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ORIGINAL PAPER

Predicting factors for the follow-up outcome and management decisions in vein of Galen aneurysmal malformations

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Abstract
Purpose Vein of Galen aneurysmal malformations (VGAMs) are choroidal arteriovenous malformations that develop during an early embryonic stage. Although recent reports have shown improved outcome for these patients, the overall outcome still is poor. In this study, we evaluated the clinical, imaging, and angiographic features that may predict the outcome in VGAM patients.
Methods Twenty-five patients diagnosed with VGAM were reviewed for clinical symptoms, including neonatal scoring systems, imaging findings, angioarchitecture, treatment decision, initial treatment age, follow-up timing, and follow-up outcome.
Results Factors that were significantly associated with a poor outcome ($p<0.05$) included neurological symptoms at presentation, a medium-to-low overall neonatal score (<12/21), a very poor score (<2/5) in one (or more) categories, focal parenchymal changes, calcifications, tonsillar herniation, arterial steal, or more than two groups of multiple arterial feeders. The venous drainage pattern and treatment age were not significantly associated with the overall outcome.
Conclusions The presence of multiple factors that are related with poor outcome may warrant withholding aggressive treatment, while a small subgroup of carefully selected patients without any of these factors who are clinically asymptomatic may have a good outcome even with conservative management and close follow-up. For all other patients in which treatment is considered, the optimal treatment time is at 4–5 months of age; however, urgent treatment, regardless of age, should be indicated in those that do not have permanent brain damage on imaging with deteriorating congestive heart failure, evidence of arterial steal, or progressive occlusion of the venous outflow.

Keywords Vein of Galen aneurysmal malformations · Management decisions · Predicting factors · Pediatrics · Management

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Introduction

Vein of Galen aneurysmal malformations (VGAMs) are arteriovenous (AV) malformations of the choroidal system that develop in the early embryonic stage [2]. They represent about 30% of all vascular malformations in the pediatric population.

The natural history and effects of management are still unclear and the overall outcome is still considered poor. With routine use of screening antenatal ultrasound, an in utero diagnosis is becoming more common and the question arises on how to manage these patients. Lasjaunias et al. proposed a neonatal scoring systems for these kinds of malformations [23, 24], which is a multi-organ evaluation, to decide upon the timing of treatment of these patients and suggested that treatment should be withheld in patients with scores lower than 8 of a total of 21. Certain imaging findings, such as encephalomalacic parenchymal change, intraparenchymal calcifications, and angioarchitecture of

the VGAM (choroidal type nidus and jugular stenosis without cavernous drainage), have been postulated to be associated with a poorer prognosis in these patients; however, there has been no previous studies that proved this by correlating imaging findings to clinical follow-up or patient outcome.

Endovascular treatment has been accepted as the first treatment option for VGAMs [12, 16, 21, 23, 24, 36]. Although the transvenous route, either as the primary or in conjunction to a transarterial route, has been reported with varying success [7, 17, 25, 27], a transarterial route with glue embolization, as proposed by the Bicetre group and as used in our institution, is more commonly preferred.

Materials and methods

The study was approved by the ethical board committee of our hospital. Retrospective review of the institutional database during September 1997 to September 2008 revealed 25 patients diagnosed with VGAM. Data collection included patient demographics, clinical presentation, evaluation of the clinical symptoms, the imaging findings, angioarchitecture, treatment decision, initial treatment age, follow-up timing, and follow-up outcome.

The clinical symptoms of each patient was evaluated using the Bicetre neonatal score for patients younger than 4 weeks old and the Bicetre admission/outcome score for patients older than 4 weeks.

All patients were evaluated with a cross-sectional imaging study, either magnetic resonance (MR) and/or computed tomography (CT), and a vascular study using magnetic resonance angiography (MRA), computed tomography angiography (CTA), or digital subtraction angiography (DSA). The initial MR and CT were evaluated for the presence of parenchymal changes, calcification, hydrocephalus, tonsillar herniation, and arterial steal. Arterial steal was defined by presence of leptomeningeal collateralization of the cortical branches of the middle cerebral artery (MCA) or the anterior cerebral artery (ACA) to the posterior cerebral artery (PCA) territories and further contributing to the AV shunt by the VGAM. Vascular studies by angiogram, MRA, or CTA were evaluated for the angioarchitecture, which includes the nidal type (mural or choroidal), arterial feeders (posterior choroidal arteries (PchA), anterior choroidal arteries (AchA), subforniceal and subcallosal branches from the ACA, subependymal arteries from the basilar tip and PCA, transdural supply from the meningeal arteries), venous drainage pattern, and the presence of jugular stenosis. The degree of jugular bulb stenosis was defined as mild (<60%), moderate (60–90%), and severe (>90%). Drainage through the connection between the deep sylvian vein and cavernous sinus was only evaluated in patients who had a conventional cerebral angiogram.

The treatment decision was classified into three groups, including withholding of treatment, treatment with transarterial glue embolization, and conservative management. In the treatment group, the timing was considered early if treated before the age of 4 months and normal if treated after 4 months. The follow-up outcome for all patients was done using the above-mentioned admission/outcome score. Good outcome was defined as a score of 3 or more, and a score of less than 3 was considered as poor outcome.

The presence of each factor was compared with the follow-up outcome of the patient. Statistical significance was calculated using Fisher exact test, chi-square, or one-way analysis of variance tests for each group and was defined at 95% confidence interval ($p<0.05$).

Results

General

The average age at presentation was 0.41 years (4.92 months), ranging from 0 to 6 years. There were 12 female patients and 13 male patients. Prenatal diagnosis was made in eight patients. Eleven patients had antenatal ultrasound, of which eight were abnormal (all performed from 26 to 36 weeks gestational age) and the remaining three, performed at a gestational age of 11 to 26 weeks, were reported to be normal.

Seventeen patients presented with symptoms of congestive heart failure (all within the first week of life), three of which had additional seizures. Hydrocephalus was the initial presenting symptom in two patients, one patient having additional ataxia and developmental delay at the age of 2 years. Five patients were initially asymptomatic and one later developed hydrocephalus from aqueductal stenosis at the age of 1.5 years. Macrocephaly alone was the presenting symptom in one patient, whom was 5 months old. In the neonatal group, congestive heart failure was the most common presenting symptom (85%—17 of 20). Additional seizures were also present in three of these patients. In infants, macrocephaly was more common, seen in 75% (three of four) patients ($p=0.007$).

Twenty patients were evaluated using the neonatal score and five patients whom were older than 1 month at the time of presentation were evaluated with the admission/outcome score. The neonatal score ranged from 7 to 21 (average of 14.35)—with 14 patients whom scored 2 or lower in one category, and the admission score ranged from 2 to 5 (average of 4.4).

Parenchymal damage was present in ten patients, including focal encephalomalacia in seven patients and diffuse brain volume loss in three patients (all of which had

hydrocephalus). One patient with an initially normal MR had progressive diffuse brain volume loss after 4–5 years follow-up. One patient that had focal encephalomalacia at 5 weeks progressed to diffuse encephalomalacic change at 1 year follow-up. One patient with diffuse brain volume loss related to hydrocephalus at birth had stabilization and slight improvement of the volume loss after being treated with early embolization. Parenchymal calcifications were present in seven of 25 cases (28%), the average age was 3.5 months (range 0–2 years), and all were periventricular in location. During the course of the disease, a total of nine patients (36%) developed hydrocephalus and three patients had evidence of tonsillar herniation (one without hydrocephalus). Eight patients had evidence of arterial steal on both MR and angiography. The presence of arterial steal was associated with focal parenchymal change in five patients while none of the patients with diffuse brain volume loss had any evidence of arterial steal ($p=0.025$).

The nidus was of a mural type in 17 patients (four single hole and 13 multiple holes) and eight had a choroidal type. Of the 20 patients in the neonatal group, there was no significant difference between the average neonatal score between the mural (14.27) and choroidal (14.60) type of niduses ($p=0.883$); however, there was a difference between the mural-single hole (21), mural-multiple hole (13.23), and choroidal (14.60) type of niduses ($p=0.043$). None of the 14 patients with a multiple-hole mural type of nidus was asymptomatic—11 presented with cardiac failure and two had neurological symptoms as presentation.

The number of patients seen for each arterial feeder is summarized in Table 1. Of the five groups of arterial feeders (PchA, AchA, ACA, subependymal, transdural), six patients were limited to only PchA feeders, three had two groups, 11 had three groups, and five patients had four groups of arterial feeders.

A fetal pattern of venous drainage was present in 19 patients and consisted of the falcine sinus in 12 patients and the occipital and marginal sinuses in 16 patients. Deep venous connection to the median prosencephalic vein was visualized and used in the AV shunt drainage in two patients. Cavernous connection and drainage of the deep sylvian vein could be evaluated in 16 patients who had angiography and was good bilaterally in ten patients, good on one side in one patient, and poor bilaterally in five patients. Significant jugular bulb stenosis (moderate to complete bilaterally) was present in seven patients (28%) and was associated with hydrocephalus in six patients (six of seven; 85.7%; $p=0.003$—Fisher)

Treatment with intra-arterial glue embolization was decided upon in 15 patients, conservative management only in six patients, and treatment was withheld in four patients. The follow-up timing ranged from 0 to 12 years (average of 3.79 years). The average outcome score was 2.48. Of the 25 patients, nine patients died (36%). Nine patients were normal at the last follow-up (36%). One had minor nonneurological symptoms that did not have to be treated, two had transient neurological symptoms which did not require treatment and/or cardiac overload controlled by treatment, three had permanent minor neurological symptoms or developmental delay up to 20%, and one had severe neurological symptoms and developmental delay of more than 20%.

Of the six patients managed conservatively, five of six were normal at follow-up, three (three of 25; 12%) of which had spontaneous thrombosis of the VGAM during the follow-up period, and one patient died at the age of 3 months from sepsis unrelated to the VGAM. Of the patients within this group, all had a neonatal score higher than 17 or an admission score of 5. None of these patients presented with hydrocephalus, macrocrania, or neurological symptoms. There were no parenchymal changes, calcifications, tonsillar herniation, deep venous drainage, or jugular stenosis present in these patients.

All four patients, in whom treatment was decided to be withheld, subsequently died. In this group, all patients were neonates, whom presented with congestive heart failure with additional seizures in one patient, the neonatal score ranged from 8 to 12, three patients had parenchymal changes of the focal type, three patients had calcifications, all had evidence of arterial steal, three patients had a mural type of nidus, and all patients had more than two groups of arterial feeders (multiple).

Of the 15 patients that were treated intra-arterially, four patients died (27%) and seven had a good outcome. The number of procedures ranged from 1 to 5 (average of 1.8 per patient). The average age at the initial treatment was 4.9 months, ranging from 8 days to 2.5 years. There were six complications, three intracranial hemorrhages (of which two patients died), one venous infarction of the caudate nucleus, one pulmonary embolism with sinus thrombosis, and one femoral artery thrombosis without any sequelae.

Correlation with follow-up outcome

The correlation between each factor and the follow-up outcome is summarized in Table 2. Factors that are statistically significantly associated with poor outcome are neurological symptoms at presentation, a neonatal score lower than 12, and patients who scored 2 or less within one or more of the categories, parenchymal changes (predominantly of the focal type), calcifications, arterial steal, and those that had more than two groups of multiple arterial feeders.

Patients with an incidentally found VGAM, with a neonatal score of 12 or higher and in whom (based on these findings) a conservative management was decided upon, had a good outcome. Although patients with multiple-hole mural type

Table 1 The frequency of each arterial supply to the VGAM

Arterial feeder	No. of patients (%)
Posterior choroidal arteries	26 (100)
Anterior choroidal artery	16 (62)
Subforniceal artery and subcallosal branches of the ACA	14 (54)
Subependymal arteries from the basilar and PCA	9 (35)
Transdural supply from the meningeal arteries	1 (4)

niduses tended to have a poorer outcome (five of 13—38%) than patients with a single-hole mural type nidus (three of four—75%) and choroidal type nidus (four of eight—50%), it was not statistically significant (p=0.437).

The pattern of venous drainage was not related to the patient outcome. The timing of treatment (earlier than 4 months versus later than 4 months) was not related to the outcome (p=0.595—Fisher exact test). The good outcome group had a slightly lower mean age at treatment than the poor outcome group (0.27 versus 0.53 years); however, this was not statistically significant (p=0.428).

Discussion

Clinical presentation

The prenatal diagnosis of VGAM on screening antenatal ultrasound can be made by visualization of a dilated often roundish vascular midline structure, representing the dilated median prosencephalic vein; however, sufficient dilatation of the vein is required before it can be seen. Eleven of our patients had antenatal ultrasound, and although the VGAM is known to develop during the choroidal embryonic stage (around 7–8 weeks gestational age) [23, 30], the prenatal diagnosis was made in only eight cases that had ultrasound between 26 and 36 weeks. In the remaining three patients that had ultrasound prior to 26 gestational weeks, the dilated median prosencephalic vein was not seen. In the previous literature, there has been only one case report by Hartung et al. [18] that the dilated median prosencephalic vein was seen on ultrasound at 22 weeks; in the other case reports, most diagnoses were made by ultrasound only in the third trimester [6, 11, 28, 31, 33, 34].

We did not find any correlation between early prenatal diagnosis of VGAM and the follow-up outcome; therefore, an in utero diagnosis of VGAM without any signs of multi-organ failure or brain parenchymal changes is in our opinion not an indication for therapeutic termination of the pregnancy. However, obtaining a diagnosis prenatally will help to decide the facilities needed for the neonatal care after delivery.

Congestive heart failure was the most common presentation in the neonatal group and is probably related to a lower cardiovascular volume of these patients. Many of the severe cases had progression to pulmonary hypertension with respiratory distress and multi-organ failure, which was reflected by a low neonatal score and subsequently had a poor outcome. This corresponds to previous studies that have shown that the prognosis of the VGAM is related to the severity of heart failure [9], and in many cases, the diagnosis of VGAM is obtained only after an investigation for the congestive heart failure [18].

The initial management of VGAM with congestive heart failure in the neonatal group consists of medical stabilization of the heart failure, typically with inotropic drugs, diuretics, mechanical ventilation, or inhaled nitric oxide [22]. In cases that the medical management fails, early partial embolization is recommended to decrease the shunting volume [9]. There have been reports that the use of prostaglandin E may be helpful in some cases to stabilize the patients while awaiting the treatment of the VGAM [22].

Although Lasjaunias at el. [24] suggested that the treatment decision should be based upon the total neonatal score, in our study, we have found that in addition to a medium-to-low overall total neonatal score of less than 12, a score of 2 or less in a *single* category and certain imaging findings also predict a poor outcome and therefore should be taken into consideration as well.

Clinical presentations with hydrodynamic disorders, such as hydrocephalus and macrocrania, were more frequent in the infantile group. A simplified diagram of the proposed pathomethanism is represented in Fig. 1. The presence of a high-flow arteriovenous shunt, as in VGAM, causes increased venous pressure within the straight sinus and torcular. In cases that the sutures are open, adaptation to the increased pressure occurs by expansion of the intracranial volume resulting in macrocrania. This expansion of the cranial vault, together with the presence of a high-flow shunt, interferes with the normal skull base development and likely results in secondary stenosis of the jugular foramen [23]. In addition, the induced intimal hyperplasia from increased shear stress to the venous wall due to the high-flow shunt may also play a role in the so-called jugular dysmaturation and is known from the peripheral veins as seen in patients with hemodialysis grafts [26]. Combination of these two factors will not only result in varying degrees of jugular bulb stenosis, which

Table 2 Correlation of the factors with the patient follow-up outcome

		Good outcome	Significance (p value)
Age group	Neonates	9/20	0.559
	Infants	2/4	
	Children	1/1	
Sex	F	6/12	0.582
	M	6/13	
Clinical presentation	Asymptomatic	5/5	0.026[a]
	CHF	6/14	
	Macrocephaly	1/2	
	CHF or Macrocephaly with neurological deficits	0/4	
Neonatal score	<8	0/1	0.03[a]
	8–12	0/5	
	>12	9/14	
Two or less in a single category	No	5/6	0.038[a]
	Yes	4/10	
Admission score	2	0/1	0.05
	5	3/4	
Parenchymal changes	No	11/15	0.003[a]
	Yes	1/11	
Calcifications	No	11/18	0.046[a]
	Yes	1/7	
Hydrocephalus	No	8/16	0.56
	Yes	4/9	
Tonsillar herniation	No	12/22	0.124
	Yes	0/3	
Arterial steal (MR/Angio)	No	12/17	0.001[a]
	Yes	0/8	
Nidus	Mural	8/17	0.613
	Choroidal	4/8	
Arterial feeders	1–2 groups	7/9	0.033[a]
	3–4 groups	5/16	
Embryologic sinus	No	2/6	0.363
	Yes	10/19	
Falcine sinus	No	5/13	0.277
	Yes	7/12	
Occipital–marginal sinuses	No	5/9	0.440
	Yes	7/16	
Deep venous drainage	No	11/23	0.740
	Yes	1/2	
Cavernous capture	None	3/5	0.549
	Poor	0/1	
	Good	5/5	
Significant jugular stenosis	No	8/18	0.450
	Yes	4/7	
Treatment decision	Withhold treatment	0/4	0.035[a]
	Embolization	7/15	
	Conservative management	5/6	

[a] Statistically significant

will lead to improvement of the cardiac overload (and therefore a paradoxical amelioration of symptoms), but will also lead to further increased venous pressure. If in these patients the cranial vault fails to expand (which is the similar pathomechanism seen in cases with severe craniosynostosis [32]), decompensation occurs, when combined with the compression of the aqueduct by the enlarged venous pouch, that leads to subsequent ventricular dilata-

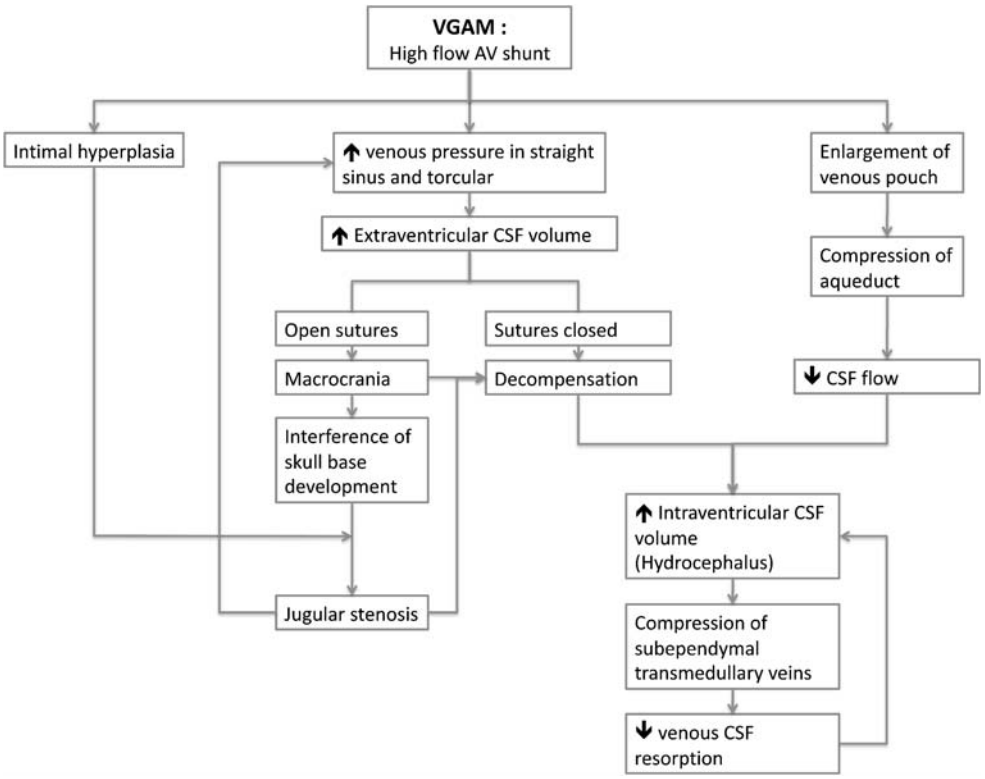

Fig. 1 Simplified diagram demonstrating the pathomechanism of the development of hydrocephalus in VGAM patients

tion. The hydrocephalus then results in compression of the medullary veins, which further decreases the cerebrospinal fluid resorption and further worsens the hydrocephalus and increased intracranial pressure. As a result, subsequent tonsillar herniation occurs. Of our cases with significant jugular bulb stenosis, 85.7% had associated hydrocephalus, proving the role of increased venous pressure in the pathomechanism of hydrocephalus. Since we did not find any correlation between the presence of hydrocephalus and the overall outcome, we believe that proper early management by decreasing the venous pressure through embolization of the high-flow shunt improves the chance for a better outcome in these patients. Early ventricular shunting in these cases is known to have a poor outcome [20, 37]; therefore, ventricular drainage should be kept only for those patients who do not improve after embolization or have a hydrocephalus unrelated to the VGAM.

The pattern of clinical presentation in our series is similar to most previous studies [21, 24]. We also found that patients who had neurological symptoms at presentation were associated with a poor outcome, likely to be related to the degree of brain damage caused by the VGAM.

Parenchymal imaging findings

The most important predictors of poor outcome on CT and MR were the presence of parenchymal changes and calcifications. The parenchymal changes seen in VGAM patients can be classified into two different types, focal encephalomalacia and diffuse brain volume loss. In our study, we found that focal encephalomalacia is related to the presence of arterial steal, which is similar to a previous study by Grossman et al. [14]. Arterial steal is usually identified as enlargement of the leptomeningeal collaterals from the MCA branches (Fig. 2), which is best seen on MR T2-weighted (T2W) images, or as delayed filling of the VGAM through branches of the MCA on DSA. Leptomeningeal collaterals from the callosomarginal branches of the ACA are uncommon and enlargement of the pericallosal branch, as an arterial feeder to the VGAM, does not represent arterial steal. Steal phenomenon may result in ischemia and subsequent infarctions, which can be detected earlier in neonates on DWI than on T2W or fluid attenuated inversion recovery images due to the normal high signal of the unmyelinated white matter in this age group. The use of DWI in antenatal fetal MR imaging of VGAM cases can occasionally help in early detection of ischemic evidence and may therefore play an important role in management decisions [5, 15]. We found that diffuse brain volume loss is often associated with long-standing hydrocephalus (Fig. 3). This has been proposed to be related to compromise of the deep periventricular venules induced by the high pressure related to the hydrocephalus, which could lead to either venous infarctions and/or decreased

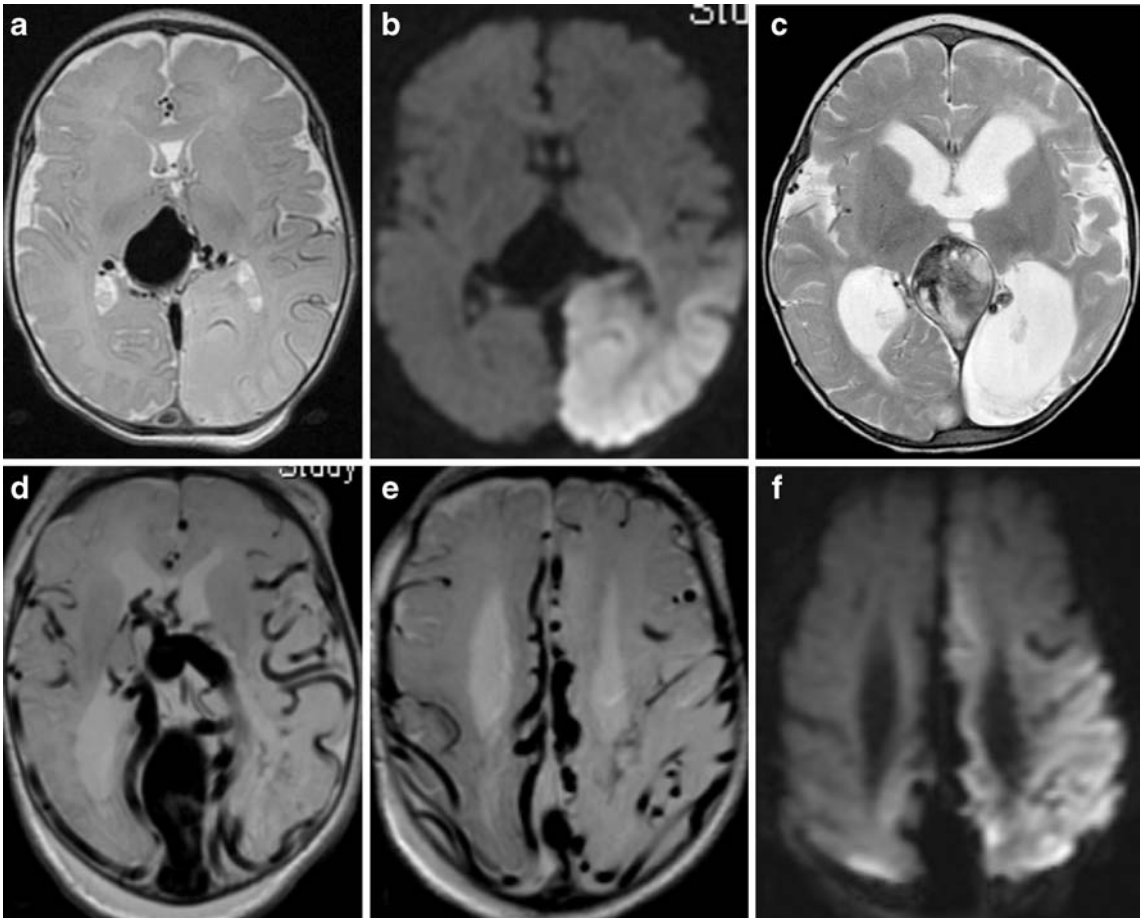

Fig. 2 Two different patients with arterial steal. **a**–**c** Case 1: a 2-day-old boy presented with congestive heart failure and seizures (neonatal score 13/21). Initial MR axial T2-weighted image (**a**) demonstrates evidence of arterial steal from the posterior left MCA branches with signal change of the left parieto-occipital lobe, which is better seen as high signal on DWI (**b**), representing acute infarction. Follow-up MR axial T2-weighted image at 2 years shows the encephalomalacic change within the region of the previously seen arterial steal. Periventricular white matter volume loss is also observed as a result of interval development of hydrocephalus between the studies. Embolic material is observed in the dilated venous pouch. **d**–**f** Case 2: a 1-day-old boy presented with macrocrania and congestive heart failure (neonatal score 12/21). Axial T2-weighted MR images (**d**, **e**) show arterial steal from bilateral MCA and ACA branches; the latter one is seen as enlarged vessels along the superior aspect of the parasagittal region. The extent of the acute infarctions is better seen on DWI (**f**) than on the T2W images. Treatment was withheld in this patient due to his unstable cardiac status and the parenchymal changes

regional cerebral blood flow followed by arterial ischemia in the region, resulting in extracellular edema and axonal damage with subsequent reactive gliosis, ongoing glial death, and atrophy, as shown in animal models [4, 10]. Stabilization of this process with mild improvement of the brain volume loss, as seen in one of our patients (Fig. 4), can be seen after proper treatment of the hydrocephalus. Our findings were similar to the series reported by Gupta et al. [16], where most patients were in an older age group and hydrocephalus was the most common finding followed by diffuse cerebral atrophy.

The presence of parenchymal calcifications is best detected on CT (Fig. 5) and is related to long-standing venous congestion [29]. There was no direct correlation between the degree of jugular bulb stenosis and calcifications in our study; therefore, we believe that the occurrence of venous congestion is likely to be multifactorial: The degree of jugular bulb stenosis, the shunt volume, and the presence or absence of cavernous drainage all have an impact on the development of venous congestion. In contrast to the subcortical calcifications related to dural arteriovenous fistulas with cortical venous reflux in adults, we observed that the calcifications seen in our study were more commonly periventricular in location. This is probably due to the increased deep venous pressure in VGAMs as opposed to the increased cortical venous pressure seen in malignant dural arteriovenous fistulas. Both parenchymal loss and parenchymal calcifications represent some degree of irreversible brain damage in most cases, and their presence was associated with an overall poor outcome of the patients.

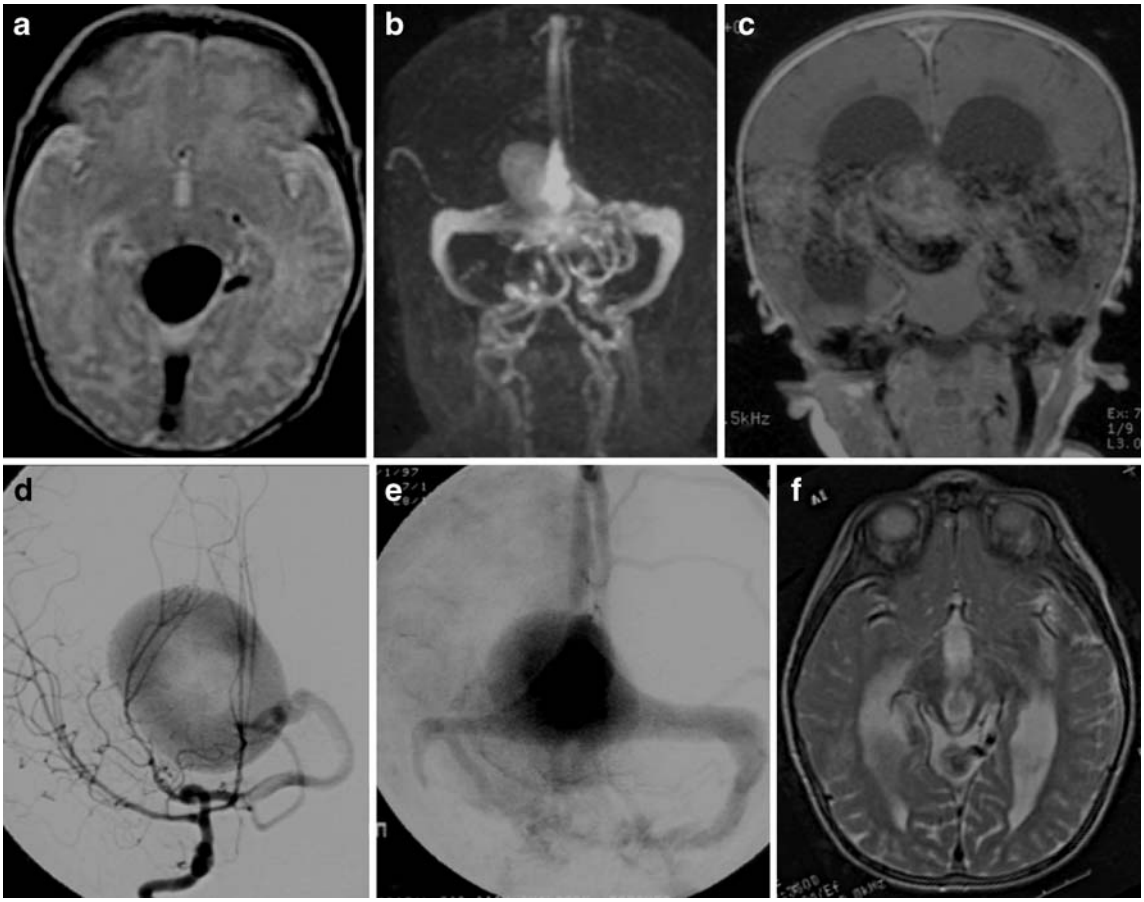

Fig. 3 A 3-month-old boy with prenatal diagnosis of VGAM and a neonatal score of 21 at birth. Initial MR T2-weighted images (**a**) and 3D TOF MRA (**b**) show normal appearance of the brain parenchyma and ventricles. Moderate stenosis of the right jugular bulb and mild stenosis of the left jugular bulb are observed. He developed macrocrania at 4 months and coronal T1-weighted MR shows newly seen severe hydrocephalus with periventricular edema. Right internal carotid artery angiograms in arterial (**d**) and early venous phase (**e**) demonstrate a mural type of nidus with complete occlusion of the right jugular bulb and severe stenosis of the left side. He was treated with transarterial embolization and cured after two sessions. Follow-up axial T2-weighted MR at 4 years of age (**f**) shows persistence of the diffuse brain volume loss, but the patient is clinically normal and doing well at school after 10 years follow-up

Angioarchitecture

In 1989, Raybaud et al. [30] were the first to describe that the venous drainage of VGAM was directed into the dilated median vein of the prosencephalon, which is the precursor of the vein of Galen and not the vein of Galen itself. The nidus is located in the midline and typically receives a bilateral symmetrical supply. Two types of niduses have been described—a choroidal type, which occurs at a very early stage of development and recruits supply from all choroidal arteries into an interposed network before draining into the large venous pouch, and a mural type. The latter type is composed of direct AV fistulas within the wall of the median vein of the prosencephalon. Multiple mural fistulas are more often encountered than a single fistula. Lasjaunias et al. have reported that patients with a mural type presented with a better clinical status [24]; however, we found that neonates who had multiple mural-type fistulas had a poorer neonatal score at presentation compared to patients with single mural-type fistulas or choroidal-type niduses, which is likely related to a higher volume of arteriovenous shunting. However, we did not find a significant correlation between the type of nidus and the follow-up outcome.

The arterial feeders relate to the choroidal supply and limbic arterial arch and therefore consist mainly of the anterior and posterior choroidal arteries, subfalcine branches from the pericallosal artery of the ACA, cortical (splenial) branches of the AchA–PCA, and subependymal arteries from the basilar tip and P1 segments of the PCA [30]. Transdural supply to a VGAM is unusual and is more likely secondary to partial thrombosis within the dilated venous pouch, often seen in older patients who have received prior treatment. There was no correlation between a particular arterial feeder and outcome; however, VGAM patients with a larger number of arterial feeding groups

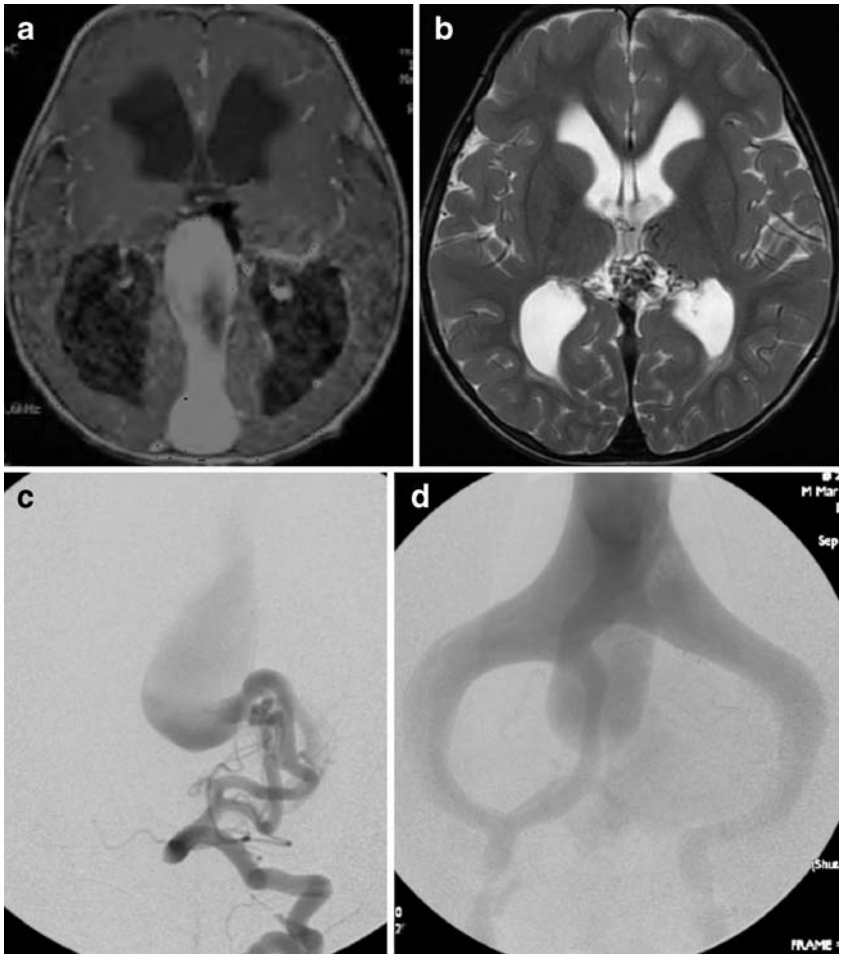

Fig. 4 A 5-month-old boy presented with macrocrania (admission score was 5). Initial axial T1-weighted MR with gadolinium (**a**) demonstrates severe dilatation of the ventricles with periventricular edema. The white matter changes and volume loss have stabilized and slightly improved after being treated with trans-arterial embolization on his 5-year follow-up axial T2-weighted MR (**b**). Residual white matter changes are still noted at the peritrigonal region. Initial left vertebral artery angiograms in arterial (**c**) and early venous phases (**d**) show a multihole mural type of nidus with moderate bilateral jugular stenosis. Note the presence of the right occipital and marginal sinuses

(reflecting a larger arteriovenous shunting volume through the lesion) had a poorer outcome than patients with fewer arterial feeders. Raybaud et al. [30] also found a correlation between the size of the dilated venous pouch and the outcome, which may again be related to the increased shunt flow and increased resistance of the venous outflow.

Although Lasjaunias et al. [24] report that there is no communication between the median vein of the prosen-

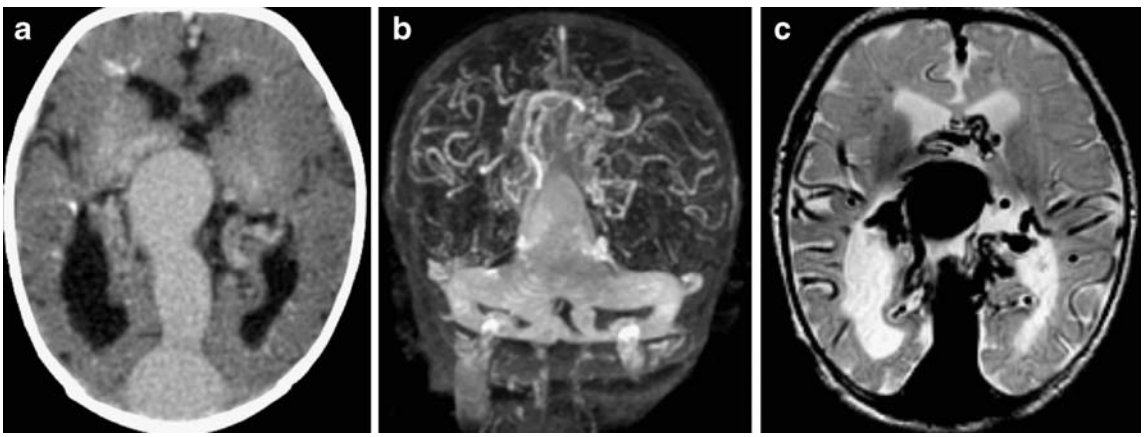

Fig. 5 A 1-day-old girl presented with congestive heart failure (neonatal score 9/21). Plain axial CT shows extensive calcifications, which are mainly periventricular in location. No significant jugular bulb stenosis was seen on the MRV study (**b**). Axial T2-weighted MR (**c**) shows evidence of arterial steal of bilateral MCA branches with volume loss in bilateral occipitoparietal lobes. Treatment was withheld in this patient due to the evidence of multi-organ failure (despite only minimal neurological symptoms), extensive calcifications, and parenchymal loss

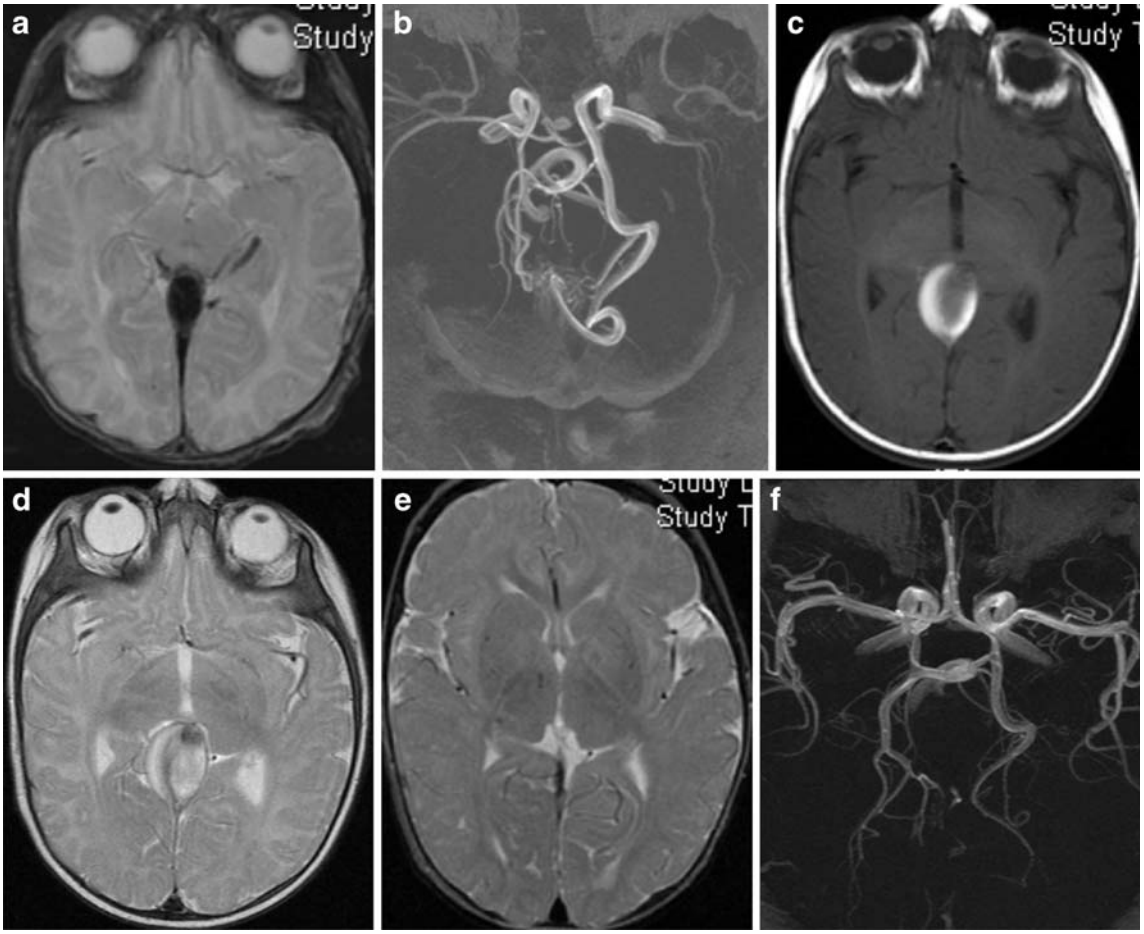

Fig. 6 A 1-day-old boy with prenatal diagnosis of VGAM remained asymptomatic after birth (neonatal score=20). Initial axial T2-weighted MR (**a**) and MRA (**b**) demonstrate a slightly dilated venous pouch with small posterior choroidal arterial feeders. No parenchymal change or calcifications are detected. Follow-up axial T1- (**a**) and T2 (**b**)-weighted MR at 4 months shows high signal T1 and T2 of thrombosis within the venous pouch. Follow-up axial T2-weighted MR and MRA at 1 year confirms the spontaneous thrombosis and closure of the VGAM

cephalon and the deep venous system, several other reports have suggested that this communication does exist in rare cases [1, 13, 19, 25]. As Levrier et al. suggested in 2004 [25], we believe that when this communication exists, it typically occurs at the posterior part of the dilated venous pouch and may not be seen on the diagnostic angiography unless there is outflow stenosis. The straight sinus may not be present and replaced by a falcine sinus [30]. There is often persistence of other embryologic sinuses, such as the median occipital and marginal sinuses. A few months after birth, cavernous drainage of the deep sylvian vein develops and offers an alternative route for the normal brain venous drainage through the orbital and facial veins [23]. We did not find a correlation between the pattern of venous drainage or the degree of jugular bulb stenosis and the follow-up outcome. This is likely because of the multiplicity of possible venous outflow routes through the vertebral venous plexus and cavernous sinuses that are apart from the jugular bulb [3]. Development of significant jugular bulb stenosis, even in the presence of cavernous drainage or vertebral venous rerouting, should still indicate prompt treatment since the progressive venous outflow obstruction will result in overloading those venous outlets that were previously used by the normal brain. This will interfere with normal brain drainage and therefore normal brain development.

Overall outcome

The natural history of VGAM described in the previous literature varies with the age group, clinical presentation, and management given in each series. Although the outcome of patients has been improving throughout the years, the overall outcome is still considered poor [12, 21, 24, 35]. In the largest series (317 patients) reported thus far [24], Lasjaunias et al. reported that approximately 19% (57 of 300; 17 lost to follow-up) were considered to be in too bad a clinical condition to be treated. Of the 216 treated

patients, 73 (34%) had a bad outcome, ranging from permanent neurological symptoms and mental retardation to death. According to these numbers, the overall poor outcome is approximately 46%. Spontaneous thrombosis of the shunt occurred in only eight of 317 patients (2.5%). In our study, the poor outcome rate was 52% and three of our cases (12%) spontaneously thrombosed during the follow-up period.

Management decision

Despite the increasing understanding of the pathophysiology of VGAMs over the years, the questions of whether and when to treat a patient still remain unanswered. In our small series, we found that a subgroup of carefully selected patients had a good outcome with conservative management and close follow-up (Fig. 6). The criteria for selection of these patients are (1) a high neonatal (>17) or admission score (>3), (2) clinical symptoms of only mild congestive heart failure well controlled with medication and no neurological symptoms, (3) imaging findings with no parenchymal loss, calcifications, hydrocephalus, tonsillar herniation, or evidence of arterial steal, and (4) angioarchitecture findings of low-flow shunts, i.e., two or less enlarged arterial feeder groups, lack of deep venous drainage, lack of jugular bulb stenosis.

The presence of severe congestive heart failure with multi-organ failure, seen as a neonatal score of <8, is probably the only single criteria indicating withholding treatment in a patient. However, a combination of other factors, most of which represent permanent brain damage, were also shown in this series to be associated with a poor outcome: an overall poor clinical status (neonatal score of <12), evidence of a single organ failure (neonatal score of two or less in a single category), neurological symptoms at presentation, parenchymal changes, arterial steal, or calcifications on imaging.

For the remaining patients, in whom treatment is considered or is indicated, its timing is still uncertain. It has been proposed that the optimal timing for embolization of a VGAM is at 4–5 months of age since this waiting period is not enough to develop permanent brain damage while offering enough benefit concerning arterial access and contrast limitation problems. A previous report by Cherif et al. [8] questions this waiting period, since the reported patient developed congestive heart failure resulting in death after being stable for 2 weeks. Since we did not find a statistical significant difference between waiting period or average age at treatment and outcome, we think that this case report highlights the necessity of closely observing the patients and adapting the treatment strategy based on the patient's individual evolution. In our practice, the following clinical conditions speak in favor of a more urgent treatment: deterioration of cardiac function (uncontrolled by medication), evidence of arterial steal, progressive occlusion of the venous outflow (jugular bulb stenosis), developing macrocrania/hydrocephalus, and, for older children, psychomotor developmental arrest or delay of more than 2 months. This necessitates close clinical observation (cardiac status, Denver developmental milestones, head circumference) and imaging follow-up (MRI at birth, at 2.5 months, and prior to treatment at 5 months in our practice). If the patient remains stable during the follow-up period, then starting the treatment at 4–5 months may be sufficient to avoid permanent brain damage.

Given the rarity of the disease, the individual patient's condition, the parents' decision, and the operator's personal experience, no general guidelines can be given, especially since it is psychologically difficult to withhold treatment in the acute setting of a newborn and since even patients with evidence of brain damage may eventually recover in part given the plasticity and adaptability of the brain in the childhood period. However, if treatment is to be contemplated, it has to be kept in mind that these patients are in a high risk group, a good outcome can therefore not necessarily be hoped for, and a higher risk of treatment related complications can be expected.

Conclusion

The management of patients with VGAM still remains challenging. There are several factors that we found to be associated with a poorer outcome, including a poor clinical status at presentation with multi-organ failure (represented as low neonatal and admission scores), presence of neurological symptoms, imaging findings of extensive encephalomalacic parenchymal changes, arterial steal and parenchymal calcifications, and evidence of high-flow multifeeder shunts. In the absence of permanent brain damage on MR or CT imaging, urgent treatment should be indicated in patients with deteriorating or severe congestive heart failure, evidence of arterial steal, and progressive occlusion of the venous outflow. It is important that all of these factors are taken into consideration when making a management decision for VGAM patients.

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