Pediatric Neurovascular Disease

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76.1 Introduction

Pediatric cerebrovascular disease comprises a diverse set of rare but nevertheless important vascular abnormalities and diseases that, while similar in some respects to those conditions found in adults, often represent distinct entities with pathophysiology, associated risk factors, and prevention and treatment considerations unique to this patient population. Additionally, despite their relative rarity, the clinical consequence in younger patients may be profound and long lasting, and the associated costs may be enormous. As such, an awareness of these lesions and their current treatments is of paramount importance. While this chapter will endeavor to present a selection of important pediatric cerebrovascular lesions and disease processes, it cannot possibly describe the full breadth of cerebrovascular disease in such a small space, nor can it hope to present those entities it does discuss exhaustively.

76.2 Aneurysms

76.2.1 Description

Cerebral aneurysms, as described elsewhere in this volume, are focal dilations of cerebral blood vessels that occur at sites of mural weakness. While the incidence of cerebral aneurysms in the pediatric population is not known with certainty, the available evidence suggests that intracranial aneurysms are much less common in children than in adults. There are several unique features of aneurysms in the pediatric population, including a male preponderance, higher relative occurrence in the posterior circulation or internal carotid artery (ICA) bifurcation, higher incidence of large or giant aneurysms, and greater relative likelihood of being fusiform or dissecting [1–4], suggesting that the etiology of these vascular lesions may be distinct from those found in adults.

Intracranial aneurysms in patients aged 18 years or younger appear to comprise between 0.17% and 5% of all aneurysms [5–8], with one study in 1966 finding only 41 of 6368 ruptured aneurysms (0.6%) in patients under 19 years old [9]. The majority of aneurysms in children are discovered in adolescence, with boys showing a gradual increase in frequency with age, while in girls the frequency peaks at menarche, resulting in a brief female predominance at age 14–15 years [10].

Most, but not all, pediatric aneurysm series appear to demonstrate a varying degree of male predominance among pediatric aneurysm case series, which appears to be in contrast with the overall female preponderance observed among adults [11, 12]. Overall, the M:F ratio among pediatric aneurysm cases appears to be 1.42:1 [10], although, as alluded to above, there is variability to this ratio with age, with the most marked male to female ratios (as high as 2.7:1 to 4:1) occurring between early childhood and puberty [3, 13]. Data regarding aneurysms occurring in children younger than 2 years is inconsistent, with at least one series reporting a marked female predominance (male to female ratio of 1:5) in this age group [14], while others report more even distribution or slight male predominance [15]. The data for this young age group is extremely limited, and therefore must be interpreted cautiously.

In general, it appears that the vast majority of aneurysms in the pediatric population produce symptoms, as evidenced by a lack of incidentally discovered pediatric aneurysms in at least one autopsy series [16]. The overwhelming majority of pediatric aneurysms appear to present with subarachnoid hemorrhage (SAH) (80–95%), with roughly half presenting with good grade (Hunt and Hess grade III or better), though it should be noted that some series report a far lower incidence of hemorrhage (as few as 20–30%) [3, 4, 17–20]. Rebleeding of unsecured aneurysms occurs in up to roughly half of children presenting with SAH [3, 21, 22]. This is considerably more frequent than in adults, for whom rebleeding occurs with a frequency of nearly 25% [3, 23], thus underscoring the urgency of treatment of ruptured aneurysms in children.

Despite this, non-hemorrhagic neurological deficits and headaches are relatively more common and more pronounced among the pediatric population than in the adult population, presumably as a result of a mass effect from the higher incidence of large and giant aneurysms [6, 17, 24]. Sharma et al. [25] reported that 18.2% of patients presented with symptoms attributable to a mass effect from giant aneurysms, while Kakarla et al. [26] reported

a frequency of 46%. These symptoms included cranial nerve deficits, headaches, seizures, or hydrocephalus, all of which occur at higher rates in children than in adults as the presenting symptom of intracranial aneurysms [10, 22].

As with aneurysms in the adult population, the majority of pediatric aneurysms occur in the anterior circulation. That said, there are some important differences with respect to the distribution of aneurysms in the pediatric population. To begin with, the most common location of pediatric intracranial aneurysms appears to be at the ICA bifurcation; this location comprises approximately 25% of pediatric intracranial aneurysms, in contrast to the 5–8% of adult intracranial aneurysms found at this location [3, 20, 27]. While anterior communicating (AComm) artery aneurysms account for nearly 50% of adult aneurysms, only 14–20% of pediatric aneurysms occur at this location [27]. Aneurysms of the middle cerebral artery (MCA) occur in adults significantly less often than aneurysms of the AComm, while in children aneurysms at this location may equal or even exceed those occurring on the AComm [9, 27, 28]. The proportion of aneurysms occurring in the posterior circulation among pediatric patients (from 17% to 60%) is significantly higher than that seen in adult patients (approximately 5.5%) [4, 5, 7, 9, 13, 14, 20, 27–30]. The basilar artery is the site of the majority of posterior circulation aneurysms.

As indicated above, giant aneurysms (>25 mm) are reported much more frequently in pediatric patients than in adults, though series vary widely in the frequency they report. Overall, it appears that roughly 20% of aneurysms in children are giant aneurysms [13, 17, 25, 26, 31, 32]. By contrast, only 3–5% of aneurysms in adult patients are classified as giant, though at least one series found the incidence to be on par with that found in children [3]. There is a clear tendency toward giant aneurysms in the posterior circulation in children: While pediatric aneurysm series report a wide range of frequencies, they appear to converge around the 80% of posterior circulation aneurysms classified as giant reported by Lv et al. [2, 3, 5, 7, 13, 17]

Saccular aneurysms are by far the most common type found in adults, while in children there is tremendous variability to the reported frequency of different aneurysm types. Both Hetts et al. [4] and Agid et al. [20] found that saccular aneurysms occur with a frequency of 46% in their series (followed by dissecting aneurysms, with frequencies of 30% and 19%, respectively), while Lasjaunias et al. [14] found that nearly 45% of aneurysms in children were dissecting, with only 32% saccular. Krings et al. [24] reported a fourfold higher frequency of dissecting than saccular aneurysms. While in general fusiform aneurysms appear to be rare in children, at least one series reported a frequency of 51% [18]. There is agreement, however, that dissecting aneurysms appear to occur more commonly in the posterior circulation [4, 14, 20].

Infectious, or «mycotic,» aneurysms occur slightly more commonly in children than in adults, though they are rare in both populations (8% vs. 5%) [10, 22]. In children, these aneurysms are most often associated with a known infectious source or immunocompromised state, such as endocarditis, meningitis, or human immunodeficiency virus (HIV) infection [3, 4]. These aneurysms carry a high likelihood of rupture, presenting with hemorrhage as often as 70% of the time [10].

Co-morbidities and risk factors implicated in aneurysm formation for adults, such as chronic, uncontrolled hypertension and cigarette smoking, do not apply to aneurysm formation in children. It is reasonable, therefore, to suspect that the etiology of aneurysm formation in children may in some ways be distinct from that of adults, a suspicion further supported by the aforementioned differences in location, size, and gender distribution.

76.2.2 Diagnosis and Treatment

In cases of abrupt neurological decline or new focal neurological deficit, an unenhanced computed tomography (CT) scan of the head is the first imaging modality employed, as it is easy to obtain, rapid, and can readily demonstrate the existence and extent of SAH, as well as associated cerebral edema or hydrocephalus (Fig. 76.1a) [33]. Further, the location of blood on CT may suggest the site of hemorrhage [34].

This imaging is best obtained within the first 24 h after ictus, as the sensitivity of CT to detect SAH declines rapidly after this period (76% after 24 h, roughly 50% after 5 days) [23]. Lumbar puncture (LP) should be performed if the initial CT is negative but high clinical suspicion for SAH persists, as CT may not demonstrate subarachnoid blood in nearly 3% of individuals with SAH [35]. Importantly, CSF obtained via LP should be centrifuged, and the supernatant evaluated for xanthochromia.

Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA) are potentially useful adjuncts for imaging of unruptured aneurysms, and may be attractive modalities for their avoidance of radiation exposure and contrast exposure (Fig. 76.1b–d). However, these studies have longer acquisition times than CT, and not all centers are able to obtain MRI or MRA sufficiently rapidly to warrant their use as the modality of choice in evaluation of suspected

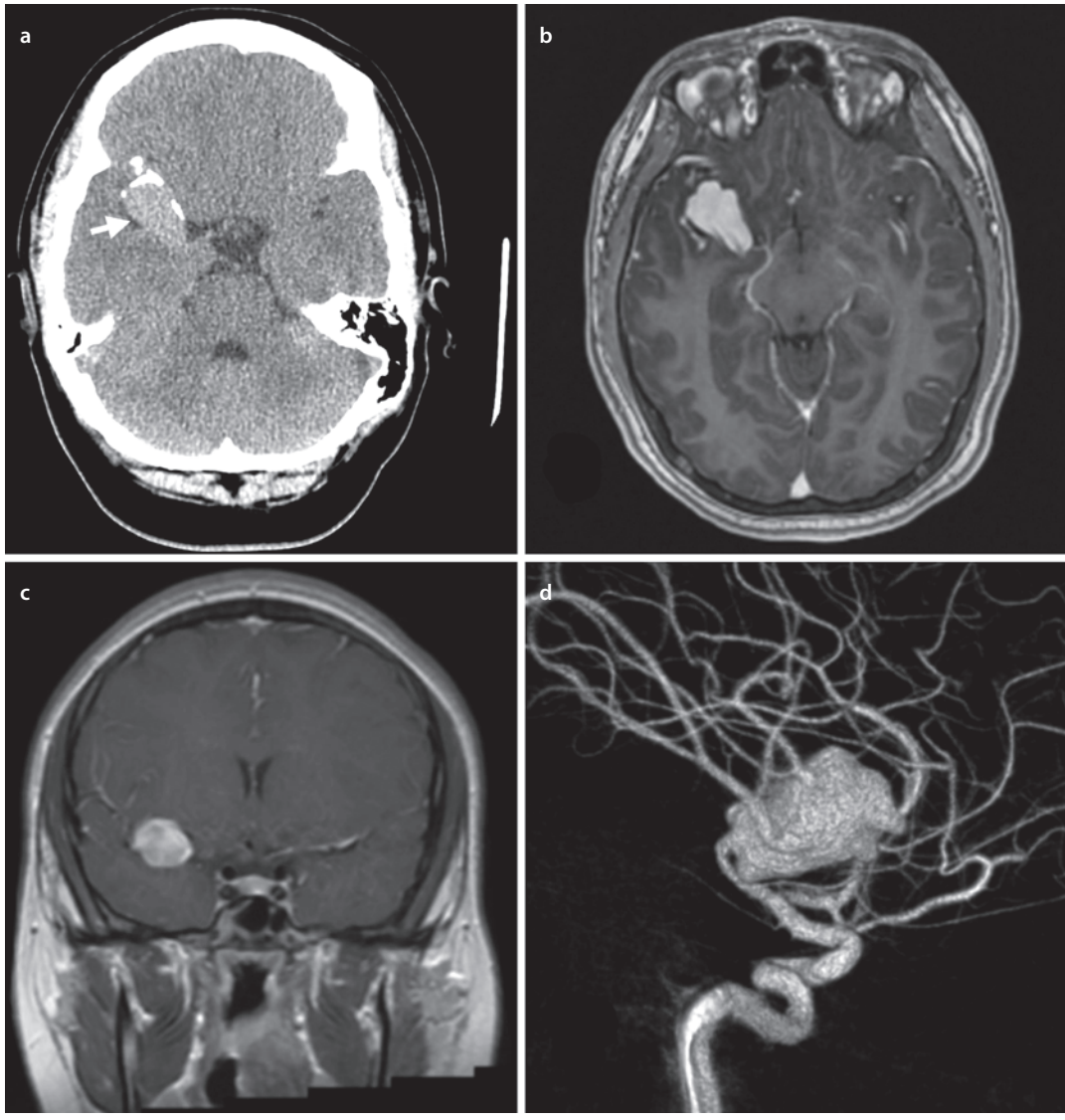

Fig. 76.1 A non-contrast head CT demonstrates a large fusiform aneurysm (*white arrow*) without evidence of subarachnoid haemorrhage. **a** The aneurysm is more clearly delineated in the T1 MRI with gadolinium in axial **b** and coronal **c** reconstructions. The MRA 3D reconstruction **d** demonstrates specific geometric details of the aneurysm

SAH. Additionally, the ability to detect small aneurysms with MRA may be limited [36].

Catheter angiography is indicated for the evaluation of aneurysms in children, and in experienced hands has a low risk and high sensitivity for detecting even small intracranial aneurysms [37, 38]. This modality has the additional advantage of permitting endovascular intervention at the time of diagnostic angiogram.

As is the case with adults, the choice of optimum treatment for pediatric aneurysms is highly dependent upon patient and aneurysm characteristics. Because these lesions are rare, data from adult aneurysm series often inform the approach to aneurysms in children, though the applicability of this data to the pediatric population is unclear. As discussed above, there are important differences between aneurysms in the pediatric population and those in adults. Furthermore, the young age of these patients raises important questions about the cumulative lifetime risk of rupture, as well as the durability of treatment.

For asymptomatic aneurysms at low risk of rupture, initial nonsurgical treatment with close follow-up and serial imaging is reasonable. Treatment options for symptomatic, high-risk, or ruptured aneurysms include microsurgical or endovascular treatment. Both techniques have benefits and risks that must be carefully weighed in each case. It is important to consider that these treatment techniques actually comprise several different therapies. Surgical interventions include direct clipping, aneurysm trapping, bypass, or some combination of these (Fig. 76.2). Endovascular treatments may include coiling, direct parent artery occlusion, stenting, flow diversion, or some combination of these. In some patients, a multimodal approach may be appropriate, with initial securing of a ruptured aneurysm by endovascular coiling, followed by subsequent surgical treatment [17, 31, 39].

Several series have investigated the role of endovascular aneurysm treatment in children. All are limited by small sample sizes, but nevertheless provide important data regarding the safety and durability of endovascular treatment in children. There are a variety of endovascular treatment methods employed, including coiling (with or without stent or balloon assistance), parent artery occlusion, and, more recently, flow diversion.

The largest series to compare surgical with endovascular treatment of pediatric aneurysms is that of Hetts et al. [4], a review of 27 years of experience treating pediatric aneurysms at the University of California San Francisco. There were 103 aneurysms in 77 patients, comprising a variety of morphologies and etiologies. Fifty-nine patients underwent treatment of their aneurysms, including endovascular coiling, parent vessel occlusion, surgical clipping, or revascularization.

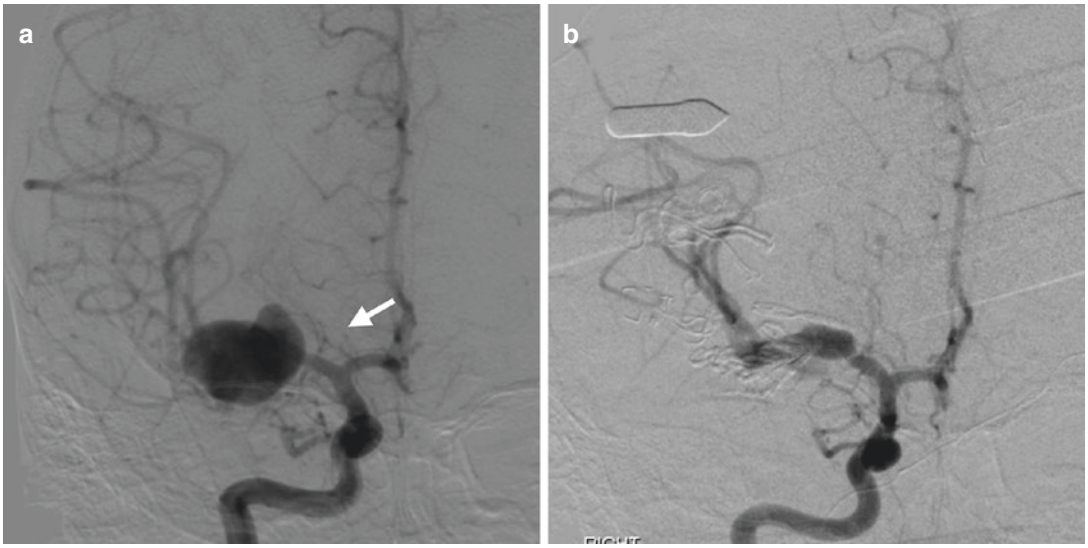

Fig. 76.2 Anteroposterior cerebral angiography of the patient in Fig. 76.1 demonstrates the aneurysm before **a** successful microsurgical aneurysmorrhaphy and vessel reconstruction with multiple clips **b**

There was low overall treatment-related morbidity and mortality for both surgical and endovascular interventions in this series; however, new ischemic stroke was observed at a higher rate with surgical treatment than endovascular treatment (14% vs. 7%, respectively). They noted a 21% retreatment rate over an average 2-year follow up among patients undergoing selective coil embolization, as well as a 10% crossover rate from coiling to surgical clipping. Importantly, this series includes 27 years of institutional experience, during which management techniques have evolved considerably.

Sanai et al. [18] reported a series of 43 aneurysms in 32 pediatric patients under 18 years of age. Thirteen patients underwent microsurgical treatment with complete obliteration in 94% in contrast to 82% in 16 patients treated endovascularly. Treatment-related neurological deficits were observed in 7.7% of patients undergoing surgery versus 6.3% of patients treated endovascularly. Recurrence was observed in 14% of aneurysms treated endovascularly, while no aneurysms treated microsurgically recurred. The superior efficacy and durability of microsurgical treatment led the authors to conclude that in most pediatric aneurysms amenable to either technique, surgery is preferable.

Stiefel et al. [31] reported on the results of treatment of 13 ruptured aneurysms in 12 pediatric patients. Surgery was employed in eight patients, while endovascular treatment was undertaken in five. The authors conclude that the two techniques were equivalent, and that either technique may be employed to treat ruptured aneurysms, though they recommend microsurgical clipping as the first-line treatment for all amenable aneurysms.

By contrast, Agid et al. [20] reviewed 37 aneurysms in 33 patients. Mortality was 11% in both microsurgical and endovascular groups, but significantly more patients experienced a good outcome in the endovascular group (77% vs. 44% in surgically-treated patients), and there was significantly less morbidity (23% vs. 44%). The authors therefore recommend endovascular treatment whenever possible.

Saraf et al. [40] reported the results of treatment of 23 pediatric patients with aneurysms of several types and morphologies, 14 of which were ruptured. A variety of endovascular techniques were employed, with 91% immediate post-procedural angiographic cure, favorable outcome in 96%, and stable aneurysmal occlusion in 96%. The authors conclude that endovascular management is a safe, effective, and durable treatment for aneurysms in children.

There are very limited data regarding the use of flow diverters in children; however, initial data is promising. A few small series have demonstrated that flow diversion may be a reasonable option in pediatric patients, with low procedure-related morbidity and good initial results [41–43]. In the authors' experience, flow diversion may be selectively used to treat aneurysms that are more difficult to treat by more traditional microsurgical or endovascular means (Fig. 76.3).

76.3 Arteriovenous Malformations

76.3.1 Description

Cerebral arteriovenous malformations (AVMs) are abnormal congenital connections between the arterial and venous circulations, without intervening capillaries. Thus, arteriovenous shunting occurs through the AVM nidus into arterialized draining veins. The prevalence of AVMs overall appears to be low, with one post-mortem angiography study demonstrating a prevalence of 0.06–0.11% [44, 45]. While these lesions are classically discovered between the ages of 20 and 40 years [46], they may also present in childhood, with hemorrhage, headaches, or seizures.

AVMs in the pediatric population are rare, composing only 3–20% of all AVMs, though they appear to be responsible for a disproportionate share of spontaneous intracranial hemorrhage in this population (as many as 50% of cases of spontaneous intracranial hemorrhage in children comprise AVMs) [47–50]. Accordingly, AVMs in childhood often present with hemorrhage (as many as 80% in one retrospective analysis). Furthermore, as an unruptured AVM is estimated to carry a 2–4% per year risk of rupture [46, 51, 52], the young age of these patients may be assumed to confer an increased cumulative risk of rupture [53]. The annual rate of rupture is similar in pediatric patients to their adult counterparts (2% vs. 2.2%) [54].

The majority of AVMs in older children and adults tend to be supratentorial and occur unilaterally [47], while infratentorial AVMs are more

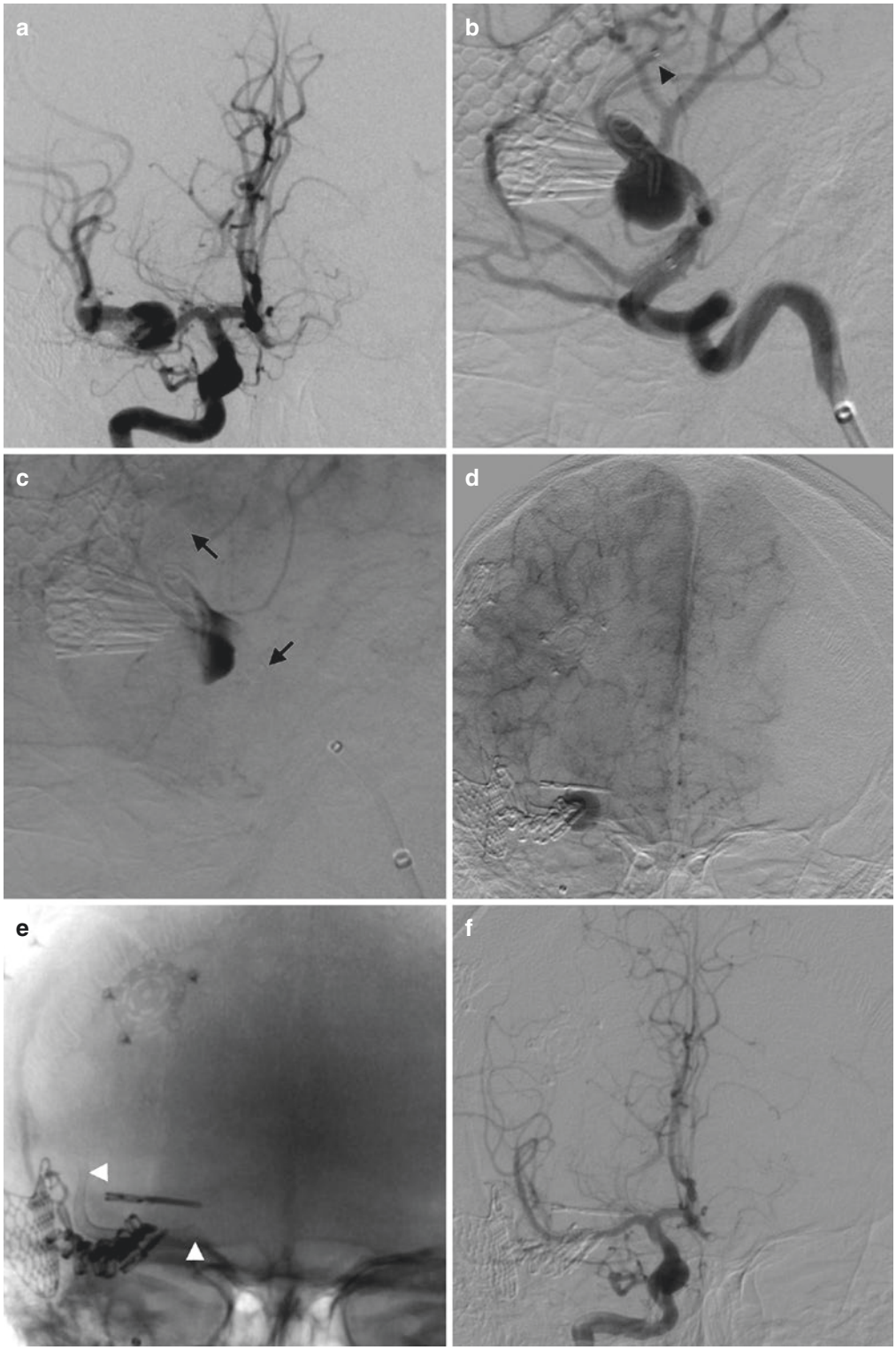

Fig. 76.3 Serial cerebral angiography of the patient seen in previous figures demonstrates regrowth of the aneurysm **a** and successful treatment with flow diversion **b**–**f**. Note the placement of the microcatheter distal to the aneurysm in the middle cerebral artery's superior division (*black arrowhead*), the stent spanning the length of the aneurysm (*black arrows*), and the final position of the stent in the unsubtracted view (*white arrowheads*)

common in younger children, infants, and neonates [55]. As deep (thalamic or basal ganglia) and infratentorial AVMs are at an increased likelihood of hemorrhage [56] or otherwise become symptomatic earlier, it should not be surprising, therefore, that these locations are more common for AVMs discovered in childhood [51].

Occasionally, AVMs present with symptoms other than hemorrhage. Headaches are occasionally the initial presenting symptom of cerebrovascular pathology, though distinguishing these headaches from other, more benign etiologies may be difficult on clinical grounds alone [57]. Epileptic seizures may arise from a focus adjacent to the AVM nidus. These events may often be focal, but can readily and rapidly generalize, thus making seizure type an unreliable clinical indicator of an AVM. The epileptogenicity of AVMs is supported by the fact that lesions involving the temporal lobe produce seizures roughly twice as often as those that do not [58]. Still other AVMs may produce intermittent ischemic symptoms via vascular steal [59].

76.3.2 Diagnosis and Treatment

As is the case with aneurysms, an unenhanced CT is often the first imaging modality used to evaluate patients with symptomatic AVMs. CT may demonstrate intralesional calcifications, hydrocephalus, or, in the case of rupture, intraparenchymal blood. In unstable patients, CT angiography is a rapid way to gain invaluable information regarding the vascular structure of an AVM. In stable patients, however, MRI/MRA reduces radiation and contrast exposure and can provide similar information, including the presence of blood or calcifications, as well as vascular architecture.

Catheter angiography remains an invaluable tool for confirming and evaluating AVMs [55]. A study that includes both internal and external carotid arteries, as well as both vertebral arteries, can effectively characterize AVM size, nidus location, feeding arteries, draining veins, and venous ectasia [60]. A repeat angiogram may be necessary if the initial study is negative, especially if a hematoma is present, as small AVMs may be obscured or compressed by hemorrhage [61, 62].

Treatment of AVMs is aimed at complete obliteration of the lesion, as the risk of rupture and rebleeding persists until that is achieved. This is a goal that may be accomplished through surgical resection, endovascular embolization, or radiosurgery, depending upon patient and lesion characteristics.

When feasible, microsurgical resection has traditionally been the gold standard for AVM treatment in children [63, 64]. This approach has the potential benefit of immediate and complete cure [65], as well as permitting evacuation of hematoma in cases of AVM rupture. In cases with favorable Spetzler-Martin grade (typically, Spetzler-Martin grades 1–3), surgical resection, either as a stand-alone treatment or as part of a multimodal treatment strategy, is associated with a high rate of angiographic obliteration (67–100%) and favorable outcome (81–95%) [50, 63, 65–67], and low associated mortality and morbidity [65, 68, 69].

With technological advances and increased experience with endovascular treatments, vascular embolization has become an increasingly important part of AVM treatment. The primary role of endovascular treatment of AVMs is preoperative embolization, as angiographic obliteration rates after embolization alone are historically low. Frizzel et al. [70] reviewed 1246 AVM cases and found complete obliteration after embolization in only 5%, though more recent series have demonstrated a significantly higher overall obliteration rate (Fig. 76.4) [71]. Additionally, recruitment of new vessels may lead to AVM recurrence in the absence of definitive obliteration [60].

As a pre-surgical adjunct endovascular embolization can be invaluable, and may not only reduce bleeding complications but can result in significant size reduction of large AVMs and enhance the durability of treatment (Fig. 76.5) [63, 65, 66, 71]. Bristol et al. [66] recommend the use of endovascular embolization as a preoperative adjunct for the treatment of all AVMs of grade II-V in children. There is variability among studies regarding the complication rate following embolization, with some series reporting complication rates near 7% [71, 72], and at least one series reporting a complication rate as high as 26% [73]. Kim et al. [74] reported a periprocedural morbidity and mortality rate of 11.8% in their series of 153 patients with AVMs, noting a direct correlation between morbidity and AVM grade.

Materials for embolization include polyvinyl alcohol particles, detachable balloons for

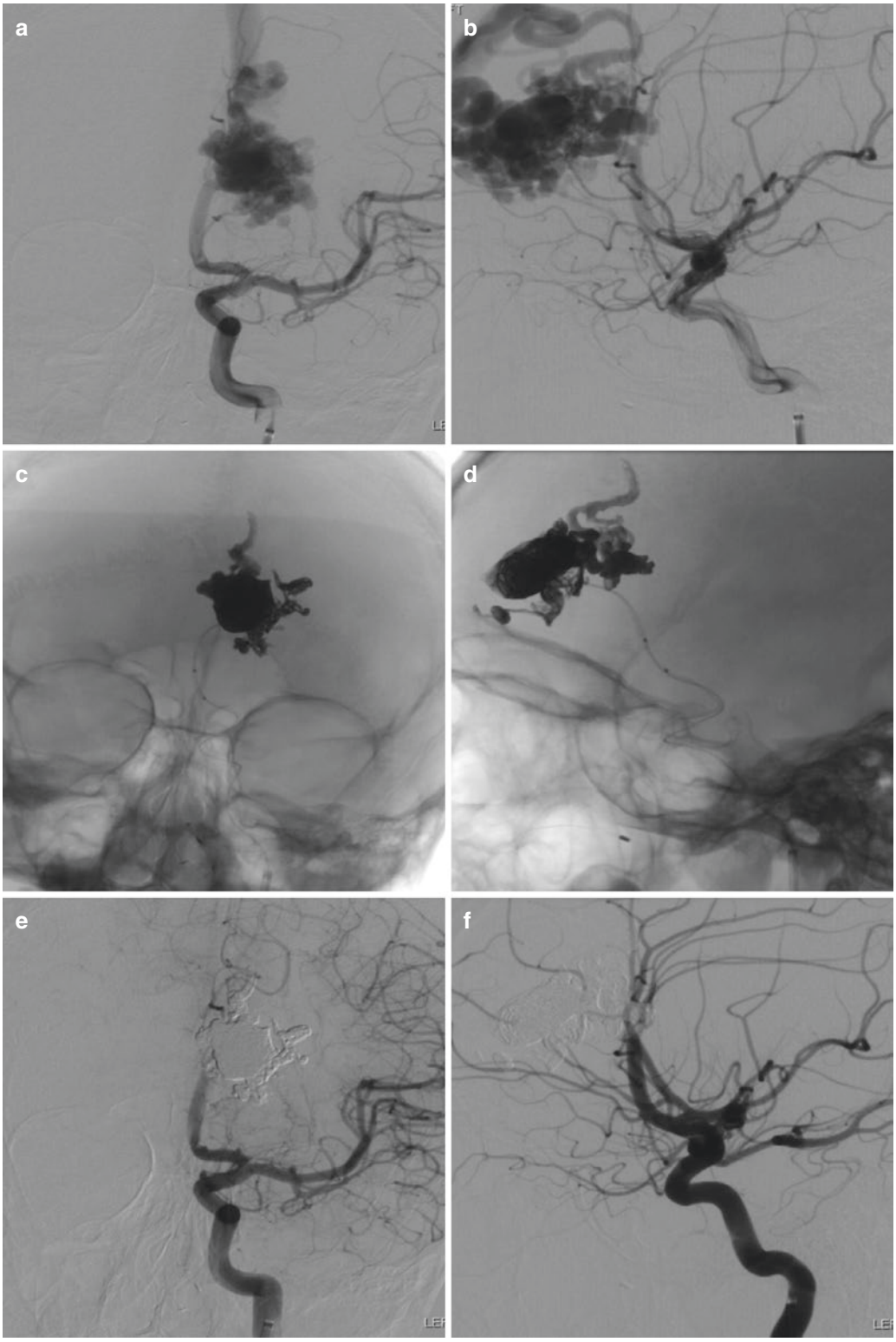

Fig. 76.4 Anteroposterior and lateral cerebral angiography **a**, **b** of a pediatric patient demonstrates a left frontal cerebral arteriovenous malformation (AVM) with contribution exclusively from the anterior cerebral artery. This AVM was treated entirely with intra-arterial embolic material **c**–**f**

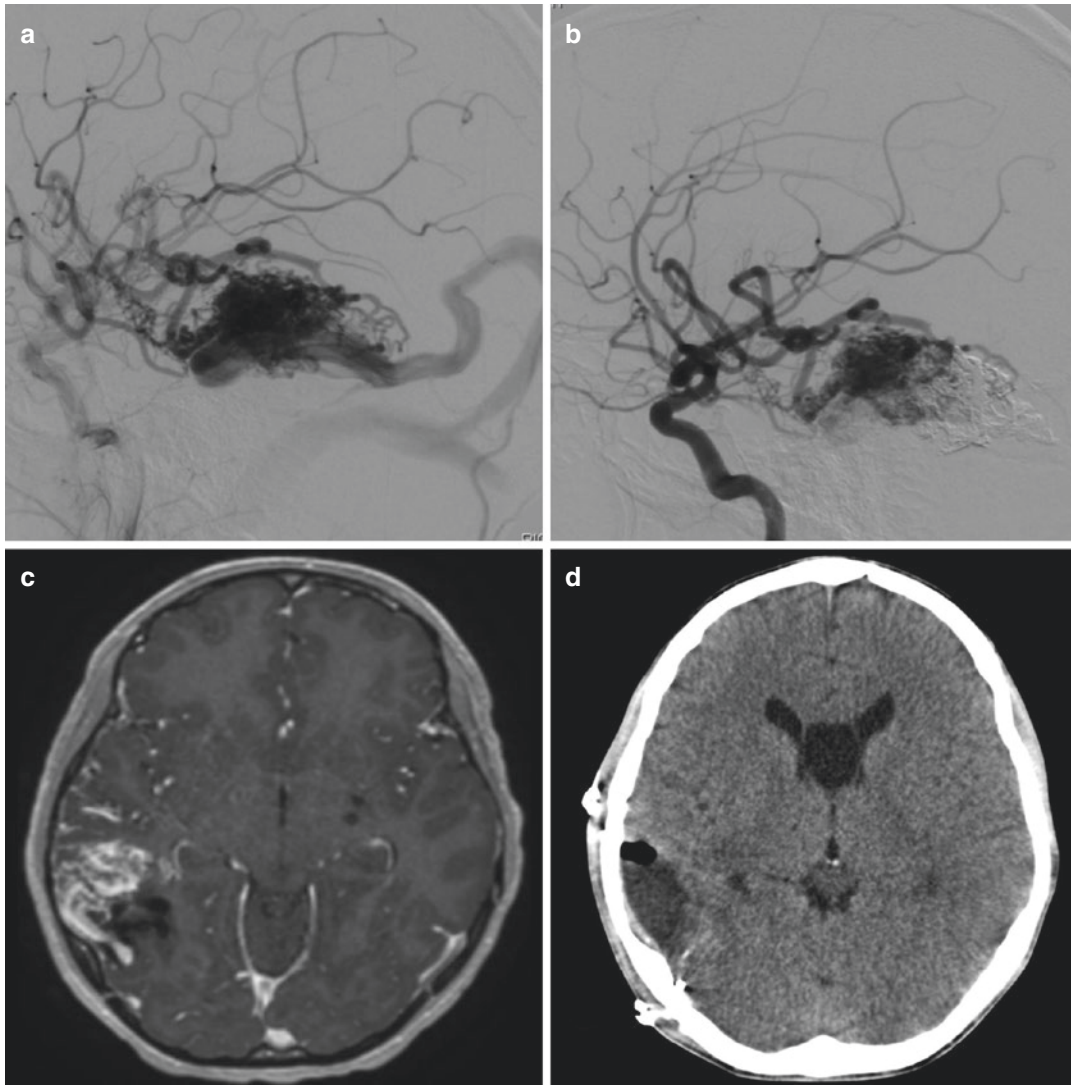

Fig. 76.5 Lateral cerebral angiography demonstrates the right temporal arteriovenous malformation (AVM) in this pediatric patient before **a** and after subtotal embolization with liquid embolic agent **b**. A T1 MRI with gadolinium **c** shows subtotal embolization of the AVM and a postoperative CT demonstrates complete resection **d**

large-vessel occlusion, coils, and liquid embolic agents such as TRUFILL (DuPuy Synthes) or Onyx (Covidien). The choice of appropriate agent is guided not only by characteristics of the lesion, including nidal size and depth, feeding vessel size, but also by provider preference and familiarity. Multiple staged embolization procedures may be required for especially large lesions.

Radiosurgery was added to the armamentarium for treating pediatric AVMs in 1989 by Altschuler et al. [75]. It is utilized for patients who are poor candidates for surgical resection or endovascular embolization (Fig. 76.6). While radiosurgery is associated with reasonably good obliteration rates and low complication rates [76–79], the long-term clinical outcomes in children after exposure to ionizing radiation are not well described and await longer follow-up.

76.4 Vein of Galen Malformations

76.4.1 Description

A specific kind of arteriovenous malformation that presents in infants and neonates deserves

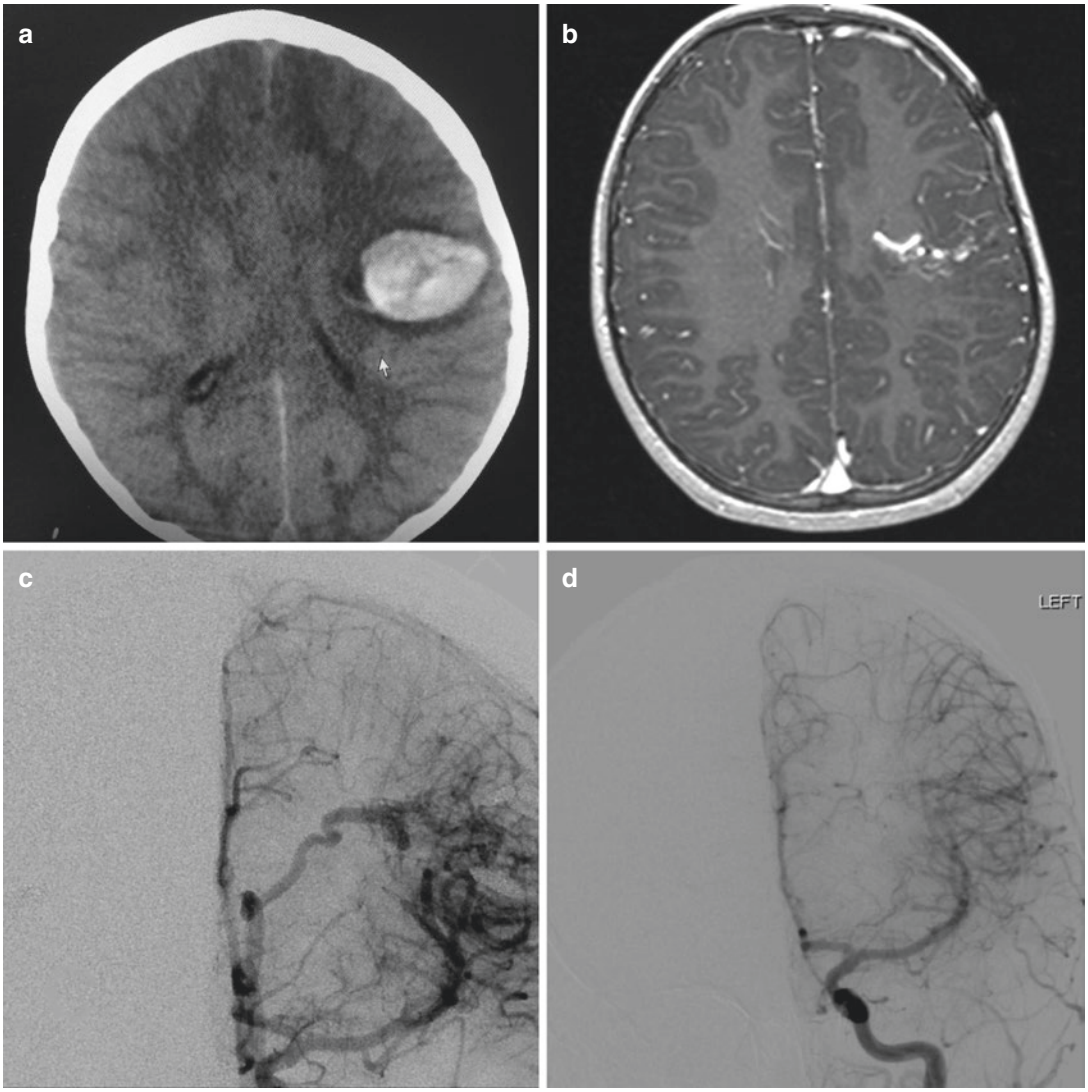

Fig. 76.6 This 6 year-old female presents with right hemiplegia and found to have an intracranial hemorrhage on CT (**a**). One year after the hemorrhage the patient underwent stereotactic radiosurgery for this arteriovenous malformation (AVM) demonstrated on T1 MRI with gadolinium **b** and cerebral angiography **c**. An angiogram performed 2 years later demonstrates complete resolution of the AVM **d**

special attention. The so-called vein of Galen aneurysmal malformation (VGAM) is a misnomer; this name actually refers to multiple arteriovenous shunts from the choroidal system draining into an embryonic forerunner of the great vein of Galen, the median prosencephalic vein of Markowski [80]. Despite representing 1% of all intracranial vascular lesions overall, they represent between 30% and 50% of vascular malformations in the pediatric patient population [80–83]. These lesions may produce a variety of symptoms and signs including heart failure.

Normally, the anterior portion of the median prosencephalic vein involutes and gives way to the vein of Galen as the developing cortical arterial system replaces the choroidal arteries. The low-flow post-capillary blood from the cortical arterial system drains into the developing internal cerebral veins, which in turn drain into the prosencephalic vein. In patients with VGAM, the choroidal arteries continue to drain directly into the prosencephalic vein without an intervening capillary bed, producing high-flow arteriovenous shunting that leads to persistence and progressive

aneurysmal dilation of the anterior portion of the median prosencephalic vein [80, 84, 85].

VGAMs are broadly divided into two general subcategories based on their angioarchitecture: The choroidal type, in which multiple bilateral choroidal arteries form a high-flow nidus anterior to a dilated draining vein, and the mural type, in which a small number of feeding vessels converge directly on the venous sac [86]. There is some evidence to suggest that the higher flow of choroidal type VGAMs results in earlier and more severe clinical presentation [86, 87]; however, not all studies have found a correlation between VGAM angioarchitecture and long-term clinical outcome [88].

The clinical presentation of VGAMs is variable. Neonates are more likely to present with high-output cardiac failure, while older infants and children more often will develop hydrocephalus and developmental delay, venous congestion, and infarction or hemorrhage [80, 81, 89]. Cardiac failure was the most common presentation reported by Heuer et al. [90] in their review of 13 patients with VGAM, and patients were frequently diagnosed within the first 2 weeks of life. Hydrocephalus may be attributable to aqueductal compression by the dilated venous pouch, or to impaired cerebrospinal fluid (CSF) reabsorption resulting from elevated venous pressure [91]. Ischemic infarct may occur as a result of arterial steal [92].

76.4.2 Diagnosis and Treatment

Today, patients with VGAM are commonly diagnosed in utero, either by fetal ultrasound or fetal MRI [93–95], although prenatal ultrasound detection of VGAM is typically not made until the third trimester, when venous sac dilation is sufficient to permit discovery [88]. Head ultrasound may reveal the VGAM in neonates, though MRI and MRA have become the primary imaging modality for evaluating these lesions [96, 97], as it obviates the need for radiation exposure, and provides detailed information regarding the angioarchitecture and flow of the malformation. It can also reliably demonstrate thrombosis, tissue ischemia, and inflammation, as well as indicators of derangements in CSF reabsorption.

Presently, VGAMs are almost always treated endovascularly, with the urgency of treatment and short-term goals of therapy guided by the patient's clinical status and presenting symptoms [82, 86, 98–101]. Long term, the goal of treatment is ultimately to obliterate the fistulae and preserve and permit neurological function and development. The immediate goals of treatment, however, are more dependent upon the nature and severity of symptoms, as well as the angioarchitecture of the lesion. Patients with choroidal-type VGAMs, for example, may require several treatments to address the multiple fistulae, with the goal to gradually reduce the magnitude of shunting and alleviate heart failure (Fig. 76.7). Overly aggres-

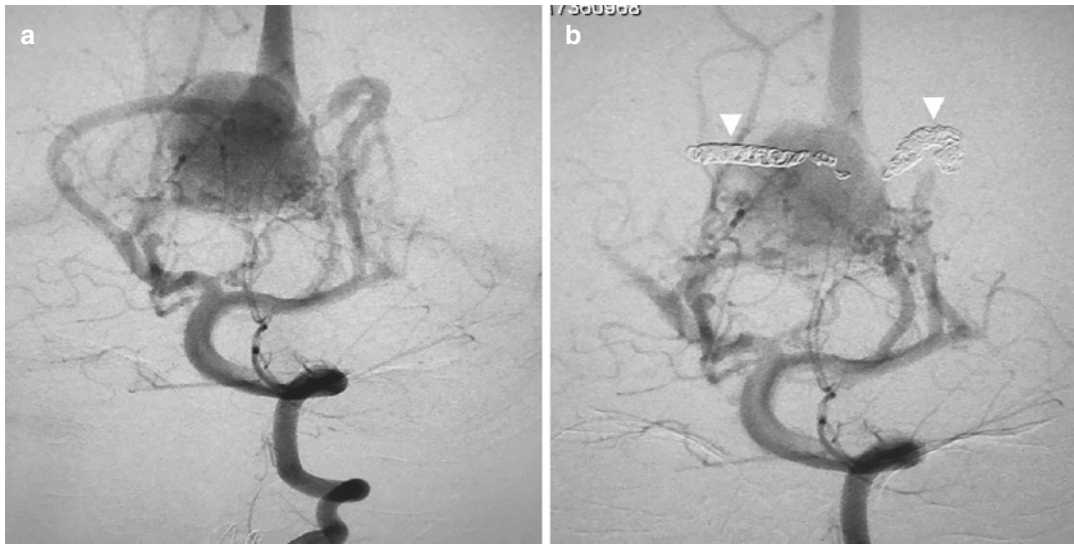

Fig. 76.7 An infant presented with heart failure and failure to thrive. The vein of Galen aneurysmal malformation was diagnosed **a**. Reduction of flow was performed until the patient did not require cardiotropic medications with subtotal embolization of arterial feeders with embolic coils (**b**, *white arrowheads*)

sive embolization should be avoided, as this can precipitate hemorrhage or, paradoxically, worsening heart failure from abruptly increased afterload [102]. Patients with mural-type VGAMs, on the other hand, may require fewer treatments, and the reduced incidence of acute cardiac complications permits delaying intervention until a later age.

Outcomes of endovascular treatment are generally good, with good outcome reported in up to 68% of patients [92]. It is important to remember, however, that case series with a younger median age will tend to have a greater proportion of patients presenting with heart failure requiring emergent treatment, while series with an older median age contain more stable patients, in whom treatment may be delayed for several months. Provided the symptoms of heart failure can be controlled with endovascular embolization of the VGAM, mortality among treated patients is relatively low. Yan et al. [92] reviewed 34 case series spanning over three decades of experience with endovascular treatment of VGAMs, and found an overall mortality rate of 16% among treated patients, despite neonates, many of whom with heart failure, making up 44% of the patient population. Other series have reported a significantly higher mortality among treated neonates with medically intractable heart failure, as high as 62%. Virtually all case series report significantly improved mortality in treated patients relative to untreated patients [82, 86, 90, 98, 99, 101, 103, 104].

As with other AVMs, there exist a number of embolic agents suitable for use in treating VGAMs, including liquid embolic agents such as TRUFILL (DePuy Synthes) or Onyx (Covidien), coils, or polyvinyl alcohol. The choice of agent should be guided by fistula angioarchitecture and provider experience and preference. Often, multiple agents are required to adequately treat the lesion. Simultaneous transvenous access permits torcular access of the lesion [80, 102, 105]. Risks of embolization are largely dependent upon the angioarchitecture of the lesion, and include hemorrhage, stroke, or death from large hemodynamic changes. Care must be taken to embolize sufficiently distally toward the arteriovenous communication, as overly proximal occlusion permits continued flow through collaterals, potentially resulting in persistence or recurrence of the VGAM, or even further dilation of the venous sac. Treatments should continue until obliteration is achieved, as incomplete embolization, while often resulting in reduction in lesion size in the short term, invariably ultimately results in VGAM recurrence [102].

76.5 Ischemic Stroke

76.5.1 Description

Stroke is rare in children (1.3–13 cases per 100,000 children under 18 years of age) [106–110], but is associated with considerable mortality and long-term morbidity, as well as potentially devastating familial and economic costs [107, 111, 112]. Up to 25% of children suffering a stroke will die, and survivors often have persistent deficits, seizures, learning disorders, or developmental problems, and 1.2–19% of patients may suffer stroke recurrence [111, 113]. From a cost perspective, the estimated cost of pediatric stroke in the USA in 2003 alone was $42 million [114].

Approximately half of all strokes in children are ischemic, which is in stark contrast with adults, in whom 87% are ischemic [110]. The risk factors associated with stroke in pediatric patients appear to be distinct from those in adults, as traditional stroke risk factors in adults, such as hypertension, hyperlipidemia, atherosclerosis, diabetes, or smoking, are rare in children. Moreover, the risk factors associated with stroke in children tend to change with age [115].

Arterial ischemic stroke (AIS) in pediatric patients may be classified as either perinatal (≤28 days of life, including stroke occurring during the prenatal period) or occurring in childhood (>28 days of life), and there are clear differences in the pathogenesis of AIS between (and within) these periods [110].

Perinatal strokes occur in 29 out of every 100,000 live births [19], and are independently associated with maternal risk factors including infertility history, pre-eclampsia, prolonged rupture of membranes, and chorioamnionitis [116], although maternal health is normal in the majority of cases [117]. Childhood strokes, by contrast, are most commonly associated with arteriopathy, especially in children aged 5–9 years, but is also associated with congenital heart defects, systemic infections, hematologic disorders, and sickle cell disease [115, 118, 119]. Head and neck trauma and infection are also independent risk factors for

pediatric AIS [120]. While not as important as a risk factor in the USA, sickle cell disease is likely a major cause of childhood AIS worldwide, as 10% of sickle cell patients studied have a symptomatic stroke by age 20 years, while another 20% may have an asymptomatic so-called «silent stroke» by that age [121, 122].

76.5.2 Diagnosis and Treatment

Non-contrast head CT, as discussed above, is a readily available, inexpensive, and rapid imaging modality for the evaluation of patients who experience an acute neurological decline. CT can reliably detect intracranial hemorrhage, differentiating AIS from hemorrhagic strokes more likely to be associated with the lesions discussed above. Infarcts may appear as regions of low density on a non-contrast CT, though the ability to detect ischemic stroke is limited within the first 12 h postictus. MRI, while more expensive and requiring longer acquisition times, is much more sensitive for early detection of acute infarct [123, 124].

There is no consensus regarding the optimal therapy for pediatric AIS. Beyond supportive therapy, which should be initiated in all cases of pediatric stroke, AIS or otherwise, there is some evidence for the efficacy and safety of anticoagulation in preventing stroke recurrence, especially in those patients with arteriopathy or hypercoagulable conditions, which may increase their risk of stroke recurrence [125–127]. The efficacy and safety of thrombolytic therapy in the pediatric population is not known, and aside from some utility in cases of venous sinus thrombosis, what data there are are extraordinarily limited, the benefits unclear, and there is therefore insufficient evidence to recommend its use in children [125, 128–131]. The Thrombolysis in Pediatric Stroke (TIPS) study by Rivkin et al. [132] sought to evaluate the safety and efficacy of thrombolytic therapy in children presenting with acute AIS, but was unable to recruit a sufficient number of patients meeting the inclusion criteria.

To date, there are no controlled clinical trials to guide the use of endovascular treatment of AIS in pediatric patients, though there exist several case reports of intra-arterial thrombolysis and mechanical thrombectomy in cases of pediatric AIS with large vessel occlusion (Fig. 76.8). A review of 34 cases of AIS by Ellis et al. [133] found that while intra-arterial thrombolysis alone resulted in a hemorrhage rate of 30.4%, mechanical thrombectomy as the sole procedure resulted in a hemorrhage rate of 9.1%, leading the authors to recommend mechanical thrombectomy over

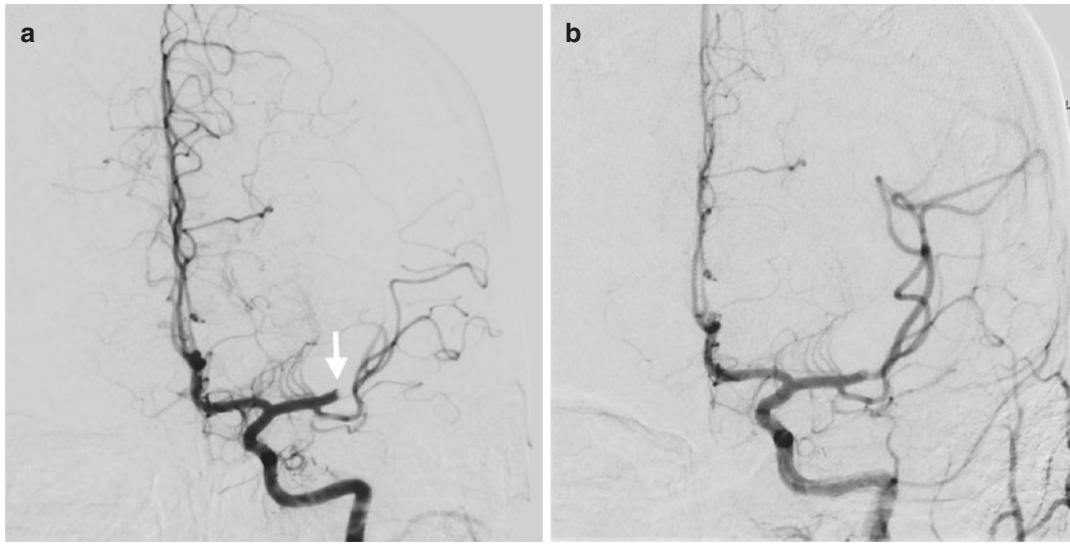

Fig. 76.8 A 16-year-old female with history of congenital cardiac abnormalities presented with right hemiplegia and aphasia. AP cerebral angiography confirms the suspected large vessel occlusion (**a**, *white arrow*) and shows subsequent return of flow after revascularization with a mechanical thrombectomy device **b**. She is now neurologically intact

intra-arterial injection of thrombolytics. A more recent review by Satti et al. [134] of 29 cases of pediatric AIS with proximal large-vessel occlusion in which mechanical thrombectomy was employed found recanalization in over 75%, with no procedure-related adverse events. It is important to note that there are no endovascular mechanical thrombolytic devices specifically tested or approved for use in children.

76.6 Special Considerations

While the entire breadth of technical differences in performing neuroendovascular procedures on pediatric patients, as opposed to their adult counterparts, cannot be fully covered by this chapter, there remain some key points to discuss when approaching the pediatric patient. First, for patients younger than 2 years old, a 4 French sheath and diagnostic catheter is used in diagnostic angiograms. Moreover, we have a low threshold to use ultrasound guidance to access the femoral artery, something not routinely done in adults. Iodinated contrast is kept to the minimum necessary amount, that is, we attempt to keep the contrast limitations to 3 ml/kg. For smaller patients, this may be challenging, so the authors often dilute contrast to 50% for most injections. In addition, contrast within the dead-space of the catheter is aspirated after the angiographic run. For patients with a history of moderate-to-severe contrast allergy, a weight-based protocol may be used similar to those used in adults, which involves prednisone 0.5–0.7 mg/kg dosed at 13, 7, and 1 h prior to the procedure and diphenhydramine 1.25 mg/kg dosed 1 h prior to the procedure. Because of the variability in weight, heparinized drips are not typically used on pediatric patients. Rather, the patients are systemically anticoagulated with heparin dosed 70 u/kg.

76.7 Summary

Cerebrovascular disease is rare in pediatric patients, but its effects may be significant, not only for the patients themselves, but for their families and caregivers. While most practitioners may see these conditions rarely outside of specialized tertiary care centers, it is nevertheless important to gain an understanding of the epidemiology, pathophysiology, and natural history of these lesions, as their effective, safe treatment depends upon this knowledge. Durability of treatment is an important consideration, given the longer expected lifespan of these patients and the attendant concerns regarding recurrence. Lastly, all treatment decisions should be individualized depending upon patient characteristics.

There is still considerable discussion regarding the best treatment approach for cerebrovascular diseases in children; existing data are limited by the rarity of the lesions in question, and the long time periods over which researchers seek to accumulate a sufficient number of patients means that outcome data may be affected by advances in technology, improvements in technique, and changes in institutional practices. Nevertheless, endovascular approaches are an increasingly important set of tools in the treatment of pediatric cerebrovascular disease, and future research will continue to refine their role in the years to come.

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