CASE REPORT

Successful endovascular treatment of three fusiform cerebral aneurysms with the Pipeline Embolization Device in a patient with dilating HIV vasculopathy

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SUMMARY

Dilating HIV vasculopathy can be a cause of ischemic and hemorrhagic stroke in patients with HIV. Although first identified in children, this condition is increasingly being recognized in adults and has a dismal natural history under medical or expectant management. Vessel wall invasion by varicella zoster virus, HIV or *Mycobacterium avium intracellulare* complex (MAI) has been postulated as a possible etiology. We present a case of an adult patient with HIV and chronic disseminated MAI infection who presented with ischemic stroke and three fusiform cerebral aneurysms that were successfully treated with the pipeline embolization device (PED). Flow diversion may be a viable treatment option for patients presenting with this serious neurovascular condition when aneurysm location precludes parent vessel sacrifice or surgical bypass. In addition, platelet function testing with VerifyNow may be valuable in selecting the appropriate P2Y12 receptor antagonist to be used in order to prevent PED thrombosis, since some of the antiretroviral drugs may inhibit clopidogrel or prasugrel metabolism.

BACKGROUND

Dilating HIV vasculopathy can be a cause of ischemic and hemorrhagic stroke in patients with HIV. This serious neurovascular condition was first identified in children and is estimated to affect up to 2.6% of patients who acquire the HIV infection in childhood,¹ usually leading to death within 6 months of aneurysm diagnosis.² With the advent of highly-active antiretroviral therapy (HAART), the condition is increasingly being recognized in adults, with 20 cases reported in the English language literature to date.^{3–9} Although the exact etiology of vasculopathy is unclear, vessel wall invasion by varicella zoster virus, HIV or *Mycobacterium avium intracellulare* complex (MAI) has been postulated.

A review of the 20 reported adult cases of dilating HIV vasculopathy (13 men; mean age 34 years (median 35 years, range 22–43 years)) shows that the natural history of this serious neurovascular condition is dismal.^{3–9} The clinical presentation was subarachnoid hemorrhage (SAH) in seven patients (35%), cerebral infarction in seven patients (35%), severe epistaxis in two patients (10%) and one patient each with intracerebral hemorrhage (ICH), a combination of ICH and cerebral infarction, seizures and cognitive impairment. Ten

patients were treated with either the institution or optimization of HAART (50%), five with endovascular or neurosurgical intervention (25%, two with parent vessel sacrifice, two with coiling of associated pseudoaneurysms and one with surgical bypass of the affected vessel) and five patients (25%) did not receive any treatment. Five of the 15 patients who received either medical treatment with HAART or no treatment were lost to follow-up. Among the remaining 10 patients, five had recurrent cerebral infarctions or ICH (50%), three died shortly after diagnosis (30%, one from a fulminating recurrent SAH) and only two had resolution of the presenting symptoms (20%). Among the five patients who underwent either endovascular or neurosurgical intervention, four had resolution of the presenting symptoms (80%) and one died shortly after diagnosis (20%).

We present a case of an adult patient with HIV and chronic disseminated MAI infection who presented with ischemic stroke and three fusiform cerebral aneurysms that were successfully treated with the Pipeline Embolization Device (PED).

CASE PRESENTATION

A 37-year-old African-American man with an 18-month history of HIV infection leading to AIDS, chronic disseminated MAI infection and a partially resected posterior fossa hemangiopericytoma presented with worsening slurred speech and right-sided weakness. At the time of presentation the patient was on a HAART regimen of ritonavir, darunavir, abacavir-lamivudine and raltegravir, with a CD4 cell count of 49 cells/ μ l and an undetectable viral load.

INVESTIGATIONS

Brain MRI demonstrated acute infarctions involving the left caudate head and posterior limb of the left internal capsule (figure 1A), with associated fusiform dilation of the left supraclinoid internal carotid artery (ICA) and bilateral posterior cerebral arteries (PCA), which was confirmed by catheter angiography (figure 1B,C). Notably, three-dimensional reconstructions of a contrast-enhanced MRI of the brain performed 6 months prior to presentation showed a normal appearance of the circle of Willis (figure 1D). Analysis of cerebrospinal fluid (CSF) showed it to be cloudy with glucose 35 mg/dl, protein 53 mg/dl, 172 white blood cells/mm³ and 1835 red blood cells/mm³.

To cite: Delgado Almandoz JE, Crandall BM, Fease JL, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2012-010634

Figure 1 (A) Axial diffusion-weighted image showing acute infarctions in the left caudate head and posterior limb of the left internal capsule. (B) Frontal left internal carotid artery (ICA) angiogram showing fusiform dilation of the supraclinoid segment of the left ICA. (C) Frontal left vertebral angiogram showing fusiform dilation of the P1 segments of the posterior cerebral arteries bilaterally. (D) Volume-rendered three-dimensional reconstruction of a contrast-enhanced MRI of the brain performed 6 months prior to presentation showing a normal appearance of the circle of Willis.

Aerobic, anaerobic and fungal CSF cultures were negative. CSF varicella zoster and herpes simplex virus PCR were also negative.

DIFFERENTIAL DIAGNOSIS

The clinical impression was that the cerebral infarctions were due to either the fusiform left supraclinoid ICA aneurysm or AIDS-related small vessel vasculopathy. The moderate number of red blood cells in the CSF without associated xanthochromia was thought to be due to either a traumatic lumbar puncture or a sentinel SAH.

TREATMENT

Given that (1) there was clinical concern for a possible sentinel SAH, (2) the patient's HAART regimen was already optimized, (3) parent vessel sacrifice or surgical bypass were not viable treatment options due to the aneurysm locations and (4) the natural history of this serious neurovascular condition under

medical or expectant management was dismal, the patient was offered endovascular treatment with the PED in an effort to prevent further thromboembolic events from the left supraclinoid ICA aneurysm as well as rupture of the P1 segment PCA aneurysms causing a fulminating SAH. After a detailed discussion of management options and the risks of thromboembolic and hemorrhagic complications associated with endovascular aneurysm treatment with flow diversion including postoperative aneurysm rupture, the patient and his family elected to proceed with endovascular treatment with the PED.

The VerifyNow test performed the day before the first procedure after seven 75 mg doses of clopidogrel demonstrated a P2Y12 reaction units (PRU) value of 399. The patient was considered a clopidogrel hyporesponder and was administered prasugrel in a 60 mg loading dose followed by 10 mg daily. A repeat VerifyNow test performed immediately before the first procedure showed a PRU of 126, which was within the target PRU range of 60–240.

Figure 2 (A) Frontal fluoroscopic image prior to pipeline embolization device (PED) deployment showing the bilateral PED inside the Marksman microcatheters. (B) Frontal fluoroscopic image showing the bilateral PEDs partially deployed into each P1 segment of the posterior cerebral arteries (PCA). (C) Frontal fluoroscopic image showing the fully deployed PEDs extending from each P1 segment of the PCAs to the distal basilar artery in a 'kissing' overlapping fashion. (D) Sagittal Dyna-CT angiogram reconstruction showing the 'kissing' overlapping PEDs in the distal basilar artery. (E) Final frontal left vertebral angiogram showing patency of the PEDs and distal cerebral vasculature with reduced flow to the left P1 segment PCA aneurysm.

The patient underwent uncomplicated treatment of the left supraclinoid ICA aneurysm with a 4.5 mm×30 mm PED and was discharged on postoperative day (POD) 1.

A repeat VerifyNow test performed on POD 7 prior to the second procedure demonstrated a PRU value of 258. The patient was considered a prasugrel hyporesponder, possibly due to a drug interaction with ritonavir,¹⁰ and was subsequently administered ticagrelor in a 180 mg loading dose followed by 90 mg twice daily. A repeat VerifyNow test immediately before the second procedure showed a PRU of 30.

The patient underwent treatment of the bilateral P1 segment PCA aneurysms under general anesthesia using bilateral transfemoral arterial access and bilateral triaxial systems in each

vertebral artery as follows: 5 Fr Shuttle sheaths advanced to their mid-cervical segments, bilateral 058 inch Reflex distal access catheters advanced to their distal cervical segments and two Marksman microcatheters advanced over Traxcess microwires to each PCA past the fusiform aneurysms (figure 2A). Subsequently, sequential deployment of a 2.5 mm×14 mm PED via each Marksman microcatheter was performed (figure 2B and video). The two PEDs were deployed from each PCA across the fusiform aneurysms and overlapped in a 'kissing' fashion at the top of the basilar artery (figure 2C,D). Patency of the PEDs and distal cerebral vasculature was confirmed with catheter angiography (figure 2E). The patient remained at his neurological baseline and was discharged on POD 1.

OUTCOME AND FOLLOW-UP

The 6-month follow-up catheter angiogram demonstrated complete remodeling of all three fusiform aneurysms along the PEDs. The left ICA was normal in caliber and the left anterior choroidal artery remained patent (figure 3). The bilateral PCA aneurysms also demonstrated complete vascular remodeling (figure 4A,B), with complete remodeling of the top of the basilar artery along the 'kissing' PEDs and four separate vascular channels for the bilateral superior cerebellar and bilateral PCAs (figure 4C,D).

At the time of the 6-month follow-up angiogram, the patient's neurological deficits had improved with mild to moderate residual cognitive impairment and mild residual right-sided weakness (4/5). The patient was able to ambulate with the aid of a walker. He received dual antiplatelet therapy with ticagrelor 90 mg twice a day for 9 months after PED deployment and 81 mg aspirin daily for life. The patient remains neurologically stable 10 months after PED deployment.

DISCUSSION

To the best of our knowledge, this is the first reported case of successfully treated fusiform cerebral aneurysms with the PED in the setting of dilating HIV vasculopathy. Given the dismal natural history of this serious neurovascular condition under medical or expectant management, flow diversion may represent a viable treatment option for these patients when aneurysm location precludes parent vessel sacrifice or surgical bypass. Platelet function testing with VerifyNow may be valuable in selecting the appropriate P2Y₁₂ receptor antagonist to be used in order to prevent PED thrombosis, since some of the anti-retroviral drugs (ritonavir in our patient) may inhibit clopidogrel or prasugrel metabolism.

Figure 3 (A) Frontal left internal carotid artery (ICA) angiogram 6 months after treatment showing complete remodeling of the left supraclinoid ICA aneurysm along the pipeline embolization device (PED) with patency of the left anterior choroidal artery and distal cerebral vasculature. (B) Lateral left ICA angiogram 6 months after treatment showing complete remodeling of the left supraclinoid ICA aneurysm along the PED with patency of the left anterior choroidal artery and distal cerebral vasculature.

Learning points

- ▶ Fusiform aneurysms due to dilating HIV vasculopathy can present with either ischemic or hemorrhagic stroke and have a dismal natural history under medical or expectant management.
- ▶ Endovascular treatment with the pipeline embolization device (PED) may be a viable treatment option for patients with this serious neurovascular condition when parent vessel sacrifice or surgical bypass is not possible.
- ▶ Platelet function testing with VerifyNow may be valuable in selecting the appropriate P2Y₁₂ receptor antagonist to be administered prior to PED deployment since some of the antiretroviral drugs used to treat the HIV infection may inhibit clopidogrel or prasugrel metabolism.

Figure 4 (A) Frontal left vertebral angiogram 6 months after treatment showing complete remodeling of the bilateral P1 segment posterior cerebral artery (PCA) aneurysms along the pipeline embolization device (PED) with patency of the distal cerebral vasculature. There has also been vascular remodeling at the top of the basilar artery along the two 'kissing' PEDs. (B) Lateral left vertebral angiogram 6 months after treatment showing complete remodeling of the bilateral P1 segment PCA aneurysms along the PED with patency of the distal cerebral vasculature. There has also been vascular remodeling at the top of the basilar artery along the two 'kissing' PEDs. (C). Anteroposterior view of a volume-rendered three-dimensional reconstruction from a rotational catheter angiogram showing vascular remodeling at the top of the basilar artery along the two 'kissing' PEDs with four separate vascular channels providing blood flow to the bilateral superior cerebellar arteries (SCA) and PCAs. (D). Posteroanterior view of a volume-rendered three-dimensional reconstruction from a rotational catheter angiogram showing vascular remodeling at the top of the basilar artery along the two 'kissing' PEDs with four separate vascular channels providing blood flow to the bilateral SCAs and PCAs.

Competing interests JEDA, BMC and DET have consulting relationships with Covidien/ev3.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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