 cm synchro2 microguidewire (Stryker Neurovascular, Salt Lake, Utah, USA) to the site and slowly dilated to 7 atm. Post-angioplasty angiography revealed improvement of the stenosis and marked spasm of the left V3 segment (Figure 2C). The slow infusion of 1 mg of intra-artery nimodipine alleviated the spasms (Figure 2D). Next, a 4.5×14 mm Enterprise stent (Codman & Shurtleff, Inc., Raynham, MA, USA) was quickly and successfully implanted in the stenotic segment. The DAC was withdrawn immediately after the control run (Figure 2E). The final run showed only minor spasms in the initial segment of the left VA (Figure 2F). The patient showed no neurologic deterioration on awakening. Proper blood pressure was maintained using intravenous urapidil, while tirofiban was used to prevent acute stent thrombosis. Four hours later, the patient developed an occipital headache and back neck pain, mainly on the left side. Postoperative CT imaging revealed nothing significant.

However, at midnight, symptoms worsened, accompanied by dysarthria, left-sided hemiplegia, and elevated blood pressure (around

TABLE 1 Timeline of clinical, imaging and procedural data.

First admission	Worsening dizziness and left-sided hemiplegia; PE: grade 0 muscle strength in the upper left extremity, grade 3 muscle strength in the lower left extremity, and left-sided hypoesthesia
Day 8	Cerebral angiography
Day 15	Discharged with grade 4 muscle strength in left extremities
Second admission	PE: grade 4+ muscle strength in left extremities
Day 6	Left vertebral artery angioplasty and stenting
4 h after procedure	Occipital headache and back neck pain
10 h after procedure	PE: dysarthria, left-sided hemiplegia and elevated blood pressure
Day 7	MRI: acute infarction of the left posterior medulla oblongata on DWI and newly developed hyperintensity in the left medulla oblongata on T2 and FLAIR Cerebral angiography
Day 11	Cervical spine MRI: hyperintensity and swelling in the cervical cord
Day 37	MRI: near-normal intensity in the medulla oblongata and cervical cord
Day 38	Discharged with grade 4+ muscle strength in left extremities
1 year	Clinical, MRI and Computed tomography angiography imaging follow up

PE, physical examination; MRI, magnetic resonance imaging; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery.

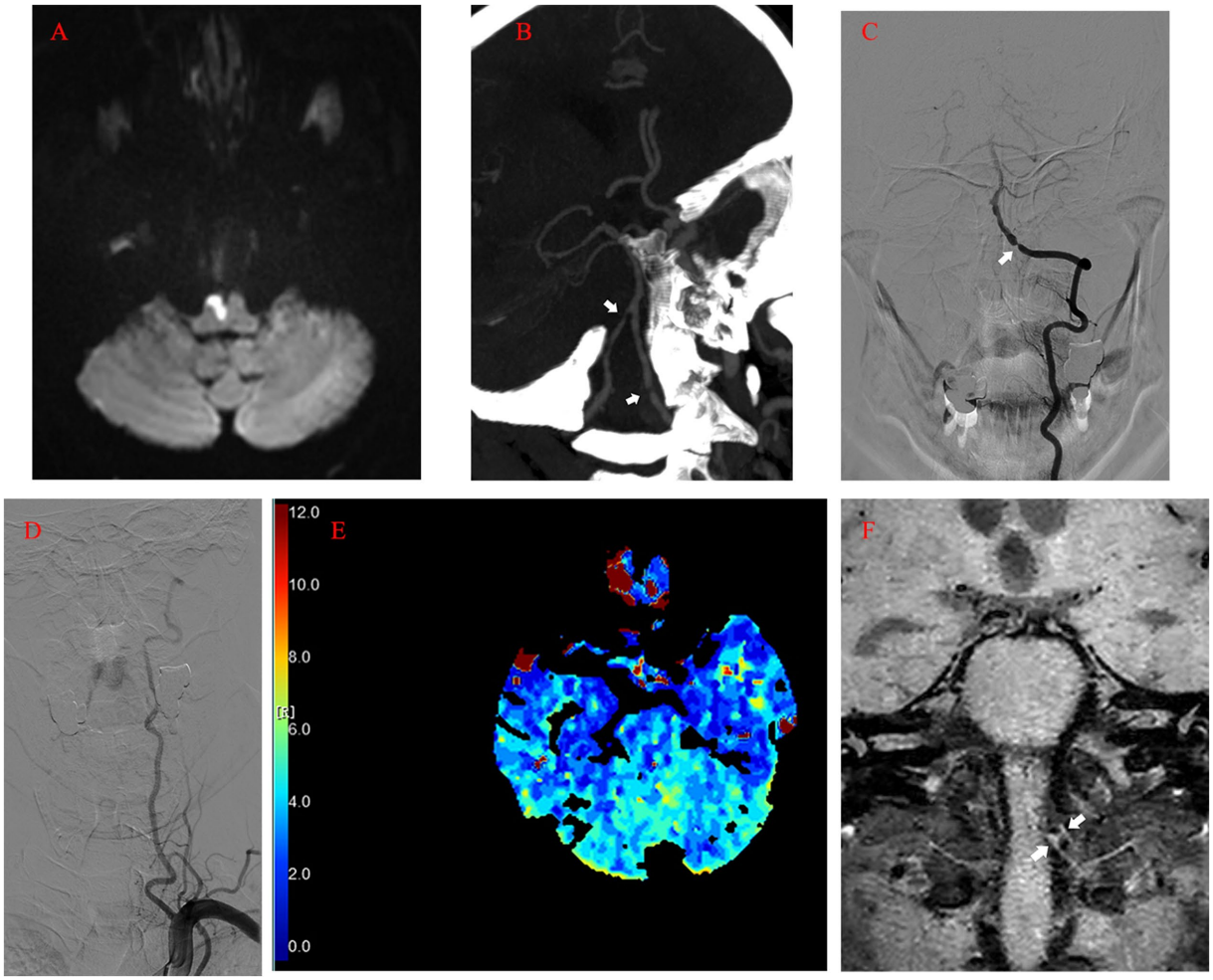

FIGURE 1
(A) Acute infarction of the right anteromedial medulla oblongata visualized by MRI (diffusion-weighted imaging). **(B)** Computed tomography angiography image showing the bilateral VA stenosis in the intracranial segment (arrow). **(C)** Left vertebral angiogram (anterior–posterior view) showing preocclusive stenosis of the left intracranial VA (arrow). **(D)** Tortuosity of the left VA revealed by angiogram. **(E)** Computed tomography perfusion showing the marked hypoperfusion in the brain stem and cerebella (Tmax). **(F)** High-resolution MRI showing atheromatous plaques (arrow) in the stenotic segment of the left VA (coronal view). MRI, magnetic resonance imaging; VA, vertebral artery; Tmax, Time to Max.

170/100 mmHg) (Table 1). Again, CT imaging showed no marked changes, while MRI revealed acute infarction of the left posterior medulla oblongata on the next morning (Figure 3A). In addition to the new infarction, T2-weighted and fluid-attenuated inversion recovery (Flair)-weighted images showed newly developed hyperintensity in the left medulla oblongata. Subsequent DSA demonstrated intact vertebrobasilar arteries and patency of the left VA, left PICA, and implanted stent (Figure 3B). To regulate blood pressure, we added an intravenous infusion of esmolol. We used Tirofiban for another 24 h before switching to routine dual antiplatelet treatment with 100 mg aspirin and 75 mg clopidogrel per day. The patient received an intravenous injection of 40 mg methylprednisolone twice per day, along with glycerol fructose and edaravone injections. Three days later, T2 and Flair images showed more profound hyperintensity in the left medulla oblongata (Figure 3C). One day later, a cervical spine MRI (T2 images) revealed unexpected findings of similar hyperintensity and swelling in the cervical cord (Figure 3D). We added an intravenous infusion of mannitol to ameliorate medulla oblongata and cord edema and started early rehabilitation.

Ten days after the operation, MRI still showed marked hyperintensity in the medulla oblongata and cervical cord, while the patient's symptoms and neurologic deficits gradually improved (Figures 3E,F). The final MRI before discharge showed near-normal intensity in the medulla oblongata and cervical cord, with only slight hyperintensity in the left region. At the 1-year follow-up, MRI showed normal intensity in the medulla oblongata and cervical cord, except for the old lesions (Figures 4A,B). Both VAs remained patent on the CTA (Figure 4C). The patient achieved a favorable outcome, with a modified Rankin scale score of 2. The physical examination revealed normal speech, grade 5 muscle strength in left limbs, and slightly increased muscle tone in the upper left limb.

3. Discussion

WCS is uncommon after cervical or thoracic spinal decompression surgery but potentially devastating (4). WCS is a possible explanation for delayed deterioration with no cause identified (5). We define our

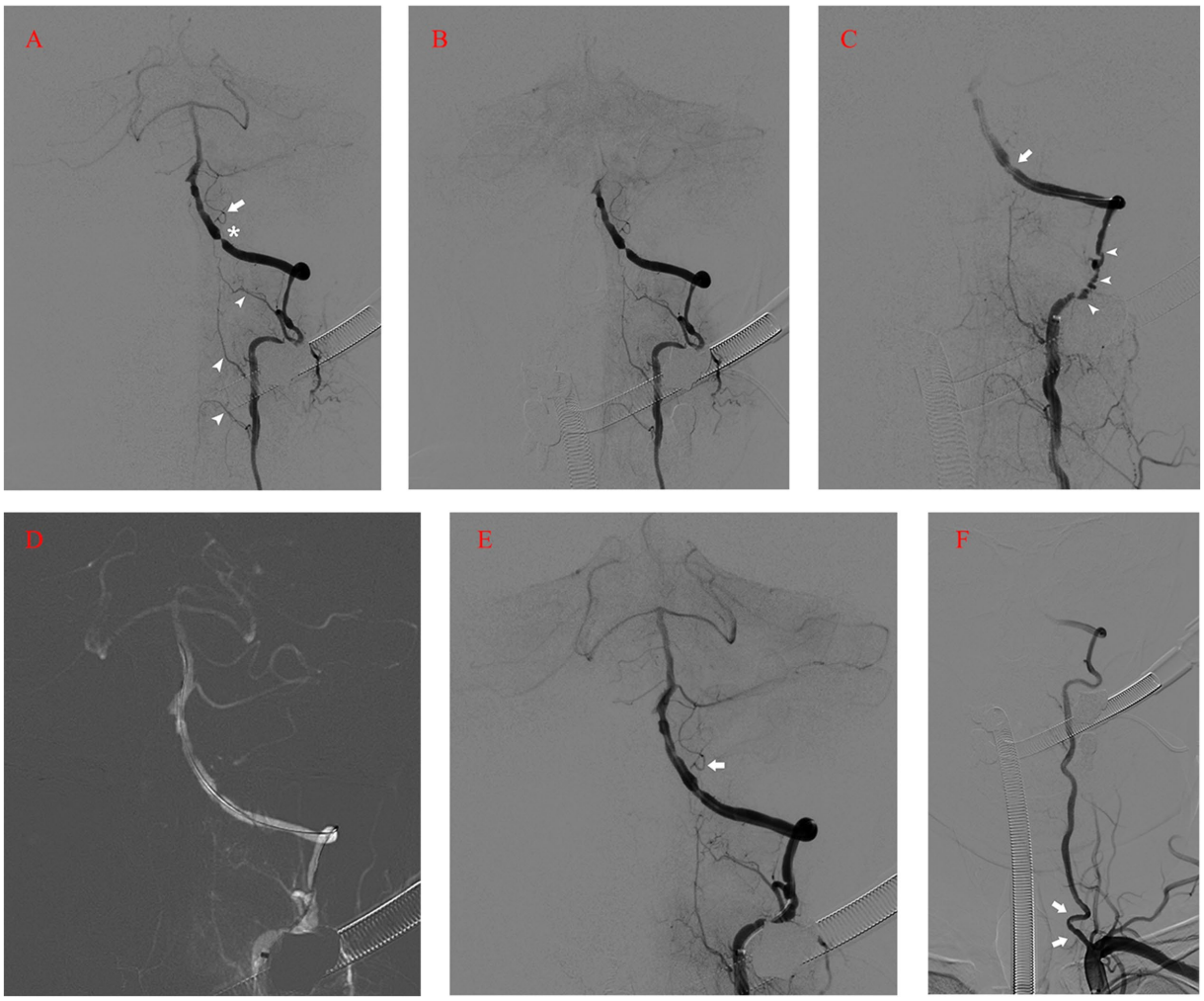

FIGURE 2
(A) Angiography with DAC in the distal V2 segment revealing severe stenosis (asterisk), dysplasia in the left PICA (arrow), and anastomosis supplying blood flow from the left VA to the cervical cord (arrowhead). **(B)** Left vertebral angiogram showing the venous phase of the intracranial anatomy and left VA flow arrest. **(C)** Post-angioplasty angiography revealing the improvement of the stenosis (arrow) and marked spasm of the left V3 segment (arrow-head). **(D)** Roadmap after intra-artery nimodipine showing the spasm mitigation process. **(E)** Control run after the deployment of Enterprise stent showing the patency of the left VA and PICA (arrow). **(F)** The final run showing the minor spasms in the initial segment of the left VA (arrow). DAC, Distal Access Catheter; PICA, Posterior Inferior Cerebellar Artery; VA, Vertebral Artery.

case as an extended version of WCS because the complication happened after VA endovascular treatment rather than after spinal surgery. The patient presented no new neurologic deficit until hours after the operation. Furthermore, to our best knowledge, the concomitant involvement of the medulla oblongata and cervical cord is rare. Using PubMed, we found one single case of WCS involving both the medulla oblongata and cervical cord. In that report, a cervical extramedullary metastatic ductal carcinoma led to cord compression and extended into both C3 neural foramina (3). Although the author did not mention why medulla oblongata was involved, we think that the removal of the tumor and decompression might have recanalized the VA and reperfused part of the medulla oblongata. The etiology of WCS is attributed to a sudden increase in blood supply to the spinal cord after decompression. The subsequent compromise of the blood–brain barrier and the blood-spinal cord barrier results in reperfusion injury (3). On the one hand, our case, in the absence of direct cord manipulation, demonstrates that inappropriate manipulation is not a causative factor of WCS in spinal decompression surgery (6). On the other hand, the underlying mechanism of our case needs further investigation due to the lack of surgical decompression.

Matsubara reported a case of ruptured VA dissecting aneurysm treated with internal trapping. The patient developed concomitant medulla oblongata and cervical cord infarction postoperatively, with a poor outcome. The author attributed the complication to the obstruction of perforating arteries supplying the medulla oblongata and ischemia of the spinal artery branches originating from the left VA (7). The upper medulla oblongata is supplied by a pair of anterior spinal arteries originating from the VA. The lateral region of the medulla oblongata is perfused by PICA or VA, while the posterior part is perfused by the posterior spinal artery, which originates from the VA or PICA (8). Tsuruta et al. found that intraoperative proximal flow arrest was performed in all four symptomatic infarction cases of VA dissecting aneurysm embolization. They believe that a long segmental flow arrest carries the risk of collateral circulation insufficiency and

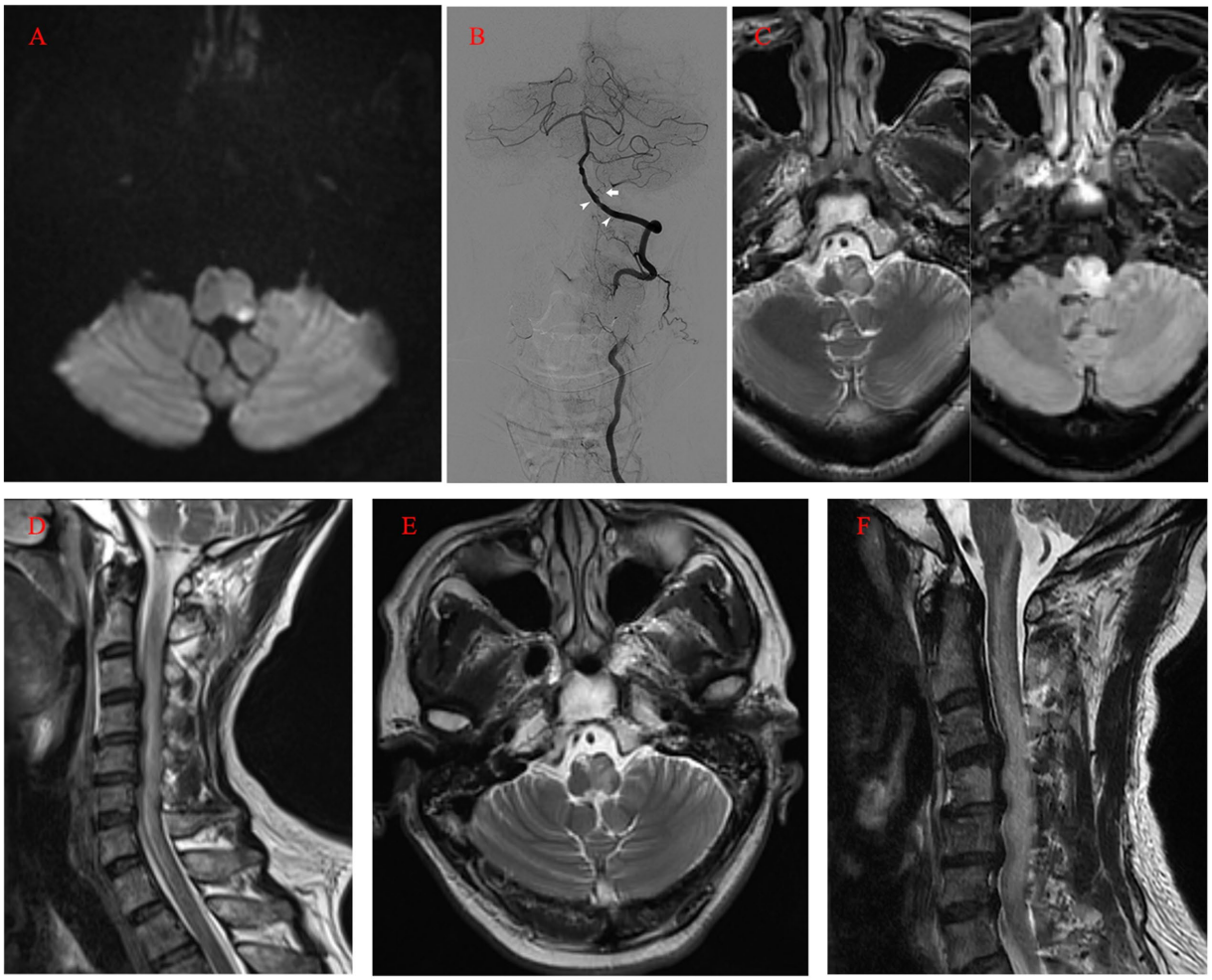

FIGURE 3
(A) MRI (diffusion-weighted imaging) on the first day after the operation showing the acute infarction of the left posterior medulla oblongata. **(B)** Postoperative angiogram showing the intact vertebrobasilar arteries and patency of the left VA, left PICA (arrow), and implanted stent (arrowhead). **(C)** MRI (T2 and FLAIR images) on the fourth day after the operation revealing profound hyperintensity in the left medulla oblongata. **(D)** Cervical spine MRI on the fifth day after the operation revealing similar hyperintensity and swelling in the cervical cord (T2). **(E, F)** Ten days after the operation, MRI still revealed hyperintensity in the medulla oblongata and cervical cord. MRI, magnetic resonance imaging; VA, Vertebral Artery; PICA, Posterior Inferior Cerebellar Artery; FLAIR, Fluid-Attenuated Inversion Recovery.

thromboembolism, resulting in medulla oblongata and cervical cord infarction (9). We used DAC to provide both steady proximal support and proximity to stenosis during the operation. However, blood flow was arrested in a long VA segment (Figure 2B) due to its tortuosity. Although we rapidly withdrew the DAC after the quick and necessary manipulations and restored blood flow (Figure 2E), reperfusion injury was initiated instead of complete infarction.

Therefore, in our case, all the branches mentioned above, supplying the left medulla oblongata and cervical cord, might have been affected due to the flow arrest in the left VA. It is likely that the temporary obstruction of perforating, anterior spinal, and posterior spinal artery branches arising from the left VA, resulting from the flow arrest by the DAC through tortuous vasculature, led to a short ischemia period and subsequent reperfusion injury. Notably, after the pass of the balloon catheter, we observed significant spasms in the V3 segment (Figure 2C). Although intra-artery nimodipine mitigated the spasms, this minor reperfusion process might have caused injury as well. The dual reperfusion may be the cause of our rare case. Either a part of the collateral network remained compromised and led to acute infarction of the left posterior medulla oblongata, or the long segmental flow arrest caused thromboembolism. The posterior spinal artery has rich collateral networks and a smaller risk of infarction (10). Although we did not perform a more complex spine MRI with diffusion-weighted imaging, we believe that the cervical cord underwent only a minor infarction based on the follow-up MRI (Figure 4B) and the patient's quick recovery and good outcome. Maintaining antegrade flow during VA endovascular treatment is crucial to prevent intraoperative infarction and postoperative reperfusion injury. Although the flow arrest should have affected the left PICA, we found no infarction or reperfusion injury in the left cerebellar on postoperative MRI because the major blood supply of the patient's left cerebellar came from the right PICA. Tanoue et al. evaluated anatomical variations of perforating arteries from VA using three-dimensional DSA. They found that non-PICA VAs give off a larger number of perforators than other types, indicating a higher risk of ischemic stroke with trapping (11). In our case, the left PICA was

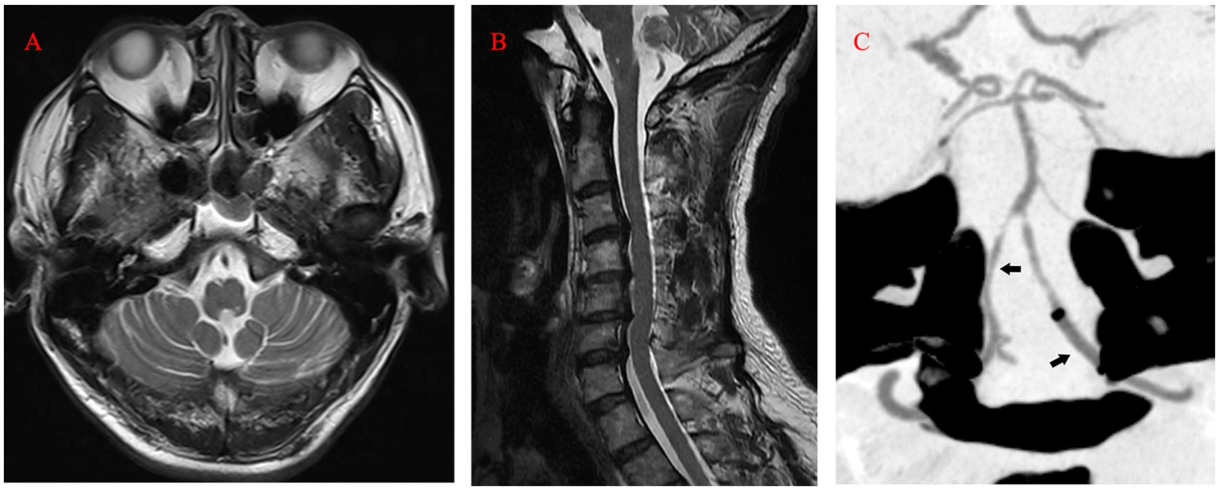

FIGURE 4
(A, B) At the 1-year follow-up, MRI (T2) showed normal intensity in the medulla oblongata and cervical cord. **(C)** Computed tomography angiography revealing the patency of both VAs (arrow). MRI, magnetic resonance imaging; VA, Vertebral Artery.

hypoplastic and, similar to non-PICA VAs, had a potentially higher risk of infarction and reperfusion injury secondary to VA flow arrest.

Cerebral hyperperfusion syndrome (CHS) after angioplasty or stenting for intracranial artery stenosis is a rare but severe complication. CHS is characterized by headaches, seizures, and neurologic deficits not caused by cerebral ischemia. Since it impairs cerebral autoregulation, CHS can present as cerebral edema, hemorrhage, or subarachnoid hemorrhage (12). In our case, the postoperative hyperintensity region was not located exactly downstream of the VA stenosis. If CHS had been the cause of the complication, the downstream regions such as the pons, midbrain, left cerebella, and left occipital lobe should have been affected.

The precise mechanism of WCS remains unclear but probably involves oxygen free radicals, lipid peroxidation, inflammation, and specific signal cascades (13–16). In our case of extended WCS, intraoperative flow arrest and restoration may have triggered a similar pathophysiological process. Therefore, we managed the complication based on the mechanism mentioned above. In an attempt to mitigate medulla oblongata and cervical cord edema, we administered methylprednisolone. A high dose might have enhanced early recovery by inhibiting inflammation and lipid peroxidation (17, 18). Nevertheless, considering gastrointestinal bleeding and hyperglycemia risks, we preferred a low methylprednisolone dose. Edaravone, a free radical scavenger, may have played a role in the patient's recovery as well. Suzuki et al. reported that edaravone protected against spinal cord ischemia–reperfusion injury in a rabbit model by reducing free radical species levels (19). Edaravone also protects against cerebral reperfusion injury *via* oxidative stress and a specific signal pathway involving mitochondrial dysfunction and apoptosis (20). Previous reports recognize physical therapy as an important treatment modality for injury and weakness (2). In our case, because the patient's respiratory and cardiac rhythm remained in the normal range despite the swelling of the left medulla oblongata, we started inpatient physical therapy four days after the complication occurrence. Next, long-term outpatient rehabilitation brought further functional improvement.

4. Conclusion

Concomitant reperfusion injury in the medulla oblongata and cervical cord is extremely rare after VA angioplasty and stenting. Nevertheless, clinicians should be fully aware of this rare but potentially devastating complication and maintain antegrade flow during VA endovascular treatment. Moreover, this complication should be added to informed consent forms, for precaution.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

Written informed consent was obtained from the participant/patient(s) for the publication of this case report.

Author contributions

GW: manuscript writing. GW, BZ, and ZY: operation. GW, JH and JJ: data acquisition. GX and ZY: review and editing. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

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Case report: A choroidal fissure pial arteriovenous malformation inducing venous congestive edema of the medulla oblongata and cervicothoracic spinal cord presented with proximal arm predominant weakness

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Intracranial dural arteriovenous fistula (DAVF) can induce remote myelopathy *via* spinal perimedullary venous drainage. In the present study, we report a rare case of intracranial pial arteriovenous malformation (AVM)-related myelopathy. A 52-year-old man presented with progressive, predominantly proximal weakness and muscle atrophy in bilateral upper limbs, urinary retention, and hyperreflexia in bilateral upper and lower limbs. Brain and cervicothoracic MRI showed longitudinal myelopathy extending from the medulla oblongata to the T6 level, with perimedullary enlarged veins from the C1 to T12 level, and remarkable enhancement in bilateral anterior horns from the C2 to C7 level. Cerebral angiography revealed a choroidal fissure AVM, which was supplied by the left anterior choroidal artery and drained exclusively by an inferior ventricular vein descending toward the spinal perimedullary veins. After endovascular embolization of the feeding pedicle, nidus, and proximal segment of the draining vein, the patient's neurological deficits rapidly improved, and a significant recovery was achieved 3 months after the procedure. This rare case indicates that intracranial pial AVM can also cause extensive congestive myelopathy with similar mechanisms underlying intracranial and craniocervical DAVF cases, and gray matter in the spinal cord might be more susceptible to ischemia induced by intraspinal venous hypertension.

KEYWORDS

choroidal fissure, intracranial arteriovenous malformation, myelopathy, interventional treatment, intracranial dural arteriovenous fistula

Highlights

- Intracranial pial AVM with spinal venous drainage can cause extensive congestive myelopathy.
- Contrasted MRI images suggest that the gray matter of the spinal cord might be more susceptible to ischemia caused by intraspinal venous hypertension.

Introduction

A series of case studies have demonstrated that intracranial dural arteriovenous fistula (DAVF) with spinal venous drainage can cause extensive myelopathy (1–4). Most of them are infratentorial, and few are supratentorial (3, 5). The supratentorial DAVF was drained downward into the perimesencephalic veins, the superior petrosal veins, and finally the anterior and posterior spinal veins (3, 6). Here, we present a rare case of a choroidal fissure pial arteriovenous malformation (AVM) with exclusive spinal venous drainage that induced venous congestive edema of the medulla oblongata and the cervicothoracic spinal cord. To the best of our knowledge, only one case of infratentorial trigeminal nerve root pial AVM-associated myelopathy has been reported, whereas no cases of supratentorial pial AVM-causing myelopathy have been described (7). In contrast to the intracranial DAVF, in which patients mainly present with ascending myelopathy (1–5), our patient presented with pronounced arm weakness with minimal leg involvement 2 months after the onset of symptoms. The likely underlying mechanisms of this unusual manifestation are discussed further in the article.

Case presentation

A previously healthy 52-year-old man initially presented with fluctuating neck tightness and predominantly proximal weakness in bilateral arms, which worsened at night and almost disappeared in the morning. Within 1 month, his symptoms became persistent and caused a deterioration in his activities. He also developed urinary retention. He was admitted to our hospital approximately 2 months after the onset of symptoms when he could not dress himself. Neurological examination revealed muscular atrophy of bilateral proximal upper limbs. Based on the Medical Research Council (MRC) scale, muscle strength was graded 2/5 on shoulders, 3/5 in proximal and 4/5 in distal upper limbs, respectively, and 5/5 in the left and normal in the right lower limb. There was hyperreflexia in four extremities, with clonus present in both ankles. There were no signs of pathological reflexes nor sensory deficits, ataxia, dysarthria, or dysphagia.

Blood and cerebral spinal fluid (CSF) routine and immunological tests were unremarkable, except for a slightly increased CSF protein level of 627.5 mg/L (normal range: 150–450 mg/L). Magnetic resonance imaging (MRI) revealed extensive longitudinal swelling of the medulla oblongata and cervicothoracic spinal cord with enlarged abnormal perimedullary tortuous vessels and notable enhancement in bilateral cervical anterior gray matter (Figures 1A–E). Source images of the brain CT angiogram showed a large abnormal vessel connected to a vascular cluster adjacent to the inferior horn of the left lateral ventricle (Figure 2A). 3D volume reconstructing images of brain CT angiogram (Figure 2B) and cerebrospinal angiography (Figures 3A, B) showed a micro-AVM on the choroidal fissure close to the left cerebral ventricular wall, which was supplied by the left anterior choroidal artery and drained exclusively by an inferior ventricular vein, connecting to the basal vein of Rosenthal, the lateral mesencephalic vein, the superior petrosal vein, then the middle cerebellar peduncle vein, and finally the anterior and posterior spinal veins, descending toward lower thoracic spinal cord (Supplementary Videos 1, 2). The left superior petrous sinus was considered to be occluded since it was not opacified in carotid and vertebral angiographies.

The AVM was treated by endovascular embolization using 18% diluted N-butyl-2-cyanoacrylate (NBCA). The feeding pedicle, nidus, and proximal segment of the draining vein were completely obliterated (Figure 3C).

After the procedure, his neck tightness significantly improved, and he was able to lift his arms and dress himself within 1 week. After 2 months, his upper limb weakness had almost completely resolved, with hyperreflexia still present in the upper and lower limbs. MRI follow-up showed a marked decrease in T2 hyperintensity in the spinal cord as well as the resolution of the abnormal perimedullary flow voids (Supplementary Figures 1A, B). His urinary retention was completely resolved 3 months after the procedure. An angiographic follow-up showed complete obliteration of the AVM (Supplementary Videos 3, 4). An MRI follow-up 9 months after the procedure showed a complete disappearance of T2 hyperintensity in the cervical spinal cord (Supplementary Figure 1C).

Discussion

Similar to those shown in intracranial DAVF cases with spinal venous drainage (1–6), cervicothoracic MRI in the current case showed venous congestive edema of the medulla oblongata and spinal cord, as well as perimedullary dilated tortuous vessels. Cerebrospinal angiography revealed a choroidal fissure pial micro-AVM with spinal venous drainage, which was considered to be the cause of extensive myelopathy. To the best of our knowledge, this is the first case of supratentorial pial AVM which leads to remote myelopathy.

Shimizu et al. (8) reported one case of anterior cranial fossa DAVF causing venous congestion of the brain stem and spinal cord. The shunt drained into the olfactory vein, basal vein, lateral mesencephalic vein, superior petrous vein, and spinal veins. The superior petrous sinus was occluded. Our case revealed a similar venous drainage route, except that the pial arteriovenous shunt initially drained to an inferior ventricular vein and then to the basal vein of Rosenthal. The superior petrous sinus was also occluded in our case. Surgical anatomic studies have demonstrated that lateral mesencephalic veins connect the basal vein to the superior petrosal vein/sinus, which may permit venous drainage from supratentorial structures directly into the superior petrosal sinus (9). We postulate that the anastomosis role of the lateral mesencephalic vein and occlusion of the superior petrosal sinus are the key factors for the exclusive spinal drainage of this supratentorial AVM case. This rare case has helped us gain insight into a unique mechanism associated with intracranial pial arteriovenous shunt-related congestive myelopathy.

Intracranial and spinal arteriovenous shunts with spinal venous drainage can lead to hypertension in the spinal perimedullary venous plexus and then in the spinal intramedullary veins (2, 3, 6). Consequently, the intraspinal arteriovenous pressure gradient is reduced, resulting in decreased tissue perfusion. Edema, ischemia, degeneration, and necrosis of the spinal cord, and rarely subarachnoid hemorrhage, may develop (10). In several autopsies,

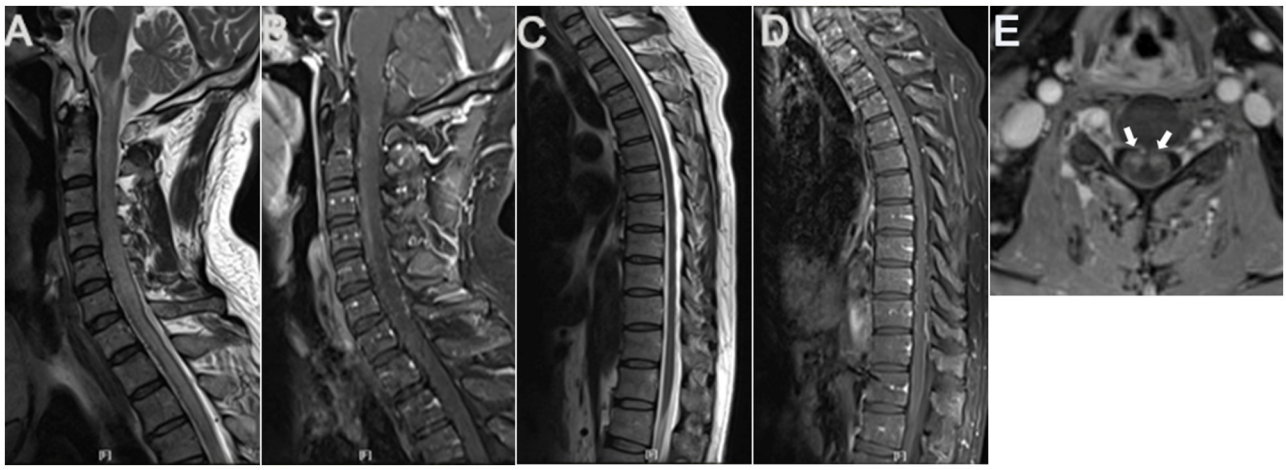

FIGURE 1
Cervicothoracic MRI. Sagittal cervicothoracic MRI T2-weighted images revealed longitudinal swelling of the medulla oblongata and cervicothoracic spinal cord extending to T6 level **(A, C)**, with apparent abnormal flow void signals in the anterior surface of the cervical spinal cord **(A)**. Contrasted MRI showed anterior and posterior perimedullary dilated tortuous veins from the cervical to T12 level **(B, D)**, apparent enhancement in cervical spinal anterior horns on both sides (arrows) **(E)**, and patchy enhancement in the whole cervicothoracic spinal cord **(B, D)**.

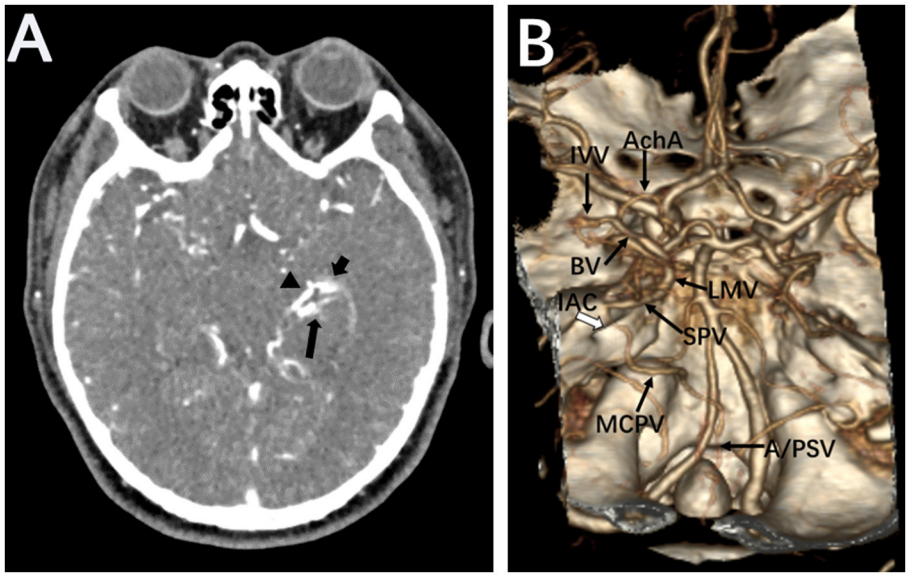

FIGURE 2
Brain CTA. Source images of brain CTA showed a large abnormal vessel (arrowhead) connecting to a vascular cluster close to the inferior horn of the left lateral ventricle (short arrow). The left posterior cerebral artery was also disclosed (long arrow) **(A)**. Volume reconstruction of CTA revealed the supplied artery and drainage veins of the micro-AVM on the choroidal fissure **(B)**. anterior choroidal artery, AchA; inferior ventricular vein, IVV; basal vein of Rosenthal, BA; lateral mesencephalic vein, LMV; superior petrosal vein, SPV; middle cerebellar peduncle vein, MCPV; anterior and posterior spinal veins, A/PSV; internal auditory canal, IAC.

severe dilation of perimedullary and intraspinal veins and arteries as well as gray matter-predominant necrosis was observed. In line with the abovementioned reports, the contrasted cervical MRI of our case also revealed a significant enhancement of bilateral gray matter. These findings indicate that spinal vein hypertension plays a key role in this process and that gray matter is more susceptible to ischemia when compared to white matter (11).

In our case, the pial AVM-induced longitudinal myelopathy mainly caused symptoms in the upper limbs. The spectrum of the clinical manifestation, in this case, is different from that in most cranial or spinal DAVF-related myelopathy cases, which tend to cause more pronounced weakness in the lower limbs than the upper ones (1, 3, 5, 6). In addition to the diffuse, patchy enhancement of the spinal cord, contrasted MRI showed the focal enhancement of bilateral cervical anterior gray matter, which may explain his symptoms of arm predominant weakness. The potential mechanism needs further investigation.

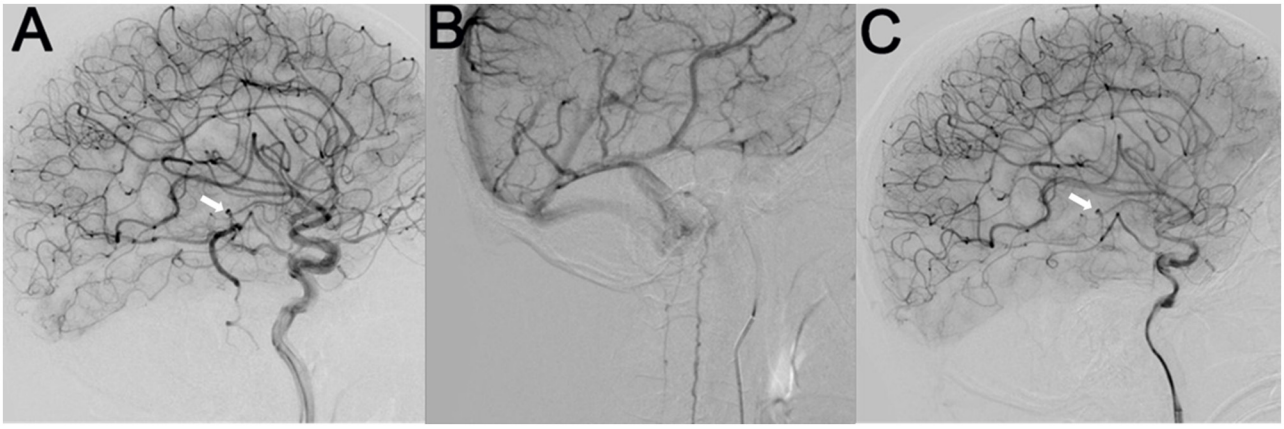

FIGURE 3
Cerebral angiography indicated a micro-AVM (arrow) supplied by the left anterior choroidal artery branch, which drained downward through a sole large vein into the anterior and posterior spinal veins **(A, B)**. After the endovascular embolization of the AVM, the draining veins completely disappeared **(C)**.

Conclusion

Pial AVM can be a rare cause of extensive congestive myelopathy, with similar mechanisms underlying those reported cases of cranial DAVF-associated myelopathy. Gray matter in the spinal cord may be susceptible to ischemia induced by intraspinal venous hypertension. The complete obliteration of the arteriovenous shunt before irreversible damage occurs is crucial for a favorable prognosis.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Beijing Hospital. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the patient for the publication of any potentially identifiable images or data included in this article.

Author contributions

YJ and JL instructed the patient's diagnosis and treatments and followed the patient. YJ drafted the manuscript. YZ, XY, and AS assisted in the patient's diagnosis and treatment. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1128366/full#supplementary-material

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Long-term outcomes of coils embolization for superior hypophyseal artery aneurysms

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Objective: Superior hypophyseal artery (SHA) aneurysms are intradural, and their rupture can result in subarachnoid hemorrhage. Considering the related surgical difficulty and anatomical restrictions, endovascular treatment (EVT) is considered the most favorable modality for SHA aneurysms; however, the long-term outcomes of EVT have rarely been reported. The study assessed the incidence of and risk factors for recurrence of SHA aneurysms after EVT as well as the correlation factors for SHA aneurysm rupture.

Methods: We included 112 patients with SHA aneurysms treated with EVT at our facility between 2009 and 2020. Here, EVT included non–stent-assisted (simple or balloon-assisted) or stent-assisted coiling. Flow diverter was not included because it was barely used due to its high cost under our national insurance's limitation, and a high proportion of ruptured aneurysms in our series. Univariate and multivariate logistic regression was performed to evaluate the correlation factors for SHA aneurysm rupture, along with the incidence of and risk factors for post-EVT SHA aneurysm recurrence and re-treatment.

Results: In our patients, the mean angiographic follow-up period was 3.12years. The presence of type IA or IB cavernous internal carotid artery (cICA) was strongly correlated with SHA aneurysm rupture. Recurrence occurred in 17 (13.4%) patients, of which only 1 (1.4%) patient had received stent-assisted coiling. All cases of recurrence were observed within 2years after EVT. The multivariate logistic regression results showed that ruptured aneurysm and non–stent-assisted coiling were independent risk factors for aneurysm recurrence. Of the 17 cases of aneurysm recurrence, 9 (52.9%) received re-treatment. Moreover, aneurysm rupture was the only factor significantly correlated with re-treatment in multivariate logistic regression. No re-recurrence was observed when a recurrent aneurysm was treated with stent-assisted coiling.

Conclusion: Type I cICA was common factor for aneurysm rupture. Although flow-diverter treatment serves as another suitable technique that was not compared with, coils embolization was effective treatment modality for SHA aneurysms, leading to low recurrence and complication rates, especially with stent use. All cases of recurrence occurred within 2years after EVT; they were strongly associated with prior aneurysm rupture. Further stent-assisted coiling was noticed to prevent re-recurrence.

KEYWORDS

stent-assisted coiling, coils embolization, aneurysm recurrence, superior hypophyseal artery, intracerebral aneurysm

Introduction

The superior hypophyseal artery (SHA) originates from the internal carotid artery (ICA) between the ophthalmic and posterior communicating (P-com) artery (1). The origin of SHA aneurysms is typically distal to the distal dural ring; therefore, SHA aneurysms are intradural, and their rupture may result in a subarachnoid hemorrhage (SAH) (2). However, most studies have included SHA aneurysms – with clinoidal, carotid cave, and ophthalmic aneurysms – among paraclinoid aneurysms (1, 3, 4), which are considered to have a low rupture rate (5, 6).

Although research on the characteristics and treatment outcomes of endovascular treatment (EVT) for SHA aneurysms has been scant, the rupture risk is higher for SHA aneurysms than for paraclinoid aneurysms (5, 7). Moreover, SHA aneurysm rupture can lead to SAH, which has detrimental clinical outcomes (8). Timely SHA aneurysm treatment is therefore necessary, and so the research article that focuses on SHA aneurysms is worth studying.

In paraclinoid aneurysm treatment, surgical clipping is considered challenging due to the related anatomical restrictions along with the adjacent delicate bony and neurovascular structures (1), which has been found to lead to high complication and mortality rates (9). EVT has consequently become the mainstream treatment modality for paraclinoid aneurysms because of its treatment safety and efficacy (1, 10). In addition, patient preference, short operative time and reducing length of stay have shifted the trend of paraclinoid aneurysm treatment toward this less-invasive technique (11).

Research on SHA aneurysms with respect to aneurysm characteristics, treatment options, and long-term follow-up has been scant. Nevertheless, Chalouhi, Tjoumakaris (7) assessed the safety and efficacy of coils embolization for SHA aneurysms, but its average follow-up period was <1 year (i.e., 10.4 months). Furthermore, the authors' study was observational and lacked any statistical analysis due to a low event number.

Here, we analyzed the features of SHA aneurysms and identified the predictors for their recurrence and re-treatment after EVT. To the best of our knowledge, this is the largest retrospective case–control study with the longest follow-up duration on EVT for SHA aneurysms. The current results may facilitate the design of personalized EVT.

Materials and methods

Patient population

We reviewed our aneurysm database for all patients with SHA saccular aneurysms who underwent EVT from January 2009 to December 2020. Aneurysms associated with fusiform dilatation or dolichoectatic change of the ICA were excluded from this study. In this study, we only focus on endovascular treatment (EVT) because surgical clipping is rarely applied in recent years at our facility since extending the exposure of skull base may damage adjacent neurovascular structures (1), and based on previous literature (7) we believe EVT nowadays has become the mainstream treatment modality that offers safe and satisfactory results. Patients who underwent flow-diverter treatment were also excluded because flow diverter is costly and our national insurance only covers multiple and giant aneurysms regardless of aneurysm location. Also, the nature of numerous ruptured cases in the study made flow-diverter unsuitable for these patients. Finally, 112 patients (23 males and 89 females) who underwent 128 sessions of treatment for SHA aneurysms were included. In the patients with acute ruptured aneurysms, non–stent-assisted procedures including simple or balloon-assisted coiling were used preferentially. Stents were applied in the cases of unstable coils mass or coils loops protruding into the parent vessel during the procedure. For unruptured aneurysms, stent-assisted coiling was typically considered first. Balloon-assisted or simple coiling was used for aneurysms with narrow necks and large dome-to-neck ratios as well as in patients who were contraindicated for antiplatelet agents. Besides, patients who presented with acute hydrocephalus all received external ventricular drainage (EVD) insertion.

All patient medical records, initial and follow-up angiograms, aneurysm characteristics, as well as aneurysm recurrence and re-treatment and EVT procedure data were reviewed retrospectively. The study was approved by the Institutional Review Board of Chang Gung Medical Foundation (IRB No: 201901382A3C502).

EVT and follow-Up

Embolization procedures were performed under general anesthesia by 4 experienced neurointerventionalists. All patients with unruptured aneurysm were treated preoperatively with a dual antiplatelet regimen comprising aspirin (100 mg) and clopidogrel (75 mg) daily for 7 days before the intervention. In patients with acute ruptured aneurysms, if the stent was necessary intraoperatively, tirofiban (a glycoprotein IIb/IIIa inhibitor) was immediately administered intraarterially and continuously through a slow venous drip for 24 h. In patients with deployed stents, continual dual antiplatelet therapy was advised for at least 3 months postoperatively, followed by single-agent maintenance for at least 1 year. The clinical treatment strategy is summarized in Figure 1.

Initial computed tomography angiography (CTA), digital subtraction angiography (DSA), and postembolization angiography data were reviewed. Cavernous ICA (cICA) was classified into 4 types according to its tortuosity—based on the angle of the anterior and posterior genus (12) —as shown in Figure 2. A type I cICA has open angles of the genus; it is subcategorized into type IA and IB when its posterior genu angle is >90° and 90°, respectively. A type II cICA is more closed than a type I cICA; in particular, the angle of a type II cICA's anterior genu is more acute. A type III cICA exhibits posterior deflection in its posterior genu. Finally, a type IV cICA is the most

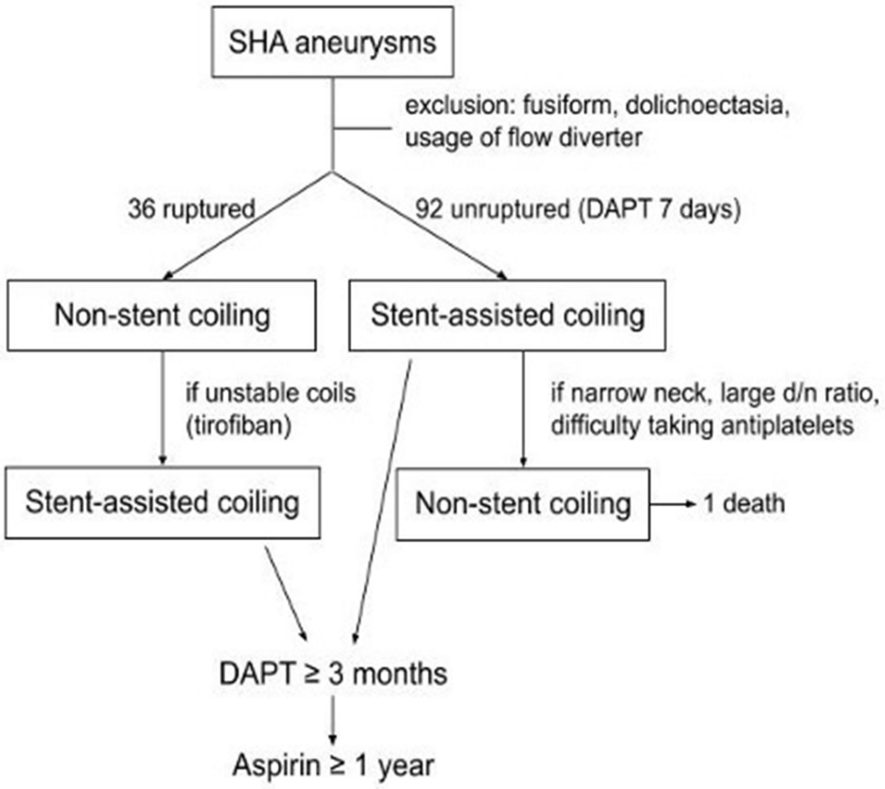

FIGURE 1
Flow of SHA aneurysm inclusion and treatment.

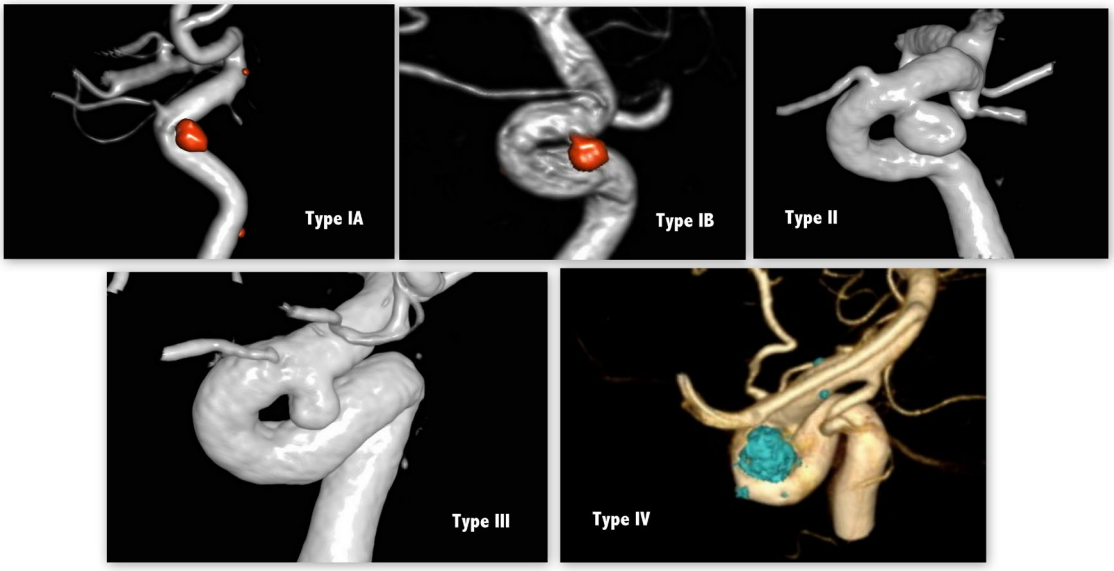

FIGURE 2
cICA tortuosity based on the angles of anterior and posterior genus.

tortuous with the posterior genu buckled more superiorly than the anterior genu.

Initial postembolization outcomes were classified as follows: complete occlusion (Raymond–Roy class I), when the aneurysmal sac and neck were tightly packed, and nearly complete occlusion (Raymond–Roy class II), when the sac was packed but a small neck remained.

Radiologic outcome data were obtained through conventional DSA at least 1 year after first treatment and through magnetic

resonance angiography (MRA) annually in the subsequent years if the previous DSA had shown no evidence of recurrence. On the other hand, DSA were arranged when MRI had suspected recurrence. The data were grouped according to the angiographic follow-up duration (Table 1). Aneurysm recurrence was defined as regrowth after previous complete obliteration or enlargement of a previous residual neck in the subsequent image. The recurrence was considered major if it was saccular and its size theoretically permitted re-treatment with coils. Major recanalization and marked residual sac flow were the basis for repeat embolization. Stent-assisted coiling was afforded the first priority as the re-treatment modality. Clinical follow-up data were collected for all patients at least until one-and-a-half years post-embolization (except in 1 patient who died of concurrent ruptured arteriovenous malformation [AVM]), and favorable outcome was defined as modified Rankin Scale (mRS) score ≤ 2 (Table 2).

Statistical analysis

All statistical analyses were performed on SPSS 25. Patient demographics, aneurysm features, and treatment characteristics were compared according to rupture by using independent t and chi-square tests, and the results were exhibited in Table 3. To examine whether patient characteristics and aneurysm features correlated with rupture, ruptured and unruptured SHA aneurysms were compared on the basis of patient sex, age, aneurysmal size, dome-to-neck ratio, multiplicity, and cICA tortuosity (Table 4). Treatment options and Raymond–Roy classes were added as independent variables in the recurrence and re-treatment analysis (Table 5 and Supplementary material, respectively). Variables with $p < 0.2$ in the univariate logistic regression analysis were further analyzed through multivariate logistic regression. Admittedly, multiple testing should be corrected when facing multiple comparisons problem. Nevertheless, we consider that this adjustment may not be best suited in the present study. Multiple testing will probably fix false positive problem (Type I error), but it also increases the false negative rate (Type II error). That is, many significant results may turn into insignificant, but those insignificant findings may not be statistically correct. This phenomenon is most evident when the number of comparisons is high, which was the situation in our series. Moreover, VIF (variance inflation) have been examined for all independent variables analyzed in the multiple regression analyses, and none of them were above 10. This means the multicollinearity problem did not occur in our analysis. Therefore, we believe the current statistical analyses were acceptable and reasonable for the present study. All statistical analyses were supervised by data analysts in Chang Gung Memorial Hospital Center for Big Data Analysts and Statistics. Notably, stent-assisted coiling was barely used for ruptured aneurysms because antiplatelet use is contraindicated to patients with intracranial hemorrhage; in these patients, simple coiling or balloon-assisted coiling was adopted.

TABLE 1 Angiography follow-up for 127 EVT sessions.

	Total	1 year	2 years	3 years	>5 years
Simple coiling	7	7 (100%)	4 (57.1%)	3 (42.9%)	1 (14.3%)
Balloon-assisted coiling	48	48 (100%)	29 (60.4%)	20 (41.7%)	12 (25%)
Non-stent-assisted coiling (simple + balloon coiling)	55	55 (100%)	33 (60%)	23 (41.8%)	13 (23.6%)
Stent-assisted coiling	72	72 (100%)	36 (50%)	24 (33.3%)	10 (13.9%)
Total	127	127 (100%)	69 (54.3%)	47 (37.0%)	23 (18.1%)

Follow-up protocol was described in the Materials and Methods section.

Results

This study included 112 patients with SHA aneurysms who underwent a total of 128 EVT treatment sessions between January 2009 and December 2020; however, 1 patient who died due to concurrent ruptured AVM was not included in further analyses.

TABLE 2 Clinical outcome of SHA aneurysms after endovascular coiling.

	Total	3 months	6 months	1 year	>1.5 year
Ruptured aneurysms	36	36 (100%)	36 (100%)	36 (100%)	36 (100%)
Favorable outcome (mRS 0–2)		28 (77.8%)	29 (80.6%)	32 (88.9%)	32 (88.9%)
Unfavorable outcome (mRS 3–5)		8 (22.2%)	7 (19.4%)	4 (11.1%)	4 (11.1%)
Mortality (mRS 6)		0	0	0	0
Unruptured aneurysms	91	91 (100%)	91 (100%)	91 (100%)	91 (100%)
Favorable outcome (mRS 0–2)		88 (96.7%)	88 (96.7%)	88 (96.7%)	88 (96.7%)
Unfavorable outcome (mRS 3–5)		3 (3.3%)	3 (3.3%)	3 (3.3%)	3 (3.3%)
Mortality (mRS 6)		0	0	0	0

mRS, modified Rankin Scale.

TABLE 3 Patient demographics, aneurysm features and treatment characteristics.

(*N*=127)		Ruptured (*n*=36)	Unruptured (*n*=92)	*P*-value
Patient factor	Female (%)	25 (69.4%)	75 (81.5%)	0.11
	Age (year)	53.17 ± 12.84	52.17 ± 11.09	0.66
Aneurysm factor	Recurrence (%)	11 (31.4%)	6 (6.5%)	<0.001
	Maximal diameter			0.37
	<3 mm (%)	4 (11.1%)	22 (23.9%)	
	3–7 mm (%)	21 (58.3%)	58 (63.0%)	
	>7 mm (%)	11 (30.6%)	12 (13.0%)	
	Dome/Neck ratio	1.71 ± 0.99	1.40 ± 0.38	0.01
	cICA type			<0.001
	Type IA (%)	24 (66.7%)	34 (37.0%)	
	Type IB (%)	11 (30.6%)	27 (29.3%)	
	Type II-IV (%)	1 (2.8%)	31 (33.7%)	
	Multiple	12 (33.3%)	29 (31.5%)	0.84
Treatment factor	Stent usage (%)	7 (19.4%)	65 (70.7%)	<0.001
	Raymond class II (%)	13 (36.1%)	23 (25.0%)	0.21

1 ruptured aneurysm was not included for recurrence analysis due to dying of concomitant ruptured AVM.

TABLE 4 Correlation factors for SHA aneurysm rupture.

				Univariate analysis		Multivariate analysis	
(*N*=128)		Rupture (*n*=36)	No rupture (*n*=92)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Patient factor	Female (%)	25 (69.4%)	75 (81.5%)	0.52 (0.21–1.25)	0.14	0.49 (0.18–1.31)	0.15
	Age (year)	53.17 ± 12.84	52.17 ± 11.09	1.01 (0.97–1.04)	0.66		
Aneurysm factor	Maximal diameter						
	<3 mm	4 (11.1%)	22 (23.9%)	0.20 (0.05–0.76)	0.02	0.39 (0.08–2.05)	0.27
	3–7 mm	21 (58.3%)	58 (63.0%)	0.40 (0.15–1.03)	0.06	0.78 (0.24–2.52)	0.68
	>7 mm	11 (30.6%)	12 (13.0%)	1.00 (reference)		1.00 (reference)	
	Dome/Neck ratio	1.71 ± 0.99	1.40 ± 0.38	2.24 (1.10–4.57)	0.03	1.72 (0.76–3.94)	0.20
	cICA type						
	Type IA	24 (66.7%)	34 (37.0%)	21.88 (2.79–171.47)	0.003	17.37 (2.17–139.21)	0.007
	Type IB	11 (30.6%)	27 (29.3%)	12.63 (1.53–104.29)	0.02	11.60 (1.37–98.41)	0.03
	Type II-IV	1 (2.8%)	31 (33.7%)	1.00 (reference)		1.00 (reference)	
	Multiple	12 (33.3%)	29 (31.5%)	1.09 (0.48–2.47)	0.84		

Follow-up outcome

Table 1 presents the summary of angiographic follow-up data for all EVT sessions. In all the included patients, the follow-up duration was at least 1 year, with it being >5 years in almost one-fifth of the patients; moreover, the average follow-up length was 3.12 years. Considering the long-term follow-up duration, the current conclusions may be substantial. Table 2 compares ruptured and unruptured cohorts by clinical outcome (mRS, modified Rankin Scale) at 3 month, 6 month, 1 year and > 1.5 year. All coiled aneurysms received clinical follow-up for at least 1.5 year. At one-year postprocedure, unfavorable outcome (mRS score ≥ 3) was observed in only 4 out of 36 ruptured aneurysms. With regard to 91 unruptured aneurysms, 3 treatment sessions resulted in unfavorable outcome: one was associated with underlying parkinsonism, one resulted from intraoperative rupture followed

TABLE 5 Risk factors for post-EVT SHA aneurysm recurrence.

				Univariate analysis		Multivariate analysis	
(*N*=127)		Recurrence (*n*=17)	No recurrence (*n*=110)	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Patient factor	Female (%)	11 (64.7%)	88 (80%)	0.46 (0.15–1.38)	0.16	1.82 (0.38–8.72)	0.45
	Age (year)	47.47 ± 12.36	53.28 ± 11.34	0.96 (0.91–1.00)	0.06	0.95 (0.89–1.01)	0.10
Aneurysm factor	Ruptured (%)	11 (64.7%)	24 (21.8%)	6.57 (2.20–19.59)	0.001	8.59 (1.36–54.22)	0.02
	Maximal diameter						
	<3 mm (%)	6 (35.3%)	20 (18.2%)	2.00 (0.44–9.13)	0.37	6.71 (0.63–71.80)	0.12
	3–7 mm (%)	8 (47.1%)	70 (63.6%)	0.76 (0.19–3.14)	0.70	0.44 (0.07–3.03)	0.41
	>7 mm (%)	3 (17.6%)	20 (18.2%)	1.00 (reference)		1.00 (reference)	
	Dome/Neck ratio	1.58 ± 0.68	1.48 ± 0.62	1.25 (0.62–2.54)	0.53		
	cICA type						
	Type IA (%)	7 (41.2%)	50 (45.5%)	2.10 (0.41–10.78)	0.37	0.50 (0.05–4.97)	0.55
	Type IB (%)	8 (47.1%)	30 (27.3%)	4.00 (0.78–20.42)	0.10	1.59 (0.20–12.46)	0.66
	Type II-IV (%)	2 (11.8%)	30 (27.3%)	1.00 (reference)		1.00 (reference)	
	Multiple	6 (35.3%)	35 (31.8%)	0.86 (0.29–2.50)	0.78		
Treatment factor	Stent usage (%)	1 (5.9%)	71 (64.5%)	0.03 (0.004–0.27)	0.001	0.03 (0.003–0.38)	0.01
	Raymond class II (%)	9 (52.9%)	26 (23.6%)	3.64 (1.27–10.38)	0.02	1.44 (0.33–6.39)	0.63

by large infarction, and the other case came from previous MCA ruptured aneurysm.

SHA aneurysm rupture

Table 3 compares the patient demographics, aneurysm features, and treatment characteristics between ruptured and unruptured aneurysms. Recurrence status, dome-and-neck ratio, cavernous ICA tortuosity and stent deployment rate were statistically different between the two groups ($p<0.05$). Notably, incomplete obliteration rate (i.e., Raymond class II) did not differ between the two groups. Table 4 lists the correlation factors for SHA aneurysm rupture in our patients. In total, our patient series had 36 ruptured SHA aneurysms (28.13% [36/128]). The multivariate logistic regression analysis results showed that cICA tortuosity was associated with aneurysm rupture. The open angles of the genus (type IA and IB) were significantly correlated with aneurysm rupture: SHA aneurysms with type IA and IB cICA were 17.37 and 11.60 times more likely to rupture than were those with type II to IV cICA, respectively ($p=0.007$ and $p=0.03$, respectively). SHA aneurysm size was more or less correlated with aneurysm rupture risk. Large (>7-mm) and medium-sized (3-7-mm) SHA aneurysms were more likely to rupture than were small (<3-mm) SHA aneurysms ($p=0.27$ and $p=0.68$, respectively). However, patient age, sex, multiplicity, and dome-to-neck ratio were not significantly associated with SHA aneurysm rupture.

SHA aneurysm recurrence

Table 5 lists the risk factors for post-EVT SHA aneurysm recurrence. Recurrence occurred for 17 SHA aneurysms (recurrence rate = 13.4% [17/127]). The recurrence rate was even lower for stent-assisted coiling (1.4% [1/72]). Notably, all recurrent aneurysms occurred within 2 years of embolization; in other words, even if residual neck presented, the sacs did not enlarge after 2 years after embolization.

Moreover, aneurysm rupture and non–stent-assisted coiling were found to be independent risk factors for aneurysm recurrence. Aneurysm recurrence was 8.59 times more likely to occur for ruptured aneurysms than for unruptured aneurysms ($p=0.02$). Furthermore, stent-assisted coiling was a negative contributor for post-EVT recurrence. Stent-assisted coiling led to 3% recurrence rate that of non–stent-assisted coiling ($p=0.01$). Patient age, sex, dome-to-neck ratio, cICA tortuosity, multiplicity, and Raymond–Roy class did not affect recurrence significantly.

SHA aneurysm re-treatment

Of the 17 recurrent aneurysms, 9 were re-treated (re-treatment rate = 7.1% [9/127]; Supplementary material). In patients who received stent-assisted coiling, the re-treatment rate was notably lower (1.4% [1/72]). In the current study, rupture occurrence was the only risk factor that correlated with SHA aneurysm re-treatment. Ruptured aneurysms were 13.66 times more likely to receive re-treatment than were unruptured aneurysms ($p=0.04$). However, patient sex, age, aneurysm size, dome-to-neck ratio, cICA tortuosity, multiplicity, stent usage, and Raymond–Roy class did not affect the odds of re-treatment significantly. No more recurrence occurred after retreatment with stent-assisted coiling.

Regarding EVT-related complications in patients with SHA aneurysms, two instances of intraoperative complications (1 bleeding

and 1 thrombus formation) occurred in the 128 embolization sessions. In the case with acute thrombosis, immediate thrombectomy was performed, and no postoperative sequela was noted. Postembolization stroke occurred in 5 cases (3 transient ischemic attacks and 2 infarctions). Moreover, intracerebral hemorrhage (ICH) occurred in 1 patient, but it was not due to re-bleeding but suspectedly due to spontaneous hemorrhage caused by coagulopathy resulting from liver cirrhosis.

Discussion

Previous studies have categorized SHA aneurysms as paraclinoid aneurysms (1, 3, 4), which are considered to have a low rupture rate (5, 6). However, consistent with the results of Chalouhi, Tjoumakaris (7), rupture occurred in a large proportion (28.1%) of our SHA aneurysm cases. Furthermore, subarachnoid hemorrhage caused by aneurysm rupture can not only lead to high mortality rate but result in high degree of disability (8). Considering their tendency to rupture and result in SAH, SHA aneurysms should be treated actively, as early as possible so as to prevent the detrimental clinical outcomes and its associated recurrence and re-treatment.

In the present study, all patients had been angiographically followed up for at least 1 years, with the average follow-up duration being 3.12 years. Therefore, the results of the current EVT series for SHA aneurysms are highly relevant and valid. Furthermore, because the main focus of this study was saccular SHA aneurysms with EVT, we excluded fusiform aneurysms and aneurysms with dolichoectasia; these variations may represent another disease entity, which may require different treatment strategy, such as the use of flow-diverter. In addition, the use of flow-diverter was excluded in the current study because it accounted for a limited proportion of our treatment sessions because of our national insurance coverage's limitation and a high number of ruptured cases in our series.

In general, cICAs can be divided into 4 types based on their tortuosity (12). In our study, SHA aneurysms with less tortuous cICA (i.e., type IA and IB cICA) tended to rupture. This result, which has not been reported thus far, may occur due to a direct bloodstream flowing into the aneurysm sac. Computational fluid dynamics, which can simulate dynamic blood flow of intracranial aneurysms, has been widely adopted to investigate the contributing factors for aneurysm rupture (13). Aneurysmal hemodynamics influence the rupture risk of paraclinoid aneurysms (14). Moreover, inflow angle—the angle between the aneurysm dome axis and the parent vessel—has been found to affect aneurysmal hemodynamics. An increased inflow angle increases peak velocity and energy transmission to the dome, followed by the achievement of a discriminate rupture status (15). Although the association between cICA tortuosity and fluid dynamics remains unknown, we hypothesized that the tortuosity of cICA is associated with the peak velocity and energy transmission of blood flow to the aneurysm sac based on the above findings. cICAs with an obtuse angle (i.e., type IA and IB cICAs) ease the blood flow into the aneurysm sac, whereas more tortuous cICAs (i.e., type II-IV cICAs) prevent this blood flow. Therefore, treating SHA aneurysms in less-curved cICAs require procedures such as stent-assisted coiling because they afford a relatively low rupture risk (16). Admittedly, additional flow dynamics studies to explore the association between vessel tortuosity and fluid mechanics are warranted.

In this study, large (>7-mm) aneurysms were to some extent associated with rupture status; this result corroborates that of previous studies (17–19): The International Study of Unruptured Intracranial Aneurysms (ISUIA) trial reported that the 5-year cumulative rupture rate was considerably lower in small (<7-mm) unruptured aneurysms, regardless of anterior or posterior circulation (19). A 2009 review also identified a size of >7-mm as independent risk factor for aneurysm rupture (18). Finally, in their long-term follow-up study with an average of 18.5-year follow-up, Korja, Lehto (17) confirmed that large (>7-mm) size is a risk factor for aneurysm rupture. As a result, large (>7-mm) aneurysms warrant timely treatment of stent-assisted coiling to prevent rupture and recurrence (16).

Large aneurysm size, aneurysm rupture, incomplete occlusion, and non-stent use have been reported to be associated with aneurysm recurrence after EVT (20–22). In the current study, aneurysm rupture and non–stent-assisted coiling, but not large size or incomplete occlusion, demonstrated similar effects on SHA aneurysms. This may be because large aneurysms accounted for only a small proportion (18.1%) of our data, and few (27.6%) of our patients demonstrated incomplete occlusion (Raymond–Roy class II or III). In contrast to angiography results reported elsewhere (21), most (72.4%) aneurysms in the current study achieved complete occlusion, possibly because of technological advancement and technical improvements since the aforementioned study was reported. In addition, compared with unruptured aneurysms (25% [23/92]; Table 2), incomplete occlusion rate was comparable in ruptured aneurysms (36.1% [13/35]; $p = 0.21$). Therefore, the claim that higher recurrence rate in ruptured aneurysms results from loose coils compaction in the fear of thromboembolism when antiplatelet therapy is contraindicated is unsubstantiated.

Consistent with previous findings (7), the post-EVT SHA aneurysm recurrence rate (13.4% in our series) was equal to or lower than that in other locations, reported elsewhere: the recurrence rates for aneurysms of the A-com artery (23), MCA (24), P-com artery (21), and posterior circulation (25) have been reported to be 14.6, 20, 37, and 24.5%, respectively. The relative lower recurrence rate highlights the satisfactory outcome of coils embolization and the importance of initial treatment for SHA aneurysms. Moreover, when recurrent SHA aneurysms were re-treated with stent-assisted coiling, no further recurrence or rebleeding occurred until the last follow-up. Therefore, SHA aneurysms can be reliably secured with stent use. Nonetheless, these findings require confirmation by studies with a longer follow-up duration and larger sample size.

Flow diverter is now considered an effective treatment tool for the management of complicated intracranial aneurysms that are difficult to treat with coiling and microsurgery (26, 27). Compared with coiling technique, it provides a higher complete occlusion rate and lower recurrence rate (28) because it can secure aneurysm sac more firmly. Although it seems an appropriate treatment modality for SHA aneurysms, flow-diverter treatment was excluded in the study. As a result, direct comparison of treatment outcomes between coiling and flow-diverter could not be achieved in the present study. However, when flow diverters are not amenable or suitable, stents can still offer satisfactory results in the SHA aneurysm treatment provided the results of the current study. Therefore, stent-assisted coiling is an reasonable treatment option for SHA aneurysms, in particular when flow diverters are not accessible and available.

Stent-assisted coiling achieves a lower recurrence rate than simple coiling or balloon-assisted coiling does (16). However, according to the 2012 *Guidelines for the Management of Aneurysmal Subarachnoid Hemorrhage*, stenting of a ruptured aneurysm is associated with

increased morbidity and mortality (29); this is because antiplatelet therapy is generally contraindicated in the acute settings (16). Therefore, ruptured SHA aneurysms were typically treated with non–stent-assisted coiling: in the current study, 29 (80.56% [29/36]) ruptured aneurysms were treated with non–stent-assisted coiling. Although the clinical outcome was favorable (mRS score ≤ 2) in 28 (96.55%) of the cases, their recurrence rate was relatively high (39.29% [11/28]). However, if the recurrence was detected early and treated with stent-assisted coiling, no re-recurrence was noted. Moreover, no recurring hemorrhages occurred during the long-term follow-up. This low recurrence rate after stent use is in line with that reported previously (7). The results reflect that stent-assisted coiling is effective in the recurring SHA aneurysms. Combined with the low complication rate for coils embolization in the present study, we therefore suggest early stent assistance in the treatment of ruptured SHA aneurysms.

Limitations

This study has several limitations. First, its retrospective nature may have contributed to selection bias. Second, operator preference and patient condition may have affected the applied treatment strategy, thus altering our findings. To mitigate subjective decision bias, we based our clinical decisions on the consensus of a multidisciplinary team. Third, comprehensive risk factors, such as hypertension, diabetes, and family history, were not considered in this analysis because a considerable amount of patient data was missing. Fourth, although all patients were angiographically followed up at 1 year post-coiling, only 23 EVT treatment sessions (18.1% [23/127]) had received image follow-up after 5 years; extended follow-up period necessitates as late recanalization may still occur even after stent-assisted coiling.

Despite these limitations, our study sheds light on the characteristics of saccular SHA aneurysms and the applicable treatment strategies, especially in areas where flow diverter was not amenable. Although this study has the longest follow-up period reported to date, a relevant study with a longer follow-up duration is warranted to investigate the long-term treatment outcomes further.

Conclusion

In this study, although flow diversion is another well-suited treatment modality for SHA aneurysms that was not compared with, EVT with stent-assisted coiling was an effective treatment modality for SHA aneurysms, with low recurrence and complication rates. Type I cICA was common factor for aneurysm rupture. In most cases, recurrence occurred within 2 years of EVT and was significantly associated with prior aneurysm rupture and non–stent-assisted coiling. Finally, further stent-assisted coiling could prevent re-recurrence.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving human participants were reviewed and approved by the Chang Gung Medical Foundation Institutional Review Board. The patients/participants provided their written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

Y-PK contributed to conception and design of the work and drafted the manuscript. C-YL performed the statistical analysis. C-TC, M-CY, P-CH, Z-HL, and C-CChu carried out techniques review and conduct. H-FW and Y-MW conducted data review and received techniques consultation. C-CChe undertook final review and interpretation. All authors contributed to manuscript revision, read, and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fneur.2023.1096970/full#supplementary-material

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Embolization of unruptured wide-necked aneurysms at the MCA bifurcation using the Neuroform atlas stent-assisted coiling: a two-center retrospective study

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Background: The management of middle cerebral artery (MCA) aneurysms remains a controversial topic, and MCA aneurysms have traditionally been treated primarily by surgical clipping. The Neuroform Atlas Stent™ (NAS, available from Stryker Neurovascular, Fremont, California) represents the latest generation of intracranial stents with improved stent delivery system capabilities.

Objective: This study aims to investigate the safety, feasibility and efficacy exhibited by NAS in treating unruptured aneurysms at the MCA bifurcation.

Methods: This was a two-center retrospective study involving 42 patients with unruptured wide-necked aneurysms (WNAs) of the MCA treated with the NAS from October 2020 to July 2022.

Results: The stent was used to treat 42 cases of unruptured WNA at the MCA bifurcation. Endovascular treatment techniques had a 100% success rate. Immediate postoperative angiography found complete aneurysm occlusion in 34 patients (80.9%) (mRRC 1), neck remnant in 7 patients (16.7%) (mRRC 2), and residual aneurysm in 1 patient (2.4%) (mRRC 3). The thromboembolic complication rate was 2.4% (1/42). The follow-up period was 8.7 months on average (3–16 months). The last angiographic follow-up results revealed complete aneurysm occlusion in 39 patients (92.9%) (mRRC 1), neck remnant in 3 (7.1%) patients (mRRC 2), no aneurysm recanalization or recurrence, and no cases of stent intimal hyperplasia. During the latest clinical follow-up, all patients had an mRS score of 0.

Conclusion: Our study demonstrates that the NAS can be applied to treat unruptured WNAs at the MCA bifurcation with favorable safety, feasibility, and efficacy.

KEYWORDS

middle cerebral artery, bifurcation, Neuroform atlas stent, stent-assisted coiling, aneurysm

Introduction

Intracranial aneurysms are increasingly treated with endovascular approaches (1). Middle cerebral artery (MCA) aneurysms account for 18 to 36% of all types of intracranial aneurysms, the majority of which are located at the MCA bifurcation (2). The treatment of MCA aneurysms remains a controversial topic. The traditional therapeutic regimen for MCA aneurysms is surgical clipping. Despite this fact, since the publication of results from the International Subarachnoid Aneurysm Trial (ISAT) and the International Study of Unruptured Intracranial Aneurysms (ISUA) on the safety and efficacy exhibited by endovascular interventions, endovascular treatments for these aneurysms have been improved for wider implementation (3). Studies have confirmed the better performance of stent-assisted coiling (SAC) than that of single embolization for both ruptured and unruptured aneurysms (4). Due to the different geometries and configurations of aneurysms, conventional simple embolization can present several complications, including coils protruding from the aneurysm lumen or even dislocating into the parent artery. The above complications can easily develop in wide-necked aneurysms (WNAs), which are aneurysms possessing a neck diameter $\geq$ 4.0 mm or a dome-to-neck ratio < 2.0. SAC is considered to be one of the most important methods for treating WNAs; it can minimize the risk of protrusion or dislocation and can effectively and safely be applied to treat these intracranial aneurysms (5, 6). The latest generation Neuroform Atlas Stent (NAS, Stryker Neurovascular, Fremont, CA) represents the latest advancement in laser-cut microstents for the brain, a low-profile self-expanding stent possessing an open-hole design. It is used to support a removable intrasaccular coil, preventing the coil from protruding out of the aneurysm lumen while providing flow redirection with low shunt rates. The original Neuroform stent was first approved more than 10 years ago, and its safety and efficacy for assisting coil embolization of aneurysms has been proven many times around the world. Considering the extensive clinical experience regarding the first-generation Neuroform stent, the new-generation Neuroform stent aims to improve the delivery of microcatheters for coil embolization in the same way. Its inner diameter is 0.0165 inches (unlike the 0.027-inch Neuroform EZ) due to its smaller size, and consequently, it can be placed in more distal vessels, such as branches of the anterior and middle cerebral arteries. Additionally, new features add a hybrid cell design, with the Atlas stent partially deployed proximally and distally to provide excellent wall apposition, aneurysm neck coverage, and robust coil support. Three years ago, the FDA approved the Atlas stent for treating WNAs during the anterior circulation. The results from multiple previous studies using the NAS for SAC of intracranial aneurysms have increased our confidence in this device (6–9). Data on safety and long-term efficacy are sparse, and further research is needed. Therefore, the present study aims to report our experience in patients with unruptured aneurysms at the MCA bifurcation using NAS-assisted embolization.

Methods

The retrospective multicenter study was approved by the hospital ethics committee, and the need for informed consent was waived.

Patients

The study conducted a retrospective analysis of all patients exhibiting unruptured WNAs at the MCA bifurcation under treatment by the Neuroform Atlas device at two institutions between October 2020 and July 2022. The study included 42 patients with WNAs at the MCA bifurcation. Inclusion of these patients was determined by an interdisciplinary consensus panel based on our inclusion and exclusion criteria. The general data and clinical data of the patients were collected. The clinical data include the basic characteristics of aneurysm (aneurysm length, aneurysm neck size, aneurysm location), treatment results, and follow-up data.

Inclusion and exclusion criteria

Inclusion criteria: (1) cranial MRA or head and neck CTA or DSA examination and confirmed unruptured aneurysm at the MCA bifurcation; (2) Refusal of surgical clipping requiring endovascular therapy; (3) adjuvant therapy with NAS when receiving endovascular therapy. Exclusion criteria: (1) dissecting aneurysm, pseudoaneurysm or ruptured aneurysm; (2) intracranial aneurysm complicated with other cerebrovascular diseases, such as intracranial arteriovenous malformation and moyamoya disease; (3) incomplete case data.

Perioperative antiplatelet management

The patients started taking aspirin (100 mg/d) combined with clopidogrel (75 mg/d) antiplatelet therapy at least 7 days before treatment. We performed a platelet function test (TEG Hemostasis System, Hemoscope Corporation, Niles, IL, United States) one week after the dual antiplatelet drugs to evaluate the inhibitory effect of dual antiplatelet drugs on platelet aggregation. When the patient failed to exhibit sensitivity to clopidogrel, ticagrelor (90 mg twice daily) was used instead of clopidogrel. Patients again underwent dual antiplatelet therapy with aspirin and either clopidogrel or ticagrelor for no less than 3 months after endovascular therapy. Clopidogrel or ticagrelor was discontinued at 3 months, and the patient was continued on aspirin for life.

Endovascular treatment procedures

After general anesthesia, all endovascular procedures were performed using Siemens Artis Zee angiography equipment. After successful femoral artery puncture, an 8F femoral artery sheath was placed, with intravenous infusion of heparin (50 U/kg) and an additional 1,000 U per hour to obtain an activated coagulation time between 2 and 3 of baseline in the process of operation 3 times. We placed the 6-F long sheath into the C1 segment of the internal carotid artery (ICA) through the 8F femoral artery sheath and the intermediate catheter into the C5 segment of the ICA through the long sheath. Based on the reconstructed images, an appropriate working projection was selected, namely, the angiographic projection that most clearly demonstrated the association of the aneurysm neck with the parent vessel. Angiographic evaluation assessed the aneurysm size and selected the appropriate coil based on the size of the aneurysm.

Excelsior SL-10 microcatheters were used to deliver the NAS. It was at the operator's discretion whether to create a "shelf" in a Y-bracket configuration for more neck coverage. One patient was treated with dual stents in the Y configuration. Considering the aneurysm neck size and the parent artery diameter, we selected a stent with an appropriate length and diameter for completely covering the aneurysm neck, and the "half-release" technique was used to release the stent while packing the coil. After the stent was completely released, stent deployment, stent adherence, stent patency, and tumor cavity filling were observed at the working angle and anterior and lateral angiography. The indwelling arterial sheath was pulled out 8 h after the operation. Immediately after the operation, a head CT scan was performed to observe whether there was intracranial hemorrhage. After recovery from anesthesia, the patients were returned to the ward. After discharge, patients were asked to return periodically for a review of their cerebral angiography and for clinical follow-up.

Angiography and clinical follow-up

The modified Raymond Roy classification scale (mRRC) assisted in assessing the effectiveness of aneurysm embolization, with mRRC1, 2 and 3 representing complete aneurysm occlusion, neck remnant, and residual aneurysm, respectively (10). The patients were instructed to return to the hospital for DSA angiography at 3, 6, and 12 months after treatment. The following two conditions were defined as aneurysm recanalization: 1. conversion of an initial complete aneurysm occlusion to a residual neck or residual aneurysm; 2. conversion of an initial residual neck to a residual aneurysm. Two experienced neurointerventionalists reviewed all images and agreed on the angiographic findings. The modified Rankin Scale (mRS) was employed to assess the clinical outcomes of patients when they were discharged and during the most recent follow-up.

Statistical analysis

SPSS 25.0 statistical software was used for the data analysis. This single-arm study only investigated the outcomes of NAS-assisted embolization in treating unruptured WNAs at the MCA bifurcation and did not compare the outcomes with those of other types of treatment; therefore, only descriptive statistics are provided. All data are presented as the means and ranges of continuous variables as well as the numbers and percentages of categorical variables.

Results

Baseline characteristics

Forty-two patients who received NAS for unruptured WNAs at the MCA bifurcation were included in our study, including 16 males and 26 females (mean age: 59.21 years; range 41–78 years). Hypertension was found in 25 cases (59.5%), diabetes in 5 cases (11.9%) and smoking in 11 cases (26.2%). Aneurysm was found on physical examination in 12 patients, headache in 14 patients, dizziness in 10 patients, and tinnitus in 6 patients. The aneurysm was located on the left side in 22 patients, and the aneurysm in the remaining 20 patients was located on the right side. The aneurysms possessed an average maximum diameter of 4.3 ± 1.0 mm (2.8–7.5 mm) and an average neck diameter of 2.8 ± 0.8 mm (1.8–6.4 mm). The mean aneurysm dome/neck ratio was 1.62 ± 0.2, and the average PHASES Score of the patients is 2.7 ± 0.6.Baseline data are shown in Table 1.

Immediate embolic effects and endovascular treatment-related complications

The endovascular treatment success rate was 100%, and there was no NAS placement failure. Immediate postoperative angiography revealed complete aneurysm occlusion in 34 patients (80.9%) after endovascular treatment (mRRC 1), 7 patients (16.7%) with neck remnant (mRRC 2), and 1 patient (2.4%) with residual aneurysm (mRRC 3) (Table 2). The thromboembolic complication rate was 2.4% (1/42). One patient developed thrombosis, which disappeared after to tirofiban bolus injection. The other patients did not experience thrombosis, postoperative intracranial hemorrhage or other surgery-related complications. The patients with intraoperative thrombosis had mild right extremity dysfunction at discharge with an mRS score of 1, and the rest possessed an mRS score of 0 when they were discharged (Table 2).

Clinical and angiographic follow-up

Clinical and angiographic follow-up results were available for all 42 patients. The follow-up period lasted 8.7 months on average (3 to

TABLE 1 Baseline and aneurysm characteristics of patients.

Variable value[a]	
Gender (n)	
Male	16 (38.1%)
Female	26 (61.9%)
Age (years)	59.21 ± 8.90
Clinical risk factors (*n*)	
Smoking	11 (26.2%)
hypertension	25 (59.5%)
diabetes	5 (11.9%)
Location	
Left	22 (52.4%)
Right	20 (47.6%)
Symptom	
Asymptomatic	12 (28.6%)
Headache	14 (33.3%)
Dizziness	10 (23.8%)
Tinnitus	6 (14.3%)
Aneurysm maximum diameter (mm)	4.3 ± 1.0
Aneurysm neck diameter (mm)	2.8 ± 0.8
Aneurysm dome/neck ratio	1.6 ± 0.2
PHASES Score	2.7 ± 0.6

[a]Values are mean ± standard deviation or number of patients (percentage).

TABLE 2 Immediate and follow-up results.

Variable value[b]	
Immediate postoperative embolism classification	
mRRC 1	34 (80.9%)
mRRC 2	7 (16.7%)
mRRC 3	1 (2.4%)
mRS score at discharge	
0	41 (97.6%)
1	1 (2.4%)
2	0 (0%)
3	0 (0%)
4	0 (0%)
5	0 (0%)
6	0 (0%)
Mean follow-up time(months)	8.67 ± 2.98
Results of the last follow-up angiography	
mRRC 1	39 (92.9%)
mRRC 2	3 (7.1%)
mRRC 3	0 (0%)
mRS score at last clinical follow-up	
0	42 (100%)
1	0 (0%)
2	0 (0%)
3	0 (0%)
4	0 (0%)
5	0 (0%)
6	0 (0%)

[b]Values are mean ± standard deviation or number of patients (percentage). mRS, Modified Rankin Scale.

16 months). The last angiographic follow-up revealed complete aneurysm occlusion in 39 patients (92.9%) (mRRC 1), neck remnant in 3 (7.1%) patients (mRRC 2), and no aneurysm recanalization or recurrence. The last angiographic follow-up showed no stent intimal hyperplasia in any patient (case illustration, Figure 1). None of the patients developed bleeding or thromboembolic events during clinical follow-up. At the most recent follow-up, the mRS score was 0 for all patients. The follow-up data are shown in Table 2.

Discussion

Endovascular treatment is challenging for many MCA aneurysms, especially aneurysms at MCA bifurcations. Although many innovative devices have emerged over the past decade with the development of neurointerventional devices, many neurovascular centers still view microsurgical clipping as the treatment of choice (1). A more complex and controversial topic lies in the management of WNAs (neck ≥4 mm) and small aneurysms located distal to the branch of the MCA (round neck ratio < 2), which are often treated with clipping (3). Conventional coil embolization specific to wide-neck MCA bifurcated aneurysms, without the assistance of stents or balloons, remains a technical challenge due to the bifurcation anatomy, wide neck, deformed shape, and angiographically unrecognizable branches, and the stability of its long-term results remains controversial (11). Wide-neck intracranial aneurysms need additional devices like balloons or stent for management (12) Stent-assisted coiling achieved better results in terms of complete occlusion and stability than balloon-assisted coiling with a lower rate of recurrence without being associated with a higher risk of intraprocedural complications (13). Woven EndoBridge [WEB (Sequent Medical, Aliso Viejo, California, USA)] is a highly innovative technique for the endovascular treatment of wide-necked bifurcation aneurysms (WNBAs), but it is more suitable for treatment of basilar bifurcation aneurysms, WNBAs with necks >7 mm, and/or those with a bifurcation angle >180° (14). With the development of various neurointerventional devices and neurointerventional techniques, many studies have revealed the effectiveness and safety of stent-assisted embolization in treating MCA aneurysms. YAN et al. reported the results of 57 patients with unruptured WNAs at the MCA bifurcation under the treatment of Low-Profile Visualization Endovascular Support (LVIS) stent-assisted embolization (15). Immediate postoperative angiography showed that 45.6% of aneurysms had Raymond 1 occlusions (45.6%), 17.6% of the aneurysms had Raymond 2 occlusions, and two patients (3.5%) experienced perioperative complications, one with a procedure-related bleeding event and the other with a procedure-related thromboembolic event. Angiographic results obtained at an average follow-up of 11.7 months after surgery showed complete occlusion in 78.7%, improvement in 6.4%, stabilization in 10.6%, and recanalization in only 4.3% of cases. During follow-up, 1 in-stent stenosis was found, and 2 patients developed stagnation or occlusion of occluded branches, but none of the three patients developed symptoms. There were no thromboembolic or bleeding events in any patient in the clinical follow-up. LVIS stent-assisted embolization has shown good long-term outcomes. Hegan et al. retrospectively analyzed the outcomes of 150 unruptured MCA bifurcations treated with coils, SAC, or intravascular shunts (WEB devices), 45 of which were stent-assisted embolizations (16). The results of this study showed that the overall surgery-related good clinical outcomes (mRS ≤2) were found in 89.9% of patients, and the mortality was 2.7%; short-term follow-up was conducted for 91.3% of patients, and the mortality was 0.7%. Long-term angiographic follow-up showed stent-assisted embolization recurrence. The treatment rate was only 5.9%. This study demonstrates that endovascular treatment has good clinical outcomes and lower mortality regardless of the structure of the MCA bifurcation aneurysm. Yunsun et al. reported the results of 14 patients suffering MCA aneurysms undergoing stent-assisted embolization of acute hypoplastic M1 branches, and 13 patients achieved an average bulk density of 30% (17). Magnetic resonance angiography at an average follow-up of 4 months (1–26 months) revealed that 11 patients had developed complete occlusion, and 3 patients had developed a residual aneurysm neck. At a median clinical follow-up of 17 months (2–26 months), there were no clinical events, with an mRS score 0. One patient exhibited thrombotic occlusion during surgery that resolved with tirofiban infusion, with no evidence of infarction or defect. Chen et al. reported the results of SAC using the solitaire AB stent at the MCA trifurcation in 57 WNA patients (18). Immediate postoperative angiography showed complete embolization in 52 cases,

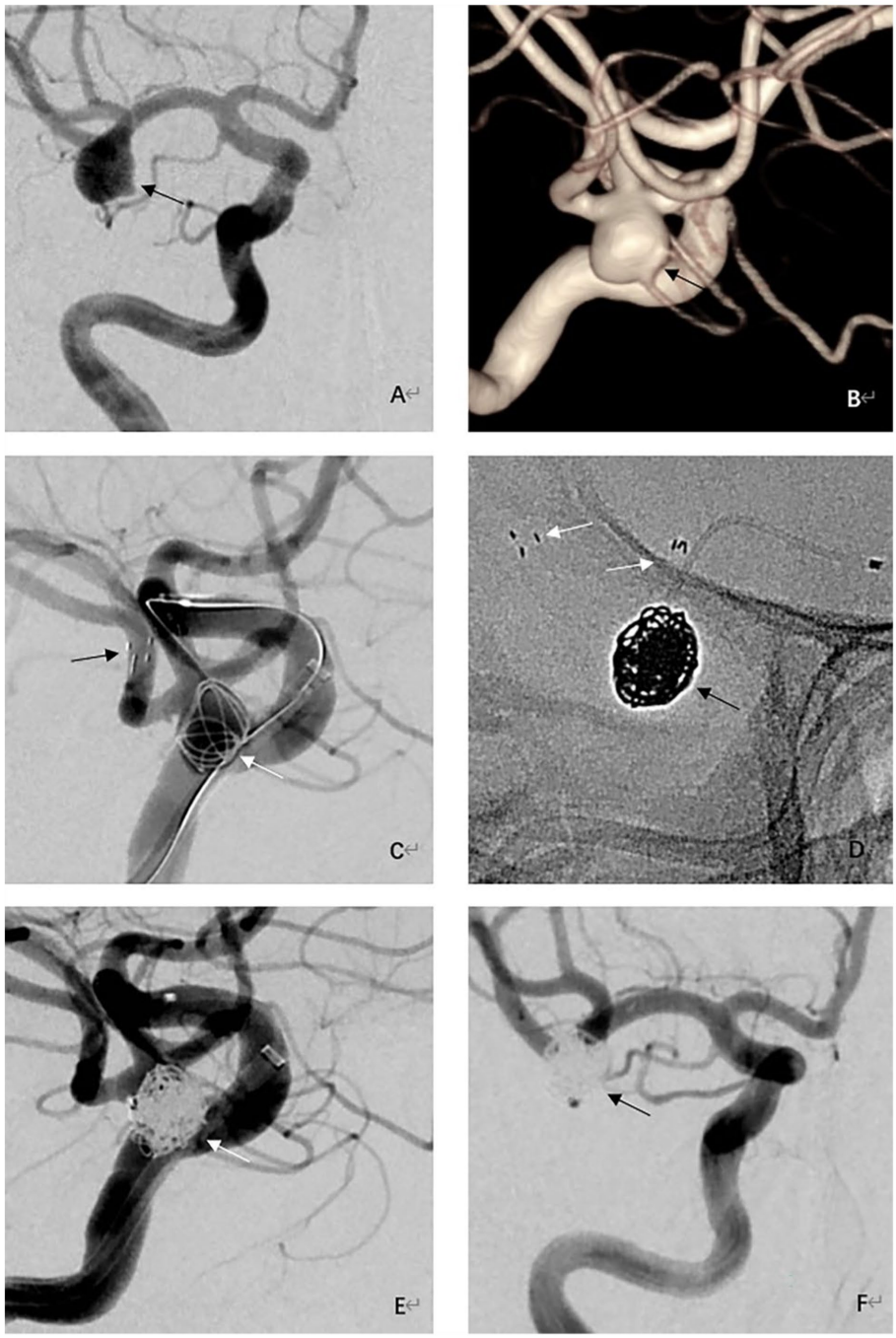

FIGURE 1
Procedural and follow-up angiographic images of an adult patient with an unruptured wide-necked aneurysm at the right MCA bifurcation. **(A)** Preprocedural right internal carotid angiography image showing a wide-necked aneurysm at the MCA bifurcation (black arrow). **(B)** Preprocedural 3-dimensional reconstructed angiography image showing a saccular wide-necked MCA aneurysm (black arrow). **(C)** Intraoperative angiographic image shows Neuroform Atlas stent (black arrows) deployed into the inferior trunks of the MCA and coils (white arrow) inside the aneurysm. **(D)** Visualization of stent (white arrows) and coils (black arrow) under fluoroscopy. **(E)** Immediate postprocedural angiographic image showing complete embolization of the aneurysm (white arrow). **(F)** 9-month follow-up angiography demonstrating complete occlusion of the aneurysm (black arrow) with good branch preservation and no in-stent stenosis.

residual aneurysm neck in 4 cases, and residual aneurysm body in 1 case. Fifty patients were followed for 6–36 months. No aneurysmal rupture or hemorrhage was observed during the clinical follow-up. According to the last angiographic evaluation, 46 patients developed complete embolization, 3 patients developed a residual neck, 1 patient developed an aneurysm body, and the other 2 patients developed a stable aneurysm. Finally, patients with residual aneurysm body were asymptomatic at follow-up review. Hidenori et al. reported the angiographic and clinical outcomes of SAC of 47 unruptured MCA aneurysms in 46 patients treated with Low Profile Visualization

Endovascular Support Primary (LVIS Jr.) stents (19). Immediate postoperative angiographic findings were Raymond-Roy class I in 31 patients (65.0%), Raymond-Roy class II in 5 patients (10.6%), and Raymond-Roy class III in 11 patients (23.4%). According to the latest angiographic results, 33 cases (86.8%) were Raymond-Roy class I, 2 cases (5.3%) were Raymond-Roy class II and 3 cases (7.9%) were Raymond-Roy class III. The aneurysm occlusion status remained unchanged in 27 cases (71.0%), improved in 9 cases (23.7%), and worsened in 2 cases (5.3%). No recurrent aneurysm required additional treatment. Two patients had significant stent thrombosis on angiography, but their clinical outcomes remained favorable. At discharge, the mRS score was 0 in 45 patients and 1 in 1 patient. Feng et al. reported the safety and efficacy of LVIS Jr. stents used for MCA aneurysm embolization (20). There were 18 MCA aneurysms, with 13 unruptured and 5 ruptured aneurysms. At the last angiographic follow-up, 8 patients (44.4%) had complete occlusion, 7 patients (38.9%) had residual neck, and 3 patients (16.7%) had partial occlusion. One patient had intraoperative stent thrombosis, which disappeared due to intravenous injection of tirofiban. At discharge, 14 patients had mRS scores of 0; 3 patients, scores of 1; and 1 patient, a score of 2.

The past two decades saw the emergence of many newer laser-cut or braided stents, such as the Neuroform EZ, Solitaire, Enterprise, LVIS and LVIS Jr. stents. Each bracket possesses advantages and limitations. Compared with closed-cell stents, open-cell stents exhibit a strong vessel wall fit but cannot be recoated, and the coils are more likely to come out in patients using open-cell stents. Braided stents increase metal coverage for better shunting but are not easy to deploy (21). Embolization of MCA aneurysms is often challenging due to the wide neck anatomy associated with bifurcations. This forces the surgeon to often choose between coiling the tumor lumen and damaging the parent or distal vessels. To this end, stents specifically developed for SAC, including Y-stents and the NAS, largely solve this problem (9). The NAS (Stryker Neurovascular, Fremont, CA, United States) serves as a laser-cut, self-expanding nitinol stent that provides good adherence and sufficient linear support in stent-assisted embolization to prevent coil prolapse. The atlas possesses a hybrid cell structure consisting of alternating 16-pole and 24-pole rows. The design aims to enhance the adherence and compliance of the stent. In addition, the NAS features a minimal see-through design. It is available in 3.0, 4.0 and 4.5 mm diameters and four lengths: 15, 21, 24 and 30 mm; the bracket is designed to be deployed on female 2–3, 3–4 and 4–4.5 mm diameters, respectively, in blood vessels. Stent systems are delivered via microcatheters, including XT-17™ Microcatheters (0.017" ID) (Stryker Neurovascular) and Excelsior SL-10® (0.0165" ID). Its small inner diameter delivery system makes it capable of increasing the aneurysm types that can be treated within the vessel, such as those that are previously inaccessible (22). Zaidat et al. reported one-year follow-up results of the NAS for anterior circulation aneurysms, achieving complete occlusion in 88.2% of patients, parent artery stenosis (>50% stenosis) in 1.3% of patients, and 7 patients underwent retreatment, 84.7% of patients achieved complete aneurysm occlusion (Raymond-Roy class 1) with retreatment of the aneurysm or stenosis of the parentless artery, and 4.4% experienced ipsilateral stroke or neurological death (7). This study demonstrates that the NAS system can assist in safely and effectively treating WNAs of the anterior circulation. Kim et al. reported data on application of the NAS in patients with ruptured and unruptured cerebral aneurysms (21). Thirty-three aneurysms in 31 patients received embolization with the assistance of the NAS. Of the 29 aneurysms under angiography after patients were followed up for 6 months, 19 (65.5%) had Raymond-Roy class I occlusions, 8 (27.6%) had Raymond-Roy class II occlusions, and 2 (6.9%) had Raymond-Roy class III occlusions. No patients experienced surgery-related bleeding complications. Sweid et al. published a retrospective multicenter study of 69 subjects treated with the Atlas stent (23). At the 4-month follow-up, 97.7% of aneurysms had Raymond-Roy class I/II occlusion results, 91.8% of patients had good clinical outcomes, and the mortality rate was only 1.4%. A meta-analysis using NAS-assisted coiled intracranial aneurysms showed that the NAS-assisted coil achieved an initial adequate occlusion rate of 88% and the perioperative complication rate was 6% (5). The immediate postoperative complete occlusion rates were 85 and 86% for unruptured aneurysms and WNAs, respectively. Kubilay et al. illustrated the results of Y-stent-assisted coiling with NAS for treating WNAs with complex intracranial bifurcation. The study included 30 patients, and 30 aneurysms were treated postoperatively (8). Immediate angiography revealed complete aneurysm occlusion in 83.3% of patients. The angiographic follow-up lasted 11.8 months on average. The last follow-up revealed complete aneurysm occlusion in 93.3% of patients. Only 6.7% of patients developed surgery-related complications, 3.3% of patients developed permanent complications, and no patients died. Hanel et al. presented results from a prospective study trial of the NAS in treating MCA aneurysms (9). A total of 35 patients (27 MCA bifurcations, 5 M1, 3 M2) were included. Twenty-six patients received digital subtraction angiography at 12 months, of whom 80.8% (21/26) had complete aneurysm occlusion. At 1 year, 84.4% (27/32) of patients had an mRS score of ≤2, and 3 patients were lost to follow-up. Stent-assisted crimping with the NAS is an alternative to surgical clipping for selected MCA aneurysms.

A total of 42 patients with unruptured WNAs at the MCA bifurcation were included in the study. The follow-up lasted 8.7 months on average. The last angiographic follow-up revealed complete aneurysm occlusion in 92.9% of patients (mRRC 1), neck remnant in 7.1% of patients (mRRC2), no patients with aneurysm recanalization or recurrence, and no patients with stent intimal hyperplasia. For all patients, the mRS score was 0 at the last clinical follow-up. The present study shows favorable results for application of the NAS in unruptured aneurysms at the MCA bifurcation.

Limitations

The present investigation has some limitations. First, it was a retrospective study with a small sample size, making the conclusions drawn less persuasive. Future studies with larger sample sizes are needed to better evaluate the safety and efficacy exhibited by the Atlas stent in treating unruptured WNAs at the MCA bifurcation. In addition, this was a multicenter study conducted in conjunction with another institution, and although uniform standards were used in data collection, interobserver and reporting biases may still have been introduced. In addition, our follow-up time was also shorter, which may not accurately reflect the aneurysm occlusion rate, requiring a longer follow-up time to draw more reliable conclusions.

Conclusion

Although many challenges remain in treating unruptured WNAs located at MCA bifurcations to date, our study demonstrates that the NAS can safely and feasibly treat such lesions. Accordingly, it is clear that the NAS contributes greatly to the treatment of intracranial aneurysms, and we have immense confidence in this device.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by Jingmen People's Hospital and Qujing Second People's Hospital (2022-073-01). Written informed consent for participation was not required for this study in accordance with the national legislation and the institutional requirements.

Author contributions

XZ, RW, and WL: designing or planning the manuscript. XZ and YD: drafting the manuscript. JZ: critically reviewing and editing. HR and WL: approving the final version. All authors contributed to the article and approved the submitted version.

Conflict of interest

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Case report: A combination of nitroglycerin and adenosine proves effective in repairing a cerebral arteriovenous malformation

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Hemorrhage secondary to rupture of a brain arteriovenous malformations (AVM) is one of the initial manifestations, and the main cause of, morbidity and mortality in patients with this condition. Current treatment strategies include endovascular embolization with the goal of AVM obliteration and neurological preservation. In the transvenous endovascular embolization procedure, adenosine is the preferred agent to induce temporary hypotension and allow adequate AVM embolization. We describe the intraoperative management of an adenosine-resistant 38 year-old male who underwent a successful intracranial AVM embolization after concomitant administration of gradually increasing doses of nitroglycerin. This report suggests that nitroglycerin infusion can be combined with adenosine boluses to create a pronounced and dose-dependent hypotension in patients partially unresponsive to adenosine alone.

KEYWORDS

arteriovenous malformations (AVM), adenosine, nitroglycerin, embolization, transvenous

Introduction

Intracranial arteriovenous malformations (AVMs) are defined as abnormal connections between the high-pressure arterial circulation and the low-pressure venous circulation (1). These connections increase venous pressure in AVMs, which contribute to their rupture and subsequent hemorrhage (2). AVMs may be discovered incidentally or as a result of various symptoms, including acute intracranial hemorrhaging, seizures, headaches, and focal neurological deficits. Although the mechanisms and contributing factors associated with AVM formation are still undefined, changes in genetic pathways and abnormal expression of inflammatory proteins have been linked to this pathology (3, 4). Endovascular techniques, invasive surgery, interventional radiosurgery, and conservative approaches have been used to lower the risk of AVM rupture and resultant hemorrhagic stroke (5). Endovascular embolization, which is a procedure that blocks blood flow through an AVM, has recently been demonstrated

to successfully obliterate these malformations (6). This approach requires close access to the nidus, while maintaining low mean arterial pressure (MAP) to prevent backflow into the venous system and avoid occlusion of the venous drainage. The effectiveness of this procedure has become reliant on the use of vasodilators to induce time-sensitive periods of systemic hypotension, which allows the embolic agents to occlude the nidus without causing neurologic effects (6). Historically, the most common vasodilators are nitroglycerin, esmolol, nitroprusside and inhalational agents (6). All these agents cause hypotension individually, and their effects are not easily reversed should hemodynamic compromise occur. Since nitroprusside is associated with a risk for cyanide toxicity and esmolol infusions are expensive, nitroglycerin is a readily available option for intracranial aneurysm surgeries. By increasing nitric oxide release in vascular smooth muscle, nitroglycerin causes vasodilation that is easily titrated during an infusion. It is also known to cause headaches after prolonged infusion and refractory hypotension in cases of hypovolemia or cardiac dysfunction. For AVM endovascular embolization, however, literature on nitroglycerin use is insufficient. Adenosine has been proved to be a better alternative for controlled hypotension due to its replicability, consistency, and minimal side effects (7). This agent is a purine nucleoside that is rapidly cleared from blood with a short half-life of 0.6–20 s. A bolus of this drug causes flow arrest and decompresses the aneurysm sac, which in turn improves visualization and clipping without prolonged hypotension. By working directly at the AV node, adenosine in high doses may cause a high-grade conduction block, leading to arrythmias, hypotension and transient cardiac arrest. Thus, patients receiving adenosine should have cardiac arrest defibrillator pads placed prior to use in case a shockable rhythm develops. Tachyphylaxis induced by adenosine, however, has been described as a possible complication when administering increased doses for supraventricular tachycardia (7). In this report, we present a unique case of an adenosine-resistant patient treated with an effective combination of adenosine and increasing doses of nitroglycerine to achieve a target systemic MAP of 50 mmHg during an AVM embolization.

Case presentation

The patient was a 38 year-old male with a past medical history of hypertension, which was adequately treated with oral nifedipine and enalapril. The patient's chief complaint was a severe headache that was accompanied by one-sided weakness of his left side and slurred speech, dizziness, nausea, and episodes of emesis, which led him to seek medical attention. Upon evaluation, he had preserved cranial nerve function and mental status with a Glasgow Coma Scale (GCS) of 15/15. There was left-side hemiparesis graded 4 out of 5, as well as a positive Hoffman sign, left pronator drift, a negative Babinski sign, and hyperreflexia (+3) of the left side. A computed tomography (CT) without contrast of the head was performed that revealed a right frontal, flame-shaped, intracranial hemorrhage (ICH) involving the cingulate gyrus and corpus callosum. To identify the source of the bleeding, further imaging was performed with computed tomographic angiography (CTA) of the brain to evaluate any anomaly in the vascular system. Due to his young age and lack of risk factors for other more common etiologies of ICH, an AVM was suspected. The CTA confirmed the presence of a right medial frontal diffuse AVM (13.40 × 12.60 × 18.82 mm), with feeders from the right anterior cerebral artery, deep venous drainage, and an associated small perinidal aneurysm (Figure 1). Venous drainage involved the internal cerebral veins, vein of Galen, straight sinus to the torcula leading to the rest of the venous system. Using the Spetzler-Martin Grading system, which considers AVM size, eloquence, and location (8), the lesion was given a grade III. The supplementary Spetzler Martin Grade is 3 points given the age of patient (between 20 and 40), the presence of prior bleeding and its diffuse anatomic nature. The patient was immediately admitted into the neurosurgery intensive care unit (ICU) for closer monitoring and treatment. During his admission, his symptoms began to improve, but did not resolve completely. Since the ICH was estimated to be around 18 mL, and the patient was clinically stable, endovascular embolization was the preferred approach for this patient without prior hematoma evacuation. In preparation for the procedure, a systemic blood pressure threshold of 150/90 mmHg was maintained with enalapril (10 mg daily). In addition, any medications or activities that could secondarily increase intracranial pressure (ICP) were avoided. One week following the diagnosis and medical optimization, the patient was taken to the operating room for a cerebral angiogram and embolization of the AVM with ONYX embolic agent (Medtronic, Irvine, CA, United States), All ASA (American Society of Anesthesiologists) monitors were placed, including defibrillator patches. A 5 mg bolus of midazolam was administered (IV) as premedication. Smooth induction of anesthesia was achieved with 150 mg propofol, 100 µg fentanyl, and 100 mg succinylcholine. He was endotracheally intubated using direct laryngoscopy with MAC blade #4 and ETT size 7.5 mm. An additional peripheral IV line and a right arterial radial line were placed. Vascular access was gained through the left femoral artery and right femoral vein for local blood flow control with balloon insertion and embolisate injection, respectively. The arterial catheter setup included a Scepter C 4 mm X 11 mm (Microvention) compliant balloon microcatheter to assist with in-flow reduction to the AVM nidus. The venous catheter setup included a DMSO compatible (Headway Duo, Microvention) microcatheter. After micro catheterization proximal to the right frontal AVM's nidus, the perinidal aneurysm was coiled under fluoroscopic guidance to reduce venous reflux of ONYX particles. The previously positioned balloon was inflated to obtain proximal arterial control and reduce forward blood flow. Following the method of Hashimoto and colleagues (9), a baseline nitroglycerin drip (5 mg/min) was initiated prior to the procedure in order to decrease MAP by 10% from baseline. Preceding AVM embolization, adenosine was used in boluses to induce short periods of target MAP (50 mm Hg that last at least 10 s). Specifically, an adenosine bolus of 12 mg (IV push) was administered, followed by two series of adenosine boluses. Each series consisted of an initial adenosine bolus (24 mg, IV push) followed by a second bolus (12 mg, IV push) after 30 s. Whereas in other patients the serial administration of adenosine induces transient hypotension, our patient did not achieve the expected hemodynamic response. In an effort to obtain the appropriate MAP reduction, the nitroglycerin drip was increased to 15 mg/min, yet the MAP remained above the target goal. Finally, the optimal MAP was achieved with an additional bolus of adenosine and an increase in nitroglycerin to 20 mg/min. AVM embolization was then performed by injecting a combination of ONYX 34 (0.6 mL) and ONYX 18 (1.0 mL). Complete obliteration of the arteriovenous defect was confirmed with a post-procedure angiogram (Figure 2). The only complication of the

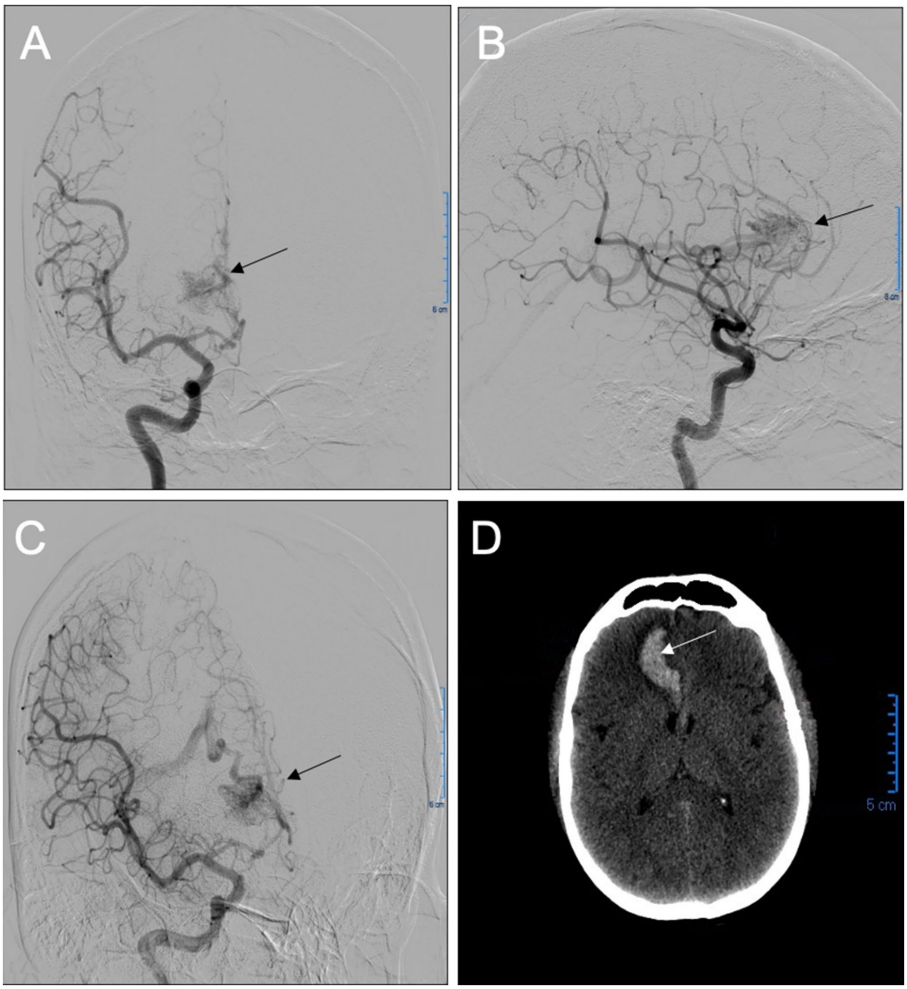

FIGURE 1
Anteroposterior **(A)**, lateral **(B)**, and oblique **(C)** projections of a preoperative digital subtraction angiography (DSA) from a right internal carotid artery injection demonstrated a diffuse right frontal arteriovenous malformation (AVM), with feeders from the right anterior cerebral artery and deep venous drainage. Preoperative head CT **(D)** shows an intraparenchymal hematoma centered in the right medial frontal lobe extending to the callosal sulcus.

procedure was a transient reactive vasospasm at the carotid bifurcation during arterial access, which was treated with verapamil (3 aliquot of 5 mg/each). Paralysis was successfully reversed with sugammadex (200 mg), and morphine (4 mg) was then administered for postoperative pain. The patient was successfully extubated and transferred to the post anesthesia care unit (PACU) for observation and was later discharged to the ICU. A postoperative head CT showed moderate enlargement of intracerebral hemorrhage presumably due to adenosine resistance during procedure, which difficulted blood pressure control during the embolization requiring increased nitroglycerin dosing. Post-operative head CT after 24 h, showed hematoma size of around 30 cc as compared to 18 cc initially, however patient remained clinically stable with mild symptomatology. A second follow up head CT scan at 48 h showed stable ICH volume. Strict blood pressure control was employed at the ICU and he was subsequently discharged 5 days later to a rehabilitation facility. Ten months after the procedure, the patient presented to the neurosurgery clinics for a follow up angiogram, revealing no evidence of AVM recurrence (Figure 3). The patient's outcome was favorable despite hemodynamic challenges, reporting resolved left hemiparesis and only mild balance deficit. Since the patient can carry out all daily without significant disability, a modified Rankin scale of 1 point was designated.

Discussion

To our knowledge, this is the first description of the concomitant use of adenosine and nitroglycerin for the successful embolization of a brain AVM. Transvenous embolization has been associated with various complications, including AVM rupture and subsequent hemorrhage (10). Thickening and arterialization of the venous walls secondary to higher-than-normal intraluminal pressures, however, make this approach a safe alternative (11). Successful application of this method requires that the embolic agent overcomes the anterograde arterial pressure and move in a retrograde fashion from the venous system into the nidus. This procedure requires pharmacological intervention to achieve the necessary reduction in MAP.

Prior to the administration of adenosine, Hashimoto and colleagues (9) used a continuous infusion of nitroprusside to decrease baseline MAP by 10%. The baseline reduction of MAP is a useful

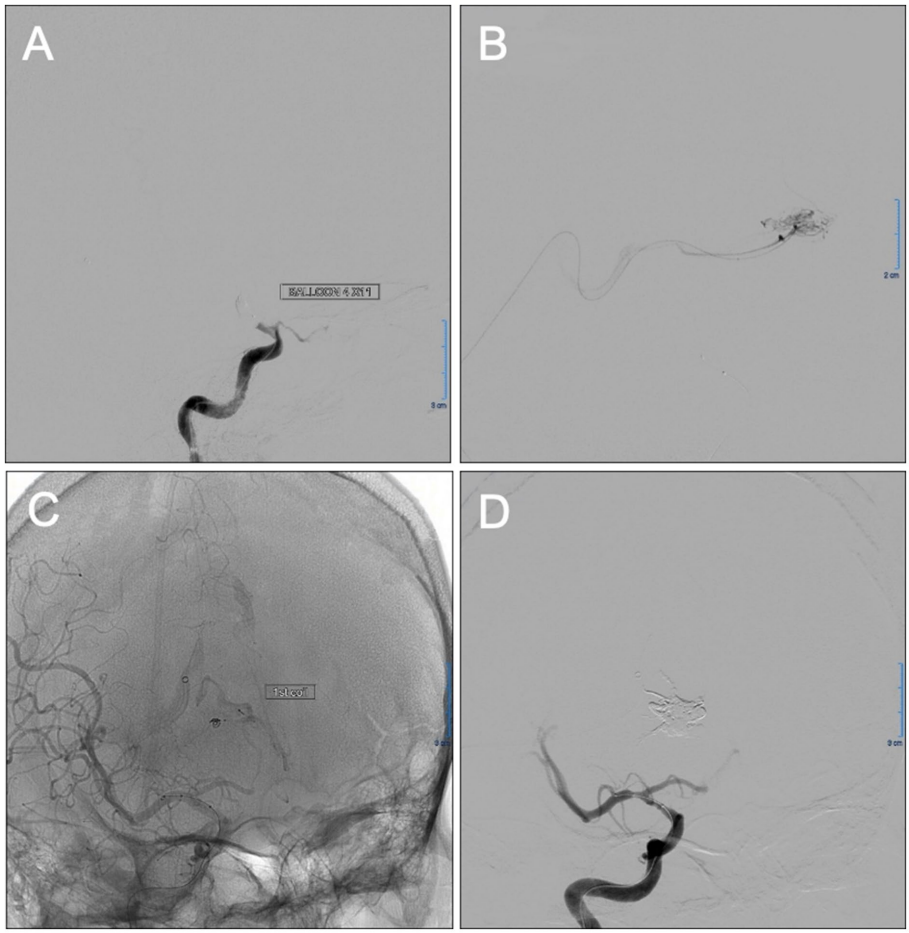

FIGURE 2
Intraoperative images showing planning and completion of the transvenous Onyx embolization of the diffuse right frontal arteriovenous malformation (AVM). Balloon test occlusion of the anterior cerebral artery A1 segment **(A)** was done during embolization for proximal vascular control of the AVM nidus flow. After superselective venous catheterization of the straight sinus, deep venous system, and right frontal AVM nidus, superselective runs **(B)** showed nidus configuration and no significant collateral reflux. Unsubstracted radiograph **(C)** shows proper placement of aneurysm coil proximal to the nidus performed under fluoroscopic guidance to reduce venous reflux of Onyx (pressure cooker technique). Oblique digital subtraction angiography (DSA) view of right internal carotid injection post-embolization **(D)** showed complete obliteration of the AVM nidus.

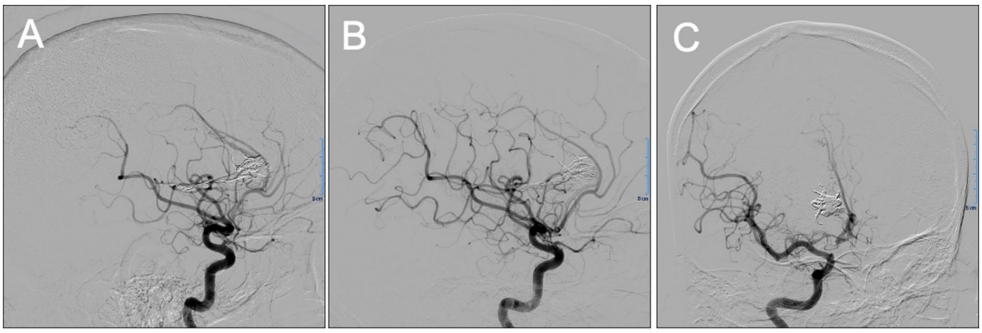

FIGURE 3
Lateral **(A,B)** and oblique **(C)** projections of control digital subtraction angiography (DSA) 10 months after embolization showing no evidence of arteriovenous malformation (AVM) recurrence.

strategy to reduce the potential for post-adenosine rebound hypertension (9). In the present report, however, nitroglycerin was selected as the vasodilator of choice because it has been associated with lower incidences of tachyphylaxis and rebound hypertension than nitroprusside (12, 13). Contrary to our expectations, repeated boluses of adenosine did not result in adequate hemodynamic control. The appropriate reduction in MAP was achieved, however, after increasing nitroglycerin infusion to a dose of 20 mg/min.

The use of adenosine alone to induce a transient arrest in the cardiac cycle during AV embolization has been described previously (6). Adenosine provides an advantage over other pharmacological agents due to its predictable duration, the extent of its effects, the reduced risk of complications, and its low side effects profile (9). Additionally, its short half-life allows for a profound and rapidly reversible transient hypotension, which increases the effectiveness of the embolic agent (6). The fact that adenosine was unable to effectively reduce MAP may indicate that this patient is adenosine resistant. It has been suggested that adenosine response and predictability are patient-dependent, and tachyphylaxis may develop after administration of repeated boluses of the drug (9, 14, 15).

After a complete AVM embolization by the transvenous route, the patient in this case showed no recurrence of his malformation in the 10 month, follow-up imaging. Such success rates following endovascular therapy alone are rare, even more so in challenging cases such as this one. The anesthetic management was of utmost importance during a procedure that relied heavily on hemodynamic control. Although the patient was only partially responsive to adenosine, nitroglycerin was able to act strategically as an adjunct by targeting a different component of the vascular response. In this way, greater control of the nidus pressures was attained, which in turn allowed for curative endovascular therapy. In conclusion, this report suggests that nitroglycerin infusion can be combined with adenosine boluses to create a pronounced and dose-dependent hypotension in patients partially unresponsive to adenosine alone.

One of the limitations of this pharmacological intervention, is that since this is a case report, the results were primarily based on a single adenosine resistant patient, who was only evaluated 10 months after the procedure. Further studies including more adenosine-resistant patients, and additional follow up interventions are needed to validate our conclusion. The findings of this study, however, provide a foundation to continue research on the concomitant use of adenosine and high dose nitroglycerine for successful embolization.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

This study involving human participant was reviewed and approved by the Ethics Committee on Biomedical Research of the University of Puerto Rico- School of Medicine. Written informed consent to participate in this study was provided by the participant.

Author contributions

VR-N worked in the conceptualization of the manuscript, writing the draft, and compiled the figures. CR-C and AR-S contributed with the writing and editing of the manuscript, and performed literature review. MR contributed with the writing of the draft and compilation of the figures. CF-V, HT-P, and PF revised manuscript and figures. MJC wrote the manuscript, revised the final version, and submitted the manuscript. All the authors read and approved the final version of the manuscript.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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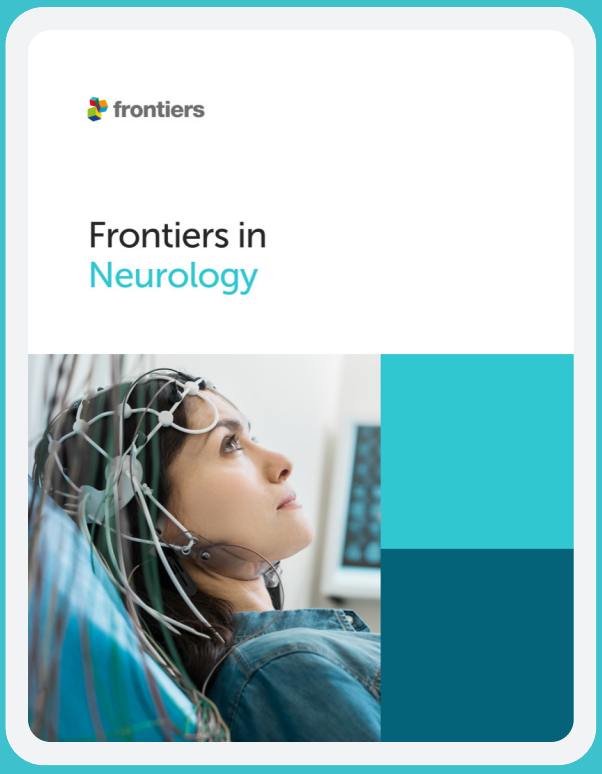

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