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ORIGINAL ARTICLE

Paediatric intracranial aneurysms: a British institutional review

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Abstract

Introduction Paediatric intracranial aneurysms are rare, with a differing natural history and thought to account for only up to 7% of all intracranial aneurysms. There is much uncertainty that surrounds the prevalence of unruptured intracranial aneurysms and it is estimated to be anywhere between 2 and 90 per 1000. This is the largest British single-centre analysis of paediatric intracranial aneurysms. We present the patient course from their initial presentations to the outcome of treatment and evaluate a serial assessment of adequacy of aneurysmal obliteration radiologically.

Results Twenty-two paediatric cases were identified that required treatment. The median age of presentation was 11.3 years (mean 9.9, range 0 to 15.9), 68% (15/22) were male and 77% (17/22) were ruptured on presentation. The majority of aneurysms were located at the anterior circulation (77% (17/22)). The overall median aneurysm size ($n = 21$) was 7.4 mm (mean 5 mm, range 2.5–19 mm). Twenty patients survived the acute phase and 80% (16/20) underwent coil embolisation and the other patients' surgical clipping. The overall outcomes were available for the 20 patients; on discharge, 90% (18/20) had a favourable clinical outcome (GOS score of 3–5). Treatment-specific clinical favourable outcomes were 88% (14/16) for coil embolisation against 100% (4/4) after surgical clipping. Of the two patients that died in the acute phase, one had sickle cell anaemia. Aneurysm aetiology was unknown in all other cases. None of the patients had a family history of aneurysms.

Conclusion Paediatric intracranial aneurysms while rare should be considered a differential diagnosis of children presenting with unexplained loss of consciousness with or without focal neurological deficit and/or headache. There is a two to one preponderance for males with a larger proportion of aneurysms within the posterior circulation (25%). Coil embolisation is the preferred method of securing a paediatric intracranial aneurysm.

Keywords Delayed ischaemic neurological deficit · Endovascular coiling · Paediatric intracranial aneurysms · Subarachnoid haemorrhage · Surgical clipping

Introduction

There is much uncertainty that surrounds the prevalence of unruptured intracranial aneurysms and it is estimated to be anywhere between 2 and 90 per 1000 [1, 2].

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Intracranial aneurysms are more common in the over 40s with a higher incidence in women than men [1, 2]. The challenge for a clinician is quantifying the annual risk of rupture. This was surmised in Brown et al. (2014), a review paper which reported a varying risk of rupture from 0.34 to 2.8% [3]. Paediatric intracranial aneurysms are rare, with a differing natural history and thought to account for less than 7% of all intracranial aneurysms [1, 2].

The first case report of paediatric aneurysms was described by the German pathologist Eppingher in the nineteenth century. Eppingher reported the finding of an incidental intracranial aneurysm on autopsy of a 15-year-old child who died of aortic stenosis [4]. In Locksley's more recent study, looking at the natural history of over 6000 ruptured intracranial aneurysms, only 4% were less than the age of 20 years [5]. In adults, there is a 3 to 2 female predominance [5–7].

The natural history of paediatric aneurysms is quite different from those that occur in the adult population. This is largely due to the absence of acquired risk factors including age, excess alcohol intake, type 2 diabetes, hypercholesterolaemia, hypertension and smoking. In children, however, there are other factors to consider including (i) cerebral arteriovenous malformations, which may carry aneurysms on feeding arteries, (ii) extracellular matrix and connective tissue disorders and (iii) other associated medical conditions such as sickle cell anaemia, tuberous sclerosis, Klippel-Trenaunay-Weber syndrome, alpha-1-antitrypsin deficiency, hereditary haemorrhagic telangiectasia and polycystic kidney disease. It is estimated there is an underlying medical comorbidity in up to a third of children with intracranial cerebral artery aneurysms [8–10].

The morphology of paediatric aneurysms differs from that of adults in that they are typically larger in size on presentation; thus, children may present with non-haemorrhagic symptoms including focal neurological deficits, headache, local mass effect and/or seizures. The rupture risk depends on the aetiology, i.e. associated with dissection, infection or trauma. Children tend to have a better initial clinical presentation as well as improved outcomes with less delayed ischaemic neurological deficit (DIND) when compared with adults [11].

The management of adult ruptured intracranial aneurysms has undergone a paradigm shift from surgical clipping to endovascular coiling. In small (≤ 10 mm) anterior circulation aneurysms, the randomised allocation to coiling was associated with a better 1-year clinical outcome (defined as survival without dependency) [12].

These findings are unlikely to be as meaningful in the paediatric population as the size of the aneurysm is usually large and the morphology is complex and in infants, endovascular access raises considerable technical difficulties to allow for equipoise in randomisation or in any comparison of these procedures [13, 14]. Similarly, the lack of clipping experience in some paediatric neurosurgeons may render equipoise unsustainable.

A review of paediatric studies of intracranial aneurysms indicates that most of these are retrospective, small numbers (largest having 54 patients) and mostly reflect surgical intervention [7–11, 13–34]. More recent comparisons between coiling and clipping are not randomised in the paediatric population as one would expect.

This review aims to provide our experience of both clipping and coiling in the paediatric population. This is the largest and most recent British single-centre analysis of paediatric intracranial aneurysms. We present the patient course from their initial presentations to the outcome of treatment and evaluate a serial assessment of adequacy of aneurysmal obliteration radiologically.

Methodology

All paediatric patients treated with ruptured intracranial aneurysm over the 13-year period from 2005 to 2018 were reviewed. Our centre takes on new patients under the age of 16 years. Data was collected retrospectively from medical records including electronic databases and radiological imaging (Fig. 1). The need for further surgery, incidence of complications (both at outset and on serial follow-up) and follow-up outcome quantified as the Glasgow Outcome Scale (GOS) at discharge and at 1 year was recorded. Endovascular interventions and surgery were performed at the Birmingham Children's Hospital, UK.

Results

Patient and aneurysm characteristics

Twenty-two paediatric cases of intracranial aneurysms were identified that required treatment. Our data excluded traumatic and mycotic aneurysm cases (Table 1). The median age of patients was 11.3 years (mean 9.9, range 0 to 15.9) and 68% (15/22) of patients were male. Two cases were detected antenatally. Overall, 77% (17/22) of aneurysms were ruptured at presentation. Of these, all had a subarachnoid haemorrhage present on CT or MRI. The overall median aneurysm size ($n = 21$) was 7.4 mm (mean 5 mm, range 2.5–19 mm).

Two patients died before a definitive treatment could be offered, one of which had known sickle cell anaemia.

The majority of aneurysms, 73% (16/22), were located in the anterior circulation. The most common locations were the middle cerebral artery (36%, 8/22) and the internal carotid artery (18%, 4/22). Aneurysm aetiology was unknown in all other cases. None of the patients had a family history of aneurysms.

Treatment and outcomes

Six patients (27%, 6/22) required immediate CSF drainage (EVD) one of which died before the aneurysm was secured. Twenty patients survived the initial acute phase with definitive treatment, 80% (16/20) underwent coil embolisation and 20% (4/20) underwent surgical clipping. A patient after coil embolisation required a craniectomy for evacuation of the SDH (Table 1).

Treatment-specific outcomes were available for the 20 patients; 90% (18/20) had a favourable clinical outcome (GOS score of 3–5). The rate of favourable clinical outcome after endovascular treatment (coil embolisation) was 88% (14/16) compared with 100% (4/4) after surgical clipping ($P = 1.00$, two-tailed Fisher's exact test) (Table 2).

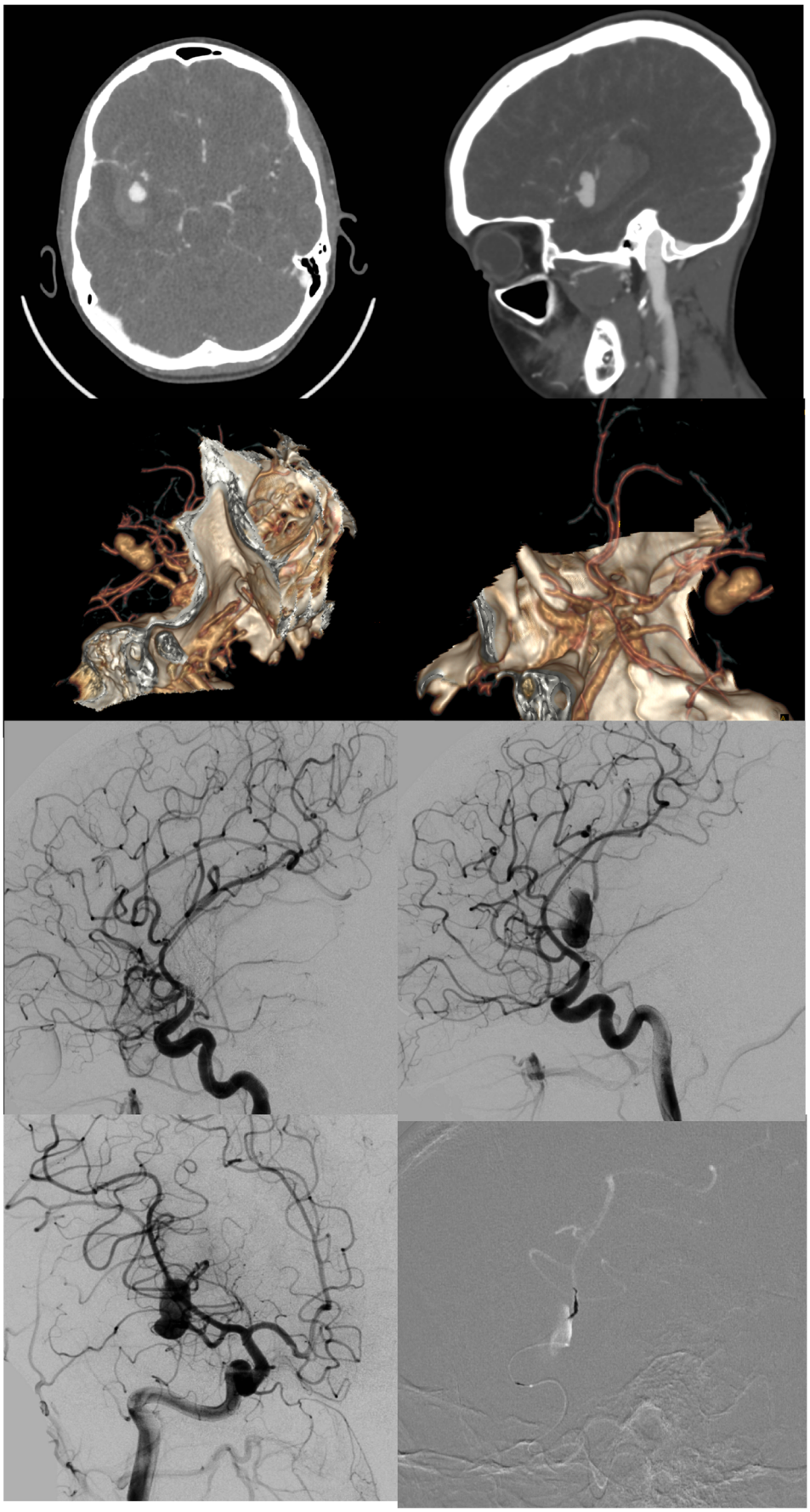

Fig. 1 Radiological imaging and endovascular treatment of an 11-year-old male that presented initially with sudden severe headache. He had urgent imaging after a seizure and reduced GCS. CT head demonstrated a subarachnoid haemorrhage with a right-sided MCA aneurysm that was coil embolisation. On discharge, his Glasgow Outcome Scale score was 5 and at 1-year follow-up

Similarly, there is no significance in the subgroup analysis of ruptured and unruptured aneurysms on comparing the two treatment modalities (Table 1).

Among all the patients, the mean duration of hospitalisation was 10.6 SD ± 7.3 days following endovascular treatment and 21 SD ± 7.4 days following surgical clipping ($P = 0.0211$, unpaired t test).

In terms of perioperative complications, there was a new post-operative clinical neurological deficit in one patient that had endovascular treatment. Two patients that had surgical clipping underwent decompressive craniectomy, one of which after insertion of their autologous bone flap developed osteomyelitis and the other required insertion of ventriculoperitoneal shunt (VPS) for post-haemorrhagic hydrocephalus.

A single patient who had received initial endovascular treatment suffered a late rebleed at 18 years of age following recurrence.

Three patients (15%, 3/20) exhibited on-going higher neurocognitive deficits on long-term follow-up.

Discussion

Natural history

The prevalence and incidence of cerebral artery aneurysms in the paediatric population are difficult to determine. A large recent review of 2726 patients with ruptured aneurysms identified that 62 were less than the age of 18, an incidence rate of 2.27% [6]. Therefore, the true incidence of non-traumatic non-infective aneurysms in those under the age of 16 is likely to be less than 2% [6–9, 14, 35, 36]. In the 13 years analysed in our study, 22 patients presented and were treated by our department that has a paediatric catchment of over 450,000 (https://www.westmidlandsdeanery.nhs.uk/Portals/0/Recruitment%202016/BCH%20%20-%20General%202016.pdf?ver=2016-05-16-143811-087).

The clinical features of children presenting with intracranial aneurysms do diverge away from what is known about adults. This is in terms of clinical presentation, aneurysm characteristics and neurological recovery. The acquired risk factors seen in adults are largely absent in children. The predominant factors in the natural history and formation of paediatric intracranial aneurysms are congenital factors and haemodynamic stresses.

Risk factors

The only association in our study was a single child with a diagnosis sickle cell anaemia that had an underlying saccular PCA/PCOM aneurysm [37]. The underlying pathophysiology is such that the abnormally adherent sickle erythrocytes injure the endothelium of the arterial wall [38]. There is subsequent fragmentation of the internal elastic lamina and degeneration of the smooth muscle layer. The haemodynamic stress at these loci of arterial wall damage results in aneurysm formation, which is particularly noteworthy as this occurred at the left PCA/PCOM junction [8–10, 38].

Aneurysms that were due to infection or head injury were excluded in our study; however, both are more common in children than in adults. It is the less developed immune system that aids in the seeding of septic emboli into intracerebral vessels. In trauma, the dissipation of kinetic energy causes structural fatigue of the vessels especially points of bifurcation [9, 17, 39, 40].

In our study series, the preponderance of aneurysms was approximately 2:1 males to females and this is similar to the proportion that is reported in other case series, although opposite to that found in adults [5–7].

Subarachnoid haemorrhage (SAH) is a common presenting feature at any age, and in our series, all the ruptured cases (77%, 17/22) presented with SAH. This is consistent with the expected range (54 to 95%) in the published literature [13]. The other 23% (5/22) had non-SAH presentations; two detected antenatally and three children with neurological symptoms including headache and seizure activity secondary to mass effect or compression exerted by the aneurysm mass. A single patient had a giant aneurysm of their left ICA and this was picked up at antenatal screening. A patient further had a giant aneurysm presenting with SAH. Giant intracerebral artery aneurysms are more common in children and clinical features of presentation are often due to the mass effect rather than haemorrhage [35]. Intracerebral aneurysms should remain a differential diagnosis in children during investigation of chronic headaches or other focal neurology where there is no subarachnoid and/or intracerebral haemorrhage as this can be a feature in 8% of clinical presentations [35].

Location and size

In our study, 77% (17/22) were located in the anterior circulation and this is significantly less than the 97% ($n = 2118$) found in ISAT. The most common specific locations in children were the middle cerebral artery (36%, 8/22) and the internal carotid artery (18%, 4/24) or combined 55% (12/22). In ISAT, 14% of aneurysms are located at the MCA and generally the anterior communicating artery (ACOM) is the more common aneurysmal site in adults accounting for up to 50% (in ISAT) [12]. In our paediatric series, only 9% (2/22) were ACOM aneurysms. This greater preponderance of ICA aneurysms in children is thought to be due to the wider angle at the ICA bifurcation

Table 1 Patients with intracranial aneurysms evaluated at our institution

Patient	Age (years)	Gender	Presentation	Location	Size (mm)	Radiological findings	Treatment	Other neurosurgery	Length of stay	GOS (at discharge)	GOS (at 1-year)
1	9.9	Male	Decline GCS	MCA	3	SAH, ICH, IVH	Surgical clipping	EVD	28	5	5
2	11.3	Male	Decline GCS	ICA	3.5	SAH	Coil embolisation		6	5	5
3	9.4	Male	Decline GCS	ICA	7	SAH, SDH	Surgical clipping		18	5	5
4	4.3	Male	Vomiting, Decline GCS	MCA	12	SAH, ICH	Surgical clipping	EVD	26	4	4
5	13.1	Male	Headache, Vomiting	ACA	4	SAH	Coil embolisation		8	5	5
6	15.1	Male	Headache, Vomiting, Decline GCS	ACOM	2.5	SAH	Coil embolisation		17	5	5
7	13.2	Female	Decline GCS, Respiratory arrest	PCA/PCOM junction	2.5	SAH	Coil embolisation	EVD	4	1	–
8	0	Female	Antenatal diagnosis	ICA	14		Coil embolisation		7	5	5
9	12.8	Male	Headache, Seizure, Decline GCS	SCA	4	SAH	Coil embolisation	EVD	13	5	5
10	11.5	Male	Headache, Decline GCS	ACA/ACOM junction	5	SAH, ICH	Died	EVD	3	1	–
11	14.5	Male	Headache, Seizure, Decline GCS	ICA	13	SAH, ICH, SDH	Coil embolisation	Craniectomy	3	1	–
12	7.5	Male	Seizure	MCA	10	SAH, ICH	Coil embolisation		13	3	3
13	13.6	Female	Headache, Vomiting, Right CN-III palsy	PCOM	6.5	SAH, SDH	Coil embolisation		14	3	3
14	11.1	Female	Headache, Right CN-III palsy	SCA	4	SAH	Coil embolisation		5	4	4
15	6.9	Male	Headache, dysarthria, paresis	MCA	13	SAH, ICH	Surgical clipping		12	3	3
16	5.6	Male	Antenatal diagnosis	MCA	4		Coil embolisation		19	3	3
17	15.9	Male	Decline GCS	PCA/PCOM junction	–	SAH	Died		1	1	–
18	4.4	Female	Elective - headache	ACA	3		Coil embolisation		2	5	5
19	0.1	Female	Seizure	MCA	11		Coil embolisation		8	3	3
20	12.4	Female	Headache, Seizure	MCA	9		Coil embolisation		9	5	5
21	11.3	Male	Headache, Vomiting, Seizure, Decline GCS	ACOM	5	SAH, IVH	Coil embolisation	EVD	31	5	5
22	13.9	Male	Headache, Vomiting, Decline GCS	MCA	19	SAH	Coil embolisation		11	5	5

Table 2 Endovascular and surgical arms of patients

$N = 20$		Coiling ($n = 16$)	Clipping ($n = 4$)
Gender	M:F	9:7	4:0
Age (years)	Median (range)	11.9 (0–15.1)	8.2 (4.3–9.9)
Length of stay (days)	Mean (SD, range)	10.6 (±7.3, 2–31)	21 (±7.4, 12–28)
Size (mm)	≤ 5 mm	9 (56%)	1 (25%)
	6–10 mm	3 (19%)	1 (25%)
	≥ 11 mm	4 (25%)	2 (50%)
Intracranial location	Anterior	12	4
	Posterior	4	0
GOS ($n = 20$) on discharge	1	2	0
	2	0	0
	3	4	1
	4	1	1
	5	9	2
GOS ($n = 18$) 1 year	1	0	0
	2	0	0
	3	4	1
	4	1	1
	5	9	2

exposing it to greater hemodynamic stresses. The 1-year ISAT data for death or dependency (modified Rankin score 3–6) after any intervention of the anterior circulation reveals a rate of 27% whereas in our paediatric cohort, the equivalent death or dependency score (GOS 1 or 2) at discharge is 12% (2/17) [12]. This figure is half in children than adults and similar to other paediatric studies, perhaps reflecting the ability of the young brain to withstand insult.

The remaining 23% (5/22) of the aneurysms were identified in the posterior circulation, eight times higher than in adults (3%, 58/2118) in ISAT. Our figure is similar to previous reports by Aryan et al. (2006) and Beez et al. (2015), 21.2% and 25%. There was an associated mortality rate of 40% (2/5). The 1-year ISAT rate for death or dependency (modified Rankin score 3–6) after any intervention of the posterior circulation was similarly high at 33% [5, 34, 41].

The proportion of aneurysms at ≤ 5 mm in our paediatric cohort (50%, 10/20) and this is comparable to ISAT 52% but higher than a similar paediatric cohort published by Yasin et al. (2018), 40.5% ($n = 37$). A significant proportion of the children, 30% (6/20), in this study had larger aneurysms of ≥ 11 mm, greater than 19% in Yasin et al. (2018) study and 7% of adults identified in ISAT [12, 14].

Outcome

The overall mortality of cases in our study prior to intervention was 9% (2/22), matching the rate in adults (12%). There is no equivalent figure reported in other similar paediatric studies.

The initial clinical presentation of patients can have a bearing on outcome recovery. In the ISAT cohort of 2143 patients, 88% had a WFNS grade of 1 or 2. In our paediatric study population, 71% (12/17) of the ruptured aneurysms had WFNS grades of 4–5. Of these, four children (4/17) died, 2 prior to receiving definitive treatment. Of the remaining 13, all made a good functional recovery at 1 year (GOS 3–5).

There is a similar mortality rate of poor grade (WFNS 4–5) in children and adults, 33% and 35% [42].

Delayed ischaemic neurological deficit (DIND) is another major complication of aneurysmal rupture especially if the initial presentation is of a poor grade (WFNS 4–5). Clinical outcomes therefore can be poor with no recovery or death (GOS 2 or 1). In our series, the rate of DIND was 20% (4/20), in keeping within the observed range of 9.5 to 23.3% published elsewhere in similar paediatric studies. The figure is significantly lower than the incidence in the adult population that can be as high as 36%. It is recognised that children generally tolerate DIND better due to greater collateral circulation than adults and the protective higher cerebral blood flow that can be up to 85% higher than that of adults [13, 36, 43].

A long-term complication of subarachnoid haemorrhage is communicating hydrocephalus that is often managed through permanent CSF diversion. The insertion of ventriculoperitoneal shunt (VPS) can often be associated with delayed complications including blockage or infection leading to significant morbidity after an initial good recovery. The VPS insertion rate following aneurysmal

SAH in adults is 31% but only one patient required a VPS in our cohort [13, 44, 45].

Of the children who survived, 44% (8/18) reported an on-going neurological sequela at 1 year. These included seizures, persistent oculomotor palsy, hemiparesis and three children with behavioural difficulties but able to attend mainstream school.

Management

There was no statistically significant difference between endovascular (80%, 16/20) and surgical treatment (20%, 4/20) on long-term clinical outcomes in children with intracranial aneurysms or any examined subgroups thereof, including those with ruptured or unruptured aneurysms.

There has been a shift away from surgical clipping to endovascular coiling after the publication of ISAT. The ISAT mortality rate immediately after intervention and at 5 years was 7.5% and 11%, while following surgical clipping, this was 8.3% and 14% [12].

While our series validates the trend towards endovascular procedures, it does not reflect ISAT's significantly better mortality rate. However, similar rates are quoted in other studies (Beez et al. 2016, mortality 11% coiling versus 3% clipping) [43].

Limitations

The main limitation to this series is the small number given the rarity of cases and the retrospective nature. There is a lack of long-term follow-up quantification of functional status, scholastic performance, behavioural issues and follow-up into adulthood. The analysis of certain subgroups with small numbers of patients may not have sufficient statistical power to discriminate differences in outcomes, even when these differences may be clinically significant.

We also note that we do not routinely screen for conditions that may be associated in particularly with paediatric intracranial aneurysm. Had we routinely screened for occult associated conditions, then we may have had a higher pick up rate.

We are now carrying out a review of the longer term outcomes of children in terms of educational achievement and cognitive deficit following treatment for paediatric intracranial aneurysms.

Conclusion

Paediatric intracranial aneurysms are rare but they should be considered as a differential diagnosis of children presenting with unexplained loss of consciousness with or without focal neurological deficit and/or headache.

Our study, like previous paediatric studies, has identified a number of differences between adult and paediatric aneurysms. These include (1) male preponderance (M2:F1), (2) a larger proportion of aneurysm within the posterior circulation (adults 2.7% versus children 25%) and (3) size (7% ≥ 11 mm in adults versus 30% ≥ 11 mm in children).

It should be considered as a differential diagnosis for acute presentations of children with neurological deficit and/or headache. This pathology does account for significant morbidity and mortality especially from posterior circulation aneurysms. The shift towards endovascular coiling is the mainstay of therapy. Unlike in adults, morbidity is mainly related to the initial pathology rather than DIND.

Compliance with ethical standards

Conflict of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

Appendix

Table 3 Glasgow Outcome Scale (GOS). Jennett, B; Bond, M (Mar 1, 1975). "Assessment of outcome after severe brain damage". *Lancet*

Score	Definition
1. Death	Death
2. Persistent vegetative state	Patient exhibits no obvious cortical function
3. Severe disability	Patient depends upon others for daily support due to mental or physical disability or both
4. Moderate disability	Patient is independent as far as daily life is concerned. The disabilities found include degrees of dysphasia, hemiparesis, or ataxia, as well as intellectual and memory deficits and personality changes
5. Good recovery	Resumption of normal activities even though there may be minor neurological or psychological deficits

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