Endovascular management of pediatric neurovascular malformations – A single-center experience from South India

Abhinav Kalvala[1], Rajakumar Padur Sivaraman[2], Shruthi Tarikare[2], Shuba Sankaranarayanan[3], Santhosh Joseph[4]

From [1]Senior Resident, [2]Associate Professor, [3]Professor, Department of Paediatrics, [4]Professor, Department of Interventional Radiology, Sri Ramachandra Institute of Higher Education and Research, Chennai, Tamil Nadu, India

Correspondence to: Dr. Rajakumar Padur Sivaraman, Department of Paediatrics, Sri Ramachandra Institute of Higher Education and Research, Chennai - 600 116, Tamil Nadu, India. E-mail: rajakumarps@gmail.com

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ABSTRACT

Background: Neurovascular malformations (NVMs) in pediatric population are highly challenging to manage and treatment options include open surgery, endovascular therapy, and radiosurgery or combined. Recently, there has been a gradual shift from conventional surgical approach toward endovascular therapies with increasing availability of technical expertise and gadgetry. **Objective:** We aimed to study the clinical profile and immediate outcome of children with NVMs, who underwent endovascular therapy. **Materials and Methods:** This retrospective observational study was conducted in a tertiary care center in South India between February 2017 and August 2018. We included children admitted in pediatric intensive care unit (PICU) with NVM and needed neuroradiological intervention. Children with thromboembolism or other NVMs who did not require intervention were excluded from the study. Data on clinical profile, endovascular procedure done, supportive therapy given, and immediate outcome were collected and analyzed. **Results:** Of 1615 children admitted in PICU, 13 had NVM (0.8%), of which five had arteriovenous malformation (AVM), three had vein of Galen arteriovenous malformation (VGAM), one had VGAM with dural AVM, one had acquired carotid-cavernous fistula, two had berry aneurysm, and one had mycotic aneurysm. VGAM presented as hydrocephalus, whereas AVM and aneurysm as intracranial hemorrhage. Endovascular embolization was done using platinum detachable coils, onyx, N-butyl cyanoacrylate glue, and coil assist stents. One child needed decompressive craniectomy and another child needed extraventricular drainage. Four children needed pre-procedure ventilation and seven children needed prolonged post-procedure ventilation. Mortality was 15%; and among the survivors, 72% had an uneventful recovery. One child had seizures and two had hemiparesis at discharge. **Conclusion:** Endovascular management is an effective intervention for pediatric NVM. Multidisciplinary team approach and good pediatric intensive care are important for successful outcome. Further studies with long-term follow-up are needed to assess the durability of endovascular therapy.

Key words: *Aneurysm, Arteriovenous malformation, Endovascular, India, Neurovascular malformation, Pediatric*

Neurovascular malformations (NVMs) in pediatric population are rare and highly challenging to manage due to the complex nature of the anomalies. The types of NVMs classified under pediatric age group are - vein of Galen arteriovenous malformation (VGAM), classic arteriovenous malformations (AVM), pial AVM, aneurysms, cavernomas, and dural arteriovenous shunts [1]. The available treatment for NVM includes surgical, endovascular, radiosurgical, or combined [2,3]. There is no consensus on the modality of choice, as each treatment modality has its own merits and demerits. Although endovascular treatment has become a standard in adults in recent times, it is rarely used in children due to technical difficulties and lack of expertise. Recently, there has been a gradual shift from conventional surgical approach toward endovascular therapies with increasing availability of technical expertise and gadgetry [3,4]. Establishment of good pediatric neurocritical care units has improved the overall prognosis of the condition. There is a paucity of data in Indian literature regarding the diagnosis and outcome of endovascular treatment strategies for NVM in pediatric population. The purpose of this article is to present single-center experience of endovascular management and immediate outcome of pediatric NVM.

MATERIALS AND METHODS

This was a retrospective descriptive study for a period of 18 months between February 2017 and August 2018, conducted in a tertiary care teaching institute with facility for interventional neuroradiology, neurosurgery, and pediatric critical care. Our pediatric intensive care unit (PICU) is an accredited Level III referral unit with an average annual admission of 1000 children. Children between 1 month and 18 years of age admitted in PICU

with diagnosis of any NVM, either congenital or acquired and who needed neuroradiological intervention, were included in the study. Children who were managed conservatively, children with other space-occupying lesions or stroke due to thromboembolism, were excluded from the study. NVMs included in the study were VGAM, AVM, and aneurysms. These children were managed according to the standard PICU protocol which had been as follows: Conventional digital subtraction angiogram (DSA) after stabilization, supportive care in the form of ventilation, active seizure management and raised intracranial pressure (ICP) management, and definitive management after multidisciplinary team meet comprising pediatric intensivist, neurologist, neuroradiologist, and neurosurgeons. Interventional neuroradiology procedures were done under fluoroscopy guidance through femoral vascular catheterization. Endovascular embolization was done using platinum detachable coils, onyx (ethylene vinyl alcohol dissolved in dimethyl sulfoxide), N-butyl cyanoacrylate (NBCA) glue, and coil assist stents.

Data was collected retrospectively from the PICU register and the case sheets retrieved from medical records department in a structured proforma. The demographic details, clinical presentation, neuroimaging findings, need for pre-procedure ventilation, anticonvulsant therapy, site and type of lesion, nature of intervention, whether elective or emergency intervention, duration of post-operative ventilation, ICU stay, and immediate outcome in terms of death or discharged home, were collected. Post-procedure ventilation was considered prolonged, if ventilated for >6 h. Categorical data are depicted as number and percentage and continuous data as mean with standard deviation and median with interquartile range.

RESULTS

A total of 1615 children were admitted in PICU during the study period. Among the study subjects, 15 patients were referred with neurovascular conditions. Two patients, one with Moyamoya disease and other with sagittal sinus thrombosis, were excluded from the study as endovascular intervention could not be done, leaving 13 children (0.8 %) with NVM for final analysis. Among 13 cases, three had VGAM, one had VGAM with dural AVM, five had AVM, one had acquired carotid-cavernous fistula, two had berry aneurysm, and one had mycotic aneurysm. Diagnosis was based on magnetic resonance (MR) angiogram and conventional DSA. In the study group, majority were male (77%) and only one child with VGAM had a family history of NVM. Table 1 depicts the demographic characteristics, site and type of lesion, presenting clinical feature, nature and type of intervention, pre-procedure ventilation, prolonged post-procedure ventilation, and immediate outcome of children.

Increasing head size due to hydrocephalus was the most common presentation of VGAM. Preceding history of headache followed by altered sensorium due to intracranial hemorrhage was the most common presentation of AVM and aneurysm. Child with mycotic aneurysm had infective endocarditis due to *Streptococcus viridans* with underlying ventriculoseptal defect (VSD). Three children with VGAM had intervention before 1 year of age while one with additional dural AVM had intervention at 17 years. The mean age (standard deviation SD) of intervention of those with AVM and aneurysm was 5.8 (2.9) years and 7 (2.9) years, respectively.

Endovascular embolization of VGAM and AVM was done using platinum detachable coils and/or onyx. Endovascular procedures for aneurysm were done with platinum detachable coils, NBCA glue, and coil assist stents. Figure 1 depicts the MR angiogram of case 13 with mycotic aneurysm and Figure 2 depicts fluoroscopy image with microcatheter *in situ* of the same case. In addition to endovascular therapy, two children needed surgical intervention but not as a definitive procedure. One child who presented with signs of uncal herniation secondary to intracerebral hemorrhage (ICH) from temporal lobe AVM had an emergency decompressive craniectomy after intubation and hyperventilation. Definitive endovascular coiling was done after 3 months and cranial vault reconstruction, after 6 months. The other child with berry aneurysm rupture with subarachnoid hemorrhage and intraventricular hemorrhage needed extraventricular drainage (EVD) in addition to endovascular embolization. Four children needed pre-procedure ventilation as they had evidence of raised ICP. The other three children who needed pre-procedure ventilation also needed prolonged post-procedure ventilation. All the four children with VGAM were ventilated for longer duration electively after the procedure. Median ventilation duration was 1 day (interquartile range [IQR] 1–4 days) while median PICU stay was 3 days (IQR 2–4 days). All the children had neuroimaging post-procedure to confirm resolution of lesion.

Mortality was seen in 15% (2/13); one child with VGAM and dural AVM had a massive ICH and died. One child with rupture of berry aneurysm of the left middle cerebral artery who had endovascular coiling 2 months earlier, presented with rebleeding. He underwent emergency endovascular coiling and stenting with EVD with a plan to do surgical clipping later, but he had features of raised ICP and died after 72 h. Among survivors, 8 (72%) made uneventful recovery and were discharged without any sequelae. Three children had sequelae at the time of discharge, of which one had seizures and two had hemiparesis. One child had post-extubation stridor needing few weeks of steroids treatment.

DISCUSSION

In this study, we report successful management of pediatric NVM using endovascular therapy. There is a paucity of literature in this subject from developing countries. Pediatric NVM differs from the adult population with respect to location, morphology, etiology, and natural history. The diagnosis is often missed or delayed, as neurovascular anomalies are not included in the differential diagnosis of headache in pediatric population. Hence, many cases are diagnosed with intracranial bleeding. This fact is brought out clearly in our study as children with AVMs and berry aneurysms, though had preceding history of headache, all were diagnosed only after intracranial bleeding.

VGAM is arteriovenous connections between multiple primitive choroidal arteries and the median prosencephalic vein

Table 1: Demographic, clinical presentation, management, and outcome of pediatric neurovascular abnormalities

Case No.	Sex	Age of intervention	Diagnosis	Location	Clinical presentation	Nature of intervention	Procedure	Pre-procedure ventilation	Post-procedure ventilation>6 h	Outcome
1	F	1 year	VGAM	Vein of Galen	Increasing head size, CCF	Elective	Endovascular embolization (glue)	No	Yes	Discharged
2	M	7 months	VGAM	Vein of Galen	Increasing head size, CCF	Elective	Endovascular embolization (glue)	No	Yes	Discharged/seizures
3	M	11 months	VGAM	Vein of Galen	Antenatal hydrocephalus, CCF	Elective	Endovascular embolization (glue)	No	Yes	Discharged
4	M	17 years	VGAM and Dural AVM	Posterior to 3rd ventricle	Increasing head size	Elective	Endovascular embolization (glue)	No	Yes	Death
5	M	3 years	AVM	Parieto-occipital lobe	Headache and visual disturbances for 1 month	Elective	Endovascular embolization (glue)	No	No	Discharged
6	F	7 years	AVM	Parietal lobe	Headache and vomiting for 3 months	Elective	Endovascular embolization (glue)	No	No	Discharged
7	M	4 years	AVM	Temporal lobe	Altered sensorium for 1 day	Emergency	Decompressive craniectomy and delayed endovascular embolization	Yes	Yes	Discharged; post-extubation stridor, left hemiparesis
8	M	4 years	AVM	Occipital lobe	Headache	Elective	Endovascular embolization (glue)	No	No	Discharged
9	M	11 years	AVM	Cerebellum	Headache and gait disturbances for 3 weeks	Elective	Endovascular embolization (glue)	No	No	Discharged
10	M	9 years	Carotid-cavernous fistula	Cavernous sinus	Proptosis H/o head trauma 1 month back	Emergency	Endovascular embolization (glue)	Yes	No	Discharged
11	M	8 years	Berry aneurysm	Left middle cerebral artery	Persistent headache for 3 months	Emergency	Endovascular coiling and stenting	Yes	Yes	Death
12	M	10 years	Intracranial aneurysm	Right posterior inferior cerebellar artery	Headache and vomiting for 2 weeks	Elective	Endovascular coiling and stenting	No	No	Discharged
13	F	3 years	Mycotic aneurysm	Left distal middle cerebral artery	VSD with altered sensorium and seizures	Emergency	Endovascular coiling	Yes	Yes	Discharged with right hemiparesis

VGAM: Vein of Galen arteriovenous malformation, AVM: Arteriovenous malformation, VSD: Ventricular septal defect, CCF: Congestive cardiac failure

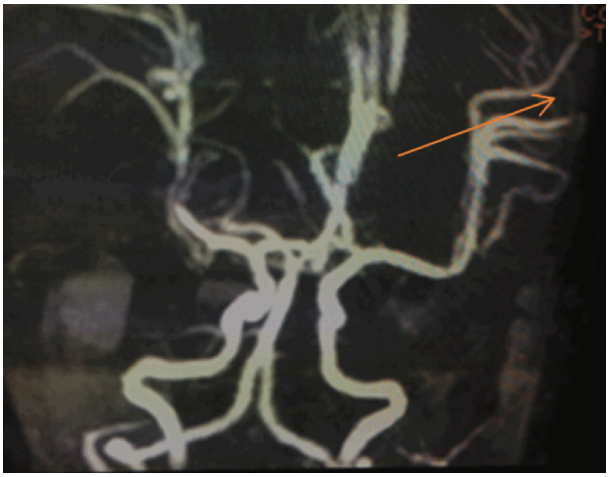

Figure 1: Magnetic resonance angiogram showing bilobed aneurysm in M4 segment of middle cerebral artery

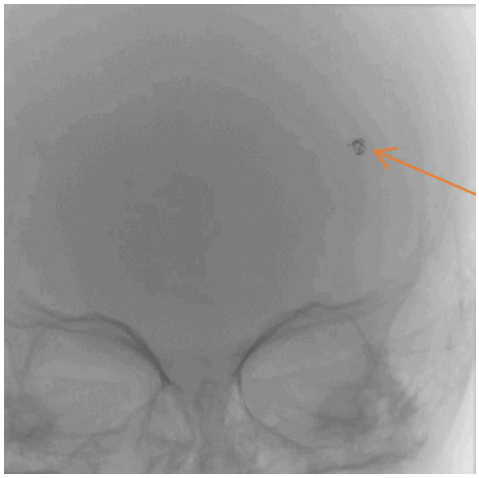

Figure 2: Fluoroscopy image of case 13 with microcatheter *in situ*

of Markowski, which is the precursor of vein of Galen [1,5]. The cerebrospinal fluid drainage in this age group is entirely dependent on the venous drainage as arachnoid granulations are not yet fully functional. Therefore, VGAM causes an increased pressure within the venous system and results in hydrocephalus [6]. All the studied children with VGAM were presented with hydrocephalus. The most disabling feature of severe forms of VGAM is congestive heart failure in infancy which, if not treated, could potentially result in multiorgan dysfunction and death. Therefore, most need intervention early in life as seen in our study. Collateral pathways of venous drainage typically develop around VGAM to accommodate the markedly increased blood volume associated with the shunt [7]. The adequacy of these collaterals is responsible for milder and late presentation in some children. The unusually late age of intervention of one child with VGAM reflects the presence of collateral drainage.

Pediatric NVM often requires complex and challenging treatment strategies and requires multidisciplinary cooperation involving neurosurgeons, neurointerventional radiologists, pediatric intensivists, and a rehabilitation team. Endovascular embolization is the most preferred treatment for VGAM as surgical intervention is associated with poor outcomes [8-10]. Choice of endovascular procedures versus microsurgical/conventional surgical techniques still remains controversial in the management of pediatric aneurysm. International subarachnoid aneurysm trial (ISAT) study showed that 1-year outcome following ruptured aneurysm is better with endovascular coiling compared to surgical clipping, if lesions are small and located in anterior cerebral circulation in adults [11]. A good candidate for surgery would be a young symptomatic patient with surgically accessible lesion and/or a significant hematoma with mass effect [12]. The advantages of endovascular therapy over surgery are decreased risk of anesthesia, less invasive procedure, and shorter anticoagulation therapy. In mycotic aneurysm due to infective endocarditis and heart disease, the need for cardiothoracic surgery with anticoagulation makes endovascular procedure the natural choice before cardiac surgery [13,14]. AVMs are considered as congenital defect with a nidus, the region where there is the absence of intervening capillary network between artery and vein. Complete obliteration of the nidus is essential for success of treatment as it ensures abolition of high-flow fistulous connection within the malformation [15,16]. There is a role for open/microsurgery, endovascular therapy, stereotactic radiosurgery, or combined therapy for AVM [2]. Open surgery is the treatment of choice for superficial lesions with mass effect [17]. Endovascular therapy is useful for small- and moderate-sized lesions. It is also a good adjunctive therapy for open surgery in large AVMs as it prevents significant blood loss. Radiosurgery is preferred in large, deep seated or eloquently located AVMs [18,19]. However, safety of maximum radiation dose and risk of long-term malignancy in children need to be evaluated [20]. All the children in our study had interventional neuroradiology procedure as choice due to availability of expertise, our center preference, and parental choice. Neuroimaging and angiography were done after the procedure confirmed resolution of lesions.

There is a wide variety of material used in endovascular therapies. NBCA glues polymerize when exposed to anions such as hydroxyl groups in water or blood and cause an acute inflammatory reaction similar to foreign body granulomatous reaction progressing over 1 month. They can be injected through very small catheters and cause permanent occlusion with minimum chance of recanalization. Most neuroradiology centers use NBCA glue as agent of choice [9,21]. Onyx is a newer addition in the armamentarium of occluding agents [22]. The use of platinum detachable coils allows placement in the exact location needed and thus decreases the risk of distal migration of embolic material. The additional benefit is that if distal migration of coils occurs, the coils can be retrieved, unlike acrylic glues. We used all the above-mentioned occluding agents in our cases.

A well-equipped neurocritical care unit is essential to manage these children. Children with raised ICP need careful stabilization, both – before and after procedure. Critical care aspects involved are controlled mechanical ventilation, osmotherapy, management of cerebral vasospasm in case of aneurysmal rupture, invasive hemodynamic monitoring, anticonvulsant therapy, safe transport for neuroimaging, optimization of hemodynamics, fluid and

electrolyte status, euthermia, and adequate analgesia and sedation. Four of 13 children in our study needed neuroprotective measures due to raised ICP before the procedure.

The goal of post-procedure care is to prevent or minimize complications related to anesthesia and the procedure, and hence, the focus is on optimizing hemodynamic, respiratory, and electrolyte parameters. The need for prolonged ventilation in more than half of our cases highlights the importance of good supportive care in determining the outcome.

We report successful outcome in 11 of 13 children (85%) in our study. This underscores the point that endovascular therapy for NVMs is an effective treatment modality.

However, the small sample size and lack of long-term follow-up were the limitations of the study. The main drawback of endovascular therapy is the risk of recurrence in the long term [23,24]. In our study, endovascular management has shown short-term success. Further studies with long-term follow-up are needed to assess the durability of endovascular therapy.

CONCLUSION

The study outcome points toward the success of endovascular but with a short-term success. Multidisciplinary team approach and good pediatric intensive care are important for successful outcome.

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