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Pediatric Intracranial Aneurysms: Experience from a Singapore Children's Hospital

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Abstract: (1) Background: Pediatric intracranial aneurysms (PIA) are rare and clinicopathologically distinct neurovascular entities. The aims of this study are to evaluate our institution's experience and corroborate our results with updated literature. (2) Methods: This is a single-institution, retrospective study. Patients with a confirmed diagnosis of PIA are included. Variables of interest include patient demographics, clinical presentation, treatment outcomes and features specific to each patient's PIA. A literature review on PIA-centric clinical studies was conducted. (3) Results: A total of 14 PIAs in 11 patients were treated from 2000 to 2022. The mean age was 5.8 years old, and most were males (90.1%). Anterior circulation PIAs constituted 78.6% of the cohort. Half of the PIAs were of the dissecting type, and 14.3% were giant aneurysms. Of interest, 14.3% of patients had subsequent de novo aneurysms after treatment of their index aneurysm. For treatment, 57.1% underwent surgery, 35.7% had endovascular intervention and the remaining 7.1% were managed conservatively. Based on the literature review, this study had congruent findings to other existing publications. (4) Conclusions: PIAs are unique neurovascular lesions that have good outcomes if managed in a timely fashion by an experienced multidisciplinary team. We recommend longer surveillance periods due to the risk of developing de novo aneurysms.

Keywords: intracranial aneurysm; pediatric intracerebral aneurysm; pediatric intracranial aneurysm

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1. Introduction

Pediatric intracranial aneurysms (PIA) are rare and account for 0.5 to 4.6% of all intracranial aneurysms [1–4]. Recent insights confirm these aneurysms are of a distinct pathological entity in comparison to their adult counterparts; thus, they require different treatment principles [5–7]. The technical aspects of intervention—that is, microsurgery, endovascular approaches or a combination of both—are somewhat similar to adult patients. However, owing to the longer life expectancy of children, the aim is to provide effective aneurysm obliteration while minimizing the risk of recurrence and peri-procedural morbidity. To date, most PIA-related publications are case series with limited patient numbers [4,8–12]. As previously highlighted by Kim et al., the existing clinical literature on PIA is mostly from Western or European centers [13–18]. Similar epidemiological studies from Asia are even fewer [4,8,13,19]. Overall, there is a paucity of information with regards to PIA from our local and regional Southeast Asian populations. Furthermore, the incidence, pathophysiology and treatment modalities used for PIA are underrepresented in the literature from our part of the world. This is a retrospective study with the primary aim

of evaluating the patient demographics, clinicopathological characteristics, management modalities and outcomes of PIA managed by our institution. Secondary aims include a focused literature review on this uncommon condition and corroborating our results with existing literature.

2. Materials and Methods

2.1. Study Design, Patient Demographics, and Variables of Interest

This is a single institution, retrospective study approved by the hospital ethics board (SingHealth CIRB Reference: 2022/2501). Data is retrieved from the hospitals' electronic medical records and/or hardcopy notes. All patients under 18 years of age with a confirmed diagnosis of PIA via neuroimaging are included. Exclusion criteria encompass the following: patients above the age of 18, PIAs secondary to other types of neurovascular anomalies (such as Moyamoya disease, vein of Galen malformation, arteriovenous malformation and so forth), and patients with incomplete clinical information. Variables of interest include patient demographics, clinical history, presenting symptoms, treatment outcomes and features specific to each patient's intracranial aneurysm. These include radiological characteristics, location, morphology, size, and etiology of the aneurysms. For this study, the World Federation of Neurological Surgeons (WFNS) Grading Scale is used to grade the severity of the aneurysmal subarachnoid hemorrhage (aSAH) [20], and the Glasgow Outcome Scale (GOS) is used to assess patient outcomes [21]. In concordance with the literature, we defined a 'giant aneurysm' as an intracranial aneurysm with a diameter of 25 mm or more [22]. Owing to the limited cohort numbers, descriptive statistics are reported. This includes mean with standard deviation for continuous data and frequency and percentage for categorical data.

2.2. Outline of Treatment Workflow

All patients diagnosed with either suspected or radiologically confirmed PIAs are referred to the Neurosurgical Service. Urgent intervention to stabilize patients is prioritized for cases where there is progressively worsening neurological deficit, and or raised intracranial pressure. As part of a close-knit healthcare cluster, our pediatric neurosurgeons work with our adult colleagues in co-managing these patients. Clinical cases are presented at regular multidisciplinary neurovascular rounds that are attended by neurosurgeons, neuroradiologists and interventionalists dedicated to the management of neurovascular anomalies. After a consensus is reached, a decision for the type of intervention is discussed in-depth with the patient and their caregivers. All patients undergo a postoperative digital subtracted angiogram (DSA) after microsurgical clipping of their aneurysm or post-embolization/coiling. Once the aneurysm is confirmed to be obliterated, the patient is transferred to the Children's Intensive Care Unit for close monitoring. As PIAs are considered rare, thorough medical investigations are performed to exclude any underlying infective, autoimmune or cardiac conditions. Following that, early referral to the neurorehabilitation team is advocated once deemed clinically stable after intervention. Upon discharge, the patients are followed up in the outpatient clinic by the pediatric neurosurgeon until 18 years of age, wherein they will be transitioned to the adult hospital for continuity of care. Given the concerns of repeated exposure to ionizing radiation [23], the choice of neuroimaging is magnetic resonance imaging (MRI) brain and angiography (MRA) during the surveillance period.

2.3. Literature Review

To identify articles pertinent to PIA, a systematic search of publications in the English language using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines was performed in PubMed, Google Scholar and Web of Science [24]. Examples of keywords used include 'cerebral aneurysm in children', 'pediatric cerebral aneurysm', 'pediatric intracranial aneurysm' and so forth. Results are individually examined and counter-checked amongst one another for duplicates. Articles focused on adult

populations, and/or without English translation of their content, and those published before 2000 are excluded. Secondary data from meta-analyses, abstracts, editorials, expert opinions or letters are also excluded. Reference lists from selected articles are also counter-checked to obtain as complete information as possible.

3. Results

3.1. Baseline Patient Characteristics

From 1 January 1997 to 31 December 2022, a total of 81 patients with intracranial vascular anomalies were managed at our institution. In this cohort, there were 11 patients with 14 PIAs. One patient was excluded due to incomplete clinical data. The mean age of our cohort was 5.8 $\pm$ 4.7 years old. There was a notable male preponderance (90.1%). Six patients presented with aSAH, whereby four (36.4%) of them were of poor grade (WFNS grade $\geq$ 3). The average duration of follow-up in our study population was 70 months (range: 3 to 185 months).

3.2. Aneurysm Features: Morphology, Location, and Aetiology

Most of the PIAs were from the anterior circulation (78.6%)—two (14.3%) anterior communicating artery aneurysms, two (14.3%) internal cerebral artery (ICA) aneurysms, and seven (50%) middle cerebral artery aneurysms. There were three (21.4%) posterior circulation aneurysms, which consisted of one anterior inferior cerebellar artery (AICA) and one posterior inferior cerebellar artery (PICA) aneurysms in the same patient, and one vertebral artery (VA) aneurysm. Out of the 14 aneurysms, 6 (42.9%) were of the dissecting type, 5 (35.7%) were mycotic aneurysms while the remaining 3 (21.4%) were saccular aneurysms. There were two (14.3%) giant aneurysms (Figure 1), whereby one of them was previously published as a clinical vignette [25]. Interestingly, three (27.3%) had two aneurysms, either at the time of diagnosis or subsequent de novo aneurysms after treatment of their index aneurysm. One of them had a background of fibromuscular dysplasia (FMD) and had one PIA successfully treated. His second aneurysm was a de novo aneurysm which was seen 3 years after his first presentation on surveillance neuroimaging. Initially, he opted for observation. However, follow-up imaging demonstrated that the aneurysm was increasing in size. The decision was then made for definitive treatment. The next patient had his index right PICA aneurysm treated with endovascular parent artery occlusion. Upon follow-up, a new PIA was found in the right AICA, and this was similarly treated endovascularly. The last patient had two right ICA mycotic aneurysms that were treated with endovascular parent artery occlusion. The following table summarizes the patients' and aneurysmal characteristics of our study population (Table 1).

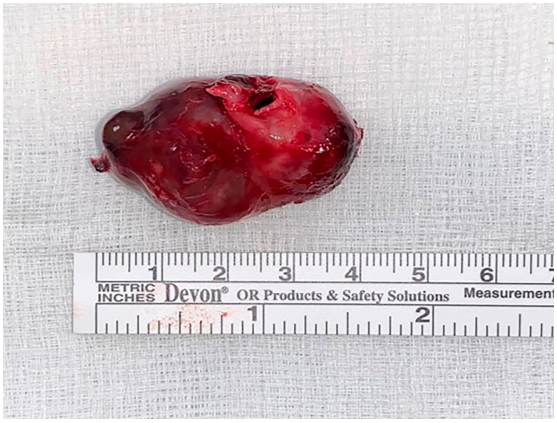

Figure 1. Photo example of an excised giant PIA from 1 of the patients in this study.

Table 1. Overview of baseline patient characteristics and aneurysm features.

Variable	*n* (%, Unless Stated Otherwise)
Age range in years (mean)	0.17 to 14 (5.8 ± 4.7)
Length of follow-up range in months (mean)	3 to 185 (70)
Number of patients	**11 (100)**
Gender	
Male	10 (90.1)
Female	1 (0.09)
Clinical Presentation	
Decreased consciousness	7 (63.6)
Headache	1 (0.09)
Cranial nerve palsy	1 (0.09)
Seizure	1 (0.09)
Incidental [1]	3 (27.3)
WFNS Grade (at first diagnosis)	
I to II	2 (18.2)
III to IV	4 (36.4)
Not applicable (as unruptured)	5 (45.5)
Glasgow Outcome Scale (GOS)	
1	0 (0)
2	0 (0)
3	1 (0.09)
4	3 (27.3)
5	7 (63.6)
Total number of PIA per patient [1]	
Single	8 (72.7)
Multiple	3 (27.3)
Total number of PIA in this study	**14 (100)**
Location	
Anterior circulation	11 (78.6)
Posterior circulation	3 (21.4)
Type of aneurysm	
Dissecting	6 (42.9)
Mycotic	5 (35.7)
Saccular	3 (21.4)
Size of aneurysm	
<1 cm	7 (50)
1 to 2 cm	5 (35.7)
≥2.5 cm	2 (14.3)
Treatment modality	
Conservative	1 (7.1)
Endovascular procedure(s)	5 (35.7)
Microsurgical clipping or excision	8 (57.1)

[1] includes patients at the time of diagnosis, and or during follow-up. (Abbreviations: PIA = pediatric intracranial aneurysm; WFNS = World Federation of Neurological Surgeons).

3.3. Treatment Modalities and Outcomes

Seven (57.1%) patients with 8 PIAs underwent microsurgical clipping or excision. No bypass procedure was performed for this subgroup in our series. There were no postoperative complications encountered. Three patients with five aneurysms were treated with endovascular therapy: one patient underwent coiling of the aneurysm sac while the other four aneurysms were treated with parent artery occlusion. Although we had two cases of de novo PIAs, no recurrent PIA was observed during the follow-up period for all patients. As previously mentioned, one patients with multiple aneurysms had a background of FMD. Despite the initially poor WFNS grade (Grade IV or V) at the time of presentation for four (36.4%) patients, three of them eventually recovered to a GOS $\geq$ 4. Although they initially had residual hemiparesis, they improved to full independence in the activities of daily living at the last outpatient review. No mortality was observed in our study cohort.

One (7.1%) patient was found to have an incidental VA PIA during neuroimaging for an unrelated condition. The decision was made for conservative management as the patient was young and asymptomatic. To date, surveillance scans report that the PIA remains stable in size.

3.4. Illustrative Case Example: Challenging Diagnosis

A 12-year-old patient with a background of native mitral valve perforation and infective endocarditis underwent a mechanical valve replacement. As part of the postoperative treatment, she was commenced on anticoagulation to retain the patency of the cardiac valve. However, the patient developed an acute onset of drowsiness, right hemiparesis and a dilated right pupil. An urgent computed tomographic (CT) brain scan reported a large acute on chronic right subdural hematoma (SDH) with significant mass effect and midline shift. Of note, there was a small, concurrent parieto-occipital lobe intraparenchymal hematoma (ICH). The initial impression was that of spontaneous hemorrhage secondary to over-coagulation. The patient underwent an emergency right decompressive craniotomy and evacuation of the SDH. Intraoperatively, no obvious vascular anomaly was observed. Owing to the recent history of infective endocarditis, a DSA was arranged. This reported a 2 mm aneurysm in the high parietal region that corresponded to the site of the previous right SDH and ICH (Figure 2). Microsurgical excision of the aneurysm was subsequently performed. Histology confirmed that it was a mycotic aneurysm. The patient's postoperative period was otherwise uneventful with good improvement of neurological function.

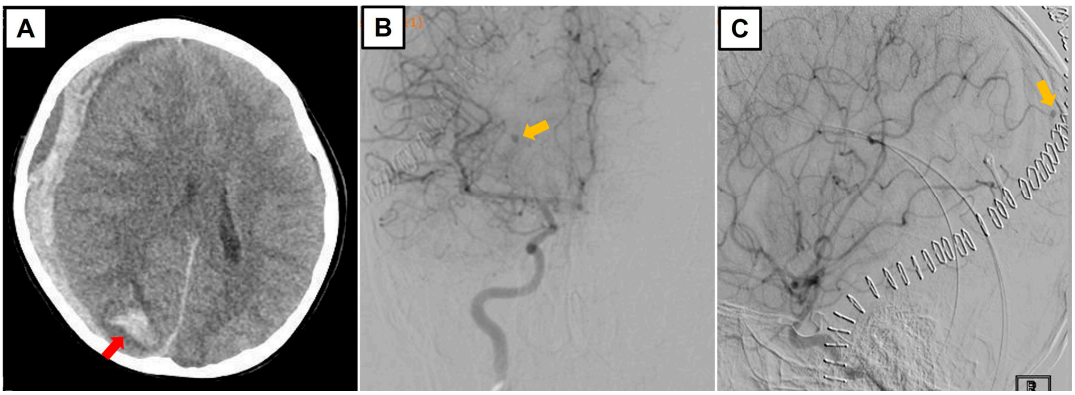

Figure 2. (**A**) Representative image of patient's non-contrasted CT brain in axial direction. There is a large right SDH causing mass effect and midline shift to the left. Of note, there is a small ICH situated in the right parietal lobe (red arrow). (**B**,**C**) depict representative arterial phase images of the patient's subsequent cerebral DSA in coronal and sagittal views. A small, saccular aneurysm is noted in the right high parietal region, corresponding to the location of the previous CT brain findings (yellow arrow). (Abbreviations: CT = computed tomographic; DSA = digital subtracted angiogram; ICH = intracranial hematoma; SDH = subdural hematoma).

3.5. Literature Review Findings

Detailed systemic reviews of PIA literature were recently performed by Brandel et al., Ciurea et al. and Yasin et al. [26–28]. Given that we aimed to compare our longitudinal clinical experience with existing literature, we prioritized studies that were similar in design to ours and within the timeframe of our study. Building on this, our focused literature search yielded 24 publications from 2000 to March 2024 [3,4,8,13,15–17,26–42] (Figure 3). For this study, we set the following parameters: exclusion of case reports with less than patients, defined case series as studies that had 5 to 20 patients and cohort studies with 20 or more patients (Figure 3). Based on these publications, our study had the following congruent demographic findings: male predilection, majority of PIAs in the anterior circulation, good neuro-functional outcomes after treatment and low mortality rates. Notably, most series

also reported higher numbers of giant and mycotic aneurysms in their study cohorts (See Table 2).

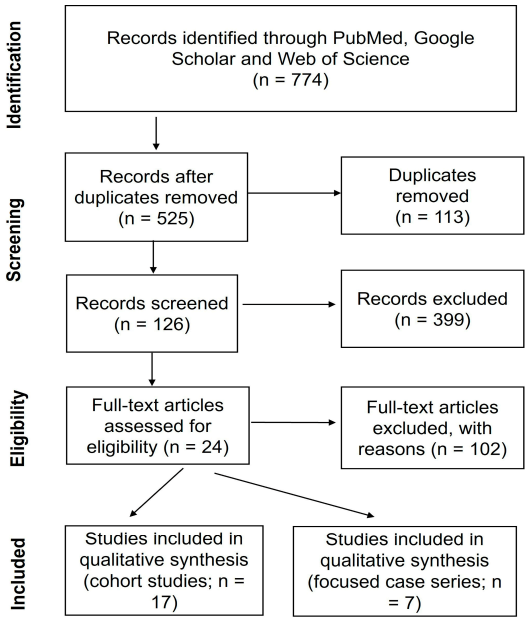

Figure 3. PRISMA flow diagram of the literature review relevant to this study.

Table 2. Summary of findings from the selected publications pertinent to our study. (Abbreviation: N.A. = not applicable; PIA = pediatric intracranial aneurysm).

Year/Authors	Patient Number (%)	Males (%)	Good Outcomes [1] (%)	Mortality (%)	Total Number of PIA (%)	Giant PIA (%)	Mycotic PIA (%)	Treatment Modality (%)
2001/Proust et al. [29]	22 (100)	16 (72)	14 (63.6)	5 (22.7)	25 (100)	3 (12)	2 (8)	Surgery 18 (81.8); endovascular 4 (18.2)
2005/Huang et al. [3]	19 (100)	13 (68.4)	18 (94.7)	1 (5.3)	19 (100)	7 (36.8)	0 (0)	Surgery 13 (68.4); endovascular 3 (15.8); conservative 3 (15.8)
2005/Lasjaunia et al. [16]	59 (100)	35 (59)	N.A.	5 (8)	75 (100)	1 (1.7)	15 (20)	Surgery 28 (37.3); endovascular 13; conservative 16 (27.1)
2005/Agid et al. [30]	33 (100)	16	21 (64)	5 (15)	37 (100)	11 (29.7)	5 (13.5)	Surgery 10 (27); endovascular 13 (35.1); conservative 14 (37.8)
2007/Sharma et al. [4]	55 (100)	38 (69)	36 (90)	2 (5)	67 (100)	13 (19.4)	2 (3)	[2] Surgery 40 (72.7); conservative 15 (27.3)
2008/Stiefel et al. [31]	12 (100)	4 (33)	9 (75)	1 (8)	13 (100)	1 (7.7)	0 (0)	Surgery 8 (61.5); endovascular 5 (38.5)
2009/Liang et al. [32]	24 (100)	14 (58)	22 (92)	1 (4)	24 (100)	8 (33.3)	1 (4)	Surgery 4; endovascular 14; conservative 5
2009/Lv et al. [33]	25 (100)	20 (80)	N.A.	1 (1.3)	25 (100)	17 (68)	0 (0)	Endovascular 24 (96); conservative 1 (4)
2009/Hetts et al. [15]	77 (100)	37 (48.1)	N.A.	1 (1)1.3	103 (100)	8 (11%)	12 (15.6)	[2] Surgery 29 (37.7); endovascular 30 (39); conservative 18 (23.4)
2009/Kakarla et al. [34]	48 (100)	28 (58.3)	44 (91.7)	1 (2.1)	72 (100)	16 (22.2)	5 (6.9)	[2] Surgery 48 (100); endovascular—done post-surgery 3 (6.3)
2013/Garg et al. [8]	62 (100)	45 (72.6)	45 (72.6)	1 (1.4)	74 (100)	11 (14.9)	2 (2.7)	[2] Surgery 43 (69.4); endovascular 19 (30.6), conservative 6 (9.7)
2015/Gross et al. [35]	33 (100)	16 (48.5)	N.A.	N.A.	33 (100)	N.A.	N.A.	Surgery 8 (24.2); endovascular 15 (45.5); conservative 10 (30.3)
2015/Vargas et al. [36]	5 (100)	5 (100)	4 (83.3)	1 (16.7)	6 (100)	4 (66.7)	0 (0)	Endovascular 6 (100)
2018/Chen et al. [37]	35 (100)	25 (71.4)	30 (85.7)	1 (2.9)	35 (100)	16 (45.7)	0 (0)	Surgery 20 (57.1); endovascular 15 (42.9)
2019/Amelot et al. [38]	51 (100)	35 (68.6)	35 (68.6)	10 (29.6)	51 (100)	3 (5.9)	N.A.	Surgery 8 (15.7), endovascular 43 (84.3)
2019/Kim et al. [13]	26 (100)	17 (65.4)	20 (76.9)	1 (3.9)	33 (100)	2 (7.7)	2 (7.7)	Surgery 10 (38.5); endovascular 10 (38.5); conservative 5 (19.2)
2019/Nam et al. [39]	23 (100)	15 (65.2)	19 (61.3)	1 (4.3)	31(100)	3 (13)	N.A.	Surgery 3 (9.7); endovascular 21 (67.7); combined surgery & endovascular 1 (3.2); conservative 1 (3.2)
2019/Thioub et al. [40]	10 (100)	4 (40)	8 (80)	1 (10)	10 (100)	1 (10)	4 (40)	Surgery 7 (70); endovascular 3 (30)
2019/Yasin et al. [27]	41 (100)	25 (61)	37 (90.2)	2 (4.9)	57 (100)	1 (1.8)	2 (3.5)	Surgery 13 (22.8); endovascular 25 (43.9); conservative 19 (33.3)
2021/Ciurea et al. [28]	47 (100)	28 (59.6)	37 (78.5)	1 (2.1)	47 (100)	14 (29.8)	N.A.	Surgery 46 (97.9); endovascular 1 (2.1)
2021/Garrido et al. [41]	18 (100)	14 (77.8)	15 (83.3)	1 (5.6)	21 (100)	4 (19)	2 (9.5)	Surgery 9 (42.9); endovascular 12 (57.1)
2021/Xu et al. [42]	47 (100)	29 (61.7)	40 (90.9)	5 (10.6)	53 (100)	10 (18.9)	1 (1.9)	Surgery 31 (58.5); endovascular 16 (30.2); medical [3] 1 (1.9)
2022/de Aguiar et al. [17]	12 (100)	5 (41.7)	10 (83.3)	2 (16.7)	17 (100)	6 (35.3)	2 (11.8)	Surgery 0 (0); endovascular 12 (70.6); conservative 5 (29.4)
2023/Brandel et al. [26]	33 (100)	21 (63.6)	21 (63.6)	6 (18.2)	37 (100)	12 (32.4)	1 (2.7)	Surgery 25 (67.6); endovascular 8 (21.6)
2024/Current study	11 (100)	10 (90.1)	10 (90.1)	0 (0)	14 (100)	2 (14.3)	5 (35.7)	Surgery 8 (57.1); endovascular 5 (35.7); conservative 1 (7.1)

[1] Reference to quantitative functional scores used in the study, namely Glasgow Outcome Scale (GOS) 4 to 5; Modified Rankin Scale (mRS) 0 to 2 or equivalent. [2] Percentage (%) quantified against the number of patients instead of total PIAs. [3] Here, 1 (1.9%) patient was given antibiotics only.

4. Discussion

4.1. Pediatric Intracranial Aneurysms: An Overview

Intracranial aneurysms in children are believed to be a distinct pathological entity in comparison to their adult counterparts, especially concerning their morphology and etiology. Clinical presentations are often diverse and variable [43]. Broadly speaking, it is believed that cerebral vessels are prone to aneurysm formation given their thin muscularis layer, as well as the lack of an external elastic lamina [44]. Acquired risk factors associated with aneurysm formation in adults such as hypertension, smoking and hypercholesterolemia are not as prevalent in the pediatric population [11]. Other associated diseases such as polycystic kidney disease, osteoporosis and atherosclerosis also tend to be more applicable to adults [45]. In children, trauma, congenital conditions and infections are reported to play a greater role in aneurysm formation [46]. Congenital conditions include systemic connective tissue disorders such as collagen deficiency, disruption of extracellular matrix, Ehlers-Danlos syndrome; congenital heart diseases; and arterio-venous malformations [47–49]. Infections, on the other hand, result in disruption of the internal elastic membrane and intima, forming a pseudoaneurysm known as mycotic aneurysm, which have a predilection for distal portions of the MCA [48,50]. Presently, it is postulated that the natural history of PIA is secondary to an interplay between aggravating external factors (such as trauma, infection, and inflammation) and an inherent defective defense mechanism (such as systemic conditions affecting connective tissues like Marfan's or Ehlers-Danlos syndrome) [5]. Nonetheless, exact details of the mechanistic factors underlying their formation are not yet fully elucidated.

For adults diagnosed with intracranial aneurysms, large multi-center, clinical trials such as the International Subarachnoid Aneurysm Trial (ISAT) [51] and Barrow Ruptured Aneurysm Trial (BRAT) [52] guide the treatment selection. Owing to the longer life expectancy and evolving developmental physiology in children, treatment guidelines for PIA need to be tailored accordingly. Under such circumstances, management protocols based on adult aneurysm trials cannot be completely extrapolated to the pediatric population [51,53]. Put together, the emphasis is on the best modality of treatment based on an individual child's aneurysm and its clinical characteristics. For instance, endovascular therapy, microsurgery, or a combination of both can be implemented for PIAs [30,33].

4.2. Aneurysm Morphology and Management Outcomes: Our Institutional Experience

Previous studies have broadly classified the etiology of PIA into traumatic, mycotic, dissecting, and saccular aneurysms. Dissecting aneurysms are reported to be four times more common in the pediatric population when compared to adults, with a purported incidence of up to 50% in some series [5,14,16,54]. In congruency with the literature, dissecting aneurysms are the most common PIA, accounting for 55% of patients in our cohort. The underlying pathophysiology is believed to be a chronic dissection process within the blood vessel wall, subsequently resulting in a fusiform-shaped outpouching. These vascular lesions often affect the parent vessel circumferentially and may become enlarged, causing local mass effects and seizures [42,54]. Unlike saccular aneurysms, the treatment of dissecting aneurysms requires either surgical excision of the aneurysm or endovascular parent vessel occlusion. While this may be tolerated if the aneurysm is located in a distal, non-eloquent vessel, a more proximal location of the aneurysm often requires a bypass procedure before parent vessel sacrifice [5,7,25,55]. Alternatively, the option of parent artery reconstruction with flow diversion has been described in selected case reports and series [36,56,57]. Separately, if the lesion is asymptomatic, some neurosurgeons may opt for conservative management with close surveillance [5]. In our cohort, we treated three anterior circulation dissecting aneurysms with surgical excision of the aneurysm, while two posterior circulation dissecting aneurysms were treated with endovascular parent vessel occlusion. One patient whose aneurysm was found incidentally remains on surveillance without any intervention. Next, giant aneurysms are relatively uncommon, comprising an estimated 5% of all intracranial aneurysms, regardless of age [58]. Up to 10%

of giant intracranial aneurysms are prevalent in the pediatric population. Here, it should be emphasized that their natural history is unfavorable, and the rupture risk generally increases depending on their size [59]. We were fortunate that our two patients with giant aneurysms underwent uneventful intervention with good recovery.

Following that, the co-existence of cardiac and or systemic vascular conditions with PIAs has previously been reported in the literature. Studies quote incidences between 8 to 50%, depending on the type of anomaly [49,60]. Various hypotheses for this association include developmental errors of the neural crest during early embryogenesis [60], and chronic hypertension affecting the medial arterial layer and hence, predisposing it to aneurysm formation, especially in children with coarctation of the aorta [61]. In the latter group, patients may still develop intracranial aneurysms several years after surgical correction for coarctation of aorta [62]. Our study cohort concurs with these findings, whereby 40% (n = 4) of our patients have associated systemic vascular or cardiac conditions..

Separately, mycotic aneurysms are reported to account for up to 15% of all pediatric intracranial aneurysms [63]. These are pseudoaneurysms that occur in response to inflammation within the blood vessel adventitia. This process then spreads into the muscularis layer, ultimately resulting in the disruption of both the internal elastic membrane and the intima [64]. Causative factors underlying the inflammation include embolization from a septic focus, and/or extension of a neighboring infection. Bacterial infections are the most common, followed by fungal and human immunodeficiency virus [65–67]. Generally, this type of intracranial aneurysm is associated with high morbidity and mortality [63]. In our series, mycotic aneurysm was identified in 25% of the patients. Similar to reports in the literature, mycotic PIAs in our cohort secondary to bacterial endocarditis tend to affect more distal intracranial vasculature while cases resulting from contiguous spread tend to be located more proximally [63,68]. As they have underlying infectious etiology, selected cases can sometimes be treated non-invasively with antibiotics. It has been shown that up to 29% of mycotic aneurysms can resolve with medical therapy alone. Surgical or endovascular intervention is often reserved for those with enlarging aneurysms despite antibiotics, and/or when an ICH is causing significant mass effect from the ruptured aneurysm which requires evacuation [63,68]. As highlighted in our case illustration, the role of a definitive cerebral DSA was necessary to exclude a mycotic aneurysm, especially in high-risk cases.

In contrast to adults, saccular aneurysms are relatively uncommon in the pediatric population and tend to occur in older children [5]. Some neurovascular experts believe that the treatment and natural history of classical saccular aneurysms in the pediatric population do not significantly differ from that in adults [5]. In essence, the approach (regardless of age) includes both microsurgical and/or endovascular treatments [43]. Treatment of saccular aneurysms is similar to their adult counterparts where coiling or microsurgical clipping of the aneurysm while preserving its parent artery is the goal [5]. Of the three (25%) saccular aneurysms treated in our cohort, two were treated with surgical clipping while one was coiled. For them, there was no significant difference in the post-treatment outcomes.

Although there is no case of traumatic intracranial aneurysm in our study population, we included the following discussion as this entity has been previously reported in children. As these are even more uncommon in the pediatric population, contemporary literature specific to them is notably sparse [2,69]. Affected patients tend to be males in the third decade of life, clinically symptomatic, arise at unusual arterial sites and are seldom multiple [2]. In the pediatric population, they have observed in both penetrating and non-penetrating trauma head injuries [69]. For the latter, three types have been described: those arising from the distal ACA, those arising at the skull base, and those arising at the cortical surface [46]. Overall, the neurosurgical management for traumatic aneurysms in children does not differ significantly from the adult population. Nonetheless, clinicians need to be mindful of this diagnosis in selected cases of presumed traumatic subarachnoid hemorrhage seen in pediatric head injuries.

4.3. Risk Factors Unique to the Pediatric Population

In adults, the formation of de novo aneurysms is exceedingly rare with reported incidences of 0 to 1.5% [70,71]. Factors associated with increased risks of developing de novo aneurysms include co-existing conditions with a predisposition for aneurysm formation and index aneurysm treatment with parent artery occlusion [72,73]. In our study, two patients developed de novo aneurysms during outpatient surveillance. One of them had a background of FMD—an idiopathic, noninflammatory, non-atherosclerotic vascular disease of small to medium-sized arteries. This finding is congruent with the high prevalence of intracranial aneurysms in patients (i.e., 21.7%), whereby up to 31% have multiple aneurysms [74,75]. Furthermore, the formation of de novo aneurysms has been reported as well in patients with FMD [76]. The other patient had an index aneurysm treated with parent artery occlusion of the PICA. On the follow-up cerebral angiogram 4 years post-treatment of the index aneurysm, the ipsilateral AICA was noted to have taken over the territorial supply of occluded PICA. Based on current understanding, we theorize that changes in cerebral hemodynamics added stress to the ipsilateral AICA by increasing the area of re-vascularized territory supplied, resulting in the formation of de novo AICA aneurysm.

4.4. Clinical Outcomes

In the adult population, a poor WFNS grade is often associated with unfavorable clinical outcomes, so much so that aggressive treatment is often withheld [20]. Despite aggressive intensive care treatment and early occlusion of poor-grade aneurysms, favorable outcomes (GOS $\geq$ 4) up to 30% have been reported in the children [77,78]. In our series, four patients were treated despite their initially poor WFNS grade (grade IV) on presentation. They eventually recovered to a GOS score of $\geq$ 4. Two patients made a full recovery without any neurological deficits. The remaining two suffered from mild hemiparesis but are otherwise independent in their activities of daily living. Similarly, a meta-analysis by Yasin et. al. reported favorable outcomes (mRS 0 to 2) in 48% of PIA with poor Hunt and Hess Scale (HHS4 to 5) presenting with aSAH [27]. Such pertinent differences highlight the ability of pediatric patients to better tolerate aneurysm or treatment-related neurological injury. We believe this is because children have higher rates of neuroplasticity to allow the brain to adapt or compensate for injuries [79].

As a child is expected to live for several decades to come, rather than mitigating hemorrhagic risk alone, the durability of treatment should be given due consideration when treating pediatric aneurysm. Here, aneurysm recurrence is of particular concern, especially for those treated endovascularly as a recurrence rate of up to 20% has been reported in adults. To date, the long-term durability of flow diversion techniques in children remains uncertain [13]. Another major concern is the use of antiplatelet therapy. A regimen for the loading and maintenance of antiplatelet doses for pediatric patients after endovascular treatment has not been established [13,80,81].

A long-term series by Sanai et. al. reported PIA recurrence rate of 15.8% in patients treated endovascularly versus 0% in patients treated surgically. Operative morbidities were similar in both treatment groups. They also found that the formation of de novo aneurysms was more prevalent in patients treated with endovascular therapy. The authors attributed this to the possible weakening of already defective vessel walls during microcatheter manipulation during endovascular therapy [7]. Unlike clinical trials in adults, which showed superiority of endovascular treatment over surgical treatment [51], a recent meta-analysis demonstrated relatively equal treatment-related outcomes between endovascular treatment and surgical treatment in the pediatric population [27]. Although we postulate that this discrepancy may likely be due to the inherent differences between adult and pediatric intracranial aneurysms, there are no large, randomized studies to objectively confirm our theory.

4.5. Aneurysmal Cerebral Vasospasm: Is This Phenomenon Less Prevalent in Children?

Cerebral vasospasm is defined as the narrowing of a cerebral blood vessel enough to cause a reduction in distal blood flow [82]. This phenomenon manifests as a potentially life-threatening clinical syndrome called delayed cerebral ischemia (DCI), whereby there is a development of new focal neurological signs, and/or deterioration in conscious levels, lasting for more than 1 h in patients with aneurysmal SAH [83]. Peak incidences usually occur around 7 to 10 days after the initial bleed [84]. Based on adult literature, up to 70% of aneurysmal SAH patients develop angiographic vasospasm, and 30% progress to neurological deficits [85]. Overall, it is generally accepted that DCI is a well-established sequelae that contributes to significant mortality and morbidity associated with aneurysmal SAH [86]. In contrast, symptomatic DCI from PIA is uncommon, and its exact prevalence is uncertain [87,88]. The rarity of this condition in children may initially mislead clinicians to consider other differential diagnoses such as Moyamoya disease, hemiplegic migraine and so forth [87]. Broadly speaking, the general principles of DCI management in adults have been reported to be successfully applied in PIA [87–89]. Nonetheless, it has been recommended that careful dose titration of nimodipine is necessary, especially in young children to avoid hypotension [88]. In our study, no case of DCI was encountered and for selected cases, the dose of nimodipine was titrated according to recommendations by the hospital pharmacist.

4.6. Study Critique and Future Directions

For this study, we acknowledge that there are noteworthy limitations. Firstly, this is a retrospective and modest population-based, cohort at a single institution. In congruency with reports from other overseas neurosurgery centers, our local incidence of PIA is extremely low. We observe similarities such as a higher number of male patients, and predilections for giant, mycotic and de novo aneurysms. Also, key challenges include diverse causes, perioperative considerations due to age-related physiology and available expertise from individuals. Owing to such heterogeneity, it is difficult at this stage to directly compare each variable meaningfully at a granular level. Overall, we are cognizant that results from our study are, at best, descriptive. Nevertheless, our study provides additional data from our region of Southeast Asia; at the same time, it reiterates findings from previous publications. We hope that our results can contribute to the growing body of literature and be incorporated into future meta-analysis efforts if needed. Separately, as part of our own institution's future work, we endeavor to collaborate with international groups focused on understanding the knowledge gaps in PIA. Examples include elucidating the links between certain genetic disorders and the risk of intracranial aneurysm formation in those affected [90]. Ultimately, the aim is to improve the management of children diagnosed with this uncommon but life-threatening entity.

5. Conclusions

Pediatric aneurysms are a heterogeneous group of lesions that are pathologically distinct from their adult counterparts. Current evidence recommends that treatment should be individualized, selecting the safer approach depending on aneurysm characteristics and the availability of local expertise. A multidisciplinary approach is paramount for good outcomes. Based on our institutional experience, longer surveillance for high-risk patients is recommended given their propensity to develop de novo aneurysms.

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