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AJNR Am J Neuroradiol 2010, 31 (6) 1139-1147
doi: https://doi.org/10.3174/ajnr.A2023
http://www.ajnr.org/content/31/6/1139

ORIGINAL RESEARCH

Treatment of Intracranial Aneurysms by Functional Reconstruction of the Parent Artery: The Budapest Experience with the Pipeline Embolization Device

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BACKGROUND AND PURPOSE: Aneurysm treatment by intrasaccular packing has been associated with a relatively high rate of recurrence. The use of mesh tubes has recently gained traction as an alternative therapy. This article summarizes the midterm results of using an endoluminal sleeve, the PED, in the treatment of aneurysms.

MATERIALS AND METHODS: A total of 19 wide-neck aneurysms were treated in 18 patients: 10 by implantation of PEDs alone and 9 by a combination of PED and coils. Angiographic and clinical results were recorded immediately and at 6 months following treatment.

RESULTS: Immediate angiographic occlusion was achieved in 4 and flow reduction, in another 15 aneurysms. Angiography at 6 months demonstrated complete occlusion in 17 and partial filling in 1 of 18 patients. There was no difference between coil-packed and unpacked aneurysms. Of 28 side branches covered by ≥1 device, the ophthalmic artery was absent immediately in 1 and at 6 months in another 2 cases. One patient experienced abrupt in-stent thrombosis resulting in a transient neurologic deficit, and 1 patient died due to rupture of a coexisting aneurysm. All giant aneurysms treated with PED alone were demonstrated by follow-up cross-sectional imaging to have involuted by 6 months.

CONCLUSIONS: Treatment of large, wide-neck, or otherwise untreatable aneurysms with functional reconstruction of the parent artery may be achieved with relative safety using dedicated flow-modifying devices with or without adjunctive use of intrasaccular coil packing.

ABBREVIATIONS: AICA = anterior inferior cerebellar artery; BA = basilar artery; Immed = Immediate; DSA = digital subtraction angiography; ICA = internal carotid artery; ID = internal diameter; MRA = MR angiography; N/A = not applicable; PcomA = posterior communicating artery; PED = Pipeline Embolization Device; PITA = Pipeline Embolization Device for Intracranial Treatment of Aneurysms; Recan = recanalization; SAH = subarachnoid hemorrhage; SCA = superior cerebellar artery; Sup = superior

The application of mesh tube implants for the treatment of intracranial aneurysms was first proposed in the early 1990s.[1-3] Early experimental work suggested 3 potential mechanisms of action: improved anatomic reconstruction of the parent artery, functional modification of flow across the orifice of the aneurysm, and biologic repair of the aneurysm neck by neointimal overgrowth.[1] Flow conditions within the parent artery and the aneurysm itself have long been thought to play an important role in aneurysm growth and rupture.[4-11] Yet, the early application of stent-assisted aneurysm therapy was primarily focused on geometric reconstruction of the parent artery through improved coil packing of the aneurysm. A few clinical case reports, however, suggested that improved outcomes associated with the use of stents may be attributable to stent-induced modification of flow within and around the aneurysm,[12,13] providing the impetus for development of higher coverage endoluminal sleeves for the treatment of cerebral aneurysms.[14] The purpose of this study was to analyze the early clinical experience with the first dedicated flow-modifying device, the PED (Chestnut Medical, Menlo Park, California).

Received September 25, 2009; accepted after revision November 16.

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This work was partially supported by a grant from the Hungarian National Scientific and Research Fund (OTKA 73773).

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DOI 10.3174/ajnr.A2023

Materials and Methods

Indications

Between February 2007 and July 2008, a total of 19 aneurysms in 18 patients were treated at the National Institute of Neurosurgery, Budapest. Nine patients were treated in a multicenter international safety trial (the PITA study) enrolling a total of 31 patients. Eight patients were treated in a single-center trial (the PITA II Budapest study), enrolling 8 patients total. These later patients were not included in the PITA trial. Both studies were conducted under an ethics

committee–approved protocol. One additional patient was treated following European conformity mark approval of the device.

Two aneurysms were treated as incidental findings; 10 because of headaches; 6 due to mass effect; and 1 due to recanalization following previous endovascular treatment. Regarding aneurysm morphology, sidewall and fusiform aneurysms were treated; we considered these to have a high likelihood of failure and/or recurrence with conventional endovascular techniques either because of a large or giant aneurysm or an unfavorable neck-to-sack ratio.

Periprocedural Angiographic Evaluation of the Aneurysms

Morphologic characteristics of the aneurysms and parent arteries, such as diameter and volume, were measured on 3D reconstructed images derived from rotational angiography before the procedure. All measurements were performed on an Advantage Windows Workstation by using ADW 4.2 software (GE Healthcare, Milwaukee, Wisconsin). Flow modification after PED implantation was classified as either complete stasis (if no contrast material entered the aneurysm following deployment of PED), significant flow reduction (if contrast stagnation was seen within the aneurysm at the late venous phase of the angiographic series), or slow flow (if the contrast circulation within the aneurysm became slower but without contrast stagnation into late venous phase images). Aneurysm occlusion was rated as either complete (if no contrast material entered the aneurysm by completion of the procedure) or incomplete (if any contrast filling of the aneurysm was seen on the last angiogram).

Operative Techniques

The Device. The PED is a woven wire mesh tube made of 25% platinum and 75% cobalt-nickel alloy. It is designed to provide 30%–35% metal coverage of the inner surface of the target vessel with a pore size of 0.02–0.05 mm^2 at a nominal diameter. The PED is attached to a pusher wire, compatible with a 3F (0.027-inch ID) microcatheter. The pusher wire has a platinum coil tip, which extends 15 mm beyond the distal edge of the PED. The device is delivered via a 0.027-inch ID microcatheter, requiring a 6F guide catheter support. Once positioned across the aneurysmal segment, the delivery wire is held while the distal one-third to one-half of the PED is carefully unsheathed. Once the unsheathed segment begins to expand, its distal end is released from the delivery wire by clockwise rotation of the wire. The proximal segment of the PED is then deployed by gentle advancement of the wire. Once the PED is fully deployed, it may be recrossed by advancing the microcatheter over the indwelling delivery wire, which can then be exchanged for a second PED. This provides a safe possibility of deploying multiple PEDs through the same microcatheter if necessary. At any point up to final deployment, the PED may be captured and removed from the body.

Procedural Protocol. In each case, a 3F neurovascular microcatheter (Renegade High Flow, Boston Scientific, Natick, Massachusetts; or Mass Transit, Cordis [Johnson and Johnson], Miami Lakes, Florida) was placed across the neck of the aneurysm either directly or over an exchange wire that was previously advanced into a distal branch with the help of a smaller microcatheter. The number of PEDs to be deployed was decided on the basis of flow reduction, but multiple coverage of clinically significant side branches (such as the anterior choroidal artery or the SCA and the AICA in the basilar territory) was carefully avoided. Clinically forgiving branches, such as the ophthalmic artery, were liberally covered by as many PEDs as thought necessary to achieve satisfactory flow reduction. Earlier in the series, several aneurysms were treated by PED-supported coil packing of the aneurysm. For those, a dual-marker microcatheter (Excelsior SL 10, Boston Scientific) was placed within the aneurysm before PED implantation to secure the possibility of additional coil placement into the sac in case flow modification was considered unsatisfactory. With growing experience, we abandoned secondary coiling except in cases in which early aneurysm occlusion of an intradural aneurysm was desirable.

Periprocedural Medication. Each patient was given 75 mg of clopidogrel and 100 mg of aspirin per day for at least 48 hours before and 6 weeks following the procedure. Aspirin, 100 mg/day, is still continued. Patients were anticoagulated by an intravenous bolus of sodium-heparin to achieve a double the normal activated clotting time value. Heparin anticoagulation was discontinued by the end of procedure.

Follow-Up

Patients were clinically followed at 30 days, 6 months, and 1.5–2 years after the procedure. Angiographic follow-up was performed routinely at 6 months. Clinical follow-up examinations were performed by the authors during office visits. Ophthalmologic symptoms were evaluated by an independent ophthalmologist. Angiographic results were evaluated by using both hard copy films and DICOM files by an independent core lab for patients treated in the clinical studies and by the authors for the first patient treated outside the studies (patient 18, On-line Table and Tables 1 and 2). Cross-sectional imaging follow-up by either CT or MR imaging was performed at 6 months for aneurysms presenting with mass effect. Eleven patients (12 aneurysms) had late imaging follow-up by MRA between 1.5 and 2 years postembolization.

Results

Aneurysm Location and Morphologic Data

Eighteen aneurysms were located on the intracranial ICA and 1, on the basilar trunk (BA). Four aneurysms were giant ($\geq$ 25 mm), 10 were large (10–25 mm), and 5 were small ($<$10 mm) according to the Yasargil classification with a mean largest diameter of 16 mm. The mean aneurysm volume was 1.26 cm^3, ranging from 0.047 to 3.969 cm^3. All aneurysms had wide necks, ranging from 4 to 18 mm, with a mean neck size of 7.4 mm (On-line Table and Tables 1 and 2).

Procedural Techniques

Ten aneurysms were treated by PED-supported coil packing, and another 9 aneurysms were treated by PED implantation alone. The mean maximum aneurysm diameter was the same in both groups (16 mm), but the volume was larger in the unpacked group (1.63 versus 0.93 cm^3). The mean volumetric packing attenuation of coiled aneurysms was 13.4%. These aneurysms were covered by either 1 (5 cases), 2 (4 cases), or 3 (1 case) PEDs. For unpacked aneurysms, a single PED was used in 2 cases; 2 overlapping devices, in 3 aneurysms; 3, in another 2; and 4 and 5 PEDs, in 1 case each. Aneurysms covered by 1 or 2 PEDs had a mean maximum diameter of 13 mm, a neck size of 6 mm, and a volume of 0.88 cm^3, while those that received $\geq$3 PEDs had a mean largest diameter of 23 mm, a mean neck length of 11 mm, and a mean volume of 2.26 cm^3 (On-line Table and Tables 1 and 2).

Table 1: Immediate and 6 months angiographic results of 19 aneurysms treated with PED

Patient ID	Side Branch Occlusion		Immed Angiographic Occlusion		6-Month Angiographic Occlusion	
	Immediate	Follow-Up	Complete	Incomplete	Complete Occlusion	Near-Complete Occlusion
1				1	1	
1				1	1	
2		1	1		1	
3			1		1	
4			1		1	
5				1	1	
6				1	1	
7	1			1	1	
8				1	1	
9				1	N/A	N/A
10		1		1	1	
11				1	1	
12				1	1	
13				1		1
14				1	1	
15				1	1	
16				1	1	
17			1		1	
18				1	1	
Total	1	2	4	15	17	1

Table 2: Complications and clinical outcome of 19 aneurysms treated in 18 patients with PED

Patient ID	Complications					Clinical Outcome		
	In-Stent Thrombosis	Side Branch Embolization	Distal Thromboembolic	Hemorrhagic	Other	Unchanged	Improved	Worsened
1						1		
1						1		
2							1	
3						1		
4					1		1	
5							1	
6						1		
7		1					1	
8							1	
9				1				
10							1	1
11						1		
12						1		
13	1						1	
14							1	
15							1	
16							1	
17						1		
18							1	
Total	1	1	0	1	1	7	11	1

Angiographic Results

Flow Modification and Aneurysm Occlusion. After placement of the PED construct, angiographic evaluation demonstrated complete stasis in 3 aneurysms, significant flow reduction in 13 (Fig 1*A*–*C*), and slow flow in 3. Complete aneurysm occlusion was found in 3 cases of PED-supported coil packing and in 1 case following flow modification alone.

Periprocedural Complications

Thirty-nine of 41 PEDs were successfully deployed in the desired position. Two PEDs were introduced into the microcatheter; however, they could not be deployed due to friction in a highly tortuous ICA. In addition, a gentle balloon dilation (Hyperform Balloon; ev3, Irvine, California) was needed to fully open the distal section of 1 device. Clinical complications occurred in 4 cases. One patient had a mild postprocedural hemiparesis lasting for 2 days. The patient fully recovered, and no ischemic changes were seen on CT. This event was primarily considered the result of contrast overload due to difficulties of catheter navigation and a lengthy procedure, but a CT-negative thromboembolic complication could not be excluded. One patient had an embolic occlusion of a retinal artery branch, resulting in a small visual field deficit following PED-supported coil packing of her complex paraophthalmic aneurysm. One patient who we subsequently learned had not taken her antiplatelet medication experienced acute intraprocedural in-stent thrombosis within the ICA. It was initially recanalized with tirofiban (Aggrastat) but re-occluded 2 days

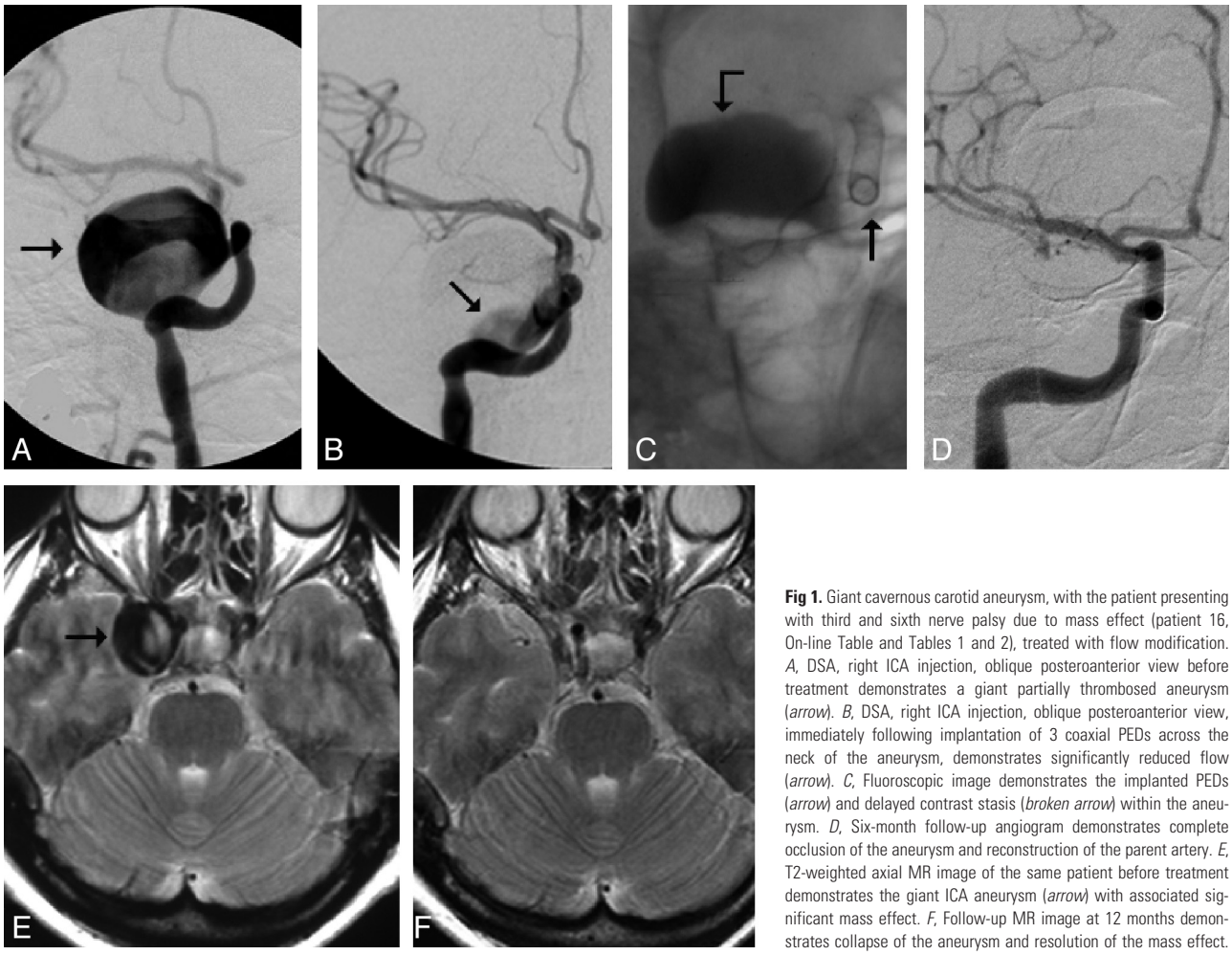

Fig 1. Giant cavernous carotid aneurysm, with the patient presenting with third and sixth nerve palsy due to mass effect (patient 16, On-line Table and Tables 1 and 2), treated with flow modification. *A*, DSA, right ICA injection, oblique posteroanterior view before treatment demonstrates a giant partially thrombosed aneurysm (*arrow*). *B*, DSA, right ICA injection, oblique posteroanterior view, immediately following implantation of 3 coaxial PEDs across the neck of the aneurysm, demonstrates significantly reduced flow (*arrow*). *C*, Fluoroscopic image demonstrates the implanted PEDs (*arrow*) and delayed contrast stasis (*broken arrow*) within the aneurysm. *D*, Six-month follow-up angiogram demonstrates complete occlusion of the aneurysm and reconstruction of the parent artery. *E*, T2-weighted axial MR image of the same patient before treatment demonstrates the giant ICA aneurysm (*arrow*) with associated significant mass effect. *F*, Follow-up MR image at 12 months demonstrates collapse of the aneurysm and resolution of the mass effect.

later, despite being treated with double antiplatelets. The patient had a transient hemiparesis. Having good collateral circulation, she fully recovered and the ICA later recanalized (Fig 2).

One patient died secondary to a diffuse SAH within 5 hours following treatment. Repeat angiography failed to demonstrate the source of bleeding; however, autopsy suggested rupture of a small coexisting ICA bifurcation aneurysm distal to the target lesion. Given the patient's tortuous anatomy and difficult catheter navigation, this could have resulted from a guidewire perforation during either the exchange manipulation or PED deployment. Small angiographically occult leakage might have led to a significant collection of blood within the subarachnoid space until it became symptomatic. Altogether, permanent nonrestricting morbidity occurred in 1, and mortality, in another patient.

Normal Branches Arising from the Parent Artery in Which the PED Would Be Deployed

A total of 28 visible side branches were covered, having an estimated diameter of 0.5–1 mm, including the ophthalmic artery in 17, the PcomA in 5, the anterior choroidal artery in 4, and the AICA and the posterior inferior cerebellar artery in 1 patient each. The ophthalmic artery was covered by 2 PEDs in 6, and by 3 and 4 in 1 case each. The PcomA was covered by 2 devices in 1 patient. The remaining branches had single coverage only. One ophthalmic artery was immediately nonvisualized on posttreatment angiography and resulted in a retinal branch occlusion. Two ophthalmic arteries, each covered by 3 or 4 devices, were found occluded at the 6-month follow-up. These delayed occlusions were clinically silent. No additional side branch occlusions were detected, including branches of the basilar trunk (Fig 3).

Imaging Follow-Up

Eighteen of the 19 aneurysms were studied by conventional angiography at 6 months following treatment (1 patient died). All but 1 aneurysm was completely occluded, without evidence of neck remnant, and exhibited smooth remodeling of the parent artery (Fig 1*A*−*D*). In the patient with in-stent occlusion of the ICA, delayed recanalization of the parent artery was associated with partial residual filling of a bilobed giant aneurysm (Fig 2). Additional coil packing did not seem to make a difference in late aneurysm occlusion (9/9 loosely coiled and 8/9 uncoiled aneurysms thrombosed completely, despite the generally larger sizes of aneurysms in the uncoiled cohort; 1.6 cm^3 versus 0.9 cm^3 by volume) (On-line Table and Tables 1 and 2, Figs 4 and 5).

Large and giant aneurysms treated exclusively with PEDs were demonstrated by cross-sectional imaging (CT or MR imaging) to have involuted, with resolution of mass effect in all

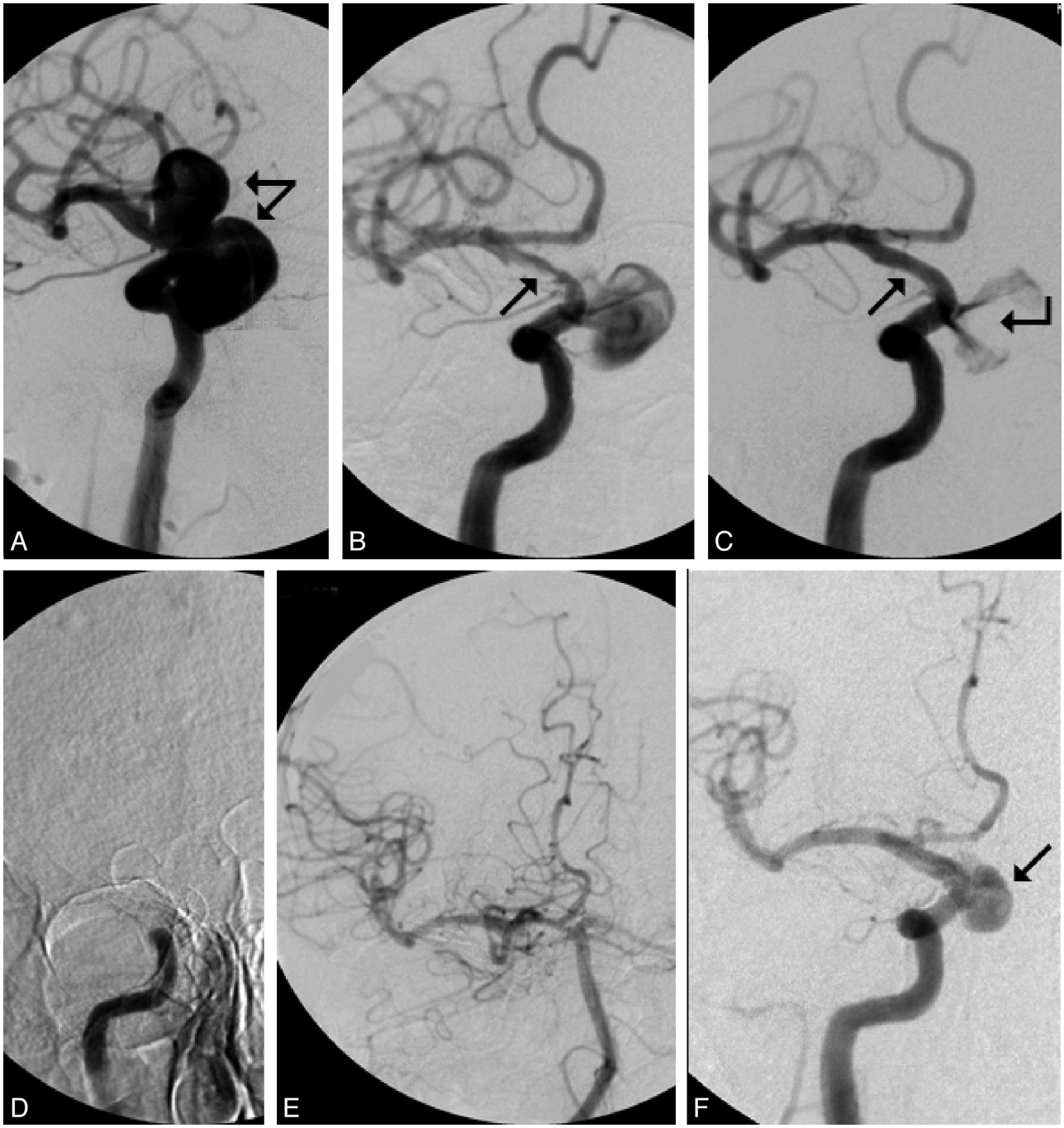

Fig 2. Giant infrasupraclinoid aneurysm of the right ICA. The patient presented with loss of vision due to mass effect (patient 13, On-line Table and Tables 1 and 2) and was treated with flow modification with transient thrombosis of the parent artery. *A*, DSA, right ICA injection, demonstrates bilobulated giant aneurysm (*arrows*). *B*, DSA, same view, following implantation of 2 coaxial PEDs, demonstrates partial in-stent thrombosis (*arrow*). *C*, DSA, same view, following tirofiban thrombolysis, demonstrates recanalization of the ICA (*arrow*) and significantly reduced flow within the aneurysm (*broken arrow*). *D*, Complete thrombosis of the ICA 2 days later. *E*, DSA, right vertebral artery injection, demonstrates good collateral circulation toward the right carotid system. No further action was taken at this time. *F*, Six-month follow-up angiogram demonstrates residual filling of the inferior portion of the aneurysm only (*arrow*).

patients at 6-month follow-up, except the patient with residual filling of her giant ICA aneurysm (Figs 1 and 3).

Clinical Follow-Up

Seven patients remained clinically unchanged. Six patients with compression syndromes have either completely or significantly improved. Five of 10 patients presenting with headaches reported relief of their symptoms. One patient died (On-line Table and Tables 1 and 2). There was no relationship between the immediate angiographic findings and clinical outcome (On-line Table and Tables 1 and 2).

Late Imaging Follow-Up

Eleven patients had late imaging follow-up by time-of-flight MRA. None of these patients had any new symptoms related to either their aneurysms or potential parent vessel stenosis or

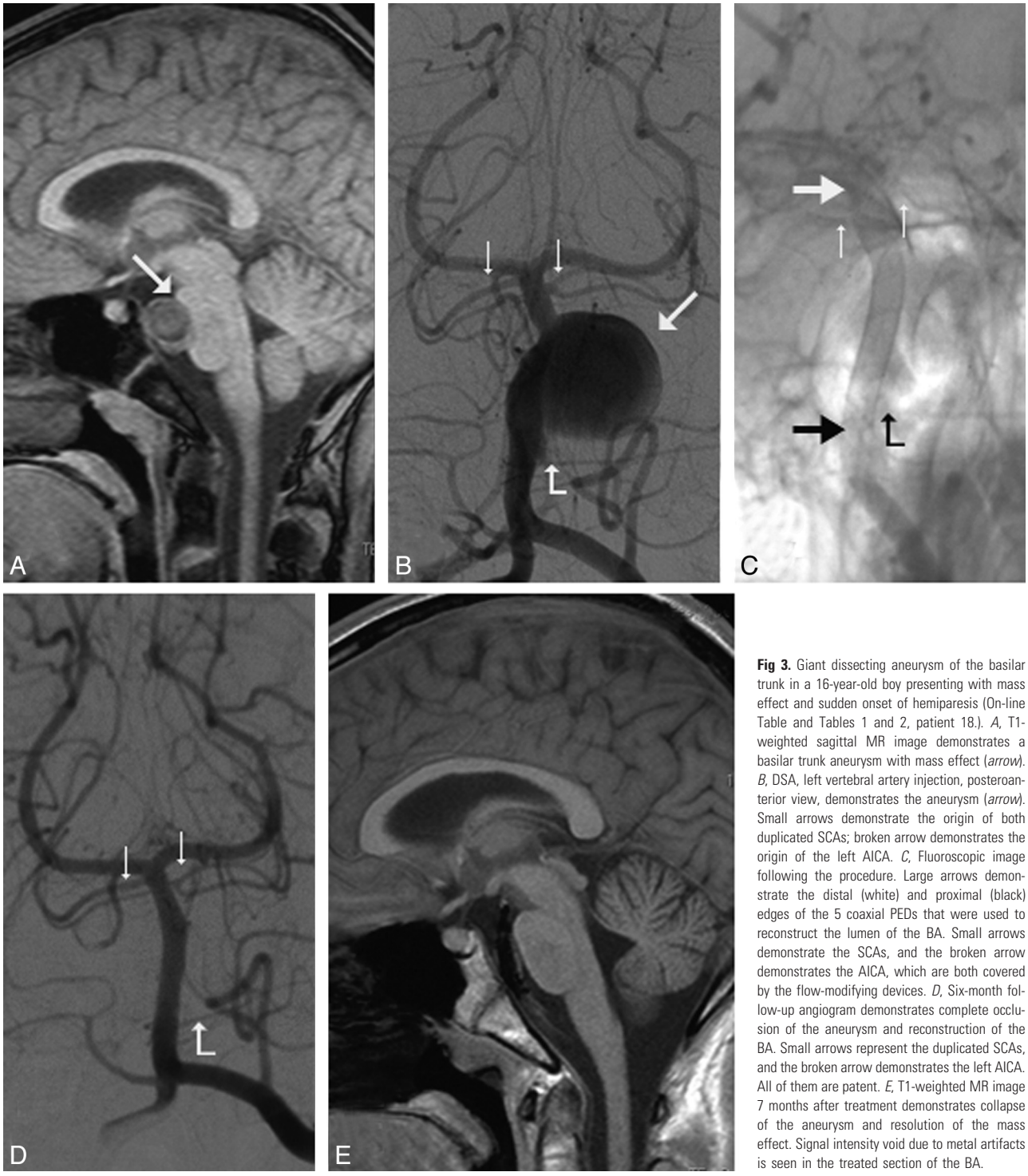

Fig 3. Giant dissecting aneurysm of the basilar trunk in a 16-year-old boy presenting with mass effect and sudden onset of hemiparesis (On-line Table and Tables 1 and 2, patient 18.). *A*, T1-weighted sagittal MR image demonstrates a basilar trunk aneurysm with mass effect (*arrow*). *B*, DSA, left vertebral artery injection, posteroanterior view, demonstrates the aneurysm (*arrow*). Small arrows demonstrate the origin of both duplicated SCAs; broken arrow demonstrates the origin of the left AICA. *C*, Fluoroscopic image following the procedure. Large arrows demonstrate the distal (white) and proximal (black) edges of the 5 coaxial PEDs that were used to reconstruct the lumen of the BA. Small arrows demonstrate the SCAs, and the broken arrow demonstrates the AICA, which are both covered by the flow-modifying devices. *D*, Six-month follow-up angiogram demonstrates complete occlusion of the aneurysm and reconstruction of the BA. Small arrows represent the duplicated SCAs, and the broken arrow demonstrates the left AICA. All of them are patent. *E*, T1-weighted MR image 7 months after treatment demonstrates collapse of the aneurysm and resolution of the mass effect. Signal intensity void due to metal artifacts is seen in the treated section of the BA.

occlusion. All parent vessels were patent proximal and distal to the aneurysm, and no aneurysm recurrence was seen by MRA. The treated segment of the parent artery could not be visualized due to the limitations of the technique.

Discussion

The potential of intravascular stent technology in the treatment of aneurysms has been proposed, and its technical feasibility, assessed in animal experiments in the early 1990s.[1-3] It was hypothesized that stent implantation may impact the results of endovascular treatment by facilitating attenuated coil-packing, modifying local flow dynamics, and providing a framework for the proliferating intima to cover the aneurysm.[1]

Further laboratory experiments demonstrated that depending on their mesh attenuation, stents alter and reduce the velocities of vortical flow within the aneurysm, increasing the intra-aneurysmal circulation time and affecting momentum exchange between the sac and the parent vessel.[15] It was also shown that in addition to the porosity, the geometry of the stent has an impact on aneurysm thrombosis, depending on the local flow patterns.[16,17]

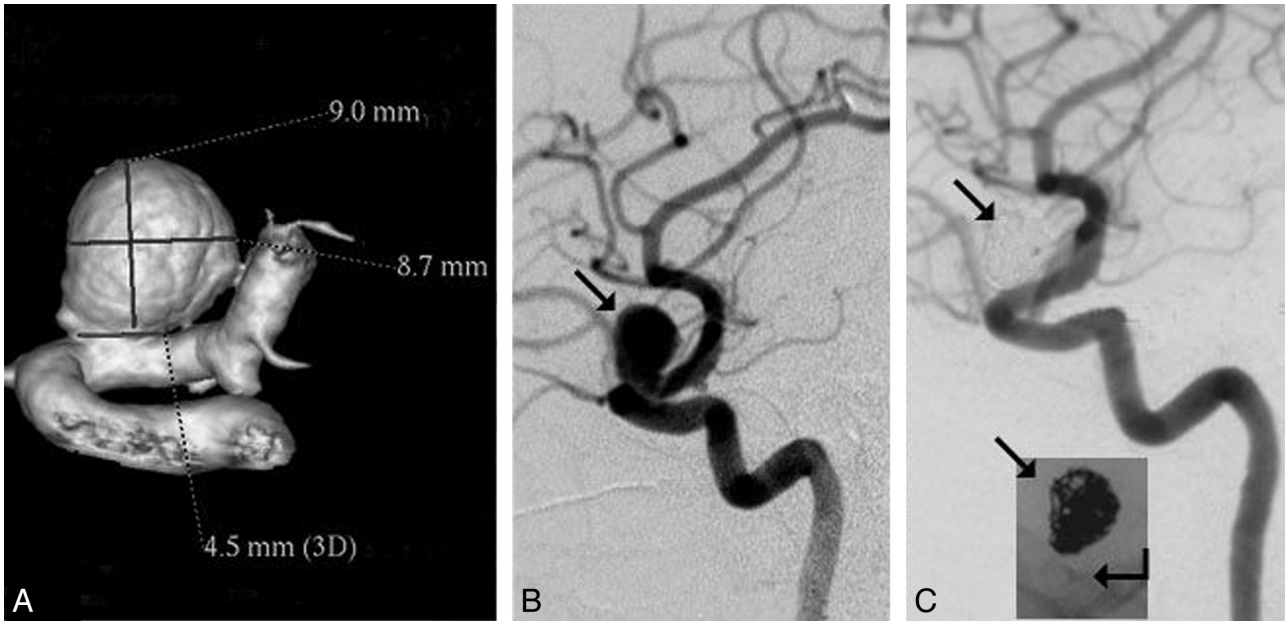

Fig 4. Results of aneurysm treatment by a combination of flow modification and additional coil packing. *A* and *B*, Nine-millimeter-diameter paraophthalmic aneurysm (*arrow, B*) treated with flow modification and coil packing (patient 3, On-line Table and Tables 1 and 2). *C*, Six-month follow-up angiogram demonstrates complete occlusion of the aneurysm with reconstruction of the parent artery. Arrows demonstrate subtraction artifacts and nonsubtracted view of the coil mass (23.3% volumetric packing attenuation); broken arrow demonstrates a single PED within the ICA.

Fig 5. Results of aneurysm treatment with flow modification only. *A* and *B*, Aneurysm with size and location similar to the one on Fig 4 (10-mm diameter paraophthalmic ICA aneurysm; *arrow, B*) treated with flow modification only (patient 11, On-line Table and Tables 1 and 2). *C*, Six-month follow-up angiogram demonstrates complete occlusion of the aneurysm and reconstruction of the parent artery (*arrow*). *D*, Arrow represents 3 coaxial PEDs implanted for parent artery reconstruction. No coils were used.

For clinical practice, following the application of modified balloon-expandable coronary stents,[18] open cell self-expandable intracranial stents became available for the morphologic reconstruction of the parent vessel across the orifice of the aneurysm.[12,13,18-24] More recently, closed cell-design stents were added to the therapeutic arsenal, presumably providing better coverage of the aneurysm neck.[25-27] Even though most clinical reports published to date have mainly focused on the utility of stents in facilitating coil packing of complex neck aneurysms, several observations suggested that stents not only promote improved packing but may independently contribute to the long-term stability of the aneurysm even with lower packing attenuation.[13,18] This assertion is supported by reports of aneurysms found to thrombose spontaneously after stent placement alone[12,13] or following double-stent coverage of the orifice without coil packing,[18] further highlighting the significance of stent design as proposed by Lieber et al[15,16] and Barath et al[17] in earlier experimental studies.

The above results allowed a conceptual change in the application of stent technology in aneurysm treatment. Instead of using stents as an adjunctive device, one can apply the intraluminar sleeves primarily for functional anatomic reconstruction of the parent artery by altering flow dynamics and inducing intimal proliferation. Early clinical experiences with 2 such devices, the Silk stent (Balt Extrusion, Montmorency, France)[28] and the PED,[29-31] have recently been reported. Nine of the 18 cases reported here are part of the first clinical trial designed to study the safety and efficacy of a flow-diverter device, the PED (the PITA trial).

Because our intention was to find an effective treatment technique for aneurysms otherwise difficult to treat, large, giant, fusiform, or wide-neck (as defined by a neck >4 mm or a

neck-to-sac ratio <1:2) lesions were treated exclusively. Overall, the aneurysms were larger compared with those in most endovascular series, having a mean diameter of 16 mm and a mean volume of 1.26 cm^3. The PED is a single layer of woven wire mesh design with a pore size of 0.020–0.052 $mm^{2.}$. Its flexibility and conformability to the implanted parent arteries were satisfactory. All devices were successfully navigated into position with moderate effort by using standard microcatheters. Two of 41 PEDs could not be deployed due to friction and were easily removed together with the microcatheter. Introduction and gentle inflation of a microballoon was necessary to release and fully open the distal tip of 1 PED that failed to detach from its delivery wire. This, too, was related to friction due to proximal tortuosity. Thirty-nine devices were acceptably deployed across the target lesion and apposed to the parent artery wall.

The exact degree of flow reduction sufficient for aneurysm thrombosis and its importance in achieving ultimate aneurysm occlusion are unclear and are likely to remain subjective in each case until flow and thrombosis simulations become incorporated into routine clinical practice. The aim is to prolong circulation time (contrast residence) within the aneurysm. Intra-aneurysmal circulation (vorticity) has been shown to be directly related to the surface area of the orifice[32-34] and can be reduced by decreasing the free surface available for fluid exchange. PED provides approximately 30%–35% surface coverage at a nominal opening as a single layer, but its design allows the overlapping of multiple devices, which can be used to strategically increase the degree of aneurysm coverage, providing 2 options for significantly reducing intra-aneurysmal circulation: the primary use of multiple coaxial PEDs or (particularly where perforator branches restrict the number of PEDs that can safely be used) reducing intra-aneurysmal flow with adjunctive coiling of the aneurysm.[10] In this series, we used both approaches.

In very large and giant aneurysms, in which it is difficult to achieve a significant effect on flow with coils, we elected to use multiple PED coverage. Aneurysms covered by ≥3 devices were practically twice as large as those treated with single or double PED coverage (On-line Table and Tables 1 and 2). To avoid occlusion of important side branches, we first used a single long bridging PED to create a stable scaffold, followed by shorter devices placed strategically over the aneurysm neck to enhance coverage of the orifice but minimize that of the parent artery proximal and distal to the aneurysm.

For smaller aneurysms, at the beginning, additional coiling was performed if complete stasis to the subjective satisfaction of the operator was not achieved. Technically, coil packing following PED coverage of the neck was very easy. With growing experience, we learned that complete stasis is not required for ultimate aneurysm occlusion; if the flow is visibly reduced by angiography, the aneurysm is likely to thrombose, and aneurysm packing is discontinued. Applying both techniques provided an opportunity for retrospective comparison of aneurysms that had additional coiling with those that were treated with PED coverage alone. Analysis of the 6-month follow-up results demonstrated that, in general, the coil-packing density was very low. Further, even though unpacked aneurysms had significantly larger volume than those that were adjunctively coiled (On-line Table and Tables 1 and 2), aneurysms of similar size and location occluded equally, regardless of coil packing (On-line Table and Tables 1 and 2, Figs 4 and 5). On the other hand, all but 1 coiled aneurysm was treated with a single PED, while unpacked aneurysms were covered by multiple overlapping devices. We concluded that for many aneurysms, PED coverage itself is an effective treatment, and for the future, we restricted additional coil packing to cases in which there is an increased risk of aneurysm rupture (such as multiple aneurysms) or the need to restrict PED coverage to a single device due to the vicinity of significant side branches.

Patency of side branches is a significant concern for the application of multilayer high-mesh-attenuation stents. In our study, 1 acute occlusion was attributed to severe catheter-induced ICA vasospasm rather than stent coverage. This was supported by the reopening of the ophthalmic artery at 6 months. Both branches that had delayed occlusion were covered by either 2 or 4 overlapping devices. A single-layer PED did not cause any side branch thrombosis. Having this positive experience in the relatively forgiving area of the supraclinoid ICA encouraged us to use the technique of targeted multilayer PED coverage in a large fusiform basilar trunk aneurysm, which was treated by 5 coaxial PEDs. In this case, coverage of the SCA and AICA segments was limited to single anchoring devices, while 3 additional short PEDs were overlapped across the aneurysm neck. No visible branches of the BA occluded, and no clinical signs of perforator-related ischemia were detected within 8 months of follow-up (Fig 3).

Another significant concern regarding high-metal-surface-area stents is their potential thrombogenicity, particularly if multiple devices are used. In-stent thrombosis occurred in 1 case in a patient retrospectively found not to have been suitably covered with antiplatelet agents. The occluded ICA reopened later, while the patient was on proper medication (Fig 2). This suggests that the PED has an acceptable thrombotic profile, but rigorous antiplatelet periprocedural medication is necessary.

Similar to the application of other intracranial stents, the necessity of aggressive antiaggregation raises further concerns about potential bleeding complications. In our study, a patient died due to diffuse SAH. This patient had a very small aneurysm on the ipsilateral ICA bifurcation distal to her giant multilobulated target aneurysm on the proximal ICA. Control angiography failed to demonstrate a source of bleeding; however, an autopsy suggested rupture of the small distal aneurysm, likely related to wire perforation. This suggests that patients having an additional aneurysm distal to the target lesion carry higher risk because perforation of the distal aneurysm may occur during the exchange maneuver or PED placement. While such perforation might otherwise remain clinically silent, it may become catastrophic under double antiaggregation. Treatment of the distal aneurysm before the target lesion should be considered.

The PED device demonstrated high efficacy, inducing complete occlusion in all but 1 aneurysm at 6 months. This was seen in the patient who had transient ICA occlusion and, for this reason, was kept on double antiplatelets for 6 months. She is due for further follow-up (Fig 2). All other aneurysms completely occluded at 6 months, with reconstruction of the lumen of the parent artery (Figs 1, 3, and 4). A minimal (15%) diameter narrowing was detected by follow-up angiography at

6 months in a single case without any flow restriction. The patient is being followed clinically and by MR imaging and MRA.

Effective treatment of mass effect is difficult with intrasaccular aneurysm packing. Treatment with flow diversion resulted not only in angiographic aneurysm occlusion but also in reduction of mass effect. This result is proved by the elimination or improvement of cranial nerve neuropathies and headaches as well as by involution of the aneurysmal mass and resolution of the mass effect at 6 months by CT or MR imaging (Figs 1 and 3).

The long-term results are yet to be studied. We do not have angiographic results for more than 6 months; however, time-of-flight MRA in 11 patients (12 aneurysms at 18–24 months) indicated persistent occlusion of the aneurysms and good flow within the parent arteries proximal and distal to the treated segments. Patients have been clinically followed for ≤12–18 months so far. No further clinical events have been recorded.

This article summarizes short-term results of only a small cohort of patients. On the basis of these results, application of this technology seems to be beneficial for patients with large and giant proximal aneurysms, particularly those having mass effect. Further studies are warranted to collect longer term follow-up data and to investigate the potential of the technique for treatment of more distally located aneurysms.

Conclusions

Treatment of large, wide-neck, or otherwise untreatable aneurysms with functional reconstruction of the parent artery may be achieved with relative safety by using dedicated flow-modifying devices. Currently available technology using the PED provides high efficacy with lasting effects in proximal intracranial sidewall aneurysms. Additional coil packing is not required to achieve aneurysm thrombosis, but it is technically feasible and can be applied if early aneurysm occlusion is desired (ie, acute SAH) or when treating aneurysms in which eloquent branch vessels limit the number of PEDs. Dual-agent antiaggregation seems to be essential in avoiding thromboembolic complications and needs to be seriously considered in cases of multiple aneurysms. Longer follow-up and larger studies are warranted.

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