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Endovascular treatment of cranial aneurysms with the pipeline flow-diverting stent: preliminary mid-term results

Celal Çınar, Halil Bozkaya, İsmail Oran

PURPOSE
We aimed to present our initial experience with a new self-expanding flow diverter device designed for wide-neck aneurysm treatment, assess its safety for intracranial deployment and efficacy of occlusion at mid-term follow-up.

MATERIALS AND METHODS
Forty-five consecutive patients with difficult aneurysmal anatomy underwent an endovascular treatment. Fifty-five intracranial aneurysms were clipped using the Pipeline flow-diverting stent (ev3 Inc., Plymouth, Minnesota, USA) between November 2009 and December 2011. Data including antiplatelet therapy, technical issues, complications, and imaging findings were recorded during the follow-up period.

RESULTS
Twenty-seven aneurysms were asymptomatic, 13 were symptomatic due to mass effect, seven were recurrent, six had subarachnoid hemorrhage, and two subjects presented with ischemia. There were 45 saccular, six fusiform-dissecting, and four blister aneurysms. The six-month control angiography was available in 34 subjects with an 85.3% (29/34 patients) complete occlusion rate. The overall occlusion rate according to the last angiography was 91.9% (34/37 patients). The following three major technical complications without clinical consequences were encountered: one distal wire fracture of the stent delivery system and two insufficient stent expansion. There was one fatal nonaneurysmal cerebellar hemorrhage. The overall mortality rate was 2.2% with no permanent morbidity.

CONCLUSION
The Pipeline flow-diverting stent represents an important advancement in endovascular therapy for cerebral aneurysms. Standard endovascular techniques are typically not suitable for these types of aneurysms. The device targets primary parent vessel reconstruction rather than endosaccular occlusion to achieve exclusion of the aneurysm and maintain a relatively high occlusion rate at six months.

From the Department of Radiology (C.Ç. ✉ *celalcinar@hotmail.com*, H.B., İ.O.), Ege University School of Medicine, İzmir, Turkey.

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The endovascular treatment of wide-neck aneurysms has been facilitated by the use of balloon remodeling and stent assistance, decreasing the recanalization rates that were seen with coiling alone (1–3). Flow-diverting stents offer a new alternative for the treatment of difficult-to-treat aneurysm morphologies, including giant, wide-necked, fusiform, and blister types. The Pipeline flow-diverting stent (ev3 Inc., Plymouth, Minnesota, USA) is a porous endoluminal sleeve designed with approximately 30%–35% surface area coverage, roughly five times that of earlier nickel and titanium alloy (nitinol) stents. The Pipeline is thought to immediately reduce the inflow and outflow jets from the aneurysm and eliminate shear stress on the aneurysm wall, while still allowing blood flow to branch arteries and perforators covered by the device (4–6). Progressive aneurysm thrombosis is anticipated within days to weeks, while neointimal growth covers the device over the course of months. Resorption of thrombus from within the aneurysm results in a remodeled blood vessel, often with virtual reconstruction of normal anatomy (7, 8). To date, a limited number of reports have described the clinical use of flow-diverting stents, with several moderate-sized series showing approximately 90%–95% occlusion rates at 6–18 months (9–11). Additionally, these devices have been successfully used in challenging cases, including fusiform, bifurcation, blister, and giant aneurysms (7, 8, 12). However, complications have been reported including branch artery occlusion and delayed occlusion of the stented parent vessel shortly after discontinuation of antiplatelet medications. These complications highlight the potential need for long-term antiplatelet therapy (11, 13–15). Reports of early successes have also been tempered by published cases of delayed aneurysm rupture, with the proposed mechanism being thrombus-associated autolysis of the aneurysm wall (16, 17). Early experience with the Pipeline has largely been confined to the treatment of unruptured (or remotely ruptured and previously treated) intracranial aneurysms (12–17).

We used the standardized grading scale described by O'Kelly et al. (18) to evaluate angiographic outcomes. This scale is based on the degree of angiographic filling and contrast stasis throughout the angiographic phases (arterial, capillary, venous) and was specifically designed to measure the outcome of flow diversion treatment.

In this study we aimed to present our initial experience with a new self-expanding flow diverter device designed for wide-neck aneurysm treatment, assess its safety for intracranial deployment and efficacy of occlusion at mid-term follow-up.

Materials and methods

Patient population

A total of 45 patients with 55 intracranial lesions were treated with the Pipeline stent at our center between November 2009 and Decem-

ber 2011. Aneurysms with the following characteristics were included: a wide neck (4 mm), unfavorable dome/neck ratio (1.6), large size, fusiform anatomy, very small, and those that had failed previous therapy. Written informed consent was obtained. Data were collected prospectively with respect to aneurysm morphology, symptoms, previous treatment, antiplatelet and anticoagulation regimens, and technical and clinical complications. At six-month follow-up, evaluation included occlusion, mass effect, delayed complications, ongoing antiplatelet therapy, and in-stent stenosis.

Pipeline flow-diverting stent

The Pipeline flow-diverting stent is a composite braided mesh tube of 48 strands comprised of 75% cobalt chromium and 25% platinum. The single wire has a diameter of 30 µm. Devices are available with a nominal diameter from 2.5 to 5 mm with 0.25 mm increments. The device is inserted via a 0.027-inch inner diameter microcatheter (Marksman, ev3 Inc., Irvine, California, USA). Once the stent has reached the desired position, deployment starts by gently withdrawing the catheter and simultaneously advancing the insertion wire. As soon as the distal end of the stent is detached from the capture coil, further deployment is a combination of advancing the insertion wire and passive backward migration of the microcatheter.

Antiplatelet and anticoagulation treatment

Patients with both ruptured and unruptured aneurysms received a loading dose of 300 mg aspirin and 600 mg clopidogrel 6–12 hours prior to treatment and a dual antiplatelet treatment of 300 mg aspirin and 75 mg clopidogrel daily thereafter. Each patient was tested for proper response to aspirin and clopidogrel with Multiplate® Aggregometry (Dynabyte, Munich, Germany). According to the "Working Group on High On-Treatment Platelet Reactivity" consensus statement, a subject with a test result higher than 468 aggregation units (AU)×min was considered a clopidogrel nonresponder (19). Only two patients were identified as nonresponders to clopidogrel, and the procedure was postponed. The next day, these two patients were given ticlopidine 1000 mg (4×250 mg) as a loading dose 6–12 hours before treatment, and the repeat test results showed good response to ticlopidine. These two patients received dual antiplatelet treatment with 300 mg aspirin and ticlopidine 2×1 daily thereafter. An intravenous bolus of heparin (5000–7500 IU) was given at the beginning of the procedure. Activated clotting time was measured.

Dual antiplatelet medication for six months was administered for aneurysms in the anterior circulation. This management strategy followed the recommendations from the largest published flow-diverting stent study. Dual agents were administered 12 months for aneurysms in the posterior circulation. Sparse data are currently available on the incidence of perforator occlusion. (9–11). Patients were monitored for clopidogrel compliance by direct questioning. A longitudinal study was undertaken beyond six months in patients with nonocclusion of the aneurysm (stopping clopidogrel at six months in the anterior circulation cases) or in-stent stenosis (maintaining clopidogrel). Patients receiving ticlopidine were controlled monthly with routine hematologic examination until the drug was discontinued.

Endovascular procedure

Endovascular procedures were performed under general anesthesia and systemic heparinization. The parent artery was catheterized with a 6 F guide catheter or with a telescoping system with a 6 F long sheath (Shuttle, Cook Medical, Bloomington, Indiana, USA) and 6 F distal access guide catheter (Fargo/FargoMax, Balt Extrusion, Montmorency, France). A system of telescopic catheters was used to achieve good support for the stent navigation. A Marksman microcatheter was inserted into the parent artery distally to the aneurysm with a 0.016-inch micro-guidewire. The correct expansion of the stent was documented under fluoroscopy. Balloon dilatation after incomplete expansion of the device was carried out in two cases. Insufficient expansion of the stent was mainly observed in vessel segments with tight or acute curves.

Follow-up

Elective patients were admitted the day before the procedure and discharged after 36–72 hours. A six-month control routine angiogram was obtained. Additional angiography was performed if the aneurysm was open or in-construct narrowing was present. In patients with mass effect, magnetic resonance imaging or computed tomography was also performed to assess interval change after treatment and, if possible, after clopidogrel was discontinued. Clinical follow-up was performed at 1, 3, 6, and 12 months, in addition to an independent evaluation by a neurologist or neurosurgeon. Patients were also seen more regularly if they had complex problems. The treatment outcome for saccular aneurysms were evaluated according to the O'Kelly-Marotta (OKM) grading scale (18).

In the case of complete aneurysm occlusion at follow-up angiography and the absence of intimal hyperplasia within the stent, we advised the patient to continue with dual antiplatelet therapy for an additional 3–6 months. The decision for repeat treatment was made individually based on the angiographic findings, patient's age, and clinical status.

Results

Patient and aneurysm characteristics

Data on 55 aneurysms in 45 patients were collected. Thirty-two females and 13 males (2.4:1) with a mean age of 48.8 years (median, 50 years; range, 8–70), mean aneurysm size of 14.2 mm (median, 10 mm; range, 2–45 mm), and mean aneurysm neck size of 6.8 mm (median, 5.5 mm; range, 2–38 mm) were included in the study. There were 9 giant (>25 mm), 22 large (10–25 mm), and 24 small (<10 mm) aneurysms. Of the 55 treated lesions, 27 (49%) were found incidentally, 13 (23%) had mass effect, seven (13%) were recurrent aneurysms, six (11%) had subarachnoid hemorrhage, and two (4%) subjects presented with ischemic symptoms. The series comprised 45 (82%) saccular, six (11%) fusiform, and four (7%) blister aneurysms. Forty-nine aneurysms were in the anterior circulation, and six were in the posterior circulation. Eight patients had received prior treatment; seven aneurysms were treated endovascularly and two aneurysms were clipped (one subject had two aneurysms treated by a coil and clip). Clinical presentation and aneurysm characteristics are presented in Table.

Treatment and procedural outcomes

Sixty-six stents were placed in 55 aneurysms (1.2 per aneurysm). Treatment with the Pipeline stent was performed

Table. Summary of the patients

No/Age (years)/Gender	Clinical presentation	Location	Type	Size/Neck (mm)	Peri-procedural complication	Late clinical complication	Control DSA (months)	Follow-up (months)/ Comment
1/46/Female	Mass effect	Carotid-cavernous	S	34/11	-	Transient increase of mass effect	Complete (6)	9/-
2/44/Female	Incidental	Superior hypophyseal	S	3/2	-	-	Complete (6)	12/-
3/42/Female	Incidental	Posterior cerebral artery P2-P3	S	10/7	Spontaneous cerebellar hemorrhage after 28 hours	Exitus at sixth day	Not available	Not available
4/59/Female	Incidental	Parophthalmic	S	15/6	-	-	Complete (6)	7/Clopidogrel resistance
5/51/Female	Mass effect	Carotid-cavernous	S	25/9-10/4	-	-	Complete (6)	26/-
6/53/Male	Ischemia	Vertebral V4	F	16/9	-	-	Complete (6)	26/-
7/50/Male	Ischemia	Vertebral V4	F	21/18	-	-	Complete (6)	13/-
8/46/Female	Incidental	Bilateral parophthalmic	S	8/6-4/4	-	-	Complete (6)	16/-
9/48/Male	Recurrent (coil) incidental aneurysms	Bilateral parophthalmic	S	24/8-5/4	-	-	Complete (6)	15/-
10/33/Female	Mass effect	Parophthalmic	S	26/7	-	-	Complete (6)	26/-
11/39/Female	Incidental	Parohthalmic-Paraclinoid	S	11/4-2/2	-	-	Complete (6)	12/-
12/39/Male	Chronic SAH	Bilateral parophthalmic	B	2/2-2/3	-	-	Complete (12)	12/-
13/70/Female	Incidental	Parophthalmic	S	26/9	-	-	Complete (6)	23/Mild stenosis
14/54/Female	Mass effect	Carotid-cavernous	S	24/11	-	Transient increase of mass effect	Complete (6)	19/-
15/51/Female	Incidental	Parophthalmic	S	9/6	-	-	Complete (6)	20/-
16/49/Female	Recurrent (clip, coil) aneurysms (acute SAH)	Supraclinoid	B	7/4	-	-	Complete (6)	25/-
17/55/Male	Incidental	Superior hypophyseal	S	10/4	-	-	Complete (6)	13/Mild stenosis
18/32/Male	Recurrent (stent+coil) aneurysm	Parophthalmic	S	14/6	-	-	Complete (6)	19/-
19/57/Female	Mass effect	Parophthalmic	S	22/8	-	-	Complete (6)	13/-
20/51/Male	Chronic SAH	Posterior communicating artery Paraclinoid	S	18/9-2/2-3/3	Insufficient expansion of proximal stent, balloon angiplasty	-	Complete (12, 18)	19/-
21/55/Male	Recurrent (coil) aneurysm	Parophthalmic	S	14/7	-	-	Incomplete (6)	27/-
22/55/Female	Mass effect	Petrous ICA	S	16/5	-	-	Complete (6)	28/-
23/55/Male	Mass effect	Superior hypophyseal	S	28/9	-	Transient increase of mass effect	Incomplete (12) Complete (18) (CTA)	18/Another stent implantation at 12th month
24/50/Female	Mass effect	Carotid-cavernous	S	22/11	-	-	Complete (6)	11/-
25/8/Female	Dysphagia	Prepetrous ICA	S	45/9	-	-	Complete (6)	23/-

Table. Summary of the patients (cont.)

No/Age (years)/Gender	Clinical presentation	Location	Type	Size/Neck (mm)	Peri-procedural complication	Late clinical complication	Control DSA (months)	Follow-up (months)/ Comment
26/52/Female	Chronic SAH	Superior hypophyseal	S	3/2	-	-	Complete (6)	19/-
27/59/Male	Acute SAH	Basilar trunk	F	14/7	-	-	Incomplete (6) Complete (12)	20/-
28/31/Female	Incidental	Bilateral parophthalmic	S	10/5-8/4	-	-	Complete (6)	18/-
29/50/Female	Chronic SAH	Supraclinoid	B	2/5	-	-	Complete (6)	16/-
30/38/Female	Incidental	Bilateral parophthalmic	S	5/4-3/3	-	Amaurosis fugax at sixth month	Complete (6)	18/Still under double antiaggregant
31/31/Female	Incidental	Parophthalmic	S	18/8	Break off the wire end without clinical consequences	-	Complete (6, 18)	19/-
32/48/Female	Incidental	Superior hypophyseal	S	4/2	-	-	Incomplete (6) Complete (12)	18/-
33/63/Female	Incidental	Paraclinoid	S	9/5	-	-	Complete (6, 12)	19/-
34/51/Female	Mass effect	Middle cerebral artery M1-M2 (partially thrombosed)	F	28/22	Transient ischemic attack	-	Incomplete (6)	9/-
35/53/Male	Mass effect	Basilar trunk (partially thrombosed)	F	36/38	-	-	-	8/-
36/50/Female	Acute SAH	Supraclinoid	B	2/3	-	-	Incomplete (6)	9/-
37/70/Male	Mass effect (contained rupture)	Middle cerebral artery M2 (partially thrombosed)	F	40/- 2/-rupture site	-	-	Complete (6) (rupture site)	6/Diminished mass effect
38/50/Female	Incidental	Superior hypophyseal	S	16/6	-	-	-	5/-
39/55/Female	Mass effect	Superior hypophyseal	S	32/8	-	-	Complete (6)	6/-
40/50/Male	Recurrent (stent+coil) aneurysm	Posterior communicating artery	S	24/7	-	-	-	5/-
41/55/Female	Recurrent (coil) aneurysm	Posterior ICA	S	8/4	-	-	-	7/-
42/43/Female	Incidental	Parophthalmic	S	10/5	insufficient expansion of stent, acute thrombosis, thrombolysis, balloon angioplasty	-	Complete (6) resistance	7/Clopidogrel
43/56/Female	Thrombosed CCF	Carotid-cavernous	S	22/9	-	-	-	5/-
44/38/Female	Incidental	Parophthalmic	S	6/5	-	-	-	5/-
45/63/Female	Incidental Recurrent (coil) aneurysm	Parophthalmic	S	3/2-2/2	-	-	-	5/-

B, blister; CCF, carotid cavernous fistula; CTA, computed tomography angiography; DSA, digital subtraction angiography; F, fusiform; ICA, internal carotid artery; S, saccular; SAH, subarachnoid hemorrhage.

in 48 (87%) previously untreated lesions. Balloon dilatation after incomplete expansion of the device was carried out in two cases. Partial expansion of the device was mainly observed in vessel segments with tight or acute curves. There were seven (13%) lesions that had been previously treated endovascularly (two with stent and coil, five with coil only). More than one stent was implanted in nine out of 55 aneurysms. The decision to implant more than one device was based on anatomical characteristics (very large neck or fusiform aneurysms) or on clinical presentation (ruptured aneurysm).

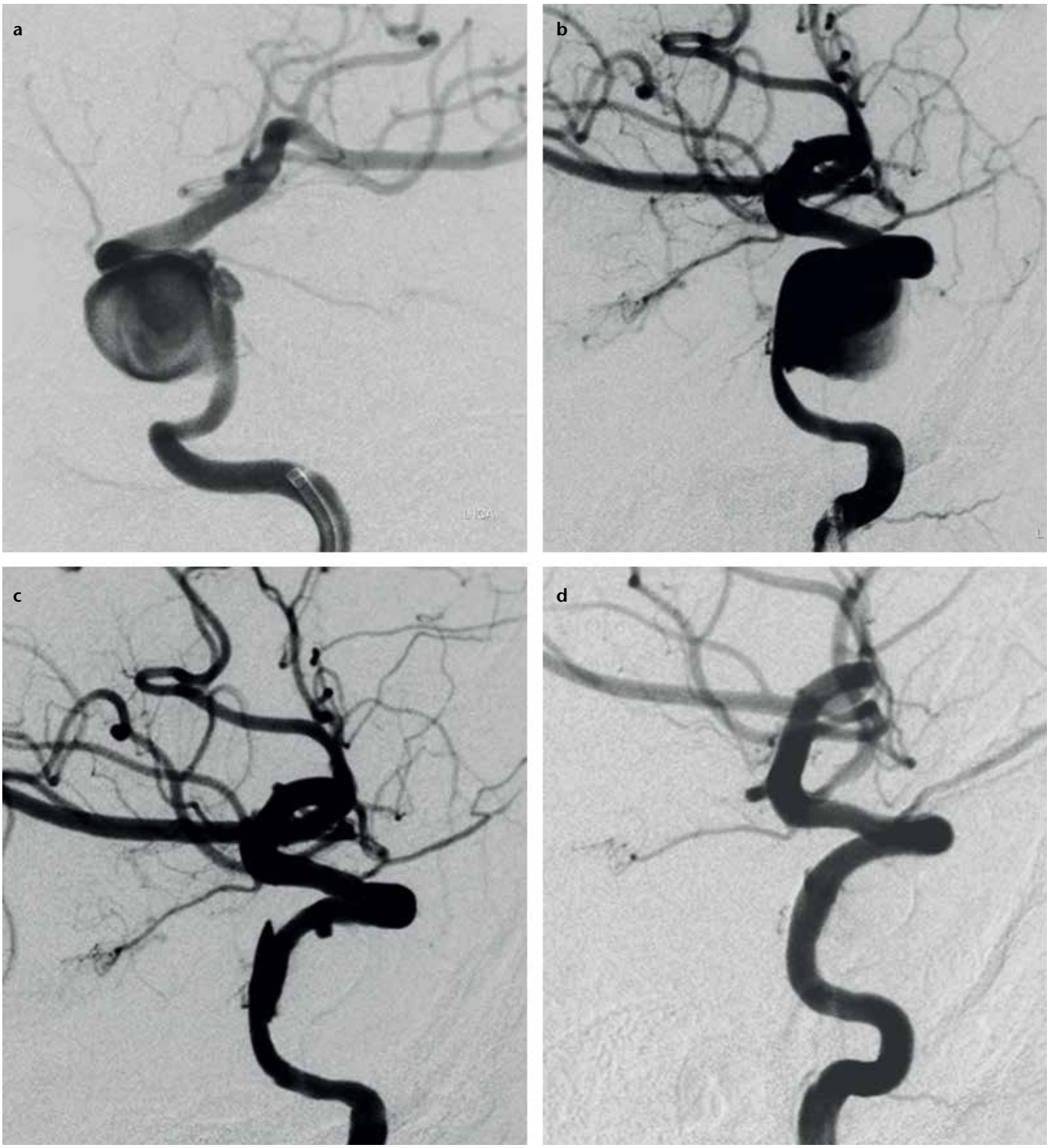

Figure 1. a–d. Case 24. Anteroposterior **(a)** and lateral **(b)** projections of the left carotid angiography show one large and two small aneurysms. Immediately after one Pipeline stent implantation **(c)** and six-month control angiography **(d)** revealed occlusion of all aneurysms.

According to this strategy, we limited the procedure to a single device if reduced aneurysm filling or contrast stagnation was visible in the venous phase, insinuating a high likelihood of intra-aneurysmal thrombosis. We did not observe any clinically relevant side branch occlusions on postinterventional or follow-up angiograms in the treated lesions (Figs. 1–5).

Procedural technical and clinical complications

Adjunctive therapies were administered in three patients, including two cases where additional balloon angioplasty was required to open the stent fully. In two of these cases, the transitory flow obstruction caused by the incompletely opened stent resulted in an immediate thrombotic event necessitating administration of tirofiban hydrochloride (Aggrastat, Merck&Co,

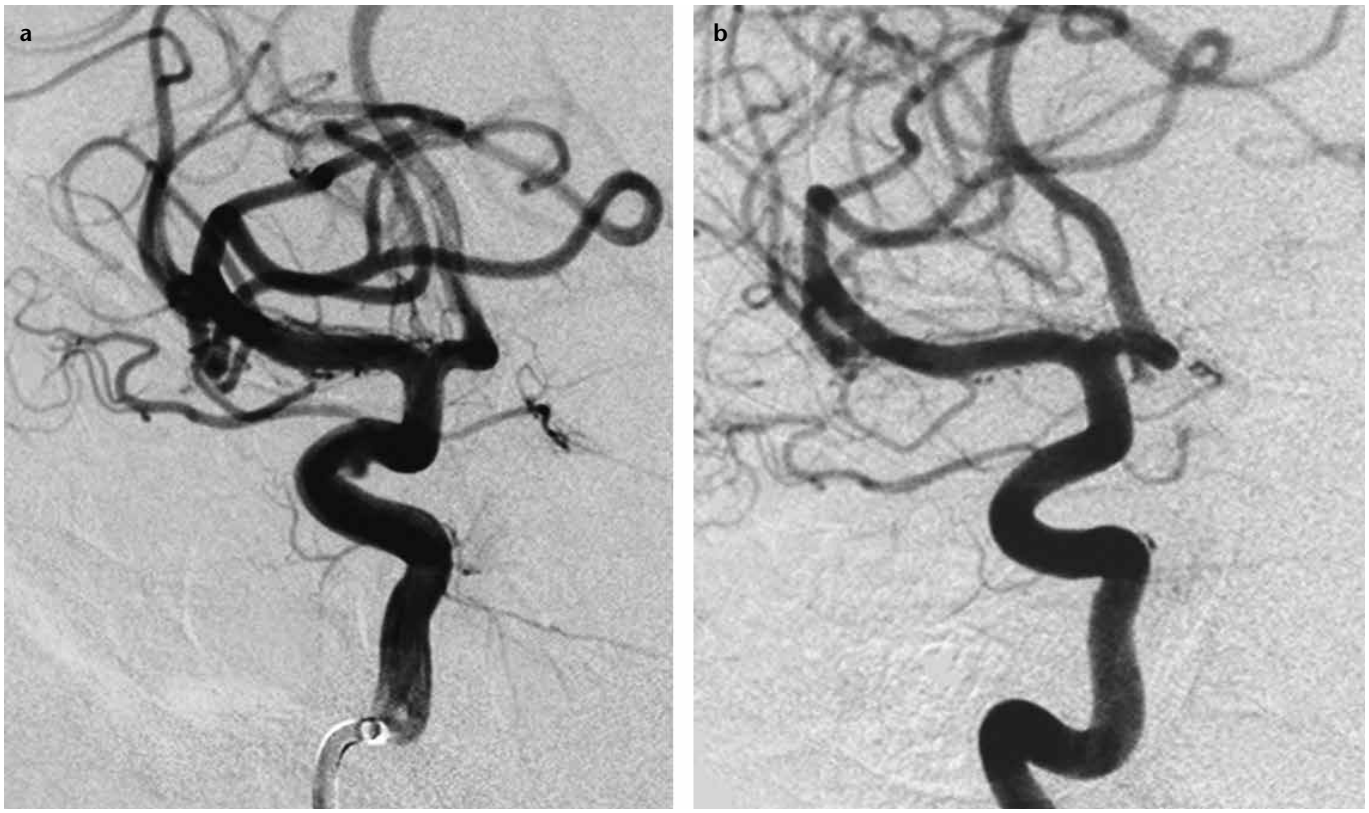

Figure 2. a, b. Case 26. Previous subarachnoid hemorrhage (chronic period). Right carotid angiogram (contralateral oblique projection) **(a)** revealed a 3 mm saccular aneurysm of the superior hypophyseal artery. After one Pipeline stent implantation, six-month angiography **(b)** showed complete occlusion.

West Point, Pennsylvania, USA). Altogether, procedural thrombotic events were treated with adjunctive medical therapy of intravenous Aggrastat in these three patients (4%). None of the subjects developed permanent neurological deficits. One major clinical complication encountered was a fatal nonaneurysmal cerebellar hemorrhage.

Aneurysm closure at follow-up

Thirty-four of 55 aneurysms were available for imaging at six months follow-up. The demonstrated aneurysm occlusion rate at six months was 85.3% (29/34), and the overall occlusion rate according to the last angiography was 91.9% (34/37). A second stent treatment was carried out in one patient because of persistent aneurysm filling on follow-up angiography. This second stent successfully excluded the aneurysm on follow-up angiography. The mortality rate in the series was 2.2% with no permanent morbidity.

In-stent stenosis and thrombosis, delayed aneurysmal rupture

Two patients had asymptomatic in-construct stenosis of less than 50%. All patients were ex-smokers, and one was noncompliant with clopidogrel. These patients, however, were asymptomatic, and no additional adjunctive therapies were applied. Both continued dual antiplatelet therapy beyond six months and remained asymptomatic.

Thirteen patients presented with focal neurologic deficits from aneurysmal compression just before the endovascular therapy. Four subjects presented acutely, and nine presented with long-standing deficits. Steroid treatment was administered in four subjects for 24 hours to prevent possible mass effect aggravation. There were three transient mass increases despite steroid treatment, which resolved completely with time (one, two, and three months) and longer steroid treatment. Acute aneurysm-provoked mass effect resolved or improved significantly in all cases by the sixth month. Two subjects had ongoing mild diplopia at six months but subsequently markedly improved. No changes were observed in the patient with long-standing aneurysmal compression. No patient developed delayed aneurysm rupture.

Discussion

Endovascular treatment of intracranial aneurysms has recently focused on an endosaccular approach to aneurysm obliteration. Following the introduction of Guglielmi detachable coils two decades ago, advances in coil technology and the use of adjunct devices, including stents and microballoons, have facilitated treatment and improved outcomes for endosaccular aneurysm embolization (20–23). Large (>10 mm) or wide-neck (>4 mm) aneurysms or those with an unfavorable dome/neck ratio are more difficult to treat and more prone to recurrence following endovascular therapy (24–26).

Flow diverters represent a novel class of endoluminal devices that promote parent vessel reconstruction, a strategy ideally suited for aneurysms with diffuse circumferential involvement of the parent vessel. Aneurysm treatment with flow-diverting devices is rapidly becoming a suitable and, in certain cases, preferred alternative to traditional endosaccular therapy with coils. Coil embolization is often criticized for high recurrence rates and incomplete aneurysm occlusion compared with

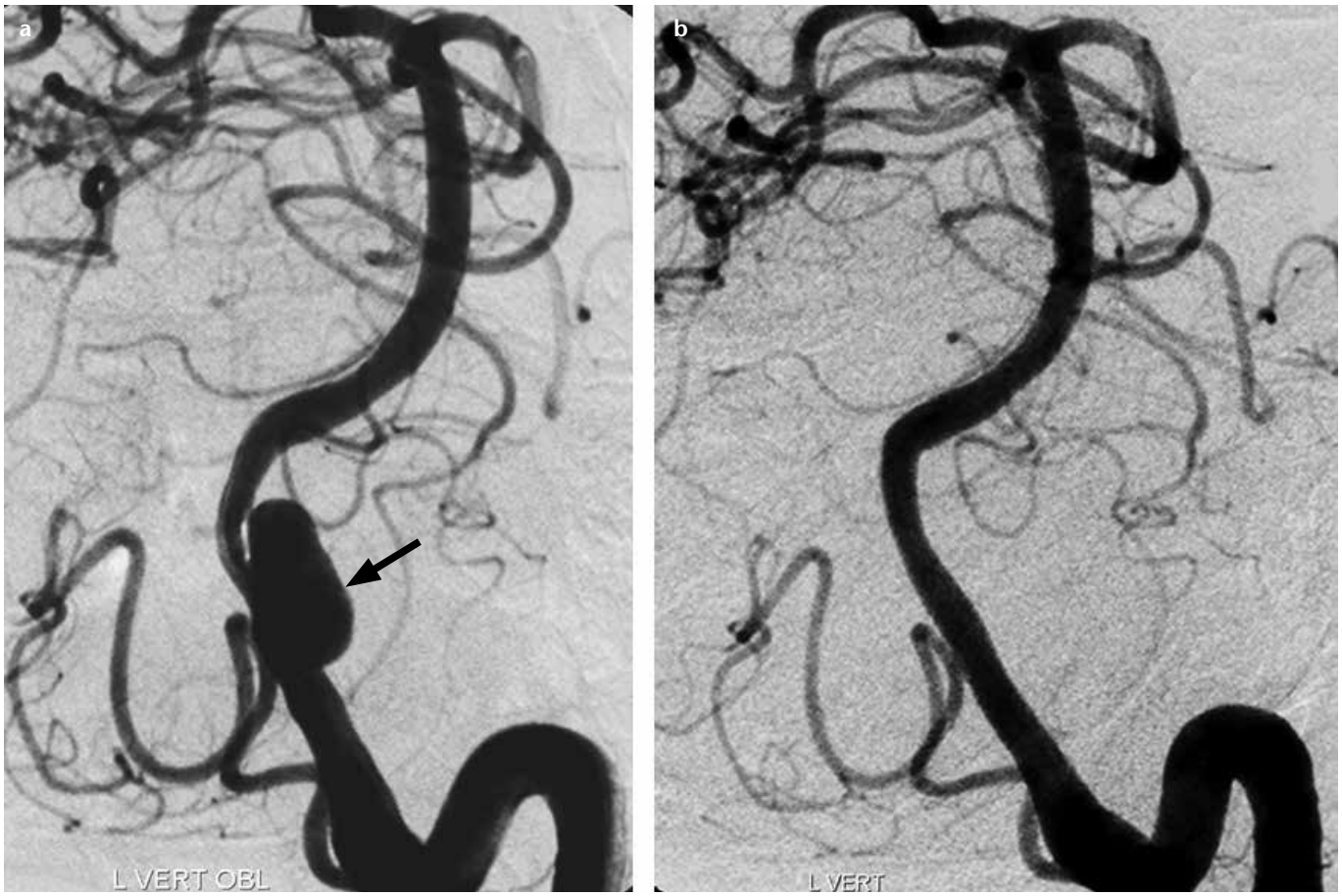

Figure 3. a, b. Case 6. Left vertebral artery V4 segment dissecting aneurysm is seen on angiography (*arrow,* **a**). After one Pipeline flow-diverting stent implantation, six-month control angiography **(b)** revealed complete occlusion.

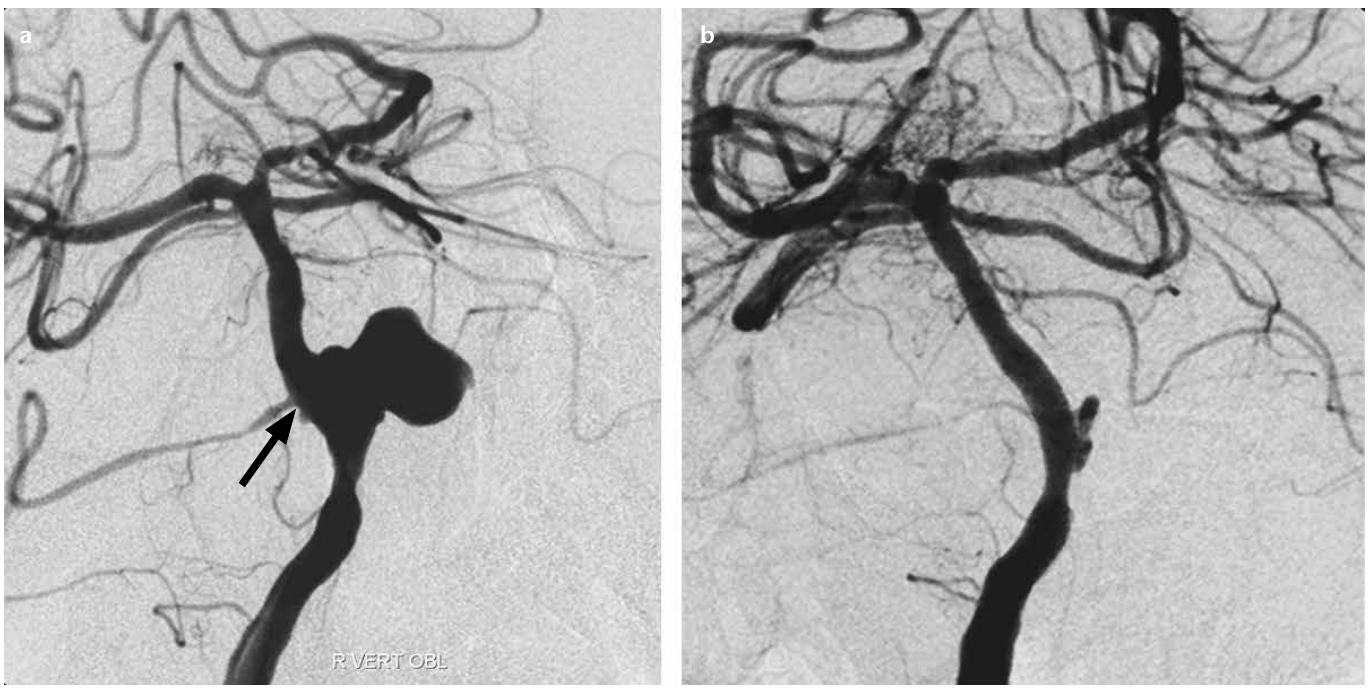

Figure 4. a, b. Case 27. Previous subarachnoid hemorrhage (acute period, 10 days). Basilar artery dissecting aneurysm is seen **(a)**. The right-sided anterior inferior cerebellar artery (AICA) arising from the aneurysm sac is also noted (*arrow*). After two telescopic Pipeline stent implantations, one-year control angiography **(b)** showed complete occlusion of the aneurysm. The right AICA proximal segment reconstruction and remodeling are seen, which originated from the aneurysm sac one year before.

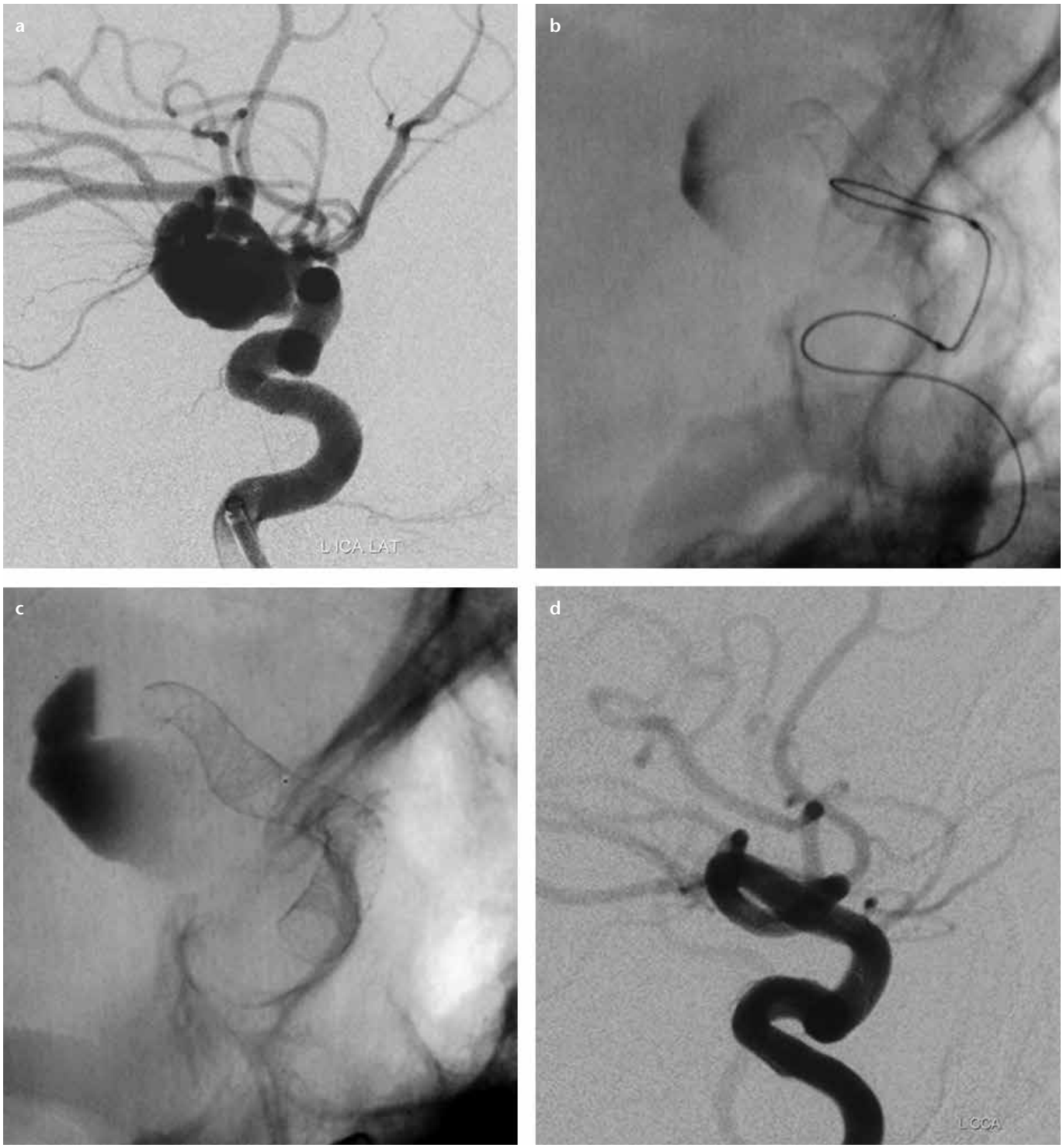

Figure 5. a–d. Case 20. A case having bilateral carotid aneurysms, which had ruptured (chronic period) and a wide-neck posterior communicating artery aneurysm on the right side. The sharp-angled multiple loops located in the distal carotid artery are noted **(a)**. Plain radiograph **(b)** shows insufficient expansion of the Pipeline stent and an angioplasty balloon inside it. Distal marker of the balloon was located at the narrowest segment of the stent. After balloon angioplasty, the stent was fully expanded **(c)**. The good conformity of the stent along the different segment of the parent artery is seen. Control angiography 1.5 years later showed complete occlusion of the aneurysm **(d)**.

microsurgical clipping, particularly in larger aneurysms and those with wide necks (27–29).

The Pipeline flow-diverting stent results in mechanical flow disruption followed by aneurysm thrombosis and ultimately parent vessel remodeling with endothelialization of the construct. When the aneurysm is completely excluded from the circulation, the thrombus resorbs and the aneurysm collapses around the construct (30). There is one other flow-diverting device called Silk stent (Balt, Montmorency, France) with encouraging initial results. It has the advantage of re-sheathable property, which may lower the likelihood of device misplacement.

Various early published trials and case series of Pipeline stent use, primarily from international groups, have demonstrated that the device is safe and effective for aneurysm treatment. The Pipeline for Uncoilable or Failed Aneurysms (PUFS) clinical study was a prospective single-arm multicenter trial that provided the primary evidence for safety and efficacy of Pipeline stent use. Patients in this trial had large or giant aneurysms with neck sizes larger than 4 mm of the paraophthalmic, cavernous or petrous internal carotid artery (31). Of the 108 patients treated, Pipeline stent placement was successful in 107 patients (99%). A total of 341 devices were implanted, with a mean of 3.1 stents placed per aneurysm. A single device was implanted in two of 107 patients (2%). Severe complications of major ipsilateral stroke or neurological death were reported in six of the 107 patients (5.6%). Intracranial hemorrhage occurred in five patients (4.7%), and four of those occurred prior to hospital discharge. No subarachnoid hemorrhage was reported. These results are similar to those in our series, in which severe complications occurred in one patient (2.2%). However, one patient in our series had an intracranial hemorrhage contrasting with five patient in the PUFS trial. Additionally, a single device was used in 82% of our cases compared with 2% in the PUFS trial.

The Pipeline stent for the Intracranial Treatment of Aneurysms (PITA) trial was a multicenter single-arm nonrandomized clinical trial conducted at three European centers and one center in Argentina and included 31 patients with 31 aneurysms that were wide-necked or had failed previous endovascular treatment (10). In this trial, 47 devices were placed with a mean of 1.52 devices per aneurysm. A single device was used in 18 of the 31 cases (58.1%). Stent placement was technically successful in 30 of the 31 aneurysms (96.8%). Severe complications of major stroke occurred in two patients (6.5%), and no minor strokes were reported.

Published reports from large series and registries show similar or, in some reports, better results. Lylyk et al. (9) reported treatment of 53 patients with 63 aneurysms with these Pipeline flow-diverting stent in Buenos Aires. Of note, however, six of these patients were also included in the PITA trial. Seventy stents were implanted and no major complications were reported. Minor complications did occur in six of the 53 patients (11%), including exacerbation of cranial neuropathy, groin hematoma, and rash. Szikora et al. (11) reported Pipeline flow-diverting stent treatment in 18 patients with 19 aneurysms in Budapest, and nine of those patients participated in the PITA study. Thirty-nine stents were implanted; one death (5.5%) occurred, and there was one case of acute in-stent thrombosis with subsequent transient hemiparesis. McAuliffe and Wenderoth (32) reported a prospective multicenter registry of 57 aneurysms in 54 patients treated with Pipeline stent in Australia. They reported a total of 98 stents placed, with no major stroke or death. Fischer et al. (33) reported a single-center case series of 88 patients with 101 aneurysms treated in Germany. One case of technical failure occurred and six patients (5.9%) developed major complications, including one death (1%).

In our series, minor complications occurred in 8.8% (three transient increase of mass effect and one transient ischemic attack) of the cases, which is in line with the rate of 11% reported by Lylyk et al. (9). Furthermore, our 2.2% rate of major complications falls in the middle of the 0%–5.9% range reported in all these series. In our series a triaxial support system was used in 44/45 (98%) of cases, as this provides the necessary support and distal access for manipulation and deployment of the stent.

The single major complication in our series of acute cerebellar hemorrhage 28 hours after Pipeline implantation occured following treatment of a wide-necked 10 mm posterior cerebral artery P2-P3 aneurysm with a single stent (patient number 3). From a technical standpoint, the embolization was uneventful and the device was implanted without any significant challenges. Emergency posterior fossa decompression revealed a huge intracerebellar hematoma in this patient. Therefore, the nonaneurysmal hemorrhage was deemed to be the cause of morbidity.

Aneurysm rupture has been previously reported following flow-diverting stent treatment of both unruptured and previously ruptured aneurysms (11, 32–34). Treatment of an aneurysm by flow diversion does not immediately exclude the aneurysm from the stresses of the arterial circulation. Furthermore, before neoendothelialization of the stent, there is still a risk of rupture . The steps leading up to aneurysm rupture following flow diversion is most likely a complex multifactorial process, with different factors involved in acute versus delayed rupture and in the rupture of small aneurysms versus large/giant aneurysms. Various hypotheses have been proposed for the etiology of aneurysm wall destabilization and rupture following implantation of a flow diverter. These include altered intraluminal and intra-aneurysmal hemodynamics and also the proteolytic, inflammatory and ischemic effects that the endosaccular thrombus has on the aneurysm wall (16, 34–36). However, further studies are needed to better understand these processes.

Two additional techniques commonly employed by the flow-diverting stent users to provide additional aneurysm protection are the placement of multiple overlapping stents and the adjunctive use of coils. Multiple overlapping or telescoped stents increase the mesh density over the aneurysm neck, thereby facilitating the flow-diverting properties of the construct. Adjunctive coils promote endosaccular thrombosis and theoretically provide increased protection of the aneurysm when combined with flow diversion. However, there are potential downsides to both of these approaches. Placement of multiple stents increases the technical difficulty of the case, prolongs the procedure time, and the additional metal in the parent artery is likely to increase the risk of intraluminal thrombosis. Adjunctive coil placement increases procedural risk of aneurysm perforation because of the need to access the aneurysm with a catheter and wire. Neither of these techniques leads to complete immediate angiographic occlusion of the aneurysm in all cases, a finding thought to correspond to maximal aneurysm protection. Furthermore, neither of these techniques fully protects against aneurysm rupture. Fischer et al. (33) reported rupture of an aneurysm despite treatment with multiple flow-diverting stents and adjunctive coils.

In-stent thrombosis is an ongoing concern in patients following implantation of a flow-diverting stent. Szikora

et al. (11) reported one case of acute intra-procedure in-stent thrombosis attributed to patient noncompliance with antiplatelet medications. The thrombogenicity of the device is a real concern, and prophylaxis requires strict adherence to a dual antiplatelet regimen, full intra-procedure systemic heparinization and, in some cases, postprocedure systemic heparinization. Postprocedure systemic heparinization was used following cases of aggressive vessel manipulation or implantation of multiple devices. In two of our cases, the transitory flow obstruction caused by the incompletely opened stent resulted in an immediate thrombotic event necessitating administration of tirofiban hydrochloride. These two cases were treated with adjunctive medical therapy with intravenous Aggrastat and balloon angioplasty. None of the subjects developed permanent neurological deficits.

Platelet inhibition assays were routinely used in our series. Only two patients were found to be nonresponders to clopidogrel and were given ticlopidine instead. Although there is growing interest in performing these tests prior to implantation of a vascular reconstruction device or flow-diverting stent, the interpretation of the results of these tests is certainly not standardized. The ideal level of platelet inhibition prior to flow-diverting stent implantation has yet to be established, and the appropriate response to perturbation of this level is not well understood. The results from the "Working Group on High On-Treatment Platelet Reactivity" have recently been published (19). Although these results are from the cardiology literature, radiologists should be aware of these results as well when performing neuroendovascular procedures.

In conclusion, flow diversion using the Pipeline stent is a technically straightforward and relatively safe treatment modality for the treatment of wide-necked saccular side-wall aneurysms, fusiform aneurysms, remnants of aneurysms after surgical or endovascular treatment, recurrent aneurysm, and dissected vessels in selected cases. Our study shows that the Pipeline flow-diverting stent is useful for endovascular treatment of complex intracranial aneurysms. Despite its potential interest to treat complex intracranial aneurysms without coils, the delayed clinical and anatomic complication rates are questionable and lead one to use this technique only in selected cases. Flow-diverting stents do not present a panacea, but new technologies and the rapid development of intracranial stents have broadened the treatment options for intracranial aneurysm and allow many previously untreatable cerebral aneurysms to be successfully managed. The immediate procedural outcomes using this technique in our series appear quite promising, although long-term results will need to be assessed.

Conflict of interest disclosure

The authors declared no conflicts of interest.

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