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Original Paper

Pipeline Flex Embolization of Flow-Related Aneurysms Associated with Arteriovenous Malformations: A Case Report

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Keywords
Cerebral arteriovenous malformations · Endovascular management strategies · Flow diversion embolization · Flow-related aneurysm · Pipeline Flex Embolization Device

Abstract
Background: An estimated 0.1% of the population harbors brain arteriovenous malformations (AVMs). Diagnosis and workup of AVMs include thorough evaluation for characterization of AVM angioarchitecture and careful assessment for concomitant aneurysms. The presence of coexisting aneurysms is associated with an increased risk of intracranial hemorrhage, with a published risk of 7% per year compared to patients with AVMs alone with a risk of 3%. Comprehensive AVM management requires recognition of concomitant aneurysms and prioritizes treatment strategies to mitigate the aggregate risk of intracranial hemorrhage associated with AVM rupture in patients with coexisting aneurysms. Endovascular treatment of these flow-related aneurysms can offer a cure, while avoiding open surgery. Successful flow-diverting embolization techniques, efficacy, and outcomes have been previously described for a variety of aneurysm types and locations. However, use of a flow diverter has not been previously described for the treatment of high-flow aneurysms on AVM-feeding vessels. ***Case Presentation:*** We report 2 cases of large AVMs within eloquent cortex associated with flow-related aneurysms in patients presenting initially with suspected intracerebral hemorrhage secondary to AVM rupture. ***Discussion:*** No consensus currently exists to guide treatment of intracranial aneurysms associated with AVMs. Surgical management addressed

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AVM embolization initially, as the vasculopathology with the highest rupture risk. Subsequently, Pipeline embolization of the associated aneurysms with adequate antiplatelet treatment was performed before scheduled radiosurgery to decrease the risk of AVM rupture or rebleed. This represents a novel and promising use of the Pipeline Embolization Device. Additional cases and longer follow-up will be needed to further assess the efficacy of this technique.

Introduction

An estimated 0.1% of the population harbors brain arteriovenous malformations (AVMs). Diagnosis and workup of AVMs include evaluation for characterization of AVM angioarchitecture and careful assessment for concomitant aneurysms [1–3]. Aneurysms in this patient population are categorized as intranidal, perinidal, flow-related, or unrelated to the AVM. Specifically, saccular and fusiform aneurysms arising along the direct course of arterial supply to the AVM are considered "flow-related" [4]. Coexisting aneurysms have been reported in up to 16.7% of cerebral AVMs [5–10]. The presence of coexisting unruptured aneurysms is associated with an increased risk of intracranial hemorrhage, with a published risk of 7% per year as compared to patients with AVMs alone with a risk of 3% [5]. Comprehensive AVM management requires recognition of concurrent aneurysms and prioritizes treatment strategies to mitigate the aggregate risk of intracranial hemorrhage associated with AVM rupture in patients with coexisting aneurysms [4–12].

Flow diversion, using stents, such as the FDA-approved Pipeline Embolization Device (PED; Medtronic Neurovascular, Irvine, CA, USA), is a well-established endovascular treatment for cerebral aneurysms. Flow-diverting embolization techniques, efficacy, and outcomes have been previously described for a variety of aneurysm types and locations [13–16]. However, use of a flow diverter has not been previously described for the treatment of high-flow aneurysms on AVM-feeding vessels. Here, we present 2 cases of staged endovascular flow diversion of feeding vessel aneurysms followed by radiosurgery for AVM obliteration.

Case Presentations

Case 1

A 69-year-old African-American woman with a long-standing history of poorly controlled hypertension and 25 pack-years of smoking cigarettes presented with a "thunderclap" headache and blurred vision. While a head computed tomography (CT) demonstrated curvilinear sulcal hyperdensities in the right frontal lobe consistent with calcifications and not hemorrhage, a lumbar puncture was positive for xanthochromia. Magnetic resonance (MR) imaging/MR angiography and CT angiography demonstrated a right frontal AVM and associated aneurysms. Cerebral catheter angiography diagnosed a right frontal pre-motor Spetzler-Martin Grade IIIb AVM supplied by a hypertrophied frontal branch of the right anterior cerebral artery with superficial venous drainage via an enlarged cortical vein (Fig. 1). Two 6-mm right internal carotid artery ophthalmic segment aneurysms were also visualized and were not considered to be sources of the hemorrhage. A multi-staged, multi-modality treatment plan was made. This included initial Onyx (Medtronic Neurovascular) liquid embolization of the AVM, staged flow diversion of the associated aneurysms, and finally stereotactic radiosurgery of the AVM nidus.

The first stage of the endovascular treatment was Onyx embolization of the primary AVM-feeding vessels. This provided a 50% reduction in arterial supply to the AVM nidus. The second stage of the endovascular treatment was planned Pipeline embolization of the high-flow aneurysms. A single Pipeline stent was positioned across the neck of both right internal carotid artery ophthalmic segment aneurysms and deployed without complications using techniques previously described [16–18]. Early follow-up angiography at 4

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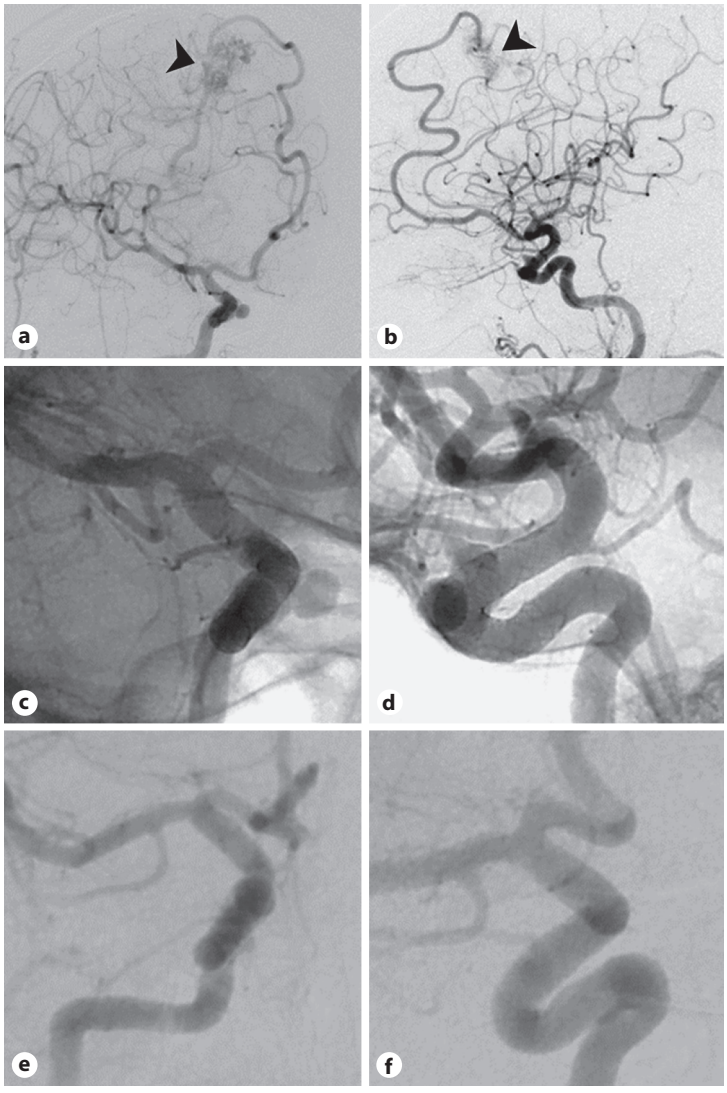

Fig. 1. Case 1: 69-year-old woman with 2 complex periophthalmic artery aneurysms. AP (**a**) and lateral (**b**) projections of ophthalmic ICA segment aneurysms in relation to the SM Grade IIIb AVM. AP (**c**) and lateral (**d**) projection of the PED Flex following deployment demonstrates apposition across the neck of the aneurysms. Four months later, AP (**e**) and lateral (**f**) projections show complete resolution of the distal ophthalmic ICA aneurysm, although there is still persistent filling of the proximal aneurysm. AP, anteroposterior; ICA, internal carotid artery; SM, Spetzler-Martin; AVM, arteriovenous malformation; PED, Pipeline Embolization Device.

months demonstrated complete obliteration of the proximal aneurysm and significant reduction of flow to the more distal aneurysm (Fig. 1). The patient was subsequently scheduled for stereotactic radiosurgical ablation of the AVM.

Case 2

A 39-year-old woman presented with a large left temporoparietal intracerebral hemorrhage (5 cm). Her exam was notable for drowsiness, expressive aphasia, right-sided hemiplegia, and hyperreflexia. Cerebral catheter angiography demonstrated a Spetzler-Martin Grade IIIb 3.5-cm AVM located within the deep eloquent left parietotemporal area. Arterial supply originated from hypertrophied left middle cerebral artery and posterior cerebral artery feeders, and venous drainage was superficial through an enlarged temporal vein. A coexisting 6-mm flow-related left vertebral artery aneurysm was also diagnosed. The treatment plan included staged Onyx embolization followed by stereotactic radiosurgery and flow-diverting stent embolization for her vertebral aneurysm.

At the time of Onyx AVM intervention, a distal middle cerebral artery pedicle was embolized to successfully reduce flow within the nidus by 70%. Six weeks later, the high-flow AVM-associated vertebral artery aneurysm was treated by Pipeline embolization (Fig. 2). Follow-up angiography demonstrated complete occlusion of the left vertebral artery aneurysm 12 months following Pipeline embolization, as seen in Figure 2. Following the embolization procedures, the patient was scheduled for definitive AVM treatment with stereotactic radiosurgery.

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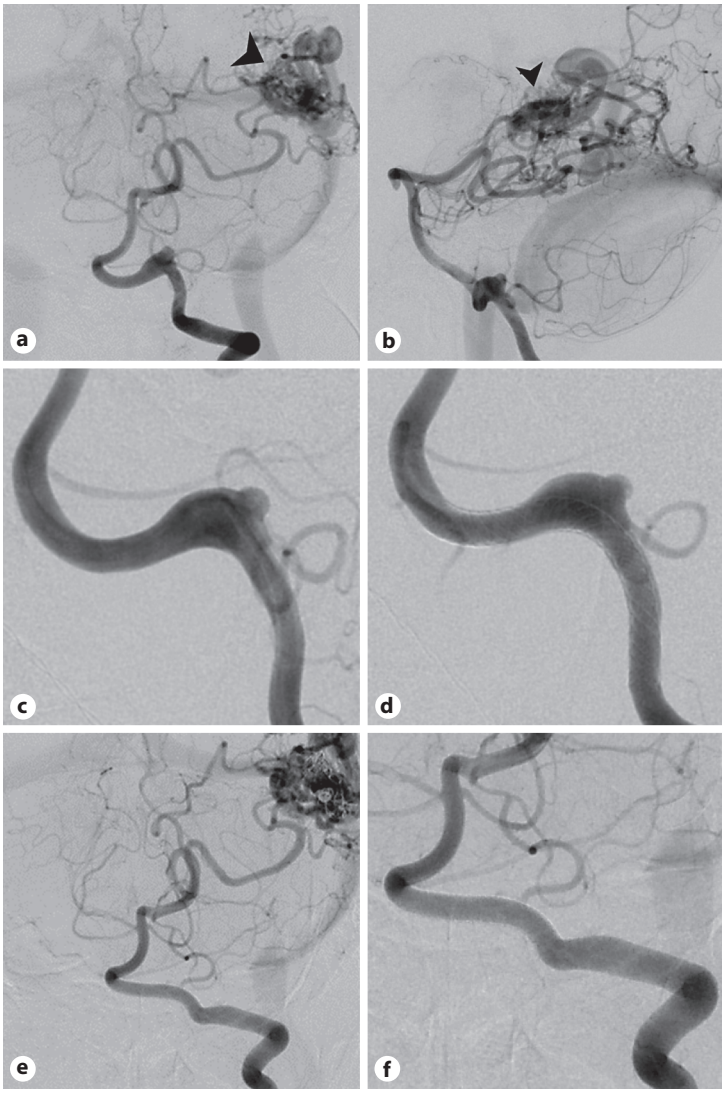

Fig. 2. Case 2: 41-year-old woman with a left temporal SM Grade IIIb AVM, as seen on the diagnostic cerebral catheter angiography. AP (**a**) and lateral (**b**) projections of a left vertebral artery fusiform aneurysm within the V4 segment. Immediately after placement of a Pipeline device (**c**), contrast stasis (**d**) can be seen. One year later, AP (**e**) and lateral (**f**) projections show complete angiographic resolution of the aneurysm. SM, Spetzler-Martin; AVM, arteriovenous malformation; AP, anteroposterior.

Discussion

Cerebral AVMs and coexisting intracranial aneurysms have been anecdotally discussed since 1942 [19]. Pathogenesis theories largely attribute the formation of AVM-associated aneurysms to pathological hemodynamics induced by the AVM, namely high proximal blood flow [4, 5, 9, 11]. Shakur et al. [20] have since expanded this theory to emphasize the biomechanical importance of AVM feeder vessel wall shear stress in coexisting aneurysm development. No consensus currently exists to guide the treatment of intracranial aneurysms associated with AVMs. However, various case series discuss current treatment strategies for surgically managing AVMs with coexisting intracranial aneurysms [4–6, 9–11, 19, 21, 22]. Rammos et al. [22] suggest that the spatial relationship between the AVM nidus and the associated aneurysm, in addition to the patient's clinical presentation, should guide treatment decisions and timing.

Case report 1 described a clinical presentation concerning for acute intracranial hemorrhage, with CT and MR imaging demonstrating only a small amount of contrast enhancement near the AVM. The MR findings represented either a region of active vascular inflammation

or a region of encephalomalacia from prior insult. The patient's initial presentation, coupled with the MR findings, necessitated expedient AVM treatment over treatment of the associated unruptured aneurysm for greater concern of AVM rupture [4–6, 9–11, 22]. Of note, the patient preferred endovascular treatment modalities. Initial treatment with AVM Onyx embolization was performed with 2 goals of therapy. The primary goal of reducing AVM size was achieved by reducing anterograde flow through AVM-feeding vessels. The secondary goal of AVM treatment, following concepts proposed by Redekop et al. [4], was to potentiate regression of the distal flow-related aneurysms [23]. On follow-up imaging, the aneurysm had not reduced in size. For this reason, Pipeline embolization was staged shortly thereafter.

Kano et al. [12] illustrated an increased risk of rebleeding following stereotactic radiosurgery in hemorrhagic AVMs with untreated associated aneurysms. The staging of treatment modalities must, therefore, be carefully evaluated. The surgical management of the high-flow posterior temporal parietal AVM, outlined in case report 2, addressed AVM embolization initially as the vasculopathology with the highest rupture risk [4–6, 19, 24–27]. Subsequently, Pipeline embolization of the associated aneurysm with adequate antiplatelet treatment was performed before scheduled radiosurgery to decrease the risk of AVM rebleeding [12].

There is no current literature to guide antiplatelet or anticoagulation use in patients with recent AVM rupture [28–30]. The risk of rebleeding must be weighed against the benefits of aneurysm treatment by flow diversion, which requires dual antiplatelet medications to prevent platelet aggregation on the device. Other treatment modalities were considered, including surgery and coil embolization alone, or stent-coil embolization. These therapies were deemed inappropriate or less effective for the proximal, wide-necked aneurysms shown in Figures 1 and 2.

To our knowledge, flow diversion of AVM-feeding aneurysms has not previously been reported in the literature. This represents a novel and promising use of the PED. Additional cases and longer follow-up will be needed to further assess the efficacy of this technique.

Statement of Ethics

This research was approved by the Johns Hopkins institutional review board.

Disclosure Statement

A.L.C. is a proctor for the Woven EndoBridge device (Sequent Medical, Aliso Viejo, CA, USA), a proctor for the Surpass device (Stryker Neurovascular, Fremont, CA, USA) and a consultant for Stryker Neurovascular, a proctor for the Pipeline Embolization Device (Medtronic Neurovascular, Irvine, CA, USA) and a consultant for Medtronic Neurovascular, and a proctor for the FRED device (MicroVention-Terumo, Tustin, CA, USA) and a consultant for MicroVention. G.P.C. receives research support from Medtronic Neurovascular and Stryker Neurovascular and is a consultant for MicroVention-Terumo. L.-M.L. is a proctor for the Pipeline Embolization Device (Medtronic Neurovascular), a consultant for Medtronic Neurovascular, and a consultant for MicroVention-Terumo. The other authors have no conflicts of interest. No author received financial support in conjunction with the generation of this submission.

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