



Original Article

Intracranial aneurysms in pediatric population treated with flow diverters: A single-center experience

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ABSTRACT

Background: Pediatric intracranial aneurysms (PIAs) are uncommon. Flow diverters (FDs) have shown to be effective on treatment of selected aneurysms.

Methods: We describe 10 cases of PIAs treated with FDs at one medical center in Mexico, from April 2015 to April 2020.

Results: Out of 230 patients treated with FDs, 10 (4.3%) were pediatric. Average age was 9.4 years old (R: 6–15). Two patients (20%) had subarachnoid hemorrhage, 3 had epilepsy (30%), 3 (30%) had clinical signs of cranial nerve compression, and 4 (40%) had only headache. Two patients were in 1a grade of Hunt and Kosnik scale. Out of the nonruptured aneurysms, 7 (70%) were in 15 points of Glasgow Coma Scale and 1 patient (10%) was in 13 points. Treatment was performed without complications; nevertheless, appropriate distal deployment was not achieved in one case. At discharge, nine patients had 5 points of Glasgow Outcome Scale. All patients underwent computed tomography angiography or digital subtraction angiography at 1, 3, 6, and 12 months, 2 patients (20%) had a 2-year follow-up, and 3 patients (30%) had a 3-year follow-up. According to Kamran grading scale, 9 patients (90%) were classified as Grade 4 and 1 patient (10%) as Grade 3.

Conclusion: Even though it is a small series, as this is an uncommon disease, we may suggest that FDs are useful to treat properly selected PIAs. Our study has consecutive imaging assessment at least a year of follow-up in which aneurysm stable occlusion was observed in 90% of patients.

Keywords: Flow diverter, Intracranial aneurysm, Intracranial pediatric aneurysm

INTRODUCTION

Intracranial aneurysms (IAs) in pediatric population (pediatric IAs [PIAs]) are rare, representing <5% of events (0.17–4.6%).^[5,8,26,30,32,33,35-37,41,46] Current therapeutic options include expectant management, surgical treatment, and endovascular treatment.^[1,2,8,10,15,16,23,46] Flow diverters (FDs) have shown to be a useful tool in the treatment of certain IAs and they are routinely used around the world.^[11,27] Nevertheless, there is still scarce experience in the pediatric population. We present our experience at La Raza National Medical Center in Mexico City with the use of FDs in the treatment of 10 IAs in pediatric patients.

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MATERIALS AND METHODS

Population

We reviewed the clinical and imaging records of all patients with IAs which were treated by endovascular means at La Raza National Medical Center between April 2015 and April 2020.

It should be noticed that our department of neurosurgery has both vascular microsurgery and endovascular intervention, and all cases are analyzed in an expert session and with Institutional Review Board approval. We registered all IAs cases which were treated with FDs and then we specifically selected patients under 18 years of age. After analyzing each case, the following characteristics were important indications for the use of the FD: (1) aneurysm fusiform appearance, (2) very wide neck, and (3) our lack of experience in by-pass in children.

Initial clinical and imaging data and follow-up imaging findings were reviewed. Before treatment, the clinical status was assessed using the Glasgow Coma Scale (GCS)^[43] in patients with nonruptured aneurysms and the Hunt and Kosnik scale for ruptured.^[18]

Incidents and complications of the procedures were registered. Patients were assessed at hospital discharge and during follow-up using the Glasgow Outcome Scale (GOS).^[28]

All patients were followed up with digital subtraction angiography (DSA) or computed tomography (CT) angiography at 3, 6, 9, and 12 months after treatment. Aneurysm thrombosis degree was assessed according to a scale proposed by Kamran *et al.*^[20]

Treatment description

Patients were submitted to double antiplatelet regime daily during 5 days before procedure, with clopidogrel 37.5 mg and aspirin 100 mg for children weighing <45 kg, and clopidogrel 75 mg and acetylsalicylic acid 100 mg for children weighing >45 kg. All patients were treated under general anesthesia at angiography suite. Femoral approach was performed using the Seldinger technique to place a 6F femoral sheath introducer. A 100 UI/Kg heparin bolus was administered to maintain a coagulation time activity approximately twice the basal value. In all cases, a 6F Chaperon guiding catheter (MicroVention, Aliso Viejo, California) was used to cannulate the cervical internal carotid artery (ICA) or the vertebral artery (VA) V2 segment, as required. In almost all cases, a 5F distal Sophia catheter (MicroVention, Tustin, California, USA) was used to reach the ICA at cavernous or clinoid segment or the VA at V3 segment. The FD selection was performed according to parent artery diameter. The deployment of the FDs was carried out using a well-known international technique, as previously

described.^[18,19] Three types of FDs were used, pipeline embolization device (PED) (Medtronic Neurovascular, Irvine, California), flow redirection endoluminal device (FRED) device (MicroVention, Tustin, California, USA), and Silk+ device (Balt Extrusion, Montmorency, France). Only in our first case, we decided to perform a “scaffold” with two Neuroform stents (Boston Scientific/Target Therapeutics, Fremont, CA) before FD deployment, preventing widening and over-shortening of the FD.

After the procedures, the patients were kept on a double antiplatelet therapy for 6 months, at the doses shown above. Subsequently, treatment with clopidogrel was continued permanently [Table 1 and Figures 1-5]. In our experience in adults, we usually continue SAPT for 1 year after treatment. We indicate prolonged SAPT in the following cases: (1) angiographic data of intracranial or extracranial atherosclerosis, (2) history of dyslipidemia, (3) personal history of coronary ischemia, (4) personal or family background of stroke, and (5) evidence in the angiographic controls of a mild degree of stenosis within the FD, in which we associate, in addition to the antiplatelet agent, some statin.

RESULTS

From April 2015 to April 2020, at La Raza National Medical Center, 505 endovascular therapeutic procedures were performed in 463 patients; 400 were IAs in 383 patients, from which 230 patients with 247 aneurysms were treated with FDs, and out of these, 10 patients (4.3%) were under 18 years old. It is worth noting that four other children with ruptured aneurysms were excluded from this study because they were treated by clipping.

Seven patients (70%) were male. The average age was 9.5 years (R: 7–15). No child had a remarkable medical history during gestation and they had no congenital disease or any important recent infectious disease. Only a 12-year-old male patient (10%) had a V4 segment dissecting aneurysm, as well as an indirect cervical trauma history due to a car accident.

The initial presentation of 2 patients (20%) was a subarachnoid hemorrhage (SAH), in 2 (20%), it was epilepsy, 2 patients (20%) had clinical signs of cranial nerve compression, and 4 patients (4%) had a history of headache.

Patients whose initial presentation was SAH were admitted with Hunt and Kosnik scale Grade 1a and were treated 20 days after the bleeding event. Of eight patients with an initial presentation different than SAH, 7 (70%) had a GCS score of 15, and 1 (10%), who had a large basilar aneurysm, had a GCS of 13 in addition to quadriplegia and bilateral paresis of the sixth cranial nerve [Table 1].

Procedures were performed without complications in all patients. For Patient 2 [Figure 1] who had a left middle

Table 1: Description of patient/aneurysms characteristics.

Case	Gender/age	Clinical	Location	Morphology	FD/No	Size (mm)	Compl./incident
1	Male/12	Trauma/SAH	V4	Fusiform/dissecting	FRED/1*	3.5×16	No
2	Male/8	Epilepsy	MCA	Fusiform	PED/1	3.25×30	Yes*
3	Female/7	pIIInc	cavICA	Large/giant	PED/1	3.0×25	No
4	Male/15	Headache/epilepsy	MCA	Fusiform	PED/6	3.5×20 (1), 3.0×14 (5)	No
5	Male/10	pVInc/quadruparesis	Basilar	Large/giant	PED/1	3.0×18	No
6	Male/6	SAH	PCA	Fusiform	FRED/1	3.0×16	No
7	Female/9	Headache	MCA	Large/giant	PED/1	3.0×12	No
8	Male/8	pIIInc	cavICA	Large/giant	FRED/1	3.0×16	No
9	Male/9	Headache	cavICA	Large/giant	Silk+/1	3.0×15	No
10	Female/10	Headache/epilepsy	MCA	Large/giant	Silk+/1	3.5×25	No

FD/N: Flow diverter class and devices number. Compl./Incident: Complications and/or incidents. pIIInc: Third cranial nerve palsy. pVInc: Sixth cranial nerve palsy. V4: Vertebral artery V4 segment. MCA: Middle cerebral artery. cavICA: Cavernous segment of internal carotid artery. PCA: Posterior cerebral artery. FRED: Flow redirection endovascular device. FRED/1*: In this case, a FRED device was used within scaffold made with two Neuroform stents. PED: Pipeline endovascular device. Yes*: Impossibility of a more distal access to MCA

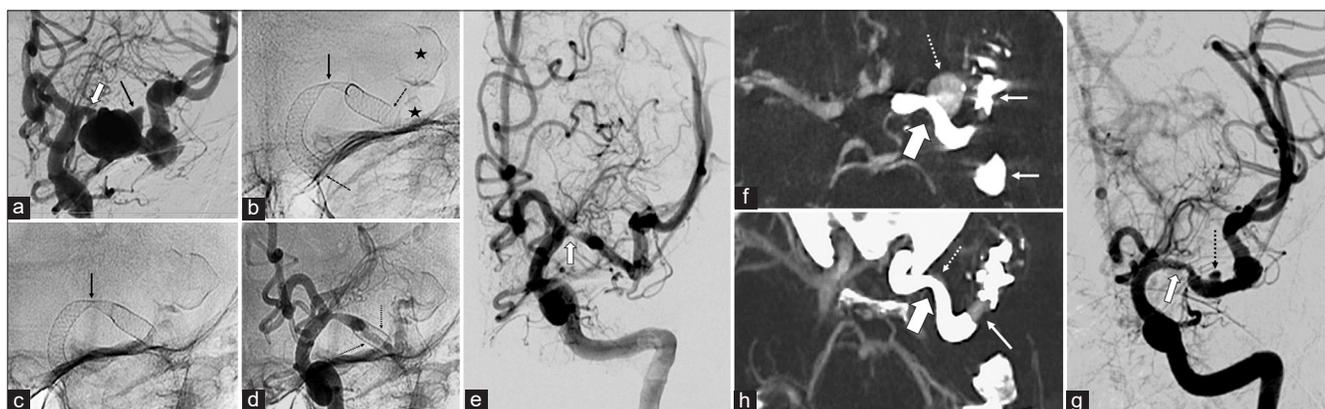


Figure 1: (Case 2) (a) Fusiform aneurysm affecting the entire left M1 segment and part of the M2 segment, together with parts of a saccular appearance, the M1 segment being the largest, with blebs (thin arrow). An stenosis at the origin of the middle cerebral artery (thick arrow) is evident. (b and c) Flow diverters (FD) deployed (dotted arrows) along the stenotic segment over the middle cerebral artery (arrow) to the M1 segment. The stenosis caused great difficulty and inability to navigate and deploy it more distally. Some calcified segments of the aneurysm (star) can be seen. In c, the arrow shows the stenotic site that only slightly widened despite being balloon treated twice. (d and e) Contrast injection revealed stent patency, which was initially slow with only flow toward the FD center (dotted arrows on d). At the end of the procedure and through a digital subtraction angiography (DSA) on AP projection, appropriate flow is observed through the FD and left middle cerebral artery, regardless of the stenotic segment (thick arrow). (f) One month follow-up transvenous contrast injection CTA with axial section where a stenotic segment is observed (thick arrow) and even residual flow on aneurysm saccular part (dotted arrow). Some calcified segments of the aneurysm can be seen (arrows). g: One-year DSA control on AP projection where an excellent flow is observed through FD toward MCA distal segments, regardless to stenotic part (thick arrow). A very reduced residual filling is seen at old saccular part at M1 segment (dotted arrow). h: A 24-month follow-up CTA on axial section where persistence of the stenotic part is seen (thick arrow) but with a filling of less than 1% regarding old saccular part at M1 segment (dotted line). Distal flow toward FD can be seen (arrow).

cerebral artery (MCA) fusiform aneurysm, the original treatment plan was to deploy FD further from Sylvian point. Although superselective microcatheterization of the distal branches of the MCA bifurcation was easily achieved, we were not able to navigate FD more distally to M1 segment despite several number of attempts. This situation conditioned the deployment just before the Sylvian point. We suspect that this was due a severe stenotic origin of the MCA [Figure 1].

Patients recovered from general anesthesia without any additional deficit and their progress was unremarkable, with

the exception of slight headache in Patients 3, 5, and 7. Based on GOS, patients were rated as follows: 9 (90%) in Grade 5 and 1 (10%) in Grade 4. The latter was the case for a large aneurysm on the basilar artery that was admitted with a GCS of 13.

In our institution, as a standard practice, we follow-up with a DSA and/or CT angiography (CTA) at 1, 3, 6, and 12 months after the procedure and subsequently every year. Ionizing radiation in children has been shown to affect the growth plates, gonads, and thyroid gland. For that reason, lead shields



Figure 2: (Case 3) (a) Digital subtraction angiography (DSA) on lateral projection showing a large aneurysm on cavernous segment with a bleb that seems to be under an intradural location (thick arrow). (b) Lateral X-ray taken immediately after placing flow diverter, highlighted with dotted arrows. (c and d) Immediate follow-up DSA on lateral projections showing reduction of aneurysm flow velocity. (e and f) Follow-up DSA in lateral and AP projections at 6 months showing the absence of intra-aneurysmal flow. Intrastent stenosis is observed (arrow), presumably due to endothelium hyperplasia. (g and h) Lateral and AP projections of follow-up at 24 months with persistent absence of aneurysmal flow. The stenosis described in E is no longer observed.

were used over some parts of the body, including the pelvis and neck. We avoided carrying out the follow-up at 1 month and 3 months in children under 10 years of age, due to the risk of leukemia or malignant brain tumor. Nevertheless; we decided that a follow-up at 6 months and at 1 year was needed, either by CTA or DSA, since the possible benefits obtained with follow-up images outweighed by far the actual and potential risks.

All patients underwent follow-up assessments at 1 year, 4 patients (40%) at 2 years, and 4 patients (40%) at 3 years. Imaging follow-up was excellent, the aneurysms showed intra-aneurysmal thrombosis progression with parent vessel blood flow patency. The final imaging studies showed nine patients with Kamran's Grade 4. It is important to mention that in Case number 2 in which we had a diverter deployment incident, DSA after 1 year showed thrombosis beyond 90%, with a Karman's Grade 3. The plan was to perform a new DSA follow-up every 2 years. However, the patient's mother refused, so a 2-year CTA was performed and the aneurysm was found to be already occluded [Figure 1].

DISCUSSION

IAs in pediatric population (PIAs) are rare, representing <5%.^[5,8,26,30,32,33,35-37,41,46] On a review made by Beez *et al.*,^[5]

they analyzed 135 articles published between years 2000 and 2015, gathering information on 573 cases with 656 aneurysms with an average age of 7.6 years (R: 3–18). In most of the papers, there was a predominance of men over women, which coincides with our study. IAs were saccular in 20–30% of cases, the most frequent being fusiform, dissecting, and giant/complex aneurysms with different degrees of thrombosis.^[1,23] About 68% of aneurysms were large/giant and 16% were fusiform. Younger children are more prone to have fusiform and/or giant aneurysms.^[2] In our study, 57% of aneurysms were fusiform while the others were large/giant.

Dissecting aneurysms are generally secondary to trauma, infection, or congenital diseases.^[13,44] In our cases, there were no cases secondary to congenital diseases, vasculitis, collagen, or hematologic diseases, such as sickle cell anemia. Nevertheless, according to literature review, some of these diseases represent between 10 and 20% of cases.^[8,38,46] One patient of our series (14%) had a traumatic dissecting aneurysm (Case 1).

Hetts *et al.*^[16] classified pediatric aneurysms as follows: (1) traumatic, (2) infectious, (3) saccular, and (4) nontraumatic and noninfectious fusiform aneurysms. It has been reported that 75% of PIAs are usually located in the anterior circulation and 25% in the posterior circulation.^[5]

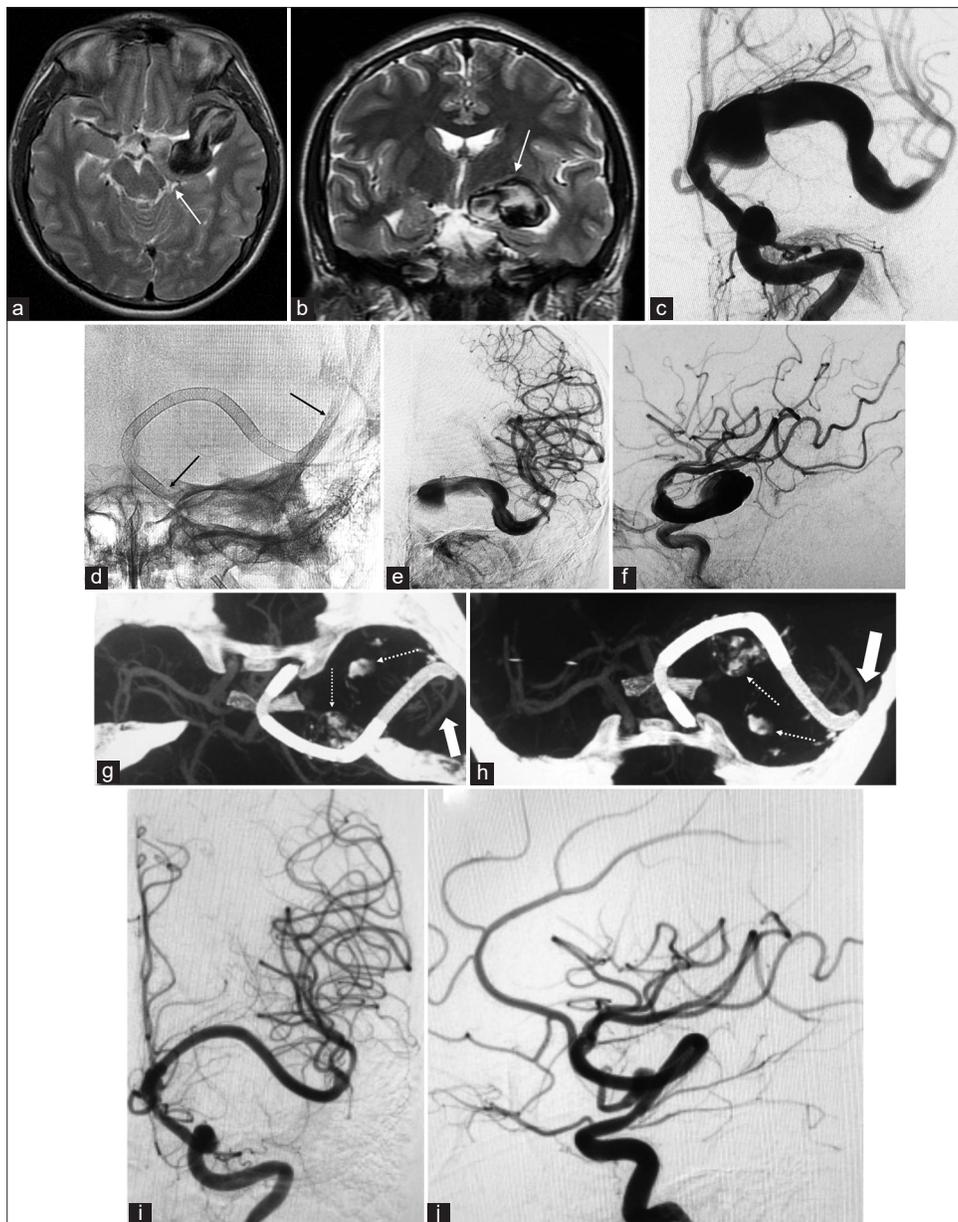


Figure 3: (Case 4) (a and b) T2-weighted MRI showing a partially thrombosed fusiform aneurysm on the left middle cerebral artery at sphenoidal segment. The lesion mass effect is very evident over cerebral peduncle as well as ipsilateral central core structures (arrows). (c) Digital subtraction angiography (DSA) in AP projection showing a fusiform aneurysm originating from the bifurcation of the internal carotid artery, in the entire M1 segment of the left MCA and beyond the Sylvian point. Inadequate iodinated contrast filling is evident in the distal branches. (d) The artery was reconstructed with six tandem flow diverters (arrows show start and end of devices). (e and f) AP and lateral projections DSA showing appropriate blood flow through flow diverters (FDs) and MCA distal branches. There are no obvious changes in the fusiform aneurysm. (g and h) One-month follow-up CTA shows no evidence of aneurysmal lesion around flow diverters as well as excellent distal flow (thick arrows). Dotted arrows show aneurysm calcifications. (i and j) Follow-up DSA with AP and lateral projections after 3 months of treatment showing appropriate reconstruction of middle cerebral artery and excellent distal flow, which, in turn, is better than the flow observed before the treatment (refer to c).

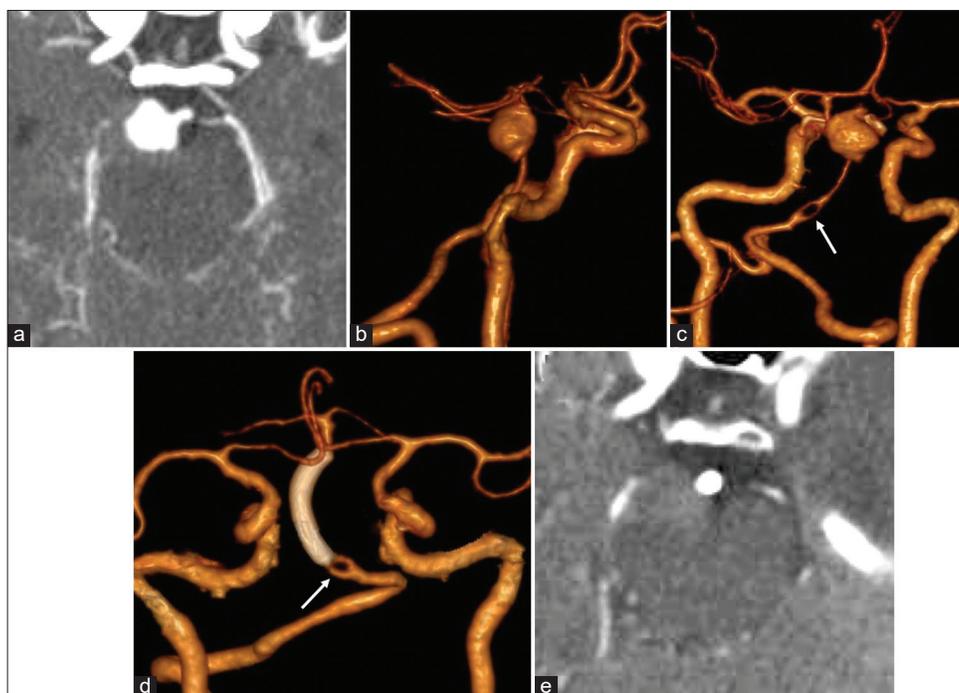


Figure 4: (Case 5) (a-c) A saccular aneurysm is seen occupying on basilar artery mid and distal portions. The MPR image clearly shows the aneurysm compressing the right midbrain peduncle (a). An fenestration related to basilar artery proximal third portion can be noticed (arrow on c). (d and e) CTA performed 2 months after the treatment showing FD with distal patency in addition to absence of aneurysm. The MPR image already shows the absence of filling of the aneurysmal sac. FD position is evident just distal to aforementioned fenestration (arrows on d).

Then, in the anterior circulation, 27% are located on ICA and 26% on MCA, while basilar artery was the most common location on posterior circulation. It has been reported that approximately 22% of cases involved multiple aneurysms.^[5]

In most cases, PIAs are symptomatic^[42] and they are usually recent incidental radiologic findings.^[16] Overall, there is a higher incidence of clinical manifestations during the first 2 years of life, with a peak during the first 6 years and during the second decade.^[31,35] Clinical manifestations include SAH, headache, or focal neurological deficit. It has been determined that in general population suffering from SAH, <1% are patients younger than 21 years of age.^[2] During pediatric age, SAH is more frequent in early childhood (under 5 years of age), as well as during mid to late adolescence, and it is less frequent on elementary schoolchildren.^[12,14,17,24,35] Of our patients, 2 had SAH (29%). In turn, 30% had initial manifestations secondary to compression effect,^[5] and within which the most frequent were cranial nerve deficits and hydrocephalus in some cases.^[40] Four patients in our series (57%) had cranial nerve palsy or epilepsy secondary to compression effect of the aneurysm.

There is no clear consensus regarding treatment of IAs on children. Treatments are based on the application of algorithms and treatment criteria created for the adult

population, with specific modifications and “customized” according to the center experience and ultimately in the surgeon’s experience.^[13] It is very common that microvascular neurosurgeons, as well as endovascular neurosurgeons, do not specifically target pediatric population, so it is essential to carry out a multidisciplinary analysis with pediatricians’ participation for adequate pharmacological and clinical management, as well a pediatric neurosurgeon in case of surgical approach. Evident treatment benefits are as follows: (1) relieving or reducing symptoms and (2) preventing rupture and/or rerupture. To already known surgical/endovascular risks in adult population, there are also general anesthesia-related specific risks. From an endovascular point of view, the risks are related to age, while the younger the patient is, the greater the complexity for handling devices. This starts with the selection of the diameter of the femoral introducer along with its compatibility with involved devices.

Already used techniques include: (a) simple clipping/coil embolization, which does not apply to dissecting, fusiform and/or giant aneurysms and (b) trapping/sacrifice, which is related to by-pass in case of poor collaterals. Although children with aneurysms usually develop adequate collaterals, it is absolutely necessary to carry out a balloon occlusion test to assess collaterals.

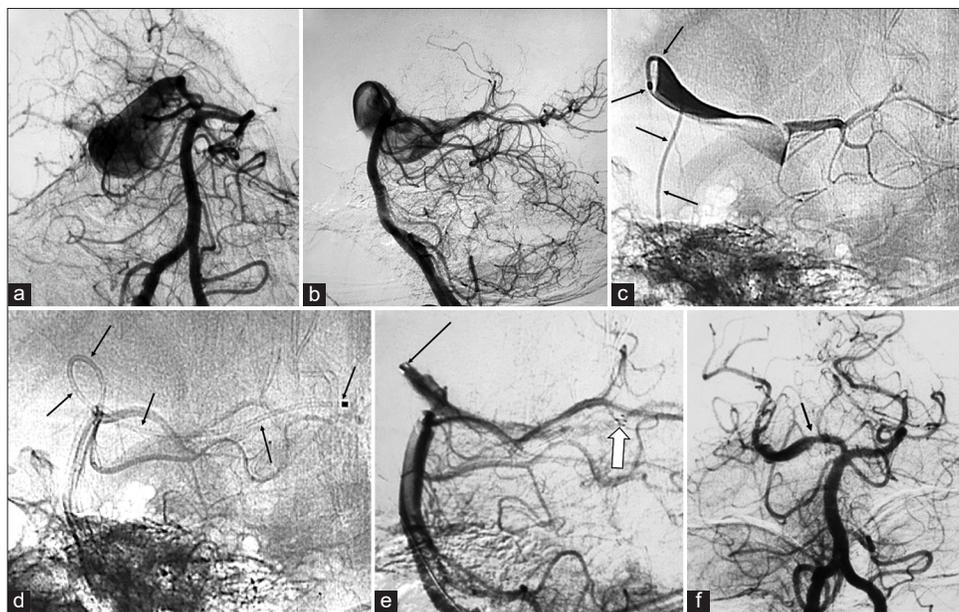


Figure 5: (Case 6) (a and b) A large fusiform aneurysm located on the right posterior cerebral artery (PCA) P2 segment is shown. (c and d) Superselective microcatheterization, initially of aneurysm with contrast injection and subsequent microcatheterization on PCA more distal segments (microcatheter is indicated by the arrows). (e) Digital subtraction angiography (DSA) in lateral projection performed during flow diverters (FDs) deployment where the distal end can be observed (thick arrow) in addition to a part of microcatheter where the device is attached (arrow) before a complete detachment. (f) One-month DSA showing absence of aneurysm with adequate artery reconstruction along and excellent distal filling. It is possible to see the proximal end of the FD (thin arrow).

Endovascular management has shown to be safe, effective, and long lasting for this type of aneurysms.^[39] Treatment with FDs in children can be justified due to the great experience globally acquired in adult treatments,^[6,7,11,22,27] as well as to the high incidence of giant and fusiform aneurysms on pediatric population, which makes them more susceptible for treatment with these devices.^[4] The treatment with FDs in Mexico was just approved at 2015, and La Raza Medical Center was the first to place one at April, being this a FRED device. Therefore, we had the first experiences both in adults and, during the same month, in a pediatric patient who had a dissecting aneurysm of the VA [Table 1].

Even today, there are not many cases of PIAs in the world treated with FDs, nevertheless, the experience continues to grow.^[4,9,13,19,21,27,44-47] According to the literature review, it should be stated that the first case of a child treated with a pipeline device (PED) was reported in 2009 by Lylyk *et al.*, along with other adult patients, but without providing specific details.^[27]

At early 2017, Barbuoglu and Arat reported a successful use of FDs on five PIAs and in their review of reports around the world, they gathered information about 15 successful PIAs treatment.^[4,19,29,46] Vargas *et al.* successfully treated five patients with FDs.^[46] The age range of the patients was from

6 to 18 years old. It should be mentioned that in Mexico, only those over 18 years of age are strictly considered adult patients. A situation limited the number of patients. In 2017, Ghali *et al.* described three successful treated with FDs.^[13] Basilar trunk aneurysms are challenging, because the FD can occlude perforating arteries. Kan *et al.* presented a case with a successful treatment.^[21] In our series, we describe a pipeline device placement in a basilar trunk aneurysm without complications [Case 5 and Figure 4].

The growth of brain arteries has been suggested as a future potential problem, for this reason, it is necessary to consider that approximately at 48 months, a vascular diameter between 81 and 99% is achieved, which, in turn, is similar to those seen in adults.^[3] In our series, the youngest patient was 6 years old, which eased the decision to use a FD. It is important to mention that follow-up images were obtained over 12 months, which demonstrated long-term occlusion stability. The risk of thromboembolic complications after stenting is lower in the pediatric population compared to adults, since the latter develop resistance to clopidogrel. It should also be noted that a lower dose per kilogram is needed in children compared to adults, to achieve a proper antiplatelet effect.^[25]

We should also mention that ionizing radiation can triple the risk of leukemia or brain tumors, especially in children

under 10 years old. However, it has been stated that the risk ratio in children under 10 years old is one new case for every 10,000 CT scans.^[34] Nevertheless, we avoided carrying out the 1-month and 3-month follow-up in children under 6 years old, but we decided that a follow-up at 6 months and 1 year was needed, either by CTA or DSA, since the possible benefits obtained with follow-up images outweighed by far the actual and potential risks.

CONCLUSION

IAs in the pediatric population are infrequent; therefore, the cases treated with FDs are few, but enough to demonstrate their efficacy in well-selected cases. It is also important to notice that in our study, all patients had consecutive imaging assessments with 100% compliance at 1 year and 74% at 2 or more years. As more cases emerge globally and patients get older, we will have more data to definitely assess effectiveness and durability of treatment with FDs.

Declaration of patient consent

Institutional Review Board (IRB) permission obtained for the study.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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