Endovascular Reconstruction of Intracranial Aneurysms with the Pipeline Embolization Device in Pediatric Patients: A Single-Center Series

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\section*{Abstract}
\textbf{Background:} Pediatric intracranial aneurysms tend to differ in etiology, size, and location from their adult counterparts, and they are often less amenable to microsurgical clip reconstruction techniques. Endovascular treatment with detachable coils is an accepted treatment technique for pediatric patients, though high recurrence rates have been reported with coil embolization of large and giant aneurysms in this population. While the Pipeline Embolization Device (PED) is FDA-approved for adult intracranial aneurysms, the use of PEDs in pediatric patients is considered off-label. 

\textbf{Case Descriptions:} We present 3 cases of pediatric intracranial aneurysms in a 5-year-old male, a 12-year-old male, and a 12-year-old female who presented with symptoms including seizure, headache, and blurred vision. The 2 male patients were found to have intradural vertebral artery saccular aneurysms, while the female patient had a paraophthalmic right internal carotid complex aneurysm. After endovascular reconstruction of the aneurysms with PEDs, follow-up angiography showed complete occlusion of the previous aneurysms with no residual aneurysm filling in all 3 cases. 

\textbf{Conclusion:} While further investigation is needed, the evidence presented here supports the conclusion that the PED can be an effective and viable treatment strategy in the pediatric population.
Introduction

Intracranial aneurysms are uncommon in the pediatric population, occurring in only 0.5–4.6% of patients 18 years of age or younger [1, 2]. Most aneurysmal risk factors in adults do not exist in pediatric patients. Pediatric patients also show different pathogenesis, demographics, and anatomical features for aneurysms, including male predominance, higher incidence in the posterior circulation, and a greater incidence of large and giant aneurysms. The initial presentations of most unruptured aneurysms in the pediatric population include headache, seizure, and mass effect [3]. Aneurysms in this population are often not amenable to direct microsurgical clip reconstruction techniques due to the predominance of unfavorable locations for surgical access [4, 5]. High recurrence rates following endovascular coiling also make traditional endovascular therapies less favored in pediatric patients [6, 7].

The Pipeline Embolization Device (PED) was approved by the FDA in 2011 for adult patients and has since been shown to provide higher aneurysm occlusion rates compared with preexisting endovascular techniques such as coiling and parent vessel occlusion, with comparable associated morbidity [8–10]. To date, however, there has been only one clinical trial comparing the efficacy and safety of endovascular coiling and clipping in children [11]. There have also been relatively few case reports on pediatric patients treated with flow diversion [3, 5, 12–14]. To illustrate the safety and efficacy of this relatively new endovascular technique in treating intracranial aneurysms in pediatric patients, we present in this article our experience in treating 3 pediatric aneurysm cases using the PED.

Case Reports

The 3 cases that will be discussed in this article are summarized in Table 1. All patients were given aspirin (81 mg) and Plavix (0.2–1.0 mg/kg/day, maximum 75 mg/day) for 5 days prior to the procedure. Platelet inhibition was measured using the P2Y12 assay. On the day of the procedure, the goal of P2Y12 reactivity between 50 and 150 was achieved. All of the procedures were performed under general endotracheal anesthesia.

Case 1

A 12-year-old male presented to the emergency department with neck stiffness of several weeks’ duration. CT of the head showed a giant left vertebral artery aneurysm at the foramen magnum level. The patient was evaluated and scheduled for an elective cerebral angiogram and possible embolization and was discharged home. He later returned to the hospital with complaints of a headache and more severe neck pain than first reported. An MRI/MRA of the patient’s head confirmed an approximately 2-cm aneurysm arising from the left vertebral artery proximal to the vertebrobasilar junction, which had enlarged since the prior CT study.

The patient was admitted and underwent cerebral angiography, demonstrating a giant partially thrombosed aneurysm originating from a distal left vertebral artery, without incorporation of the vertebrobasilar junction (Fig. 1). The left posterior inferior cerebellar artery originated just proximal to the aneurysmal segment. A left lateral medullary perforator (bulbar artery) originated 7 mm proximal to the aneurysmal segment. Other than the symptoms of a severe headache and neck pain, the patient’s history and neurological examination were unremarkable.

To treat this patient, a 4-gauge French sheath was placed in the right femoral artery, and diagnostic angiography was performed using 4-gauge French diagnostic catheters. The diagnostic catheter and sheath were then exchanged for a 088 Neuron Max guide catheter. The aneurysm was selectively catheterized using an Echelon-10 microcatheter. The aneurysm neck was then crossed with a Marksman microcatheter, which was advanced into the distal basilar artery. The aneurysmal segment of the left vertebral artery was reconstructed with five overlapping PEDs, telescopically deployed from proximal to distal across the aneurysm neck, in such a way that the proximal perforator and the vertebrobasilar junction were preserved. Once the pipeline reconstruction was completed, the aneurysm fundus was coiled with multiple detachable platinum coils. This final step was based on growing evidence in the IntrePED database supporting the addition of coils for large and giant aneurysms [15]. Since treatment with the PED takes a few months to fully secure the

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**Table 1.** Case summaries

| Patient | Symptoms | Aneurysm location | Aneurysm size | Aneurysm morphology | PEDs/coils | Follow-up |
|---------|----------|------------------|--------------|---------------------|------------|-----------|
| **Case 1** | 12-year-old male | headache, neck stiffness | intradural left vertebral | 24 × 16 mm with a neck size of 19 mm | saccular aneurysm | 5 PEDs plus coiled aneurysm | 6-month DSA showed no residual aneurysm filling |
| **Case 2** | 12-year-old female | headache, blurred vision | right ICA paraophthalmic to terminus | 1.2 cm | complex dysplastic distal ICA involving origin of PCOM, MCA, and ACA; accessory MCA arising from A1 distal to aneurysm | 4 PEDs | 8-month DSA showed no residual aneurysm filling |
| **Case 3** | 5-year-old male | seizure | intradural left vertebral | 7 × 4 mm with a neck size of 7 mm | saccular aneurysm | 2 PEDs | 1-year DSA showed no residual aneurysm filling |

ACA, anterior cerebral artery; DSA, digital subtraction angiography; ICA, internal carotid artery; MCA, middle cerebral artery; PCOM, posterior communicating artery; PEDs, Pipeline Embolization Devices.
Aneurysm, coiling on top of the PED is done in order to secure the aneurysm faster, especially with warning signs such as growth of the aneurysm.

At the 6-month follow-up, the patient was neurologically intact and was taking aspirin (81 mg) and Plavix (50 mg) daily. His 6-month follow-up angiography demonstrated complete occlusion of the previously known left vertebral artery aneurysm, without residual aneurysmal dome filling.

Case 2
A 12-year-old female presented to the emergency department complaining of frontal and left occipital headache lasting 1 week and a 1-h episode of blurred vision. The initial head MRI/MRA showed a complex aneurysm arising from the terminus segment of the right internal carotid artery (ICA). The patient underwent elective cerebral angiography that demonstrated a complex dysplastic segment of the distal ICA associated with a fusiform aneurysm of the supraclinoid segment of the right ICA. The patient’s past medical history and physical examination were otherwise unremarkable.

Diagnostic angiography was performed using a 5-gauge French diagnostic catheter that was then exchanged for a 6-gauge French Neuron Max guiding catheter over an exchange-length wire. The tip of the guiding catheter was positioned within the bulb of the ICA. A 5-gauge French Navien catheter was placed in the horizontal petrosal segment of the ICA. Subsequently, using roadmap guidance, a Marksman catheter was positioned using a 0.014 Transend wire into the A1 segment of the right anterior cerebral artery. The aneurysms and dysplastic segment were treated using a partially overlapping construct of four PEDs, spanning the A1 to cavernous segments, in the setting of an accessory middle cerebral artery variant (Fig. 2).

At the 8-month follow-up, the patient was neurologically intact and was taking aspirin (81 mg) and Plavix (50 mg) daily. Her 8-month follow-up angiography demonstrated complete occlusion of the previously known complex aneurysm of the distal right ICA, without residual aneurysmal dome filling. There was also reconstruction of the dysplastic segment.

Case 3
A 5-year-old male with a history of tuberous sclerosis, seizures, and cardiac rhabdomyoma was found to have a left-sided vertebral artery aneurysm during a tuberous sclerosis workup. He was electively admitted for a diagnostic cerebral angiogram. After discussion with the referring physician, the decision was made to perform pipeline embolization of the left vertebral aneurysm.
A diagnostic angiogram was performed using a 5-gauge French Envoy catheter. Following angiographic evaluation, the aneurysm was crossed with a 0.014 Transend guidewire over which a 2.8-French Marksman microcatheter was advanced past the aneurysm and into the basilar artery. The catheter was positioned with its distal tip just proximal to the basilar artery. The aneurysm was subsequently treated by placing two overlapping PEDs (Fig. 3).

At the 1-year follow-up, the patient was neurologically intact and was taking aspirin (81 mg) and Plavix (25 mg) daily. The 1-year follow-up angiogram did not demonstrate any residual aneurysm filling.

**Discussion**

Pediatric intracranial aneurysms are rare lesions, representing only about 1.0–4.6% of all reported intracranial aneurysms [12, 16]. The long life expectancy of most children and the associated disability-adjusted life years among this population necessitate a form of treatment that demonstrates both high obliteration and low recurrence rates. Up to 40% of all pediatric intracranial aneurysms are giant (> 25 mm in diameter), and up to 51% exhibit fusiform/dolichoectatic morphologic features [17, 18]. Researchers have reported that among the 42% of pediatric aneurysms involving the posterior circulation, 32% were in the posterior cerebral artery, and that among the 58% of pediatric aneurysms involving the anterior circulation, 26% were at the terminal and cavernous portion of the ICA [18]. Thus, the frequency of intracranial aneurysms not amenable to open surgery or coil occlusion is quite high in pediatric patients.

Studies have shown more favorable outcomes after coil embolization, compared with open surgery, for aneurysms involving the posterior circulation [19]. Furthermore, aneurysms in the cavernous segment of the ICA, which are often difficult to treat with microsurgery, can readily be approached by endovascular methods [19]. Endovascular treatment of aneurysms is associated with lower mortality compared to microsurgical clipping in the pediatric population [20].

Back in 2003, after conducting an 11-year follow-up study of 916 coiled aneurysms, Murayama et al. [21] found that aneurysm size and morphology were the critical variables...
leading to incomplete initial occlusion and later recurrence in endovascularly treated aneurysms. This study also found that in giant aneurysms, incomplete coiling occurred in 63% of cases, with a recurrence rate of 60% of incompletely coiled and 42% of completely coiled aneurysms. Other researchers found that endovascularly treated pediatric aneurysms with coiling had significantly higher rates of recurrence and formation of de novo aneurysms compared to a surgical cohort that underwent microsurgical treatment [22]. In addition, a large coil mass was associated with continued mass effect in large and giant intracranial aneurysms, leading to devastating neurological deficits [4]. The PED was developed to help with these problems and to improve the effectiveness of endovascular treatment. The Pipeline for Uncoilable or Failed Aneurysms (PUFS) trial demonstrated the safe and effective use of the PED in the treatment of large and giant anterior circulation intracranial ICA aneurysms, evidenced by low permanent morbidity or mortality (5.6%) and high rates of complete aneurysm occlusion, with durable results now demonstrated up to 5 years post treatment [16, 23].

The use of PEDs to treat intracranial aneurysms was approved by the FDA for adults in 2011. However, there is not as much accumulated evidence for the use of this approach in pediatric patients, where it is still considered an off-label treatment. The cases presented here make an important contribution to this needed evidence. All of the cases involved complex lesions located in the distal vertebral artery and the supraclinoid segment of the ICA. All were felt to be difficult surgical cases and either not amenable to coil occlusion or at high risk for recurrence with existing coil or stent-coil methods [24]. Thus, a PED approach was selected based on the apparent durability of pipeline-based vessel reconstruction, resulting in endothermalization of the neolumen and long-term aneurysm exclusion from parent circulation [25, 26].

Pipeline embolization has several potential advantages, especially in the pediatric population. The risk of intraoperative blood loss is considerably less when using endovascular methods for small children. Other advantages include relatively straightforward access to all vascular locations, less dependency on a large coil volume, and the ability to reconstruct whole vascular segments without the need for parent vessel occlusion. However, there are also some limitations. Pipeline embolization requires a largely empiric dual antiplatelet regimen, which in young, active children might be problematic. Moreover, if PED treatment fails, the low porosity of the device construct may preclude access to an aneurysm for further coiling. This can limit downstream options to vessel sacrifice, with or without bypass. It is also still unclear how exactly PED treatments will adjust to vessel growth in children.

While the findings of the current study are extremely promising, additional research needs to be carried out beyond these 3 cases. More long-term studies are also needed. Our patients’ aneurysms were reconstructed using two to five overlapping PEDs per aneurysm, and follow-up diagnostic angiographies up to 1 year following the procedures demonstrated complete occlusion of the aneurysms and no residual filling defects. Future studies will need to investigate additional PED procedures in pediatric patients and to examine long-term complication and regrowth rates beyond 1 year. At the current time we can say that surgical management and endovascular coiling are likely to remain the major treatment strategies in the armamentarium of pediatric neurosurgeons and neurointerventionists, but PED treatment should be considered as a robust alternative for the occlusion of large to giant pediatric aneurysms.

Conclusion

Pediatric intracranial aneurysms are more amenable to endovascular therapies compared to microsurgical constructive and deconstructive techniques. Endovascular coiling treatments lead to a high recurrence rate in pediatric aneurysms. Moreover, the mass effect exerted
on adjacent vital structures from a giant coiled aneurysm can lead to continued or worsening neurological deficits. Pipeline embolization may be a more effective treatment for completely eliminating aneurysms and reconstructing dysplastic vascular segments in the pediatric population. This article presented 3 cases of pediatric patients who were successfully treated using PEDs, thus demonstrating the potential value of the PED approach. The evidence for the success of PED treatment as an alternative to currently available therapeutic strategies for appropriately selected pediatric cerebral aneurysms warrants further investigation with long-term follow-up.

Statement of Ethics

The authors would like to state that subjects or their legal parents have given their informed consent and that the study protocol was approved by the institute’s committee on human research. No animals were involved.

Disclosure Statement

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