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Research Article

Intracranial Aneurysms Treatment with Flow Diverters in Pediatric Population: A Single-Center Experience

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Abstract

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

Patients and methods: We retrospectively describe 10 cases of PIAs which were 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 (R:6-15). Two (20%) had a subarachnoid hemorrhage, 3 had epilepsy (30%), 3 had clinical signs of cranial nerve compression (30%) and 4 (40%) had cephalea.

Two patients were in 1a grade of Hunt and Kosnik scale. Out of the non-ruptured aneurysms, 7 (70%) had a Glasgow Coma Scale (GCS) of 15 and 1 (10%) of 13. Treatment was performed without complications; nevertheless, in one case the distal deployment was not achieved.

Upon discharged, nine patients had a Glasgow Outcome Scale of 5. All patients were submitted to CT angiography or digital subtraction angiography at 1, 3, 6 and 12 months, including two patients (20%) that had a 2-year follow-up and 3 patients (30%) with 3-year follow-up. According to Kamran grading scale, 9 patients (90%) were classified as grade 4 and 10%) as 3.

Conclusions: Although is a small population since this is an uncommon disease, it suggests that FDs are useful to treat properly selected PIAs. Our study has consecutive imaging assessment of more than 1-year follow-up and through which it was observed that in 90% of patients there was evidence of results durability.

INTRODUCTION

Intracranial aneurysms in pediatric population (PIAs) are rare, representing less than 5% of events (0.17-4.6%) [1-11].

Current therapeutic strategies consist of expectant management, surgical treatment and endovascular treatment [8,11-17]. Flow diverters (FDs) have shown to be a useful tool in the treatment of certain intracranial aneurysms (IAs) and they are object of routine use around the world [18,19], nevertheless, there are still few experience in pediatric population. We present our experience at La Raza National Medical Center in Mexico City regarding the use of FDs in the treatment of 10 IAs in pediatric patients.

MATERIALS AND METHODS

Population

We reviewed the clinical and imaging records of all those patients with IAs which were treated endovascularly at La Raza National Medical Center between April 2015 and April 2020. It's important to note that our Neurosurgical Department has Vascular Microsurgery and Neurosurgical Intervention services, and all cases are held in session.

We recorded all IAs cases which were treated with FDs and out of them we specifically selected patients of less than 18 years old. Initial clinical and imaging data and follow-up imaging findings were reviewed. Before treatment, clinical condition was assessed using Glasgow Coma Scale (GCS) [20] in patients with non-ruptured aneurysms and Hunt and Kosnik Scale was used for ruptured IAs [22].

Procedures incidents and complications were registered. Patients were assessed at hospital discharge and during follow-up period using Glasgow Outcome Scale (GOS) [22].

The patients were follow-up with digital subtraction

angiography (DSA) or CTA at 3, 6, 9 and 12 months after treatment. Aneurysms' thrombosis degree was assessed by Kamran et al., scale [23].

Treatment description: Patients were submitted to double-antiplatelet regime daily during 5 days prior to procedure, with clopidogrel 37.5 mg and aspirin 100 mg in children weighting <45 kg, and clopidogrel 75 mg and acetylsalicylic acid 100 mg in children weighting >45 kg. All patients were treated under general anesthesia at angiography suite. Femoral approach was performed using Seldinger technique in order to place a 6F femoral sheath introducer. A 100 UI/Kg heparin bolus was administered to maintain a coagulation time activity approximately twice than ~~the~~ basal value. In all cases a 6F Chaperon catheter (MicroVention, Aliso Viejo, California) was used to catheterize cervical internal carotid artery (ICA) or vertebral artery (VA) V2 segment, as required. In almost all cases, a 5F distal access Sophia catheter (MicroVention, Tustin, California, USA) was used to reach ICA at cavernous or clinoid segment or vertebral artery at V3 segment. Flow diverter selection was performed according to parent vessel diameter. FDs deployment was carried out under internationally known technique, previously well described [18,19]. Three types of FDs were used, Pipeline device (PED) (Medtronic Neurovascular, Irvine, California), FRED device (MicroVention, Tustin, California, USA), and Silk+ device (Balt Extrusion, Montmorency, France) Only in our first case we decided to carry out an "scaffold" with two Neuroform stents (Boston Scientific/Target Therapeutics, Fremont, CA) before FD deployment, in order to prevent flow diverter widening and over-shortening.

After the procedures, the patients were kept on a double antiplatelet therapy for 6 months, at the doses determined above. Subsequently clopidogrel was continued permanently (Table 1, Figures 1-5).

RESULTS

Between April 2015 and April 2020 at La Raza National Medical Center, 505 endovascular therapeutic procedures were carried out, including 400 were IAs, 230 patients were treated with FDs and out of these, 10 patients (4.3%) were younger than 18 years old.

Male gender predominated, with 7 patients (70%). Average age was 9.5 years (R:7-15). No child had any known medical history during pregnancy and didn't have any congenital disease or recent important 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 two patients (20%) was a SAH, in 2 (20%) it was epilepsy, 2 (20%) had clinical signs of cranial and/or motor nerve compression and 4 (4%) had cephalea history.

Patients that started with SAH were treated after the acute phase and therefore were admitted under Hunt and Kosnik scale grade 1a. Out of the 8 patients that did not had an initial presentation with SAH, 7 (70%) had a GCS score of 15, and 1 (10%), which suffered from a large basilar aneurysm, had a GCS of 13.

Procedures were performed without complications in all patients. During treatment for patient 2, (Figure 1) whom had a left middle cerebral artery (MCA) fusiform aneurysm, the original plan was to deploy FD further from Sylvian point. Although MCA bifurcation distal branches' super selective microcatheterization was easily achieved, we were not able to navigate FD more distally to M1 segment despite many attempts, situation that conditioned deployment just prior to the Sylvian point. We suspect that this was due a severe stenotic origin of the MCA (Figure 1).

Patients woke up from general anesthesia without any additional deficits and their progression went without adverse events, with the exception of slight cephalea on patients 3, 5, and 7. By using GOS, patients were rated as follows: 9 (90%) grade 5 and 1 grade 4. The latter was the case with a large aneurysm on basilar artery that was admitted with a GCS of 13.

Table 1: Patients and treatment characteristics.

Case	Gender/Age	Clinical	Location	Morphology	FD/Nº	Compl./Incident
1	Male/12	Trauma/SAH	V4	Fusiform/Dissecting	FRED/1*	No
2	Male /8	Epilepsy	MCA	Fusiform	PED/1	Yes*
3	Female/7	pIIInc	cavICA	Large/Giant	PED/1	No
4	Male /15	Cephalea/Epilepsy	MCA	Fusiform	PED/6	No
5	Male /10	pVInc/Quadriparesis	Basilar	Large/Giant	PED/1	No
6	Male /6	SAH	PCA	Fusiform	FRED/1	No
7	Female/9	Cephalea	MCA	Large/Giant	PED/1	No
8	Male/8	pIIInc	cavICA	Large/Giant	FRED/1	No
9	Male/9	Cephalea		Large/Giant	Silk+/1	No
10	Female/10	Cephalea/Epilepsy	MCA	Large/Giant	Silk+/1	No

FD/Nº: Flow diverter class and devices number. **Compl./Incident:** Complications and/or incidents.
pIIInc: 3rd. cranial nerve palsy. **pVInc:** 6th 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 re-direction endovascular device. **FRED/1*:** In this case a FRED device was used within scaffold made with 2 Neuroform stents. **PED:** Pipeline endovascular device.
Yes*: Impossibility of a more distal access to MCA.

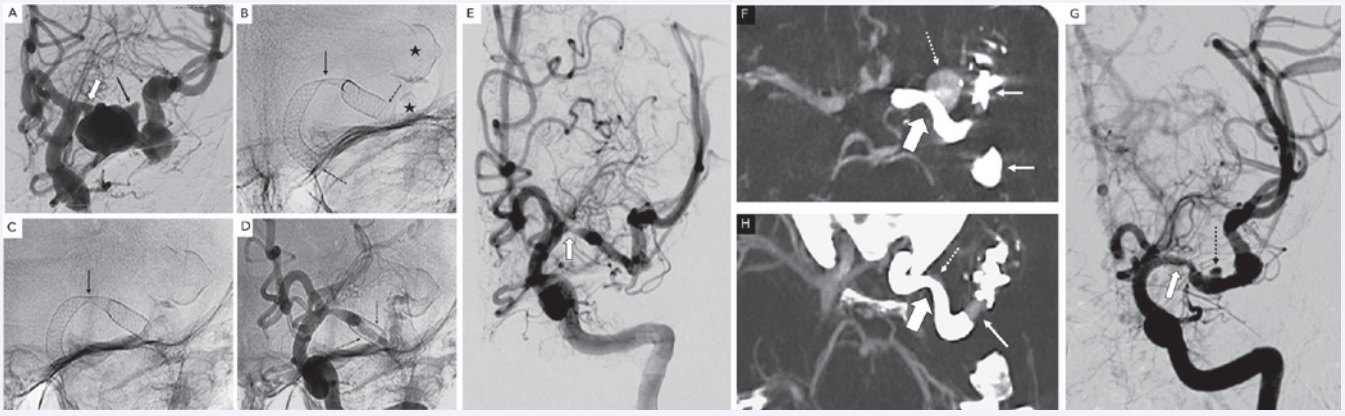

Figure 1 **Case 2:**

A: Fusiform aneurysm involving the entire M1 segment and part of the M2 segment of left middle cerebral artery along with saccular aspect segments, that on M1 segment being the largest one with a bleb (thin arrow). A stenotic segment is seen at the origin of middle cerebral artery (thick arrow).

B and C: Deployed FD (dotted arrows) along with stenotic respective segment on middle cerebral artery (arrow) that created a great difficulty and impossibility to navigate and deploy FD more distally. Certain aneurysm's calcified segments (star) can be seen. On **C**, the arrow points at the stenotic site that opened discreetly regardless of having been treated with a balloon twice.

D and E: After contrast injection, stent patency was seen, same which was initially very slow with flow only towards FD center (dotted arrows on **D**). At the end of procedure and ~~by way~~ through a DSA on AP projection, good flow is observed through FD and left middle cerebral artery, regardless to stenotic segment (thick arrow).

F: Monthly follow-up transvenous injection CTA with axial section where a stenotic part in the stent is observed (thick arrow) and even residual flow on aneurysm's saccular portion (dotted arrow). Some aneurysm's calcified segments can be seen (arrows).

G: After one year of treatment, DSA on AP projection where an excellent flow is observed through FD towards MCA distal segments, regardless to stenotic portion (thick arrow). A very reduced residual filling is seen on M1 saccular old segment (dotted arrow).

H: 24-month follow-up CTA on axial section where it is seen that stenotic portion persists (thick arrow) but with a filling of less that 1% regarding M1 old saccular segment (dotted line). Distal blood flow toward FD can be seen (arrow).

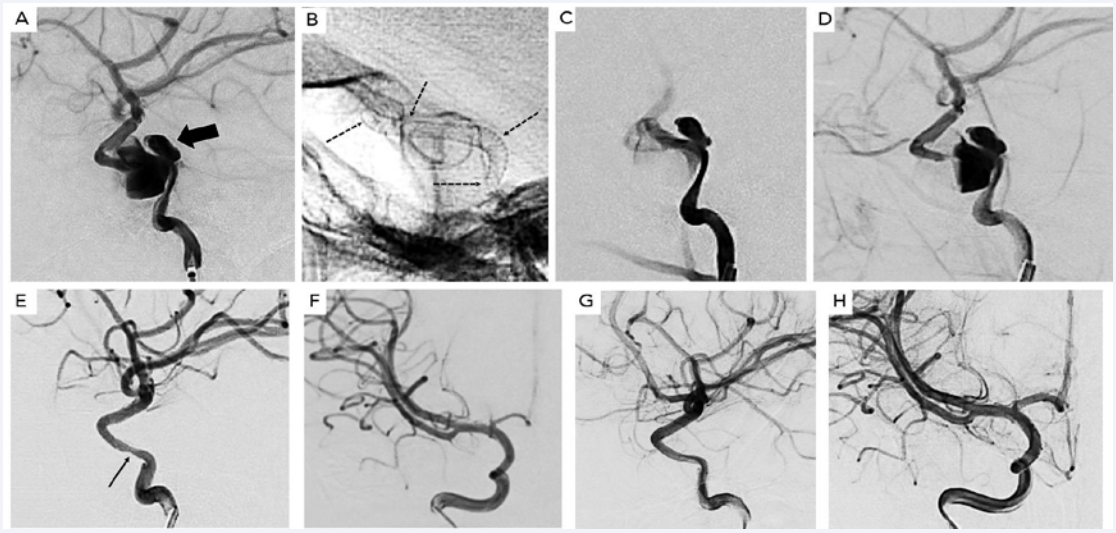

Figure 2 **Case 3:**

A: 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 that shows reduction of aneurysm's filling velocity.

E and F: Follow-up DSA in lateral and AP projections at 6 months showing the absence of aneurysm's filling. Intrastent stenosis is observed (arrow on E), presumably due to intra-stent hyperplasia.

G and H: Follow-up lateral and AP projections at 24 months with persisting absence of aneurysm's filling in addition to not observing the stenosis described in E.

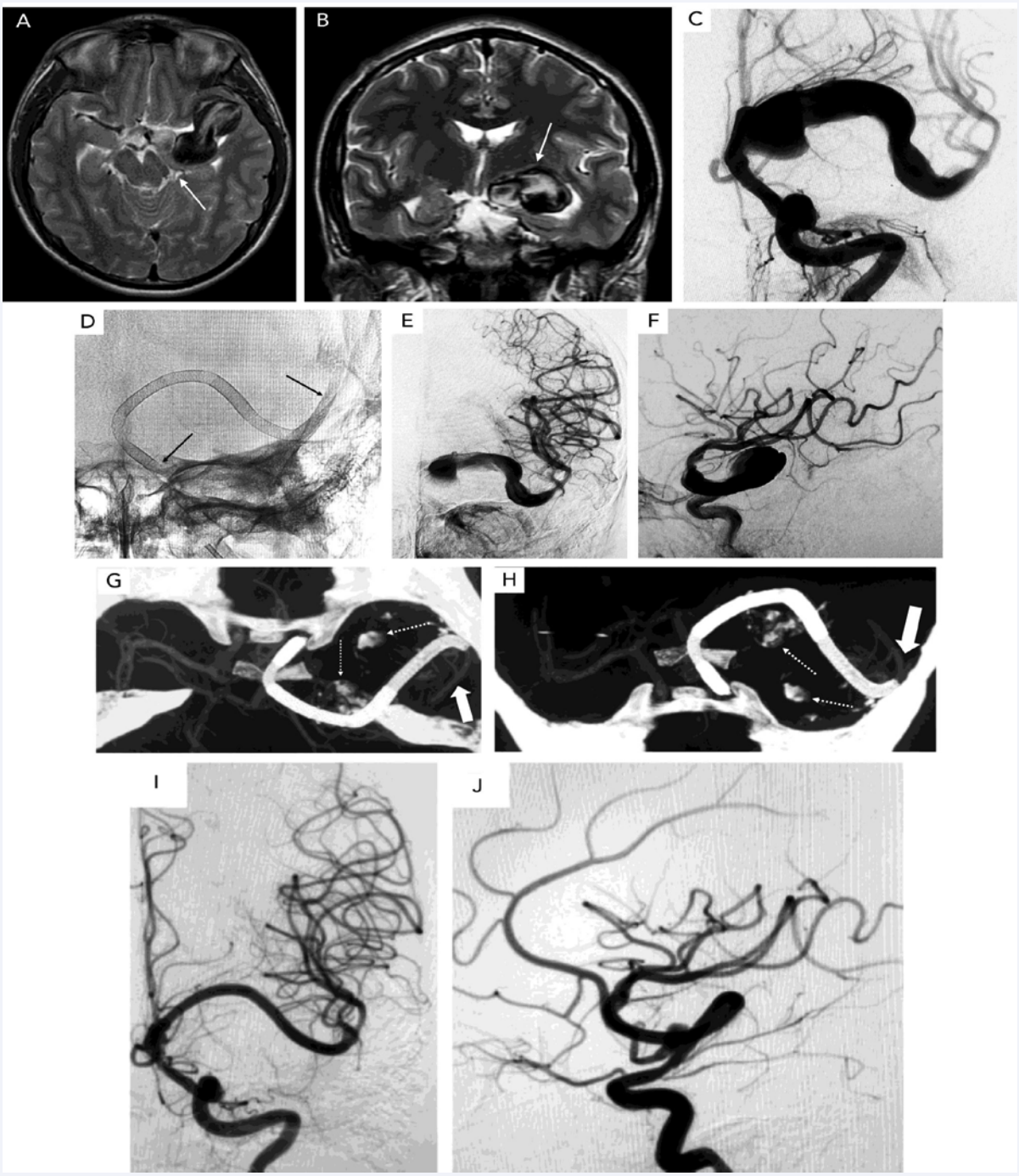

Figure 3 , Case 4:

A and B: T2 weighed MRI that shows a partially thrombosed fusiform aneurysm on left middle cerebral artery in the sphenoidal segment territory. The lesion mass effect is notorious and very evident over cerebral peduncle as well as ipsilateral central core structures (arrows).

C: AP projection DSA that shows a fusiform aneurysm originating from internal carotid artery bifurcation and entire left MCA M1 segment territory. Inadequate contrast is ~~notorious~~ evident on MCA distal branches.

D: Artery was reconstructed with 6 tandem flow diverters (arrows show start and end of devices).

E and F: AP and lateral projections DSA show adequate blood flow through diverters and MCA distal branches. Without evident changes in the fusiform aneurysm.

G and H: One month follow-up CTA shows no evidence of aneurysmal lesion around flow diverters along with excellent distal flow (thick arrows). Dotted arrows indicate some aneurysm calcifications.

I and J: Follow-up DSA with AP and lateral projections after 3 months of treatment showing adequate rebuilding of middle cerebral artery and excellent distal flow, which in turn is better than the flow observed before treatment (refer to **C**).

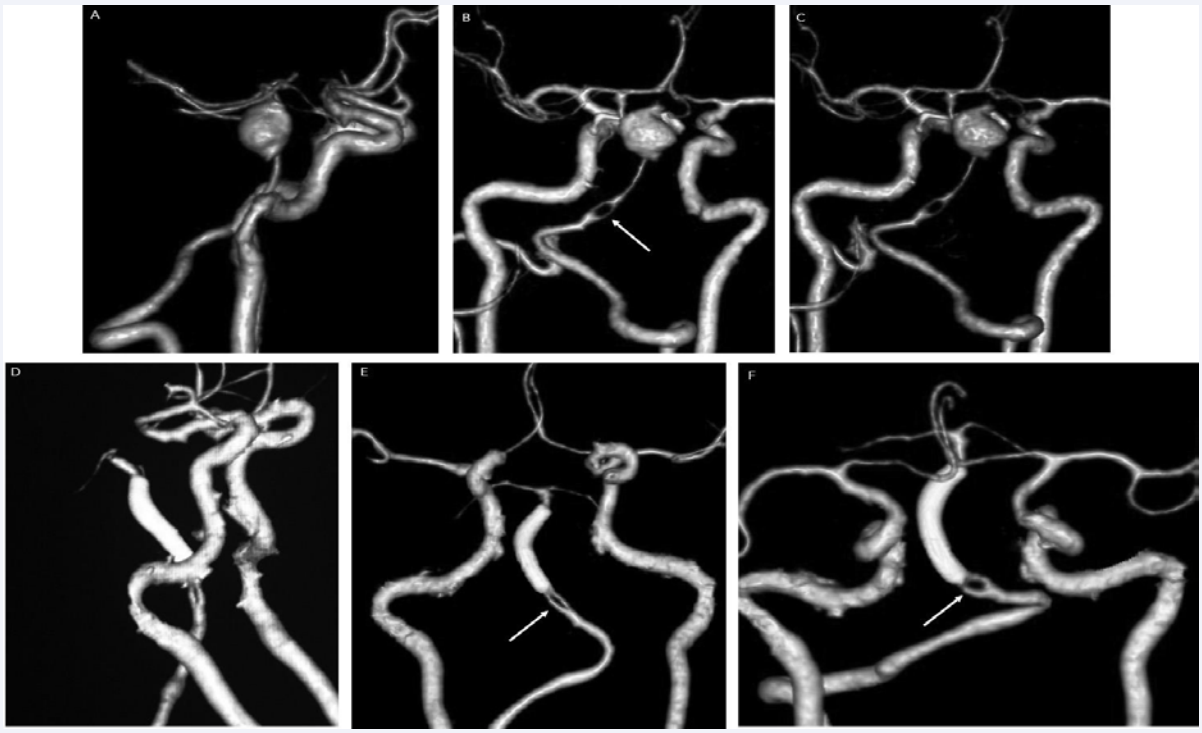

Figure 4 , Case 5:

A-C: On these diagnostic images a saccular aneurysm is seen on basilar artery distal third portion. A fenestration related to basilar artery proximal third portion can be noticed (arrow on **B**).

D-F: CTA performed two months after treatment showing FD with distal patency in addition to absolute absence of aneurysm. FD position is evident just distal to aforementioned fenestration (arrows on **E** and **F**).

In our institution, as a standard practice, we carry out DSA and/or CTA follow-up at 1, 3, 6 and 12 months after procedure and subsequently every year. Ionizing radiation in children has been shown to affect the growth plates, the gonads and the thyroid gland, reason why lead shielding over some parts of the body, including the gonads and the thyroid gland, was performed. We avoided carrying out the follow-up at one month and three months in children under 10 years of age, because the risk of leukemia or malignant brain tumor, nevertheless we decided that follow-up at 6 months and one year was necessary, either by CTA or DSA, assessing the benefit obtained with images, which may outweigh by far the actual and potential risks.

All patients were submitted to follow-up assessments at 1 year, 4 patients (40%) at 2 years and 4 patients (40%) up to three years. Imaging follow-up was excellent, with aneurysms showing progression regarding thrombosis with blood flow permanence, reason why final studies showed 9 patients with Kamran´s grade 4. It is important to mention that in case number 2 in which a diverter deployment incident took place, DSA after one year showed thrombosis beyond 90% regarding a Karman´s grade 3. The plan was to perform a new DSA follow-up every two years, nevertheless, the mother´s patient refused to do so, and therefore a CTA was carried out and showed occlusion stability of the aneurysm (Figure 1).

DISCUSSION

Intracranial aneurysms in pediatric population (PIAs) are rare, representing <5 % [1-11]. In an article by Beez et al. [10], 135 papers between years 2000 and 2015 were analyzed, gathering information on 573 cases with 656 aneurysms and where average age was 7.6 years (R: 3-18). In most of the papers, there was a male to female predominance, which coincides with our study.

In the literature, IAs were saccular in 20 to 30% of cases, being the most frequent fusiform, dissecting and giant/complex aneurysms with different degrees of thrombosis [12,13]. On a review made by Beez et al. [10], 68% of aneurysms were large/giant and 16% were fusiform. Younger children are more prone to have fusiform and/or giant aneurysms [16]. In our study, 57% of aneurysms were fusiform and the rest were large/giant.

Dissecting aneurysms are generally secondary to trauma, infection or to congenital diseases [24,25]. In our cases, there were no cases secondary to congenital diseases, vasculopathies, collagen diseases, hematologic diseases, such as sickle cell anemia, nevertheless, according to literature review, some of these diseases represent between 10 to 20% of cases [8,11,26]. One patient of our series (14%) had a traumatic dissecting aneurysm (Case 1).

Hetts et al. [15], classify pediatric aneurysms as follows: 1) Traumatic, 2) Infectious, 3) Saccular, and 4) non-traumatic and non-infectious fusiform aneurysms. It has been described that PIAs are usually located 75% on anterior circulation and 25% on posterior circulation [10]. Then on anterior circulation, 27% are located on ICA and 26% on MCA, while basilar artery was the most common location on posterior circulation. It was described that approximately 22% of cases involve multiple aneurysms [10].

In most cases, PIAs are symptomatic [27], nevertheless, they are usually recently identified with relative frequency as radiologic findings [15]. Overall, there has been 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 [7,28]. Clinical manifestations include SAH, cephalea or focal neurological deficit. It has been determined that in general population suffering from SAH, less than 1% are individuals younger than 21 years of age [16]. During pediatric age, SAH is more frequent on early childhood (less than 5 years old) as well as during mid to late adolescence, being less frequent on elementary school children [7, 29-32]. Out of the patients included in this article, two presented with SAH (29%). In turn, 30% presented with compression effect derived manifestations [10], and within which the most frequent were cranial nerve deficit and in certain cases there may be hydrocephalus [33]. Four patients in our series (57%) presented with some cranial nerve palsy or epilepsy conditioned due to a compression effect of the aneurysm.

There is no clear consensus regarding treatment of intracranial aneurysms on children. Treatments are based on algorithms application as well as adult's treatment criteria with specific modifications and "customized" according to acquired experience on centers and ultimately on surgeons experience [25]. It is very frequent for vascular neurosurgeons as well as for interventional neurosurgeon not to have as their specific objective pediatric population, reason why it is fundamental to carry out a multidisciplinary analysis with pediatricians participation, for example, for adequate pharmacological management (hydration, antiplatelet agents, etc.) as well as that of pediatric neurosurgeon in case of surgical approaches. Evident treatment benefits are: 1) relieving or reducing symptoms, 2) preventing rupture and/or re-rupture. To already known surgical/endovascular risks in adult population, there are also general anesthesia related specific risks. From an endovascular point of view, risks are related to age, while, the younger the patient is, the higher complexity for handling devices, which starts with femoral introducer diameter selection along with its compatibility with involved devices.

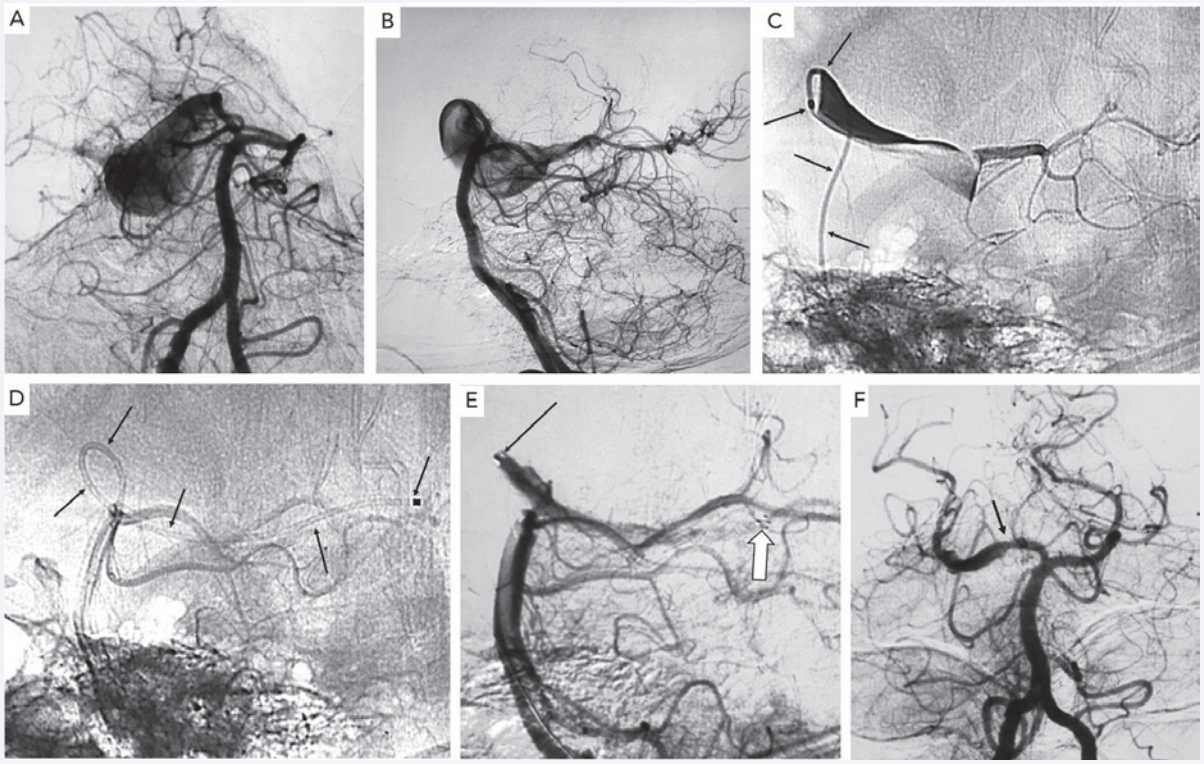

Figure 5 **Case 6:**
A and B: A large fusiform aneurysm located on right posterior cerebral artery (PCA) P2 segment is evident.
C and D: Super selective cannulation, initially of aneurysm (C) with contrast injection and subsequent cannulation on PCA more distal segments (microcatheter is indicated by the arrows).
E: Lateral projection DSA performed during FD deployment where stent's distal end can be seen (thick arrow) in addition to a part of microcatheter where stent is mounted (arrow) before complete detachment.
F: A one-month follow up DSA showing absence of aneurysm's filling with adequate artery reconstruction along with excellent distal filling. It is possible to see flow diverter stent's proximal end.

Already used techniques include: a) simple clipping/coils embolization and which in turn do not apply to dissecting, fusiform and/or giant aneurysms; b) trapping/sacrifice which in turn are 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 collaterality.

Endovascular management has shown to be safe, effective and long-lasting for this type of aneurysms [34]. Treatment with FDs in children can be justified due to the great experience globally acquired in adults treatment [18,19,35-37]. As well as to the high incidence of giant and fusiform aneurysms on pediatric population and which makes them more susceptible for the use of respective devices [38]. The use of FDs in Mexico was just approved on 2015, and it was La Raza Medical Center the first to place one on April, being a FRED device, thus obtaining the first experiences both on adults, and, during the same month, on a pediatric patient which had a vertebral artery dissecting aneurysm (Table 1).

Even today, there are not many cases of PIAs in the world treated with FDs, nevertheless, the experience continues growing [11,18,24,25,38-43]. According to that reported through literature, it can be said 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 [18].

In early 2017, Barboroglu et al., reported successful use of a FD on 5 PIAs and on their analysis of reports around the world, they gathered information about 16 successful PIAs treatment, with the exception of one [11,38,41,44]. Vargas et al., successfully treated 5 patients with FDs [11]. The age range of the patients was from 6 to 18 years old, being important to mention that in Mexico, only strictly considered as adults patients are those older than 18 years old, situation that limited the number of patients. In another article on 2017, Ghali et al., described 3 successful cases of FDs use [25]. Basilar trunk aneurysms are challenging disease, because of the flow diverter can occlude perforator arteries. Kan et al., presented a case of successful treatment [42]. In our series, we describe the use of a Pipeline in a basilar trunk aneurysm without complications (Case 5, Figure 4)

It has been suggested that a future potential problem is the growth of brain arteries. For this reason, it is necessary to consider that approximately at 48 months, a vascular diameter between 81 to 99% was achieved, which in turn is similar to those seen in adults [45]. In our series, the youngest patient was 7 years old, situation that made the decision to use a FD easier. It is important to mention that we obtained follow-up images that mostly exceed 12 months and that observed long-lasting thrombosis stability.

Thromboembolic complications risk after stenting are lower on pediatric population when compared with adults and this is due to resistance to clopidogrel. It is also necessary to point out that on children a lower per kilogram dosage is necessary, compared to adults, to achieve effective antiplatelet course [46].

It is important to note that ionizing radiation can triple the risk of leukemia or brain tumors, especially in children under 10 years of age. However, it has been determined that the risk ratio in children under 10 years of age is one new case for every 10,000 CT scans [47]. Nevertheless, we avoided carrying out the follow-up at one month and three months in children under 6 years of age, but we decided that follow-up at 6 months and one year was necessary, either by CTA or DSA, assessing the benefit obtained with images, which may outweigh by far the actual and potential risks.

CONCLUSIONS

Due to the fact that PIAs are uncommon, cases treated with flow diverters are scarce but sufficient to evidence that they are effective for adequately selected cases. It is also important to mention that in our study all patients had consecutive imaging assessments with 100% compliance at one year and 74% at two or more years. As more cases emerge at a worldwide level and patients grow (age wise) we will have more data to definitely assess effectiveness and durability of treatment with flow diverters.

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