Case Report

Brain Arterio-Venous Malformation in Children. Always a Late Diagnosis

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Abstract

Brain arteriovenous malformations (AVMs) in the pediatric population is a relatively rare occurrence representing 3% of all AVMs though the frequency of rupture is greater than in adult population. Most of the cases described in the literature have been diagnosed after rupture of the malformation and the onset of neurological symptoms. Computed tomography (CT) is often performed on patients but the malformation can sometimes go undetected in the imaging. Conventional cerebral angiography remains the gold standard for the diagnosis of AVMs. The risk of rupture and re-rupture from an AVM persists until the AVM is completely obliterated. Thus, the cornerstone of AVM treatment is to achieve complete angiographic obliteration with minimal neurological sequelae. The options available for AVM management in children have widely increased. Endovascular embolization is possible in pediatric AVMs with the potential for complete obliteration in small AVMs or, as an effective adjunctive therapy with micro or radiosurgery in larger AVMs.

Both cases presented are examples of where the AVM diagnosis was established following the rupture of the malformation. In one of the cases, the CT and angio-CT did not identify the AVM. In both cases, the AVM was clearly identifiable after angiography and treatable with endovascular embolization. We summarize the different treatment strategies as optimal management for pediatric AVMs remains controversial.

ABBREVIATIONS

AVM: Arterio-Venous Malformation; AV: Arterio-Venous; GCS: Glasgow Coma Scale; ICP: Intracranial Pressure; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; PICU: Pediatric Intensive Care Unit; MDT: Multidisciplinary Team; EVD: External Ventricular Drainage; MAP: Mean Arterial Pressure; ICH: Intracranial Hemorrhage; IVH: Intraventricular Hemorrhage; DC: Decompressive Craniectomy

INTRODUCTION

Arterio-venous malformations (AVMs) are lesions that are defined by the presence of arteriovenous (AV) shunting through a nidus of coiled and tortuous vascular connections that connect feeding arteries to draining veins [1,2]. The direct AV shunting due to the lack of capillaries between the feeding arterial and draining venous components of AVMs leads to hypertrophy in the arterial and venous components of the AVMs. The embryological basis of AVMs is due to either the persistence of a primitive AV connection or the development of a new connection after a normal closure process. Even though the precise pathophysiologic events by which such malformations form are unknown, it is hypothesized that most malformations occur during the third week of embryogenesis [2,3].

The natural history of AVMs in children is not well studied or understood; in part this might be due to the initial emergent therapy of these lesions [2].

AVMs are rare in the pediatric population, estimated to represent 3% of all AVMs [4-6] although, they tend to rupture more frequently than in adults [1,4,6-11].

AVMs are considered the most frequent abnormality of intracranial circulation in childhood [12], and they are the most common cause of spontaneous intraparenchymal hemorrhage in children. The annual hemorrhage rate has been reported to be between 2 and 10% [13-17].

The re-rupture rate is estimated to be 2 – 4% with a mortality rate up to 25% per each event; this risk is higher in the first 5 years after diagnosis [4,16,18]. The risk of rupture is conflicting related to the AVM size [16,17] but also to other risk factors as previous history of hemorrhage, deep-seated or infratentorial AVMs, deep venous drainage, female sex, associated aneurysms, and diffuse AVM morphology [16,17,19].

Examined below are the cases of two pediatric patients with intracranial bleeding following a rupture of the AVM with a description of the subsequent treatment used. Because of the AVM’s characteristics, and the center’s experience, the treatment adopted in both cases was the endovascular embolization of the malformation. Both cases exemplify the success of this particular method of treatment in selected AVMs. [20].

Endovascular embolization is often performed before surgery to reduce the AVM size and risk of operative bleeding. The advantage of this treatment is that it is less invasive than surgery and can be used to treat deep or inoperable AVMs. Disadvantages include the risk of embolic stroke from the catheter and re-bleeding [21] because the AVM is not completely obliterated. Multiple treatments may be necessary [22].

Additionally, we have examined the most frequent treatments found in the literature as optimal management for pediatric AVMs remains controversial.

**CASE PRESENTATION**

**Case 1**

12-year-old male patient without previous medical history suffered a sharp cephalica at home accompanied with irrepressible vomiting and a subsequent episode of irritability and loss of consciousness. Upon arrival of the emergency services, he had a Glasgow Coma Scale [GCS] of 7 and was therefore intubated and transferred to the reference hospital. At the hospital, a cranial CT (Figure 1) was done, which revealed a tetra-ventricular hemorrhage with secondary obstructive hydrocephalus and left parietal intraparenchymal hematoma. This was consistent with findings of vascular malformation, most likely an arteriovenous shunt. A cerebral angiography for diagnosis and therapy was then carried out which confirmed the appearance of a pial plexiform AVM with an anterior and posterior pericallosal component (Figure 2). Following MDT discussion between the neuro-radiologists and neurosurgeons, the decision was made to proceed with embolization of the malformation. The embolization with Glubran 2 acrylic resulted in the complete occlusion of the posterior compartment. There was evidence of Control cranial CT without re-bleeding. The patient was then admitted to the Pediatric Intensive Care Unit [PICU] with external ventricular drainage [EVD] and Intracranial Pressure [ICP] monitoring throughout. He then suffered episodes of increased ICP due to catheter’s obstruction as a result of blood clots. The patient required intraventricular fibrinolytic therapy to remove clots during obstruction episodes with late recovery and normalization of ICP. An optic nerve sheath ultrasound upon admission revealed pathological values (Figure 3). ICPs were kept at normal values during admission with regular intensive treatment [sedation and relaxation, hyperosmolar treatment, relative hypernatremia and noradrenaline used to regulate MAP]. Good clinical progress with serial CTs showing decreased intraventricular bleeding. Intensive treatment continued for 8 days and the ICP monitoring ceased upon satisfactory extubation of the patient. Prior to extubation, an MRI was carried out revealing persistent parasagittal and an intraventricular hematoma with less bleeding and associated right occipital stroke.

The patient was discharged after 14 days admission conscious and oriented with: attention problems and management function problems, pragmatics language alteration and prosody, normal cranial nerves, homonymous hemianopia, reduced strength in lower limbs [4/5] and left upper limb [3/5], global increased muscular tone but asymmetric with left predominance, hyperreflexia, stiffness and intentional shaking and postural in left forearm and left hand, independent walking with advanced...
shaft and inclination to forefoot support, normal sensibility, negative Romberg.

The arteriography prior to discharge (Figure 4) showed that in the posterior embolized malformative pericallosal nidus, there was a small recanalization from the right perforated pericallosal branch with venous drainage continuing to the internal cerebral vein and straight sinus.

Case 2

14-year-old male awakens in the morning with sharp cephaliea. This is followed by a convulsive episode with complex and generalized crisis beginning with tonic movement of the right upper limb and claw hand, progressing through the left half with general disconnection and ocular deviation to the right side. The patient has a previous medical history of partial atresia of the right naris following an examination 3 weeks prior. The patient’s older brother died 9 years ago having suffered acute myeloblastic leukemia. Upon arrival of the emergency services, the patient had GCS of 6, generalized hypotonicity and reactive and unequal pupils with right mydriasis. He was sedated and intubated at home before being transferred to the reference hospital. Upon arrival, cranial CT (Figure 5) showed acute intraparenchymal hemorrhage of 1.5 cm diameter with discrete peripheral vasogenic edema at left parahipocampal level with exit at lateral ventricles with dilatation of the posterior horn of the left lateral ventricle, III and IV ventricles. There was discrete uncal herniation and hypodensity of the brainstem. On the angio-CT there was no clear underlying aneurysm or extravasation through the intravenous contrast or pathological enhancement, even if there was no dismiss of vascular lesion that could be compressed by the hematoma.

Following neuroimaging, the patient was transferred to the vascular interventionist neuroradiology department, where the arteriography was carried out (Figure 6) revealing a small left ventricular AVM receiving arterial flow through the left posterolateral choroidal artery. Due to its characteristics, embolization is decided to be done with Glubran 2 acrylic glue and the malformation is completely occluded. During the procedure, the patient exhibited signs of intracranial hypertension which presents a risk of immediate death, so a right parieto-temporal decompressive craniectomy was carried out and a ventricular drainage was settled. The patient was admitted to PICU with ventricular drainage with continuous monitoring of the ICP. There was evidence of sporadic obstruction of the ventricular drainage due to clots so intraventricular fibrinolytic therapy was necessary. The optic nerve sheath ultrasound showed pathological numbers upon admission [optic nerve sheath diameter of 0.61 cm]. ICPs were kept at physiological level with regular intensive treatment. Extubated was carried out after one week of admission, followed by drain removal after 14 days. Later neuroimaging control by sonography of the area where craniectomy was performed did not show signs of hydrocephalus. Upon discharge, patient was perplexed by alteration of all upper cortical functions. GCS 10-11. Symptoms included: equal pupils and responsive with light reflex, consensual and normal accommodation, look straight slightly dissimilar asymmetrical tetraparesis with left predominance and especially upper limbs, left more damaged, augmented tone in distal area of the upper limbs with thumb included in palm.
and lower limbs, deep elated muscular reflex and increase of the reflexogenic area, ankle clonus, cutaneous plantar reflex bilateral extensor, no abnormal posture or movements, normal breathing pattern.

The control angio-MRI after 15 days being discharged showed no arterio-venous malformations rests but showed signs of ischemic residual areas (Figure 7,8).

**DISCUSSION**

AVMs are usually diagnosed after their rupture as exemplified in our cases. Computed tomography is often performed to evaluate the location and size of the hematoma. Magnetic resonance imaging (MRI) along with magnetic resonance angiography is crucial for better AVM localization and therapy planning. Conventional cerebral angiography, including external carotid artery angiogram, is still the gold standard for the diagnosis of AVMs [2].

In these instances, the angiography was performed upon admission of the patient. In the first case, the CT and angio-CT was conclusive for the diagnosis of AVM. In the second case however, it was not until the angiography was performed that the diagnosis was established. In both cases the angiography identified the AVM size, location, feeding vessels, drainage veins and location of the nidus. It was also deemed to be therapeutic due to its embolization in the same process.

Following MDT discussion, it was decided that the endovascular embolization would be the therapeutic option in both cases. Radiosurgery could have been considered as a further option. The endovascular embolization was chosen due to its capacity to completely obliterate the AVMs presented or as an effective therapy with posterior micro or radiosurgery.

The risk of rupture and re-rupture from an AVM persists until the AVM is completely obliterated. Thus, the cornerstone of AVM treatment is to achieve complete angiographic obliteration with minimal neurological sequelae. In our case, the first patient was discharged with a residual persistent small arteriovenous shunt. The risk of re-rupture was carefully considered and the decision of re-intervention [embolization or radiosurgery] was upheld but with additional controls given the substantial risk of re-bleeding in the future [23].

The Optic nerve ultrasound showed its utility as a non-invasive way to measure the ICP [24-26]. The threshold of the optic nerve sheath diameter beyond which it is considered pathological is poorly defined. Most of the studies considered pathological to be a threshold of more than 4.5 mm in the pediatric population [24, 27-29]. Both of our cases measured higher than this figure.

Placement of an ICP monitor provides the clinician with the ability to dynamically monitor cerebral perfusion pressure. The AHA recommends [30] the practice of ICP monitoring for patients with the following: a GCS of less than 8, clinical evidence of transtentorial herniation or significant intraventricular hemorrhage or hydrocephalus. In both cases, the ICP monitoring was performed through the EVD and was able to relieve elevated ICP [30,31].

It remains unclear whether decompressive craniectomy [DC] improves the functional outcome in patients with intracranial bleeding and refractory raised intracranial pressure. The recent DECRa study [32] revealed that decompressive craniectomy decreased intracranial pressure and reduced the length of time patients with traumatic brain injuries spent in ICU, though it was associated with more unfavorable outcomes. DC in patients with IVH is considered to be controversial [33]. Further investigations, including a prospective randomized trial, are needed to confirm the safety and efficacy of DC for the treatment of large AVM-ICH.

In one of the cases, the decompressive craniectomy was necessary due to the ineffectiveness of medical treatment to decrease ICP and the substantial risk of death in such a circumstance.

Extension of intracranial hemorrhage [ICH] into the ventricles or intraventricular hemorrhage [IVH] has been consistently demonstrated as an independent predictor of a poor outcome [34]. Such patients [34,35] should be considered a priority for treatment to avoid re-bleeding.

For patients with intraventricular hemorrhage, several investigators have examined whether infusion of thrombolytic agents directly into the ventricles can provide benefit [36]. By accelerating the time to breakup of the clot, the risk of obstructive hydrocephalus can be minimized, and perhaps intracranial pressure can be reduced. An EVD is placed, and thrombolytics are infused at specific time intervals. Animal studies initially demonstrated the value of this approach in minimizing the risk of hydrocephalus [37]. In humans, some studies have suggested improved secondary outcomes, including an observational
cohort study [38] and a small randomized controlled trial [39] in which intraventricular infusion of thrombolitics led to more rapid resolution of intraventricular blood. More recently, the CLEAR III study [31,40] showed reduced mortality rates in the IVH treatment by intraventricular fibrinolysis.

In both these cases, intraventricular fibrinolytic was necessary to avoid clots in the drainage and allow for its permeability.

The available options for AVM management in children have grown rapidly with technological advances in microsurgical resection and radiosurgery with or without endovascular embolization. The risks and benefits of each of these treatments are not completely understood. We present a literature review of different approaches to treat pediatric AVMs:

**Conservative management**

Not common in kids due to their longer expectancy compared to adults and the higher risk of AVM rupture. Also, the pediatric nervous system has more capacity to retain its functions after injury. The more aggressive management approach is therefore essential in this age group.

**Surgical resection**

The complete surgical resection remains the gold standard of AVM treatment if it is feasible with a minimal rate of morbidity. Rapid advances in microsurgical technology made this mode of treatment the fastest and most complete method in achieving complete obliteration [5,7]. In acute ruptured settings surgery has the advantage of hematoma removal. Surgical resection has been advocated, as a single modality or as part of multimodality approach with radiosurgery or embolization. Complete obliteration after surgical approach varies between studies from 67% to 100% [7,8,13,41]. Postoperative complications such as hemorrhage, hyperperfusion, edema, seizures, vasospasm, vascular thrombosis and stroke could be observed, and patients should be closely monitored to avoid any delay of immediate management.

**Radiosurgery**

It is indicated to maintain AVM obliteration without inducing new neurologic deficits in deep seated AVMs, which are not easily accessible by microsurgery, or lesions in the eloquent cortex. It could be utilized as a primary mode of treatment or as part of multimodality therapy. Several studies have reported the efficacy and safety of stereotactic radiosurgery in children [9,42,43,44]. Long-term follow up is needed since long-term effects of ionizing radiation on the developing nervous system have not yet been fully evaluated [44]. Complications such as intracranial malignancy or neuropsychological retardation [44,45] have been reported but are still not well studied.

**Embolization and endovascular treatment**

The rapid evolution of endovascular technology has led to the continuous increase in endovascular treatment utilization in pediatric AVM therapy. The completely obliteration rate with this technique vary between 5% to 21.2% with an average size reduction of 78% [46,47]. The complication rate is 7.3%. Thus, endovascular embolization is feasible in pediatric AVMs with the capability of complete obliteration in small AVMs or as an effective adjunctive therapy with micro or radiosurgery in larger AVMs.

**REFERENCES**


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