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Special Neurocritical Care Review Article

Pediatric Intracranial Aneurysms and Subarachnoid Hemorrhage: Review

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Introduction

Intracranial aneurysms (ICA) are rare in the pediatric population (age< 18 years). German pathologist Eppinger first reported a case of childhood aneurysm in a 15-year-old boy who collapsed during strenuous gymnastics. His postmortem examination revealed a ruptured saccular aneurysm of the right anterior cerebral artery[1].After several years Edward Bull described the first ante mortem casein a 17-year-old girl who presented with severe headache and her diagnosis of a ruptured posterior communicating artery aneurysm was subsequently confirmed on autopsy[2].In the current era, modern neuro - imaging techniques and availability of angiography has greatly enhanced the ability of physicians to diagnose cerebral aneurysms. However, even today timely diagnosis of a pediatric aneurysm and aneurysmal subarachnoidhemorrhage continues to be challenging.

Incidence

Intracranial aneurysms are extremely uncommon in the pediatric population with a reported prevalence ranging from 0.5% to 4.6%. There is an overall male predominance (male: female ratio 1.75:1)[3].

Location of Intracranial Aneurysms

More than 80% of the pediatric ICA are located in the anterior circulation while about 15% are located in the posterior circulation. The most common site in the anterior circulation is the internal carotid artery bifurcation (26%), followed by the anterior communicating artery complex (19%) and middle cerebral artery bifurcation (17%)[3]. Multiple aneurysms in children are uncommon and seen in less than 5% of all pediatric cases.

Etiology/Pathophysiology

The ICA can be congenital or acquired. The congenital (also known as berry or saccular) aneurysms are found in about 30% of cases[4]. The exact pathophysiology of congenital ICA is debatable. It is likely due to a combination of congenital and degenerative factors. The pathological specimens show an absence of internal elastic lamina and tunica media at the site of aneurysm formation. The consensus view is that the transition zone from normal vessel into the aneurysmal sac is characterized by a congenital defect of the internal elastic lamina and tunica media. This site undergoes additional degenerative changes throughout life and turbulent blood flow can cause a saccular out pouching at the area of defect. This combined effect of underlying congenital defect in the vessel wall along with additional degenerative factors is responsible for the rarity of aneurysms in children and their increasing incidence in adulthood[3]. Acquired causes of ICA in children include trauma, infection and dissection. According to Krings et al. dissecting aneurysms are the most often encountered pediatric aneurysm and may account for up to 50% of all aneurysms in this age group[4]. Traumatic aneurysms account for 14 to 39% of all pediatric aneurysms in different case series, and may occur after both penetrating and nonpenetrating trauma. Infectious aneurysms account for up to 2 to 10% of all pediatric aneurysms. They are most often of bacterial origin and are rarely caused by fungal infections. The most common organism is staphylococcal aureus, followed by streptococcus viridians and other gram-negative organisms.

Other conditions associated with increased risk of ICA are polycystic kidney disease, coarctation of aorta, sickle cell anemia, Ehlers-Danlos syndrome type 4, collagenopathy, and pseudoxanthoma elasticum.

Clinical Presentation

The most common presentation of ICA in children is an acute aneurysmal rupture with subarachnoid

hemorrhage (SAH). The signs and symptoms of SAH in neonates or infants are nonspecific and include irritability, drowsiness, poor oral intake, or vomiting. Symptoms in older children are similar to those in adults, such as acute headache, nausea, vomiting, photophobia, neck stiffness, loss of consciousness and neurological deficits. Seizures are common in both infants and older children.

An unruptured aneurysm may be asymptomatic and present as an incidental finding on neuroimaging or may cause symptoms due to mass effect such as partial complex seizures, cranial nerve palsies, or focal neurological deficit. These symptoms are more frequently seen in children than in adults.

Aneurysms presenting with SAH tend to re-bleed. If left untreated, 2 to 4 percent bleed again within the first 24 hours after the initial episode, and approximately 15 to 20 percent bleed a second time within the first two weeks[5]. The risk of rupture of an ICA that is found incidentally is much less certain.

Diagnosis

The timely diagnosis of an ICA and SAH depends on high index of suspicion. If SAH is suspected, urgent computed tomography (CT) scan of the head without the administration of contrast material should be performed to confirm the clinical impression. Patients with a negative CT but a high index of suspicion should be considered for lumbar puncture. In those with SAH, the red blood cell (RBC) count is usually >100,000 cells/mm^3 in the third tube of the cerebrospinal fluid (CSF) collection, and xanthochromia is present. The more sensitive and specific test to diagnose SAH is the measurement of excess bilirubin content in the CSF sample.

The next step after making a definitive diagnosis of a SAH should be to determine the etiology and to see whether an aneurysm is the cause of SAH in this patient. To do so, there are different imaging modalities currently used in clinical practice. The three imaging techniques to rule out an intracranial aneurysm and to delineate its size and morphological features are CT angiography (CTA), magnetic resonance angiography (MRA), and conventional catheter angiography.

The sensitivity and specificity of CTAto diagnose ICA varies from 0.77 to 0.97 and 0.87 to 1.00 respectively[6]. However, the sensitivity for aneurysms less than 3 mm is low and is estimated to be 0.40 to 0.91. Its drawback is thatit involves the use of intravenous contrast medium and thus it is contraindicated in patients with renal failure or in those who are allergic to iodinated contrast dye. (Fig 1-shows left terminal internal carotid artery aneurysm)

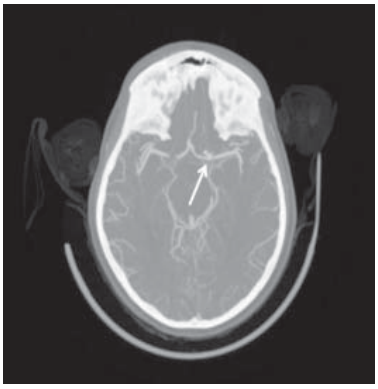

Figure 1: CTA showing lobulated aneurysm arising from left terminal Internal carotid artery.

Magnetic resonance angiography (MRA) produces images of the intracranial vasculature by detecting a specific range of blood flow velocities allowing the isolation of intracranial arteries. It is highly sensitive (0.69 to 0.99) and specific (1.00) in detecting aneurysms >3 mm in diameter[6]. Its advantage is that it does not require intravenous contrast agent, however, it takes considerably longer time than CTA and thus is more difficult to use in critically ill patients.

Conventional cerebral angiography is the "gold standard" for imaging of ICA. It provides exceptional resolution, can detect small aneurysms and demonstrate dynamic flow of cerebral vasculature and of the aneurysm itself. It is a safe diagnostic modality in infants and children with low risks particularly in the hands of an experienced operator.

SAH Grading scales

Numerous SAH grading scales have been proposed in the past, with the aim to stratify the patients into various risk categories based on their presenting signs and symptoms. The most commonly used are Hunt and Hess scale and Fisher scale. Hunt and Hess scale (Table 1) is used to describe the neurological

condition on admission and is considered a good predictor of ultimate outcome[7]. The Fisher grade (Table 2) uses a four-point scale to describe the amount of blood on non-contrast-enhanced CT of the head and has been shown to correlate with the development of vasospasm[8].

Table 1: Hunt and Hess grading system for patients with SAH

Grade	Neurological status	Percent risk of death as reported originally
1	Asymptomatic or mild headache and slight nuchal rigidity	11
2	Severe headache, stiff neck, no neurological deficit except cranial nerve palsy	26
3	Drowsy or confused, mild focal neurological deficit	37
4	Stuporous, moderate or severe hemiparesis	71
5	Coma, decerebrate posturing	100

Table 2: Fisher grade of cerebral vasospasm risk in SAH

Group	Subarachnoid blood distribution
1	None
2	Thin distribution with vertical layers < 1mm
3	Thick localized clots or vertical layers > 1mm
4	Diffuse or no SAH, but with intracerebral or intraventricular hemorrhage

Management

A multidisciplinary team including neurosurgeon, interventional neuroradiologist, neurologist and pediatric intensivist best managepediatric ICA. Theinitial treatment of a child with ruptured ICA focuses on maintenance of adequate ventilation, hemodynamic stabilization, maintenance of cerebral perfusion, preventing intracranial hypertension and minimizing the risk of re-bleeding. The unconscious patients or those with a falling Glasgow Coma Scale (GCS) should be intubated and ventilated. Prior to securing the aneurysm, blood pressure should be adequately maintained, as hypertension increases the risk of re-bleeding while excessive fall in blood pressure increases risk of cerebral ischemia. Some of the patients may develop hydrocephalus as a result of aneurysmal SAH and may need external ventricular drain placed for initial stabilization before aneurysm obliteration. The ruptured ICA should be secured as soon as possible after initial stabilization as the greatest risk of re-bleeding occurs within the first 24 hours.

Securing the aneurysm:

There are three options for treating ICA: observation, clipping and endovascular coiling. The management of unruptured aneurysms that are discovered incidentally depends on the patient's clinical condition, and size and locationof the aneurysm. Depending upon their size and location, they can be either observed with routine periodic follow-up imaging or treated electively. All ruptured aneurysms should be secured as early as possible by either clipping or coiling.

Clipping of aneurysms requires craniotomy and placement of MRI compatible permanent clips across the neck of the aneurysm, excluding it from the circulation (Fig 2 A). During the last decade endovascular procedures have been increasingly used to treat ICA. An interventional neuroradiologist usually performs endovascular coiling. With the use of angiographic techniques, a microcatheter is advanced into the aneurysm, and detachable coils of various sizes are deployed to decrease the amount of blood or to stop blood from filling the aneurysm (Fig 2 B).

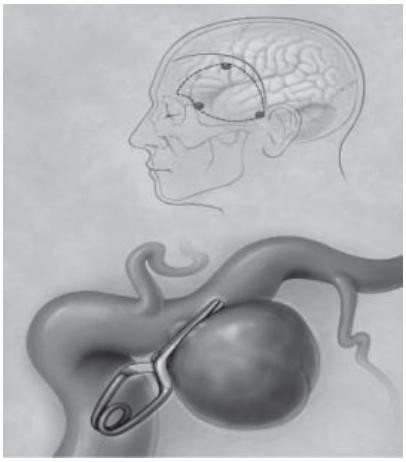

Figure 2 (A): Microsurgical Clipping of an Aneurysm.

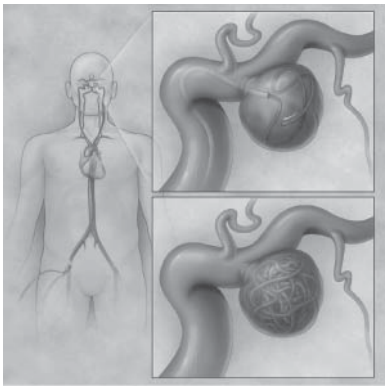

Figure 2 (B): Endovascular Occlusion of an Aneurysm. Adapted from N Engl J Med 2006; 354:387- 396

Clipping or Coiling

Both the techniques have their own advantages and disadvantages. Though successful clipping is generally associated with definitive protection against re-rupture, it has risks associated with craniotomy. Endovascular coiling does not need craniotomy but aneurysms treated with coiling may reoccur and there is a risk of rupture of the aneurysm during catheter advancement into the aneurysm or during coil placement.

The International Subarachnoid Aneurysm Trial (ISAT) was a large, multicenter prospective study in adults comparing endovascular and surgical techniques for aneurysms presenting with SAH. Though the trial was criticized for many reasons, it showed an improvement in early survival in selected patients receiving endovascular therapy[9]. There are very few pediatric studies comparing both modalities of treatment. In the study by Agid et al, 77% of the patients in the endovascular group had good recovery as compared to 45% of the patients in surgical group[10]. In their study Sanai et al, had shown that patients treated with clipping had more complete obliteration of their aneurysm and significantly lower recurrence risk as compared to patients in coiling group[11]. Stiefel et al, found no difference in outcome of patients treated with either clipping or coiling[12].

On the basis of literature, it remains controversial whether a given ICA should be treated surgically or managed endovascularly. However, recent American Heart Association (AHA) guidelines for the management of SAH in adults have recommended that in patients with ruptured aneurysms who are technically amenable to endovascular coiling and surgical clipping, the former should be considered[13]. However, there are no pediatric guidelines and the decision to do surgical clipping or endovascular coiling should be taken after discussion with multidisciplinary team.

Medical management of aneurysmal subarachnoid hemorrhage

The medical management of pediatric patients with aneurysmal SAH is as important as the surgical or endovascular intervention in ensuring a favorable outcome. Following securing of the aneurysm, management of SAH involves close neuromonitoring, prevention or treatment of vasospasm and other complications. Most of these patients need admission to the intensive care unit.

Vasospasm and Delayed Cerebral Ischemia

Vasospasm causing delayed cerebral ischemia (DCI) is defined as any neurological deterioration, including focal neurological deficits and altered consciousness, of which no other cause can be identified by radiographic, laboratory or electrophysiological investigations. It is very common in adult population with an incidence of about 30% but incidence of both radiographic and symptomatic vasospasm in pediatric population is much less. It usually happens between days four and ten after initial hemorrhage and persists for several days.

Diagnosis and monitoring for Vasospasm

All patients with aneurysmal SAH should be closely monitored clinically. Reduction in the level of consciousness with or without focal neurological deficit should raise suspicion of vasospasm. Digital subtraction angiography remains the diagnostic gold standard however CTA and MRA can be helpful at initial suspension (Fig 3). Transcranial Doppler Ultrasonography measures blood flow in basal cerebral arteries and is a useful noninvasive method to detect vasospasm.

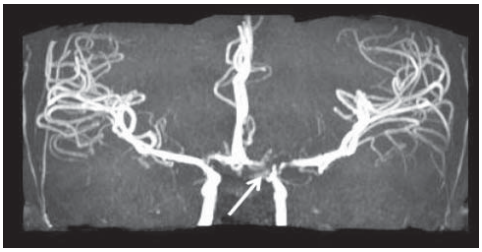

Figure 3: MRA showing severe segmental narrowing in the terminal left Internal Carotid Artery due to vasospasm

Treatment of Vasospasm

Several pharmaceutical agents like magnesium, anti-fibrinolytics, anti-platelets, and statins have been tried for the prevention and treatment of vasospasm but none has any proven benefits except Nimodipine. Nimodipine is the only agent that has been shown to reduce the incidence of vasospasm and DCI and improve neurological outcome[14]. The AHAguidelines recommend that oral nimodipine should be administered to all the patients with aneurysmal SAH immediately after diagnosis. The recommended dose in adults is 60 mg every four hours and is usually continued for 21 days. Although intravenous nimodipine is sometimes used, this route of administration remains unproven.

Another therapy that has been widely used to prevent and treat vasospasm is Triple H (hypertension, hypervolemia and hemodilution) therapy. However, this combination therapy has never been clinically proved to be useful and hypervolemia can be potentially harmful to critically ill patients. As per the recent guidelines, euvolemia rather than hypervolemia is recommended for both prophylaxis and treatment of vasospasm, and that hemodilution is not recommended[13]. Hypertensive therapy (induction of hypertension with vasopressors) is only recommended in patients with symptomatic vasospasm. Patients with symptomatic cerebral vasospasm, particularly those who have no response to medical treatment should undergo cerebral angioplasty of the narrowed vessels and/or selective intra-arterial vasodilator therapy[13].

Management of other complications

Seizures

Seizures occur commonly in patients after aneurysmal SAH. The routine long term use of anticonvulsants is not recommended but the use of prophylactic anticonvulsants may be considered in the immediate post hemorrhagic period[13]. Levetirecetam is preferred and phenytoin should be avoided because of associated cognitive effects and poor outcome[15].

Fever

Fever occurs in up to two-third of patients with aneurysmal SAH. Although the cause of fever can be related to the hypothalamic effects of subarachnoid blood, an infective cause should always be ruled out. Fever should be aggressively controlled with a target to achieve normothermia by the use of standard or advanced temperature modulating systems.

Dysnatraemia

Both hypernatremia and hyponatremia can occur in patients after aneurysmal SAH. Hyponatremia can develop from different mechanisms after SAH. It can be related to the syndrome of inappropriate antidiuretic hormone secretion (SIADH), cerebral salt wasting syndrome or iatrogenic hemodilution. It is important to monitor and diagnose hyponatremia as treatment varies with etiology.

Anemia

Anemia is common after aneurysmal SAH and may compromise brain oxygen delivery. Current guidelines recommend that the use of packed red cell transfusion to maintain hemoglobin concentration between 8-10 g/dl is reasonable in patients with SAH[16].

Cardiac dysfunction

Left ventricular dysfunction requiring inotropic support can occur in patients after SAH. It results from excessive catecholamine release in response to intracranial hemorrhage. In most cases it is temporary and resolves spontaneously after a variable period.

Outcome

Outcomes after aneurysm surgery and aneurysmal SAH are much better andfavorable in children as

compared to adults. In general, children have a lower incidence of vasospasm, which accounts for most of the morbidity and mortality associated with aneurysmal rupture. Overall, in different case series 90-95% of pediatric patients has good outcome with Glasgow coma outcome scale of 4 or 5.

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