Endovascular management of vein of Galen aneurysmal malformations: case series and review of the literature

Abstract

**Background:** Neonates with vein of Galen aneurysmal malformations (VGAMs) who present with heart failure have a high rate of morbidity and mortality, while those who present later in childhood have considerably better outcomes.

**Aim of the work:** determine the factors that have the greatest predictive value in predicting long-term results in children with VGAM.

**Patients and methods:** Between June 2015 and June 2020, 15 patients (7 infants, 8 children) were diagnosed with symptomatic VGAMs, 4 of whom were suffering from intractable high-output heart failure and received initial endovascular treatment. All of them treated by endovascular procedures. Staged Trans-arterial route was the management approach with embolic agent with different concentrations.

**Results:** In the four patients, immediate outcomes included management of heart failure and normal neurological performance. On follow-up examination, 11 (73.33 percent) children had no evidence of neurologic abnormality or heart failure; 4 (26.66 percent) infants had mild developmental delays, two of them improved with time. On digital subtraction angiography follow up, twelve had no additional shunting, two had limited flow, and one was awaiting follow-up imaging.

**Conclusion:** Even in the most high-risk neonates and children with VGAMs and heart failure, endovascular therapy combined with current neuroanesthetics and neurointensive care can provide good outcomes.

**Key words:** VGAMs, cardiac failure; endovascular management, embolization.

**Introduction**

Vein of Galen aneurysmal malformations are uncommon congenital interacerebral arteriovenous shunts that affect newborns and infants. Although VGAMs account for about 1% of interacranial vascular malformations, they account for approximately 30% of all vascular malformations in the paediatric age group.18

Vein of Galen aneurysmal malformations are caused by the persistence of an embryonic vascular structure called the median prosencephalic vein,
which generally regresses by the eleventh week of pregnancy except for the caudal end, which represents the true vein of Galen.  

The Vein of Galen aneurysmal malformations (VGAM) should be recognized from what’s called aneurysmal dilatation of the true vein of Galen caused by an adjacent brain AVM (vein of Galen aneurysmal dilatation or VGAD) which characterized by a higher incidence of bleeding tendencies.  

VGAMs is a group of arteriovenous fistulas (AVFs) draining into the dilated median prosencephalic vein. Anterior and posterior choroidal arteries, the pericallosal artery, and perforators from basilar tip represent the main feeders of these fistulas.  

VGAMs are classified into mural, choroidal, and mixed types. In the mural type; a direct high flow shunt is located within the wall while in the choroidal type; there is interposition of the arterial feeders and the venous aneurysm and the mixed types have the two components. The mural kinds of VGAMs are more commonly presented in late infancy with macrocephaly or failure to thrive, and may present with moderate heart failure or asymptomatic cardiomegaly. The choroidal types of VGAMs usually cause cardiac output failure in newborns.  

The introduction of endovascular therapy changed the management and outcome of VGAM patients dramatically. The emergence of intensive care units and clinicians specialized in the management of severely ill neonates has also played a significant role in the current positive outcomes.  

The aim of this study was to identify those factors that have the greatest predictive value in predicting long-term results in children with VGAMs.
Study details

Patient population

15 cases of VGAMs were diagnosed and treated between the period of June 2015 and June 2020. 7 infants and 8 children were included in this study. 10 of them were males and 5 were females.

Preoperative evaluation

All patients were properly assessed clinically and radiologically by CT and/or MRI brain and supplementary digital subtraction cerebral angiography.

Clinical presentation and Outcome were assessed by the neurological and developmental findings which are staged into five grades. With grade 4 representing patients with normal development, grade 3 representing patients having mild level of impairment, grade 2 representing patients having intermediate level of impairment affecting their ability of daily achievements and require obvious help in their interactions but in low need for medications, grade 1 representing patients having severe form of neurological deficits requiring aggressive care and medical treatment, and grade 0 representing mortality cases.

Treatment strategy

Endovascular management through transarterial route was the treatment choice in all cases. Treatment plan and stages were individualized according to the clinical, radiologic presentations, and angiographic architecture of the lesions.

All the 15 patients underwent endovascular embolization in our neuroendovascular intervention unit. Staged transarterial approach was the selective technique used to treat all cases using different
concentrations of liquid acrylic embolic agents such as Histoacryl opacified with tantalum powder as lipidol according to the shunt flow.

**Results:**

Fifteen patients with VGAMs were treated in Matarya Teaching Hospital between June 2015 and June 2020. Two of the children were diagnosed when they were neonates, five between the ages of 6 and 19 months, six between the ages of 3 and 5 years, and two at the age of 12 years. All of the patients who presented during the neonatal period had some degree of cardiac output failure at the time of presentation.

Four of the patients had intractable high-output heart failure and were treated with endovascular intervention at the outset after initial emergency pediatric cardiology consultation and assessment. Mild cardiac output failure was noted in nine cases associated with neurological symptoms due to hydrocephalus in five cases. Neurological symptoms due to hydrocephalus were the main presentation in two cases.

At presentation, one child had moderate developmental delay requiring significant supportive social and medical treatment. Five cases had mild neurological developmental delay requiring some sort of educational support, and the other cases were neurologically normal apart from some of the manifestations of increased intracranial pressure.

The minimum duration of follow up was 12 months and the maximum duration was 3.5 years with a mean 23.47 months. During this period the cases were followed clinically and radiologically by CT and/or MRI brain and supplementary digital subtraction cerebral angiography.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>sex</th>
<th>Follow up</th>
<th>Age at intervention</th>
<th>presentation</th>
<th>Clinical score</th>
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<tbody>
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<td>1.5 months</td>
<td>CHF</td>
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<td>8 months</td>
<td>Mild CHF, dilated scalp veins, hydrocephalus</td>
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<td>9 months</td>
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</tr>
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<td>14 months</td>
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<tr>
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<td>9</td>
<td>Female</td>
<td>20 months</td>
<td>3.5 years</td>
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<td>Mild CHF, hydrocephalus</td>
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Table (2): Fistula classification, CSF diversion, and outcomes

<table>
<thead>
<tr>
<th>Case No.</th>
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<th>VP Shunt /or not</th>
<th>Outcome score</th>
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<tr>
<td>2</td>
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</tr>
<tr>
<td>3</td>
<td>Mixed</td>
<td>Not shunted</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Choroidal</td>
<td>shunted</td>
<td>3</td>
</tr>
<tr>
<td>5</td>
<td>Mural</td>
<td>Not shunted</td>
<td>4</td>
</tr>
<tr>
<td>6</td>
<td>Mixed</td>
<td>Not shunted</td>
<td>3</td>
</tr>
<tr>
<td>7</td>
<td>Choroidal</td>
<td>Not shunted</td>
<td>4</td>
</tr>
<tr>
<td>8</td>
<td>Choroidal</td>
<td>shunted</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
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<tr>
<td>10</td>
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<td>Not shunted</td>
<td>4</td>
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<tr>
<td>11</td>
<td>Mural</td>
<td>Not shunted</td>
<td>4</td>
</tr>
<tr>
<td>12</td>
<td>Choroidal</td>
<td>Not shunted</td>
<td>3</td>
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<tr>
<td>13</td>
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<td>Not shunted</td>
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<tr>
<td>15</td>
<td>Mixed</td>
<td>Not shunted</td>
<td>4</td>
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</tbody>
</table>
Nine of the fifteen malformations were classified as choroidal, three were mural, and three were mixed indicating the presence of both choroidal and mural components. Three patients of the nine cases classified as choroidal VGAMs were having some sort of neurological delay, one of them improved neurologically and two cases remain unchanged. Of the mural types two cases were having a degree of neurological delay and both improved neurologically after intervention. Mild neurological developmental delay was noted in one case of both mural and choroidal architecture which remained unchanged. All cases showed no worsening of their neurological or cardiac condition and those patients that remained unchanged neurologically required mild supportive and educational treatment.

Three cases required cerebrospinal fluid shunting procedure. Ventriculoperitoneal shunt was inserted pre-intervention in two patients, and post-intervention in one case. All the three cases were of choroidal architecture. Radiological hydrocephalic changes and clinical symptoms improved after intervention in the rest of patients without any shunting procedures. Neuroophthalmological manifestations were noticed in three patients, one in the early infancy and two are older children, in form of loss of upward gaze, nystagmus and strabismus. One of them required surgical correction of squint after finishing stages of endovascular management.

Staged intervention was the treatment strategy in all cases. Two sessions were required to treat all cases with mural architecture, three sessions for five cases with choroidal architecture, and four sessions for the rest of cases of choroidal architecture and cases with mixed choroidal and mural architectures.
Histoacryl opacified in lipidol was the embolic agent injected through the microcatheters via arterial route in all cases. (Table 2)

Discussion

VGAM represents a rare vascular anomaly characterized by arteriovenous fistulas and shunts that drain into a dilated median vein of Markowski.2

The lesion is in the midline and is frequently supplied by the limbic system, which includes bilateral choroidal arcades, pericallosal arteries, varied transmesencephalic arteries, and midbrain perforators.14

The age of the child, the size and location of the VGAMs, the status of venous drainage, such as outflow stenosis or thrombosis, which can redirect venous outflow of the brain and/or the malformation through alternative venous channels such as the cavernous sinus, and/or transosseous veins, all influence the clinical presentation of VGAMs.13,17

In particular, venous hypertension can lead to cortical calcifications or even a condition known as "melting-brain syndrome," which is an irreversible condition.13

Typically, neonates present with signs of severe cardiopulmonary distress and/or high-output heart failure. Macrocephaly, hydrocephalus, and/or seizures are common in infants.7,9 Developmental delay or failure to thrive associated with complicating medical factors (e.g., long-standing cerebral venous hypertension, cardiac decompensation) are the presenting symptoms in some infants.9 Cranial bruit, dilated scalp veins, proptosis, and/or recurrent epistaxis are some of the other presenting signs and symptoms.7

The advent of endovascular neuro-interventional techniques has significantly improved the prospects for successful management of
patients with VGAM lesions, which were previously bleak. Several treatment strategies have been advocated in the medical literature raising the questions about the proper timing of intervention, suitable technique of approach (arterial or venous), embolization agents, and timing of management of concomitant hydrocephalus.\textsuperscript{10}

The use of liquid acrylic embolic agents is advocated by several researchers in endovascular procedures for treating patients with VGAMs.

Among the advantage of these agents is the ability to inject them through very small catheters, which are suitable to navigate the tortuous anatomy of VGAMs. Acrylics provide permanent occlusion, reducing the possibility of recanalization. In the hands of a skilled operator, their use can significantly reduce procedure time.

In our study, 15 cases of VGAM were diagnosed and treated between the period of June 2015 and June 2020. 7 infants and 8 children were included in this study. 10 of them were males and 5 were females. Two of the patients were diagnosed when they were neonates, five between the ages of six and nineteen months, six between the ages of three, and five years, and two at 12 years of age.

Thirty-one youngsters (18 males, 13 girls) were included in the Gopalan et al.\textsuperscript{8} study, with 28 of them still alive. The median age at presentation was 9.6 months (range 1.2 months to 11 years and 7 months), with the majority of children presenting in their first year of life. The most prevalent clinical manifestation (n=24) was macrocrania. Parents' observations of prominent facial veins (n=9), developmental delay (n=8), focal neurological impairments (n=8), heart failure (n=7), seizures (n=5), and headache (n=5) were among the other clinical symptoms (not
mutually exclusive). Headache and prominence of facial veins were noticed only in patients presenting after the age of 2 years.

Nine of the 15 malformations in this study were classified as choroidal, three were mural, and three were mixed indicating the presence of both choroidal and mural components. Of the nine choroidal cases three patients were having some sort of neurological delay, one of them improved neurologically and two cases remain unchanged. Of the mural types two cases were having a degree of neurological delay and both improved neurologically after intervention. Mild neurological developmental delay was noted in one case of both mural and choroidal architecture which remained unchanged.

Seven of Jones et al.\textsuperscript{10} cases were classed as mural, five as choroidal, and one as having both mural and a more complex nidus anteriorly. Five of the mural cases had some form of congestive heart disease.

Only partial occlusion of the shunt, according to certain interventionists, should be done in a single session. In some circumstances, complete occlusion has been found to be harmful because of normal perfusion pressure breakthrough in previously underperfused parts and consumptive coagulopathy with resulting bleeding problems.\textsuperscript{20}

In this study, two sessions were required to treat all cases with mural architecture, three sessions for five cases with choroidal architecture, and four sessions for the rest of cases of choroidal architecture and cases with mixed choroidal and mural architectures. Histoacryl opacified in lipidol was the embolic agent injected through the microcatheters via arterial route in all cases.
In the Mitchell et al. trial, four out of five patients had staged embolization, with the interval varying based on the anatomical and clinical findings post-embolization. A single procedure was performed in the one patient who died in this series. In nine (60 percent) of the 15 interventions, transarterial embolization was used in combination with other techniques; the preferred agent was NBCA, which was used alone (seven procedures) or in combination with coils (two procedures).\textsuperscript{16}

With transvenous embolization, knowing when to stop could be a difficult decision because when stop too early, recurrence is almost guaranteed while stop too late, total occlusion might aggravate heart failure due to acutely increased afterload.

Endovascular embolization in the treatment of VGAMs has resulted in a significant improvement in patient outcomes. Our preferred access is the transarterial embolization, which is more effective in managing heart failure when there are only one or a few arterial feeding pedicles.

Mitchell et al.\textsuperscript{16} found in their study that the presence of multiple tiny feeders that couldn’t be navigated easily during the trans-arterial technique especially in unstable newborns evolves the concept of starting the treatment plan with trans-venous approach for transient control of cardiac output failure to allow improving the patient’s general condition and anatomical architecture to give chance for second intervention through the arterial side.

In a recent systematic evaluation of 667 patients who underwent endovascular embolization between 1987 and 2014, Yan et al.\textsuperscript{20} found that 68 percent had a favorable outcome and 32 percent had a poor outcome, including 10 percent who died.
This study showed that immediate control of heart failure with normal neurological function had been achieved in the 4 cases. On follow-up examination, 11 (73.33%) infants exhibited no signs of cardiac failure or neurologic impairment; 4 (26.66%) infant showed mild developmental delay, two of them improved in the follow up visits. With long term follow up excellent cognitive and functional outcomes are achieved.

On digital subtraction angiography follow up, twelve had no additional shunting, two had limited flow, and one was awaiting follow-up imaging.

Over a course of 21 years, Lasjaunias\textsuperscript{14} found that 74 percent of VGAM patients treated with endovascular embolization had normal neurological development, 15% were moderately retarded, and just 10% of the surviving patients had severe neurological abnormalities. There were 23 youngsters that died.

Jones et al.\textsuperscript{10} found that after endovascular embolization, 7 of 13 patients (2 of 8 patients presented as neonates with heart failure and the other 5 patients presented beyond the neonatal period) had a normal or near-normal performance from 1987 to 2001.

Also Fullerton et al.\textsuperscript{6} found that 14 of 23 children who had VGAM endovascular treatment between 1983 and 2002 get a good outcome without neurological deficits.

Ellis et al.\textsuperscript{5} recently reported excellent long-term cognitive and functional outcomes following VGAM endovascular occlusions.

In Rodesch et al\textsuperscript{19} study, from the 16 neonates who had systemic cardiac signs as their first VGAM symptoms, Twelve of them were successfully controlled with digitalis diuretic therapy and were embolized in infancy, with a 67 percent survival rate and normal cerebral development. The
four babies who were not treated after diagnosis died soon after birth from severe heart failure or multiorgan failure, as well as serious brain damage. The authors emphasized the need for transarterial embolization and avoiding treatment during the early neonatal period before total stabilization of general condition.

About one-third of neonatal patients in the largest series reported by Lasjaunias et al. were deemed unsuitable for intervention due to poor general condition. 36.4 percent of the 88 newborns who treated by endovascular embolization technique are alive and have normal neurologic development, 54.5 percent have moderate psychomotor maldevelopment, and 9.1 percent have severe psychomotor maldevelopment. This age group had a 52 percent overall death rate.4

In a separate study, Khullar et al.12 found that 32.7 percent of neonatal patients had satisfactory outcomes, with normal development or mild developmental delay. The mortality rate among newborns was 35.6 percent, whereas 31.7 percent had a "fair" prognosis, with moderate or severe functional and neurological developmental delays.

In presence of evident imaging diagnostic criteria suggesting the presence of high flow lesions, Mitchell et al.16 recommended that treatment should be planned for 6 months of age even if there’s no neurological developmental delay, but frequent radiological and clinical evaluations are indicated to detect any signs of cerebral ischemia or hydrocephalus if the management of lesions is delayed beyond the age of 6 months. Endovascular embolization would subsequently be used as soon as possible; hydrocephalus often reacts to the obliteration of the arteriovenous shunt.
The Bicetre-score can be used to assess and draw the management plane for newborns presented with VGAMs. It is based on the Lasjaunias research group's experience with over than 300 VGAM patients.\textsuperscript{14} The patients are classified according to their cerebral, cardiac, respiratory, hepatic, and nephrological states.\textsuperscript{1} It is suggested to postpone treatment until the child is 5 to 6 months old if cardiovascular and neurologic symptoms are stable (Bicetre-score > 12). An emergency endovascular embolization should be performed if the Bicetre-score is 8–12 points. There is no reason for an aggressive intervention in the case of presence of serious neurological deficits or medically uncontrolled cardiac insufficiency (Bicetre-score 8).\textsuperscript{14}

CSF diversion for treatment of hydrocephalus in children with VGAMs remains a point of controversy, as pre-embolization ventricular drainage might exacerbate problems that could affect the cerebral venous circulation. The definite causes of hydrocephalic changes are not exactly listed. Many radiological findings were noticed in different studies and clinical trials including compression of cerebral aqueduct, downward displacement of cerebellar tonsils and impaired cerebral venous outflow with subsequently impaired CSF circulation. Some caregivers experienced serious complications after CSF shunting done before endovascular embolization including intraventricular hemorrhage, intracerebral hemorrhage, and progressive parenchymal damage. Hemorrhagic cerebral insults diagnosed in patients with VGAMs in some studies were supposed to be a result of changes in venous pressure gradients in underdeveloped subependymal vessels. Fortunately we didn’t have any serious hemorrhagic insults in this study.

It is better to postpone ventricular drainage until all embolization procedures are complete as the hydrocephalic findings mostly improve
and no CSF diversion procedures needed as noticed in most of our cases apart from the two cases that required preintervention shunting and the other one that required postintervention CSF diversion.

In this study, escape of glue to the venous sinuses occurred in 12 sessions of 9 patients with no significant sequelae or further needed management. Small hematoma at site of femoral artery puncture occurred in 4 patients and managed conservatively.

Intraventricular hemorrhage and subarachnoid hemorrhage were among procedural complications experienced by other caregivers. Jones et al.\textsuperscript{10} had three of their patients complicated by Intraventricular hemorrhage two of whom were premature neonates. Subarachnoid bleeding occurred in one child during the embolization process, possibly as a result of vascular injury during catheter installation, perfusion pressure breakthrough, or a combination of both. An episode of intracranial bleeding as a result of shunt insertion was reported in one patient in this study.

In a study by GoPalan et al.\textsuperscript{8} nineteen embolizations in 14 patients complicated by intraprocedural problems. The most prevalent of these (n=12) was glue escape into the venous sinuses, which was related to venous sinus thrombosis in four cases. The 4 cases managed by endovascular procedures with no residual neurological deficits. Iliac artery occlusion (n=1) and intraventricular hemorrhage (n=1) were among other complications.

Some researchers believe that venous stenosis is a risk factor for the development of cerebral bleeding in those patients with VGAM during the journey of management \textsuperscript{15}.
**Conclusion**

Staged endovascular transarterial embolization using liquid acrylic embolic agent by different concentrations according to shunt flow represents an effective strategy with a good long term outcome in treating patients with VGAMs who are properly selected according to an accurate clinical scoring system. This technique also represents an initial safe and promising approach to control cardiac output failure in newborns with VGAMs when medications fail.

**References**


