Giant intracranial aneurysms (>25 mm) are associated with high morbidity and mortality from rupture (11). These lesions can also exert significant mass effect on the surrounding anatomy, resulting in progressive neurological decline secondary to local mass effect, stroke from perforating vessel occlusion or distal embolism, or obstructive hydrocephalus. Symptomatic giant aneurysms are associated with a 60% 2-year mortality rate, with nearly all surviving patients affected by severe, progressive neurological symptoms (6). Giant aneurysms of the midbasilar artery are among the most difficult of these lesions to treat. Both open surgical and endovascular treatment options have high morbidity and mortality rates, and complete cure is not often possible without a significant risk of morbidity and mortality (9, 10).

The Pipeline embolization device (PED) (Chestnut Medical Technologies, Inc., Menlo Park, CA) is a self-expanding, microcatheter-delivered, cylindrical mesh device composed of 48 individual braided cobalt, chromium, and platinum strands. The device has a 30 to 35% metal surface area when fully deployed (2, 3). Multiple devices can be deployed within each other (telescoped) to create a composite endovascular construct (3). The degree of metal surface area coverage can be manipulated by
varying the technique of device deployment as well as by judiciously choosing the number of devices placed in a particular vascular segment. We report the results of treating a 13-year-old girl with a giant, partially thrombosed midbasilar trunk aneurysm which was anatomically reconstructed with the PED.

CASE REPORT

A 13-year-old girl presented with a 9-month history of intermittent headache. Initially, she had no neurological deficits, but she developed left gaze nystagmus and left upper-limb ataxia 1 month before treatment with PED. Computed tomographic angiography, magnetic resonance angiography, and cerebral angiography showed a 39-mm partially thrombosed midbasilar artery aneurysm. The proximal basilar artery measured 2.9 mm, and the distal basilar artery measured 2.5 mm. The aneurysm “neck” circumferentially encompassed a 29-mm-long segment of the midbasilar artery (Fig. 1). The patient sought consultation from a series of neurosurgeons, each of whom declined to offer open surgical treatment because of an unacceptably high risk of periprocedural morbidity and mortality. The patient was then referred to a regional center for a second opinion from an endovascular neurosurgeon, who recommended endovascular treatment. The patient underwent angiography in anticipation of conventional stent-assisted coiling of the aneurysm, but the procedure was aborted without stent placement or coiling. The patient was ultimately referred to our center for possible treatment with the PED. The procedure was performed under a United States Food and Drug Administration exemption for compassionate use and with local institutional review board approval. Patient- and procedure-specific, institutional review board-approved written consent was obtained before proceeding.

The patient was pretreated with aspirin and dipyridamole, and response to both agents was confirmed using platelet aggregometry. The patient was placed under general anesthesia, and systemic anticoagulation was achieved with intravenously administered heparin to increase the activated clotting time to 250 seconds. A 6-French guiding catheter (Cordis Neurovascular, Miami Lakes, FL) was manipulated into the distal aspect of the left cervical vertebral artery. Under roadmap guidance, a Renegade Hi-Fló microcatheter (Boston Scientific, Fremont, CA) and 0.014-inch Synchro-2 microwire (Boston Scientific) were advanced across the aneurysm and into the distal basilar and left posterior cerebral artery. A PED construct was built, spanning from the normal-appearing basilar artery distally to the normal-appearing basilar proximally (Fig. 2, A and B). The final construct was comprised of 7 PEDs, which were sequentially placed in a telescoping manner to achieve a stable, solid bridge across the aneurysmal segment.

The sequence and sizes of the Pipeline devices deployed are shown in Table 1. PEDs were placed to achieve maximum metal surface area coverage over the length of the aneurysm neck while limiting the amount of metal coverage over the perforators arising from the proximal and distal basilar artery. After each PED was deployed, the microcatheter was driven back through the construct over the deployment guide wire to maintain microcatheter access across the construct. After a complete bridge across the aneurysmal segment was completed, subsequent PEDs were placed over the aneurysm neck, with an emphasis on “packing,” to achieve the highest possible metal surface area coverage with the device. This technique of “packing” consists of deploying the PED while maintaining forward pressure on the delivery microcatheter. With this technique, the device is deployed to its maximal possible diameter and, to some extent, compacted to achieve the greatest density of braids possible over the length of the deployed device.

At the conclusion of the procedure, control angiography was performed, as was a postprocedural DynaCT scan (Siemens Medical Solutions, Erlangen, Germany) (Fig. 2C). Completion angiography showed significant flow reduction into the aneurysm, with stasis into the venous phase of angiography (Fig. 3, A and B). The entire procedural time for the case was 90 minutes (from first to last angiographic image). The patient was maintained on a low dose of intravenously administered heparin (300 U/h) for 24 hours after the procedure. There were no immediate complications noted from the treatment, and the patient emerged from anesthesia without neurological complications. Within 24 hours of placement of the construct, her presenting neurological symptoms of headache, left gaze nystagmus, and left upper-extremity ataxia had resolved completely.

Repeat angiography on postoperative Day (POD) 2 showed marked interval progression of aneurysmal thrombosis, with continued filling of the central portion of the aneurysm (Fig. 3, C and D). On POD 7, she was discharged to a local hotel. Final periprocedural angiography, performed on POD 7, showed complete occlusion of the aneurysm with anatomic reconstruction of the basilar artery (Fig. 4). She returned home on POD 8 and returned to school on POD 10. She has resumed all normal activities and remains neurologically normal without deficits or headache at 10 weeks. A follow-up angiogram revealed persistent aneurysm thrombosis, and a cerebral angiogram was performed to confirm anatomic reconstruction of the basilar artery.
weeks. She will be maintained on dual antiplatelet medications for 6 months.

**DISCUSSION**

The presented case illustrates 3 important concepts directly related to the future application of the PED for the treatment of intracranial aneurysms: 1) as previously demonstrated (2), the PED can be used to reconstruct and definitively treat intracranial aneurysms that are not amenable to other open surgical or conventional endovascular techniques; 2) complete aneurysm occlusion can be achieved without adjunctive embolization coils; and 3) the PED, when applied strategically to create an endovascular construct, may be safely deployed within a parent vessel that is rich with eloquent perforators.

**TABLE 1. Pipeline embolization device sizes and placement sequence**

<table>
<thead>
<tr>
<th>PEDs placed</th>
<th>Size (mm)</th>
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<tbody>
<tr>
<td></td>
<td>Diameter</td>
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<tr>
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<td>6</td>
<td>3.5</td>
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<td>7</td>
<td>3.25</td>
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*PED, Pipeline embolization device.

**Definitive Anatomic Reconstruction of Complex Intracranial Aneurysms with PED**

Giant intracranial aneurysms, particularly those that are very wide necked or fusiform, are among the most daunting vascular lesions to treat (10). They are characterized by a dismal natural history, marked by a high likelihood of rupture and a course of progressive enlargement with neurological decline related to local mass effect, stroke, or hydrocephalus (6, 11). Constructive surgical treatment is often very difficult or impossible, particularly when the lesion is partially thrombosed or calcified. Attempted open surgical treatment is typically associated with high rates of periprocedural morbidity and mortality. In the present case, the location of the aneurysm (midbasilar trunk), its circumferential morphology, its size, the volume of thrombus within the aneurysm sac, and the magnitude of local mass effect essentially precluded any safe surgical access aimed at reconstructive treatment. Parent vessel occlusion, or in the present case, bilateral vertebral occlusion to elicit flow reversal, represents a strategy with significant risk and unpredictable efficacy. Moreover, this deconstructive strategy eliminates any future access for endovascular therapy.

Constructive endovascular treatments using conventional, commercially available devices represent a significant technical challenge. In addition, with very large wide-necked, giant, and fusiform aneurysms, these techniques typically yield only a partial treatment, which almost inevitably leads to a series of repeated recurrences requiring multiple retreatments (1, 5, 7). In the present case, the complexity of the lesion precluded an attempt at stent-assisted coil embolization at an outside institution by an experienced team of endovascular neurosurgeons. Although Zenteno et al. (12) recently described endovascular reconstruction with more conventional balloon-expandable stents as a stand-alone treatment for wide-necked posterior circulation aneurysms, it is unlikely that the length of the vascular segment involved in the present case could be safely or effectively reconstructed with these devices. At the same time, the experience of these authors does provide evidence that endoluminal constructs can induce flow changes that are suffi-
The conceptual basis for the procedure is also fundamentally superior to conventional stent-supported embolization with coils. With the PED, a dense cylindrical mesh is built to reconstruct a de novo vessel through the diseased segment. In a rabbit elastase aneurysm model, Kallmes et al. (3) demonstrated that this endovascular mesh acts as a scaffolding for endothelial and neointimal overgrowth, which forms a contiguous layer that eventually completely covers the aneurysm neck. In these models, the endothelium growing over the devices was noted to be contiguous with the endothelium of the parent artery both proximal and distal to the in situ PED construct, bridging the aneurysm neck and diseased vascular segment from “normal vessel” to “normal vessel.” As such, once the construct is in place and the aneurysm is completely occluded on angiography, there is no mechanism whereby the aneurysm should recur, considering that the treated segment has been circumferentially and contiguously reconstructed. After the construct has been completely incorporated and the “endovascular repaving” completed, the treated segment represents, essentially, a “steel-reinforced” artery. There are no coils to compact, there is no “untreated” neck remnant that can grow, and there is no adjacent portion of untreated parent vessel that can reconstitute an aneurysm.

The previous PED cases presented by Fiorella et al. (2) were angiographically stable at the time of the 1-year follow-up evaluation. These findings provide some preliminary evidence to confirm the hypothesis that once angiographic aneurysm obliteration has been achieved with PED, the reconstructed vessel is durable thereafter. This is analogous to the results achieved with successful surgical clipping.

Complete Aneurysm Treatment without Coils

The treatment of large and giant aneurysms with coils, although sometimes effective, is often incomplete, frequently not durable, and typically very expensive (5, 7). During coil embolization, the strategy is to achieve thorough coverage of the aneurysm neck with embolization coils to disrupt flow

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**FIGURE 3.** Immediate posttreatment and 48-hour angiography. Immediate completion angiography in the posteroanterior (A, C) and lateral (B, D) projections showing markedly reduced filling of the aneurysm with more physiological flow through the normal vertebrobasilar circulation. At this point, contrast entering the aneurysm was static into the venous phase of angiography. C and D, the 48-hour follow-up angiography showed further reduction of flow into the aneurysm, with progressive thrombosis and further restoration of more normal, physiological flow within the vertebrobasilar circulation.

**FIGURE 4.** Postoperative Day 7 angiography. Angiography in the posteroanterior (A) and lateral (B) projections showing definitive anatomic reconstruction of the basilar artery, occlusion of the aneurysm, and complete restoration of normal physiological flow within the vertebrobasilar circulation.
into, and out of, the aneurysm, thereby creating a physiology favorable to aneurysm thrombosis and durable occlusion. Embolization coils distributed in the saccular portion of the aneurysm, near the dome, function primarily to stabilize those coils distributed in the region of the aneurysm neck and, to a lesser extent, to facilitate thrombosis within the aneurysm fundus. With large and giant aneurysms, the packing densities achieved are far lower than those seen with small aneurysms (8). Even in glass models, maximum embolization volumes achieved with platinum coils packed as tightly as possible have been reported in the 30 to 40% range, indicating that two-thirds of even the most densely packed aneurysms are composed of free space (4). In addition, when the mural defect is large and involves the parent vessel wall circumferentially, as is inevitable in large aneurysms, it becomes increasingly difficult to recreate the absent vessel wall with coils alone. As such, the intraaneurysmal coil mass, although often very effective in smaller aneurysms, is prone to compaction over time, particularly in large and giant aneurysms. These results manifest clinically as very high rates of aneurysm recurrence and correspondingly low rates of complete aneurysm occlusion at the time of follow-up. For example, Murayama et al. (5) reported angiographic recurrence rates of 35.3% for large aneurysms and 59.1% for giant aneurysms at the time of follow-up. Similarly, Raymond et al. (7) reported 12-month complete occlusion rates of only 38.3% for a series of aneurysms with an average size of just under 10 mm.

With the PED, 100% of the metal within the device is targeted to the occlusion of the aneurysm neck and the reconstruction of the parent vessel over the segment that gives rise to the aneurysm. Once the inflow and outflow of the aneurysm have been sufficiently disrupted, the aneurysm proceeds to thrombosis. The present case shows that, even in one of the most extreme cases possible, the flow disruption achieved with an adequately built PED construct is sufficient to create complete aneurysm thrombosis without adjunctive endovascular occlusion with coils. Because the construct is anchored within the parent vessel itself, no coil mesh within the aneurysm fundus is necessary to stabilize the neck coverage created by the PED. Ultimately, the in situ PED construct provides an anatomic scaffolding over which endothelialization and neointimal growth can occur to provide a homogeneous and contiguous barrier of tissue over the mural defect. This anatomic reconstitution of a normal endovascular surface over the aneurysm neck represents the hallmark of an anatomic cure, which is seen only rarely after embolization with coils.

Application of PED in a Parent Vessel Giving Rise to Eloquent Perforators

Through a strategic placement of the PEDs, we were able to build a stable intravascular construct which provided very high metal surface area coverage concentrated over the aneurysm neck and much lower metal surface area coverage over the normal-appearing proximal and distal basilar artery segments. Thus, we were able to create an in situ PED endovascular construct designed specifically to occlude the aneurysm while maintaining enough porosity to allow perfusion of the vital perforators arising from the normal proximal and distal basilar artery segments. Unlike the aneurysm filling, which is governed by parent vessel geometry and flow dynamics alone, flow into perforating vessels is maintained by a pressure gradient. These perforators present a lower-pressure “run-off” to the parent artery and, thereby, maintain their patency even when a significant percentage of the ostial surface area is covered.

Our results in the present case are analogous to those demonstrated by Kallmes et al. (3) in their experiments in which they implanted PEDs within the rabbit aorta. Although the PEDs within the parent aorta were generally covered with a homogeneous, contiguous layer of endothelium, there were focal rounded defects corresponding to the origins of the lumbar arteries. In these regions, the construct remained bare, preserving the patency of these ostia and continued perfusion (3). No branch vessels covered by the PED constructs implanted in either the rabbit subclavian artery or abdominal aorta went on to occlusion at the time of follow-up. Similarly, the angiographically visible branch vessels covered with PED constructs in our 2 previous human patients have also remained patent (2).

When applying the PED in arterial segments giving rise to potentially eloquent perforators, caution must be exercised to avoid multilayer or densely packed coverage. It is also critical that adequate dual antiplatelet medication has been administered and that therapeutic procedural heparinization has been instituted.

CONCLUSION

The PED provides a means by which to achieve definitive endovascular reconstruction of even the most complex cerebral aneurysms. The PED construct alone can create aneurysm thrombosis, without adjunctive embolization coils. When used strategically, the PED can be deployed within arterial segments giving rise to eloquent perforators. PED reconstruction offers a much less invasive, more technically straightforward, and more physiological treatment of many aneurysms than do other contemporary open surgical and endovascular therapies. Given the results achieved with the PED thus far, it seems difficult to justify heroic open surgical or conventional endovascular reconstructive treatments, deconstructive treatments, or flow reversal procedures for complex aneurysms that might otherwise be amenable to a safer and more straightforward curative reconstruction with PED.

Disclosure

Peter K. Nelson, M.D., is a stockholder in Chestnut Medical Technologies, Inc. None of the other authors have personal financial or institutional interests relevant to this article.

REFERENCES


COMMENTS

Fiorella et al. present a study of significant interest and value to the neurosurgical community. They describe a case wherein the PED is used to treat a giant midbasilar aneurysm. The patient experienced no untoward event, and the original vessel was completely reconstructed without evidence of residual aneurysm.

The PED will soon be available in the United States as part of several research trials. This article, along with its predecessor (1), should provide impetus to the neurosurgical community-at-large to make every effort to direct patients with pathologies such as those described herein to centers participating in PED investigations, for it is only with carefully designed clinical trials, supported by adequate patient enrollment, that we will learn the true value and efficacy of the PED.

In that vein, we also would offer a strong word of caution. We, at the University at Buffalo, have performed numerous similar procedures with different devices (the Magic Wall stent and/or Jostent), but to essentially the same end. Although we have experienced many outstanding outcomes, similar to the results reported by Fiorella et al., we have certainly also experienced the occasional poor outcome—usually the result of delayed thrombotic events upon cessation of anticoagulation. Therefore, we caution readers of this exciting report (for it is exciting) that there will be alternative outcomes experienced with this technology as well, and many aspects need further evaluation before this device is heralded as the obvious treatment of choice for these lesions. This will be the task for those performing the soon-to-be-begun clinical trials.

J Mocco
L. Nelson Hopkins
Buffalo, New York

Fiorella et al. present a very interesting case report describing the application of an endovascular remodeling device, the Pipeline stent, as the sole modality of treatment. Although not currently approved by the Food and Drug Administration, this device has been used in animal studies and initial clinical trials outside the United States with intriguing and encouraging results. This case presentation demonstrates the significant potential of this technology in rendering high-risk or previously untreatable aneurysms treatable with acceptable risk.

Flow diversion for aneurysm treatment has been a concept that endovascular therapists have considered and anecdotally observed, although not with any clear predictability. Zenteno et al. (1) recently described this phenomenon with the use of this stent.

Further studies and reports will provide clinicians with important long-term results related to possible delayed stenosis, a finding that has been noted in some patients with Neuroform stents. Nonetheless, this stent provides an additional technological advance that expands the role of endovascular remodeling in the treatment of complex intracranial vascular disease.

Charles J. Prestigiacomo
Newark, New Jersey