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CASE REPORT

Transvenous approach for the treatment of direct carotid cavernous fistula following Pipeline embolization of cavernous carotid aneurysm: a report of two cases and review of the literature

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SUMMARY

Flow diverters are increasingly used for the endovascular treatment of cerebral aneurysms. A rare complication from flow diversion is delayed aneurysm rupture, which can lead to carotid–cavernous fistula (CCF) in the setting of cavernous carotid aneurysms (CCAs). Direct CCFs pose unique management challenges, given the lack of transarterial access to the fistula. We present two cases of direct CCFs following treatment of CCAs with the Pipeline embolization device (PED). Case 1 was a middle-aged patient with a symptomatic 10 mm wide-necked left CCA. Six weeks after PED treatment the patient developed diplopia secondary to direct CCF. Case 2 was a middle-aged patient with a symptomatic 17 mm left CCA treated with PED. One-month follow-up angiography demonstrated a direct CCF. Both patients underwent successful coil embolization of the CCF through a transvenous approach. Direct CCF formation following PED deployment for CCA is a rare complication. Parent vessel sacrifice may be avoided with transvenous occlusion of the fistula.

BACKGROUND

Flow diverters such as the Pipeline embolization device (PED; Covidien, Mansfield, Massachusetts, USA) are a new class of low porosity endoluminal devices that promote parent vessel reconstruction and aneurysm occlusion for otherwise difficult-to-treat cerebral aneurysms. To date, national and international clinical experience with the PED has demonstrated its effectiveness, durability and safety of endovascular reconstruction.[1–6]

A rare complication following PED placement is delayed aneurysm rupture. Analysis of the International Retrospective Study of Pipeline Embolization Device (IntrePED) registry of 580 aneurysms treated worldwide with PED revealed only three spontaneous aneurysm ruptures after PED implantation, an incidence of 0.6%.[7] Additionally, the European Society of Minimally Invasive Neurological Therapies (ESMINT) Retrospective Analysis of Delayed Aneurysm Ruptures (RADAR) study found 14 delayed aneurysm ruptures among 1421 aneurysms treated with flow diverters, an incidence of 1%.[8]

Various hypotheses for delayed rupture include altered intraluminal and intra-aneurysmal hemodynamics and the proteolytic/inflammatory/ischemic effects of the endosaccular thrombus on the aneurysm wall.[9] In the treatment of cavernous carotid aneurysms (CCAs) with flow diversion, delayed aneurysm rupture can lead to a direct carotid–cavernous fistula (CCF). Although direct CCFs are typically treated via the transarterial route, a direct CCF following PED poses a unique situation given that the endoluminal device excludes transarterial access. We describe two cases of direct CCF following treatment of CCA with PED alone and also present our treatment strategy using coil embolization via a transvenous approach.

CASE PRESENTATION

Case 1

A middle-aged patient presented with worsening left retro-orbital headache and vertical diplopia over a 1-week course. Ophthalmologic examination revealed left trochlear nerve palsy. Brain MRI and MR angiography showed multiple, not partially thrombosed intracranial aneurysms (figure 1A); digital subtraction angiography (DSA) confirmed a 10 mm wide-necked aneurysm along the horizontal segment of the left cavernous carotid artery (figure 1B, C) and a 5 mm wide-necked bilobed aneurysm along the anterior genu of the right cavernous carotid artery. The PED was chosen over stent coiling because of the need to reconstruct a diseased segment of the vessel and to prevent additional mass effect that comes with the use of coils. Seven days prior to the procedure the patient was started on aspirin 325 mg and clopidogrel 75 mg. The PED was delivered transfemorally using a triaxial system as previously described.[10] A 5 mm×18 mm PED was successfully deployed across the aneurysm neck without complications. Control DSA images demonstrated significant contrast stasis within the aneurysm consistent with flow remodeling after PED placement (figure 1D–F). The patient had an unremarkable postoperative course and was discharged at neurological baseline with daily aspirin 325 mg and clopidogrel 75 mg. Six weeks later the patient returned for scheduled embolization of the right-sided CCA. At this time the patient was noted to be wearing a new left eye patch and reported having worsening diplopia for the past several weeks.

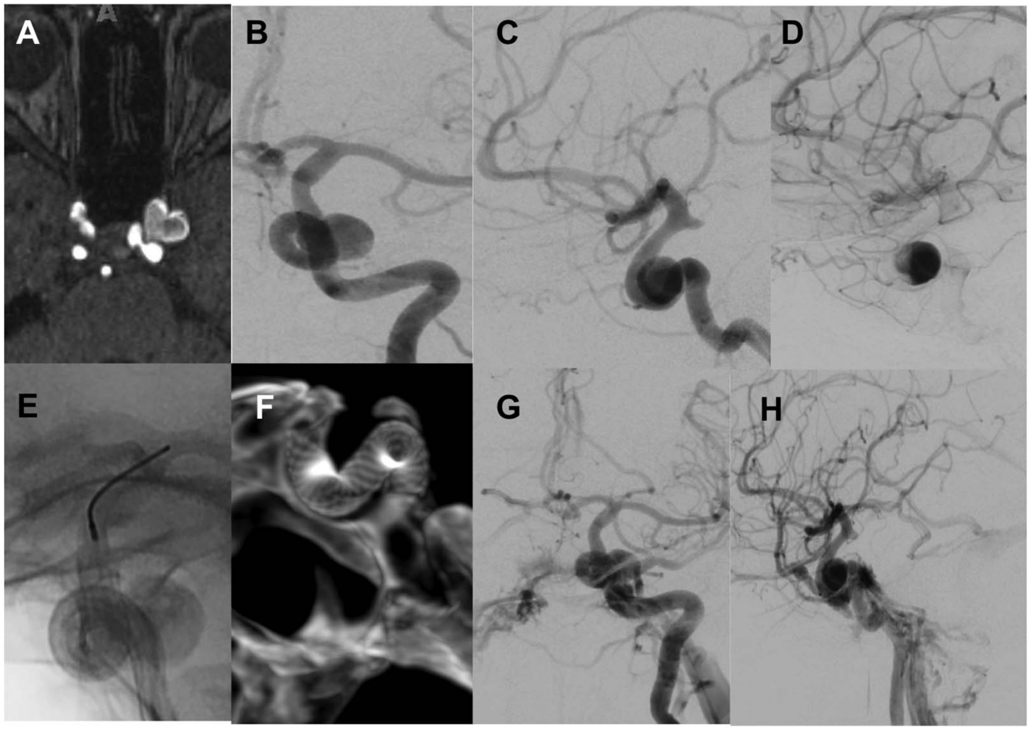

Figure 1 Case 1: left cavernous carotid artery aneurysm (CCA) and direct carotid cavernous fistula (CCF). (A) MR angiography of left internal carotid artery (ICA) aneurysm, non-thrombosed. (B, C) Left common carotid digital subtraction angiography (DSA) (B: anteroposterior view, C: lateral view) demonstrating 10 mm wide-necked aneurysm along the horizontal segment of the left cavernous carotid artery. (D) Left ICA DSA (lateral view) after implantation of the Pipeline embolization device (PED) with pronounced contrast stasis within the aneurysm consistent with flow remodeling. (E) Magnified view of PED showing adequate vessel wall apposition to the device. (F) Dyna CT without contrast reconstructed images of the implanted PED. (G, H) Left common carotid artery DSA (G: anteroposterior view, H: lateral view) 6 weeks post PED demonstrating the direct CCF with opacification of the cavernous sinus as well as the inferior petrosal sinuses and retrograde cortical venous drainage through the left superficial Sylvian vein, vein of Labbe and basal vein of Rosenthal.

Case 2

A middle-aged patient with a known and conservatively managed non-thrombosed 10 mm left CCA (figure 2A) presented with acute left abducens nerve palsy. Given the new symptoms, the patient underwent DSA which demonstrated interval growth of the aneurysm to 17 mm (figure 2B, C). Seven days prior to the procedure the patient was started on aspirin 100 mg daily and ticlopidine 250 mg twice a day. The patient underwent transfemoral delivery of a PED via a 6F Envoy guide catheter (Codman, Raynham, Massachusetts, USA) and 135 cm Marksman microcatheter (Covidien). A 4.5 mm×20 mm PED was successfully deployed across the aneurysm neck without complications (figure 2D, E) Control DSA images demonstrated a satisfactory PED position and vessel wall apposition; there was also contrast stagnation within the aneurysm sac, as expected from interval flow remodeling post PED placement (figure 2F, G). On post-procedure day 3 the patient described hearing a humming sound, giving concern for pulsatile tinnitus. Head CT angiography was unremarkable for an underlying fistula. At 1-month follow-up the patient reported increased intensity of the pulsatile tinnitus with persistent abducens nerve palsy.

INVESTIGATIONS

Case 1

New DSA images from the left internal carotid artery (ICA) injection demonstrated interval development of a direct CCF with opacification of the cavernous sinus and inferior petrosal sinuses as well as retrograde cortical venous drainage through the left superficial Sylvian vein, vein of Labbe and basal vein of Rosenthal (figure 1G, H).

Case 2

New CT angiography images showed a direct CCF with prominence of the cavernous sinus and inferior petrosal sinuses. These findings were confirmed with DSA (figure 2H–J).

TREATMENT

Case 1

A transvenous approach was selected for treatment of the CCF. A 5-French sheath was introduced in the right common femoral artery and a JB-1 glide catheter (Terumo, Somerset, New Jersey, USA) was then introduced. The JB-1 was positioned in the left ICA to provide roadmap guidance and control angiography. The left common femoral vein was accessed with a 6-French sheath. A 5-French Envoy MPC guide catheter (Codman) was coaxially introduced into the left femoral venous axis up the inferior vena cava into the superior vena cava and positioned in the proximal left internal jugular vein. An Echelon 10 microcatheter (Covidien) was then advanced over a Synchro 2 standard microwire (Stryker, Freemont, California, USA) coaxially through the Envoy guide catheter and advanced up through the left inferior petrosal sinus into the left cavernous sinus and positioned near the fistulous point (figure 3). Coil embolization was performed using Axium (Covidien) and Cashmere (Codman) coils (table 1). Coil loops provided coverage in the cavernous sinus near the fistulous connection and some loops formed within the actual

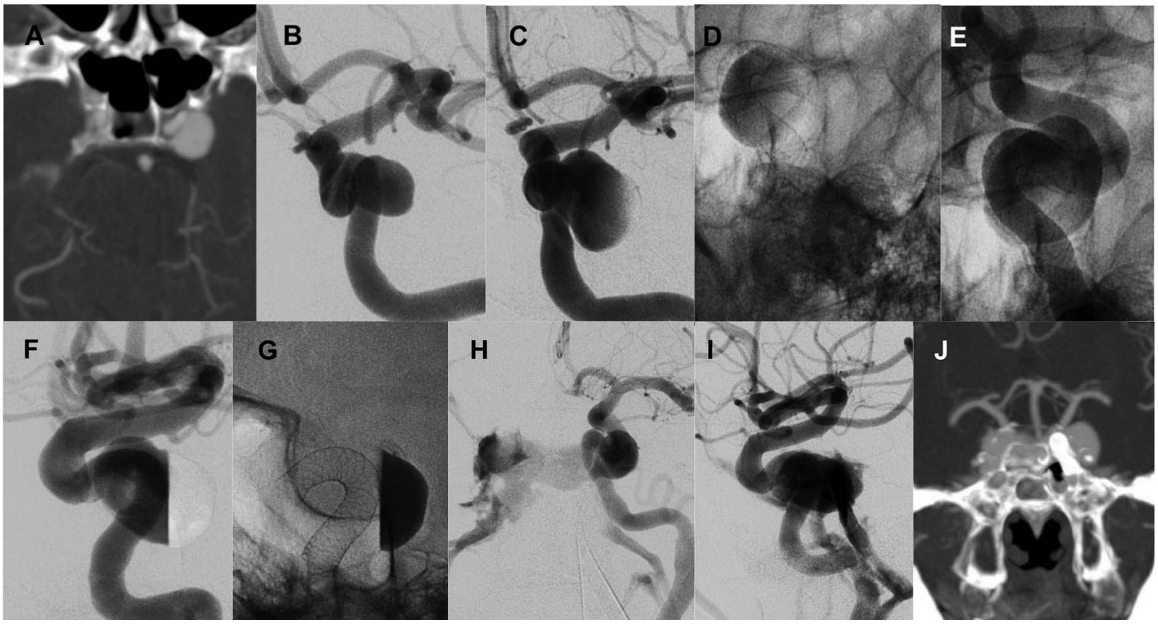

Figure 2 Case 2 left cavernous carotid aneurysms (CCA) and direct carotid–cavernous fistula (CCF) one month after Pipeline embolization device (PED) implantation. (A) CT angiogram of left internal carotid artery (ICA) aneurysm, non-thrombosed. (B) Left common carotid artery digital subtraction angiography (DSA) (anteroposterior view) demonstrating a 10 mm left CCA. (C) Left common carotid artery DSA (anteroposterior view) 23 months later demonstrating growth of the left cavernous carotid artery aneurysm to 17 mm. (D, E) Magnified view of PED demonstrating adequate vessel wall apposition of the device. (F) Left common carotid artery DSA (lateral view) after PED implantation demonstrating pronounced contrast stasis within the aneurysm consistent with flow remodeling. (G) Lateral native fluoroscopy image post PED. (H, I) Left common carotid artery DSA (H: anteroposterior view, I: lateral view) demonstrating direct CCF one month post PED with opacification of the cavernous sinus and inferior petrosal sinuses. (J) CT angiogram demonstrating a direct CCF with prominence of the cavernous sinus and inferior petrosal sinuses.

aneurysm sac. Control DSA images demonstrated complete occlusion of the CCF with significant contrast stagnation within the left CCA and complete resolution of the retrograde cortical venous reflux (figure 3). There were no complications and the patient had an uneventful post-procedure course.

Case 2

The patient underwent a transvenous approach via the contralateral internal jugular vein, inferior petrosal sinus and intercavernous sinus for treatment of the CCF. First, the right common femoral artery was accessed with a 5-French sheath. A 5-French

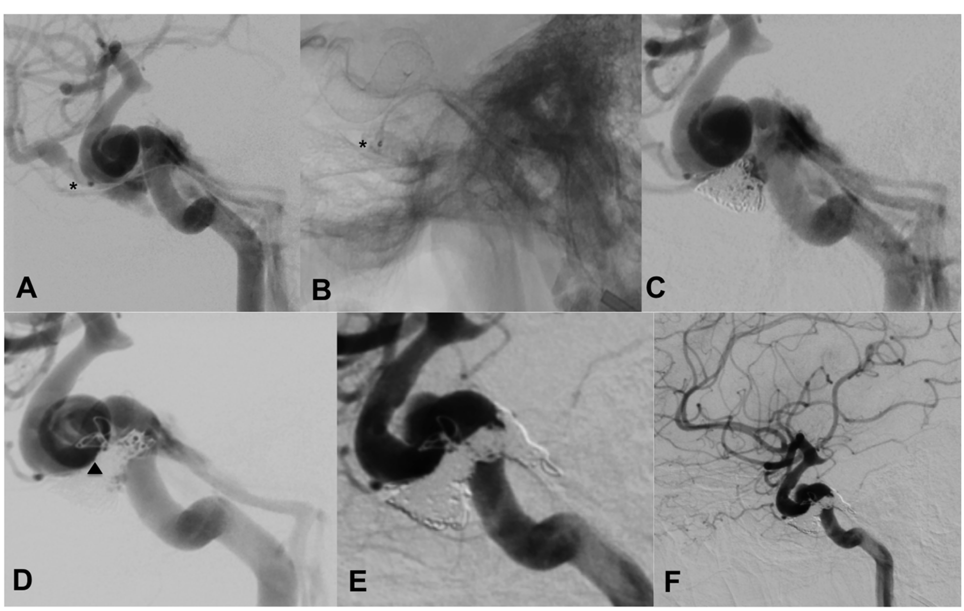

Figure 3 Transvenous coil embolization of case 1 direct carotid-cavernous fistula (CCF). (A) Left internal carotid artery (ICA) digital subtraction angiography (DSA) (lateral view) demonstrating distal microcatheter position (asterisk). (B) Lateral native fluoroscopy demonstrating microcatheter position (asterisk) in the fistulous connection. (C) Left ICA DSA (lateral view) after deployment of six coils. (D) Left ICA DSA (lateral view) after deployment of 12 coils with a few coil loops in the aneurysm sac (arrowhead). (E, F) Left ICA DSA (lateral view) final run after 19 coils with complete occlusion of the direct CCF and contrast stasis within the aneurysm.

Table 1 Coils used during transvenous coil embolization of the two carotid–cavernous fistulas occurring after treatment of cavernous carotid aneurysms with Pipeline embolization device

Coil no.	Case 1	Case 2
1	Axium 5 mm×15 cm 3D coil	Penumbra 16 mm×60 cm
2	Axium 4 mm×10 cm coil	Penumbra 12 mm×45 cm
3	Axium 4 mm×10 cm coil	Penumbra 6 mm×15 cm
4	Axium 4 mm×8 cm coil	Penumbra 5 mm×13 cm
5	Axium 3 mm×8 cm coil	
6	Axium 2 mm×8 cm helical coil	
7	Axium 2 mm×8 cm helical coil	
8	Axium 3 mm×8 cm 3D coil	
9	Axium 3 mm×8 cm 3D coil	
10	Axium 4 mm×8 cm 3D coil	
11	Axium 4 mm×8 cm 3D coil	
12	Axium 5 mm×15 cm 3D coil	
13	Axium 5 mm×15 cm 3D coil	
14	Cashmere 14 4 mm×8 cm microcoil	
15	Cashmere 14 3 mm×6 cm microcoil	
16	Cashmere 14 3 mm×6 cm microcoil	
17	Cashmere 14 3 mm×6 cm microcoil	
18	Axium 3 mm×8 cm helical coil	
19	Axium 3 mm×8 cm helical coil	

Hinck catheter (Terumo, Somerset, New Jersey, USA) was then introduced and positioned in the left ICA. The right femoral vein was then accessed with a 6-French sheath. A 6-French Envoy guide catheter (Codman) was coaxially positioned in the right internal jugular vein. The cavernous aneurysm was then accessed through the rupture point using a PX 400 Penumbra microcatheter (Penumbra, Alameda, California, USA) (figure 4). Four Penumbra coils were deployed within the aneurysm sac and neck, as well as the fistulous site (table 1). Control DSA images demonstrated complete occlusion of the CCF (figure 4). No complications were encountered and the patient had an uneventful hospital course.

OUTCOME AND FOLLOW-UP

Case 1

The patient was discharged home on post procedure day 1 with daily aspirin 325 mg and clopidogrel 75 mg, and follow-up angiography performed 6 months thereafter demonstrated complete occlusion of both the direct CCF and the aneurysm. The clopidogrel was discontinued after the 6-month follow-up and the patient was maintained on daily aspirin 325 mg. The patient's diplopia was improved from baseline and an eye patch was no longer required.

Case 2

The patient reported immediate resolution of the pulsatile tinnitus. Brain MRI and MR angiography performed 1 month later demonstrated persistent occlusion of the CCF without any evidence of residual or recurrence. The patient continued double antiplatelet regimen for 1 month and then aspirin 100 mg daily for 3 months. Two months later the patient reported complete resolution of the abducens nerve palsy. Follow-up cerebral angiography at 6 months demonstrated complete occlusion of the direct CCF and the aneurysm (figure 4).

DISCUSSION

In this report we describe the first occurrences of delayed CCA rupture after PED treatment with resultant direct CCF. An extensive literature search found only four other cases of direct CCFs occurring after delayed rupture of treated CCAs (table 2).[11–13] One CCF involved stent-assisted coiling of a 9 mm symptomatic CCA which resolved spontaneously.[11] The other three cases involved the Silk Flow Diverter (Balt Extrusion,

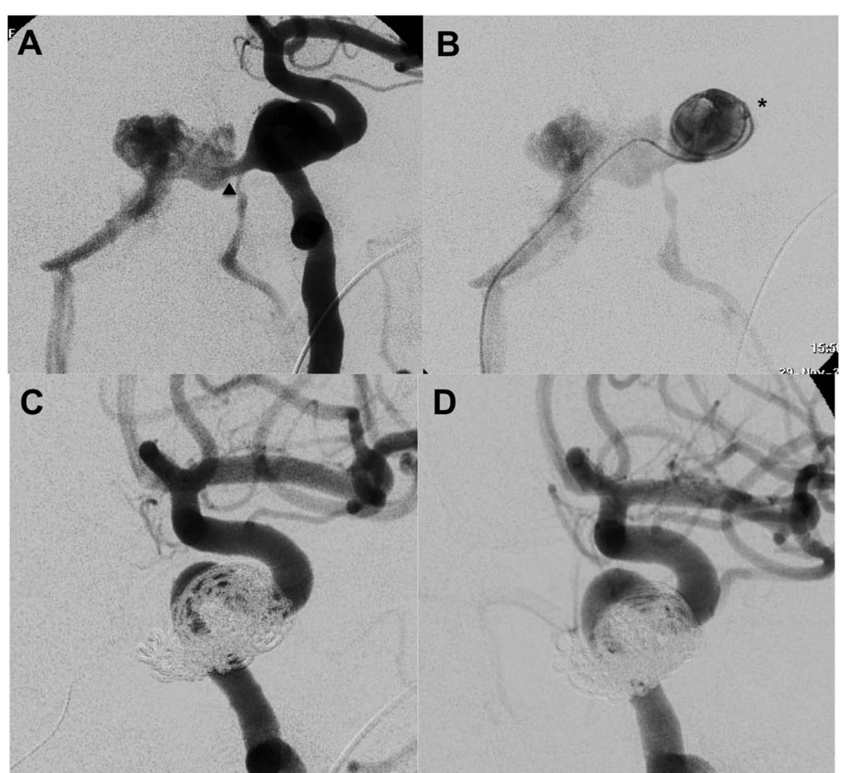

Figure 4 Transvenous coil embolization of case 2 direct carotid-cavernous fistula (CCF). (A) Left internal carotid artery (ICA) digital subtraction angiography (DSA) (anteroposterior view) demonstrating the fistulous connection (arrowhead). (B) Microcatheter supraselective DSA (anteroposterior view) demonstrating the microcatheter position (asterisk) within the aneurysm sac. (C) Left common carotid artery DSA (anteroposterior view) after transvenous coil embolization of the fistulous connection demonstrating complete occlusion of the direct CCF and the aneurysm. (D) Left common carotid artery DSA (lateral view) 6 months after transvenous coil embolization of the fistula with complete occlusion of the aneurysm and the direct CCF.

Table 2 Published cases of carotid cavernous fistulas (CCFs) after rupture of treated cavernous carotid aneurysms

Authors (year)	Age (years), sex	Symptoms	Aneurysm size (mm)	Aneurysm treatment	Interval to rupture (days)	CCF treatment
Chan *et al* (2011)	58, F	Right retro-orbital pain, blurred vision	9	Neuroform+6 Axium coils	30	None (resolved spontaneously)
Kulcsar *et al* (2011)	74, F	None	20	1 Silk	3	Parent artery occlusion
Kulcsar *et al* (2011)	48, F	Diplopia	24	1 Silk	110	Parent artery occlusion
Mustafa *et al* (2010)	39, F	Right hemifacial pain	17.6	1 Silk	14	Transvenous coiling

Montmorency, France).[12 13] Two of these cases were treated with parent artery occlusion while the other was managed with transvenous coil embolization. The incidence of delayed spontaneous aneurysm rupture after treatment with a flow diverter ranges from 0.6% to 1%.[7 8 12] The only identifiable risk factor for delayed rupture is size of 10 mm or greater.

Direct CCFs resulting from rupture of an untreated CCA are typically managed through transarterial obliteration of the fistulous site. The goal of treatment is to occlude the site of communication between the ICA and the cavernous sinus while preserving the patency of the ICA. Traditionally, flow-directed detachable balloons positioned to seal the tear in the ICA had been the standard treatment of choice until their removal from the international market secondary to problems with the balloon valve mechanism. Since then, coil embolization to occlude the fistula has become the mainstay transarterial option in managing direct CCFs. During transarterial coil embolization a temporary balloon or a self-expanding stent such as the Neuroform (Stryker Neurovascular) or Enterprise (Cordis Neurovascular, Miami, Florida, USA) may be placed in the parent ICA across the rupture site to protect the parent vessel and prevent coil migration or prolapse.[14]

Management of direct CCFs following CCA treatment with flow diverters represents a novel challenge. First, treatment is recommended as the fistulas will not spontaneously thrombose. Furthermore, the transarterial approach is not a viable option because the low porosity of the PED prevents transarterial access into the aneurysm and subsequently into the rupture site or fistulous connection. Therefore, the remaining treatment options available are parent artery sacrifice or a transvenous embolization.

The transvenous route to treat direct CCFs is typically selected when severe tortuosity or inaccessibility of the proximal ICA obviates transarterial options.[15] Occlusion of a direct CCF transvenously most commonly involves a posterior approach through the inferior petrosal sinus via the internal jugular vein. The location of the shunt involving the cavernous sinus is then accessed through the inferior petrosal sinus. If the inferior petrosal sinus is occluded, the cavernous sinus may be accessed through an anterior approach through the superior ophthalmic vein via the facial vein. Once access in the cavernous sinus is obtained, transvenous embolization of the direct CCF is accomplished by disconnecting the venous outflow at the level of the fistula with detachable coils. If the direct CCF occurs prior to complete endothelialization of the PED, the antiplatelet agents would need to be continued. However, this continuation of the antiplatelet agents may conversely hinder closing of the fistula.

In both cases we proceeded with a transvenous approach in attempts to preserve the parent artery and obtained microcatheter access to the cavernous sinus through the inferior petrosal sinus via the internal jugular vein. In the first case, a few coil loops fortuitously went into the aneurysm sac to occlude the aneurysm and the fistula. With the second case, we navigated the microcatheter further through the rupture site into the actual CCA, allowing coil embolization of the aneurysm sac back through the fistulous connection into the cavernous sinus. This ability to access the actual aneurysm sac perhaps allowed for less coil mass in the cavernous sinus to still achieve closure of the fistulous connection. Occlusion of the direct CCF was achieved in both cases. Since flow diverters such as the PED are now increasingly used to treat ICA aneurysms, it is important that neurointerventionalists be cognizant of CCF formation as a potential complication and be able to treat such CCFs without parent vessel sacrifice.

CONCLUSION

Direct CCFs may occur following CCA treatment with flow diverters. Although this is a rare complication, neurointerventionalists ought to be mindful of such occurrences given the unique challenges of managing the CCF in this setting. Parent vessel sacrifice may be avoided in such situations with transvenous occlusion of the fistulous connection. The need to continue post-procedure antiplatelet agents may delay complete occlusion of the fistula.

Learning points

- Direct carotid–cavernous fistula is an uncommon but important complication of delayed cavernous carotid aneurysm (CCA) rupture after Pipeline embolization device (PED) treatment.
- Patients may present with ophthalmoplegia from CN III, IV, and VI palsy or with pulsatile tinnitus from the fistula.
- CCF cannot be treated via a transarterial approach in patients treated with PED due to the low porosity PED device preventing access into the aneurysm.
- Transvenous endovascular embolization can be through the internal jugular vein to the inferior petrosal sinus or through the superior ophthalmic vein via the facial vein. Additionally, if the actual aneurysm sac can be accessed through the fistulous connection, this may allow less coil mass in the cavernous sinus to still achieve fistula closure.

Contributors ALC designed the data collection tools, monitored data collection for the whole case report, wrote the statistical analysis plan, cleaned and analyzed the data, and drafted and revised the paper. He is guarantor. L-ML, GPC, and BJ analyzed the data and drafted and revised the paper. GP and EB contributed their clinical expertise and initiated the collaborative project.

Competing interests ALC is a proctor and consultant for MicroVention, Stryker, and Covidien and a proctor for the PED. EB is a proctor for the PED. The other authors have no conflict of interest with the generation of this submission. There is no financial disclosure. No author received financial support in conjunction with the generation of this submission. There are no other conflicts of interest of any form involving any of the authors.

Patient consent None.

Ethics approval Ethics approval was obtained from Johns Hopkins IRB.

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