Vein of Galen aneurysmal malformations: critical analysis of the literature with proposal of a new classification system

A review

Vein of Galen aneurysmal malformations are a rare and diverse group of entities with a complex anatomy, pathophysiology, and serious clinical sequelae. Due to their complexity, there is no uniform treatment paradigm. Furthermore, treatment itself entails the risk of serious complication. Offering the best treatment option is dependent on an understanding of the aberrant anatomy and pathophysiology of these entities, and tailored therapy is recommended. Herein, the authors review the current concepts related to vein of Galen aneurysmal malformations and suggest a new classification system excluding mesodiencephalic plexiform intrinsic arteriovenous malformations from this group of malformations. (http://thejns.org/doi/abs/10.3171/2013.5.PEDS12587)

KEY WORDS • vein of Galen aneurysmal malformation • vein of Galen dilation • vein of Galen varix • median prosencephalic vein of Markowski • Litvak • Yaşargil • Lasjaunias • vascular disorders

A frontal AVM with partial drainage through the vein of Galen was first described by Steinheil in 1896. In 1923, Wohak published the first autopsy report on a vein of Galen aneurysm. However, he did not seem to recognize the pathological relationship between the aneurysmal malformation and shunting. Jaeger and colleagues15,16 were the first to describe vein of Galen “aneurysms” in 1937, a misnomer according to the current understanding of this lesion. An understanding of the true nature of these malformations has evolved over the years, from initially being thought of as a diffuse group of aneurysms and AVMs toward an understanding of their true nature as AVFs.

True VGAMs are AVFs, supplied by a variety of arterial feeding vessels that drain into the aberrantly persistent fetal median prosencephalic vein of Markowski,29 an embryonic precursor of the vein of Galen. Joseph Markowski, a Polish anatomist, was the first to describe this fetal vein during the period from 1911 to 1922. The embryonic nature of the draining vein was confirmed by Raybaud et al. in 1989.35 The arterial supply can arise from the anterior and/or posterior circulation. Due to the observed dilation in the usual location of the vein of Galen, these malformations were originally named vein of Galen “aneurysms.” Yaşargil39 described them as a group of AVMs with or without AVFs. Since they are not true aneurysms and actually are malformations involving the persistent fetal median prosencephalic vein and not the true vein of Galen, the term vein of Galen aneurysm is slowly being replaced by VGAM.

Due to significant diagnostic confusion among practitioners regarding various vascular malformations that lead to dilation of the vein of Galen or its embryonic precursors, the incidence of true VGAM is difficult to determine. According to the literature, the incidence of “vein of Galen malformations” is reportedly less than 1% of all vascular malformations, irrespective of the true nature of the lesion. In the pediatric population, 30% of brain vascular malformations have been reported to be due to vein of Galen aneurysms.2,6–8,12,18,23,28,30,31,36

Abbreviations used in this paper: AV = arteriovenous; AVF = AV fistula; AVM = AV malformation; VGAM = vein of Galen aneurysmal malformation.
egorization of these lesions in the absence of a uniform classification system is difficult. Furthermore, due to the different types of malformations affecting different age groups and resulting in different clinical sequelae, a definitive and universal treatment paradigm does not exist.

Overview

Anatomy of VGAM

Normally, septal and thalamostriate veins come together to form the internal cerebral vein. The internal cerebral vein, basal veins of Rosenthal, atrial veins, and pericallosal veins fuse to form the single great vein of Galen. The inferior sagittal sinus converges with the vein of Galen to form the straight sinus that flows toward the confluence of the sinuses. Important relationships to the vein of Galen are the third ventricle anteriorly, the quadrigeminal cistern posteriorly, the posterior commissure ventrally, and the habenular commissure dorsally. The splenium is superior and the tectal plate is inferior to this vessel. In the abnormal anatomy of VGAMs, venous blood drains from the dilated persistent median prosencephalic vein of Markowski into the straight sinus, which may be stenotic or duplicated; such lesions have been demonstrated in a publication of Yaşargil in 1988.39 The straight sinus can also be absent. In this case, the venous flow can find alternative pathways. It can flow through an aberrantly persisting falcial sinus and then into the superior sagittal or posterior venous sinuses. All the alternate venous pathways will be described later in the paper.

Because there is not usually a normal connection to deep cerebral veins, deep brain structures use alternative drainage pathways, which include thalamic and subtemporal or lateral mesencephalic veins.13 Arterial supply can arise from the anterior and/or posterior circulation. When arising from the anterior circulation, arterial blood comes through the anterior choroidal and pericallosal arteries, with distal branches of the latter being the most usual supply from the anterior circulation. The posterior circulation contributes through branches of the posterior cerebral arteries including the posterior callosal and choroidal arteries, perforating arteries from posterior communicating arteries, and P1 segments (Fig. 1).

Embryological and Pathophysiological Characteristics

The median prosencephalic vein of Markowski usually regresses during the 11th week of gestation, and by 3 months of gestation the posterior part of it joins the internal cerebral veins and basal veins to form the vein of Galen. In a VGAM the arterial tributaries to the median prosencephalic vein persist, along with the median prosencephalic vein itself. Failure of the normal degeneration of the median prosencephalic vein and persistence of its primitive arteriovenous fistulous connections are the central events leading to persistence of this vein instead of the vein of Galen. It has been postulated that the development of a VGAM might be an acquired event between the 6th to 8th weeks and the 11th week of gestation.13 Secondary to aberrantly persistent AVFs and malde-

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Development of the normal venous vasculature, the straight sinus might be stenotic, fenestrated, duplicated, or absent. An accessory torcular might be present, especially in light of the fact that the cavernous sinuses are underdeveloped in early life. Fully developed cavernous sinuses are first seen after 6 months of age, and therefore there is a higher outflow through the posterior venous pathways prior to 6 months of age. The transverse sinus may also be stenosed. Secondary to the outflow obstruction, engorgement and enlargement of an accessory straight sinus (parietooccipital vein) or falcine sinus and reflux to the internal cerebral vein might be seen (Fig. 3).

Classification of VGAMs

**Litvak Categories**

In 1960 Litvak et al.\(^25\) were the first to recognize a need for a classification system of vascular malformations involving the region of the vein of Galen. Based on a review of the literature, his personal experiences, clinical and pathological considerations, and the amenability to surgical treatment, he suggested the following 3 categories. Category A, termed “Aneurysms of the great vein of Galen,” included a singular dilation of the great cerebral vein of Galen contiguous with a dilated straight sinus and torcular, fed by anomalous branches of the anterior and posterior circulation. Category B, termed “Racemose conglomerations of blood vessels deep in the cerebral structures with dilated deep venous structures,” included a vermiform cluster of arteries and veins located in the midline and deep cerebral structures draining centrifugally into dilated deep veins and sinuses that may not include the vein of Galen itself, even though it might be displaced or engorged. “Angiomas and hemangiomas” are terms used for this vermiform cluster. In comparison with Category A, Category B tends to become symptomatic at an older age and manifests with hemorrhage rather than hydrocephalus and cardiac failure. Category C, which is named “Transitional types of midline arteriovenous shunts” (thus lesions that would not belong to either category), included singular vascular dilations other than the vein of Galen draining into dilated sinuses and deep veins; midline “angiomas” or “racemose vascular conglomerations” in combination with one or more aneurysmally dilated vessels, including the vein of Galen; and direct arterial shunts to deformed and dilated venous sinuses. Based on interpretation of descriptions and illustrations, the vascular lesions that Litvak referred to as Category B are probably true AVMs. The dilated and deformed venous sinuses directly fed by arteries of Category A or C are probably dural AVFs.

The Litvak classification system lost popularity after the 2 newer classification systems were proposed.\(^22,39\) Laşjaunias’s classification takes into consideration the fis-
tulous connection at the anterior or lateral aspect of the median prosencephalic vein, the number of feeding arteries, and the presence of venous stenosis. Interestingly, the degree of heart failure appears to be independent of the characteristics of the AV shunt because high-flow lesions are frequently well tolerated and small shunts can lead to multiorgan failure.

Lasjaunias Types

Lasjaunias described 2 groups. Type I, the choroidal type, is the most common and more complex type and has multiple feeding arteries that enter the anterior aspect of the median prosencephalic vein via tributary veins (Fig. 4A). The arterial feeders are all choroidal arteries, including bilateral anterior and posterior choroidal arteries, anterior cerebral arteries, and frequently, the thalamoperforating and collicular or quadrigeminal arteries. Clinically, this type is the most severe form of the disease, causing high-output cardiac failure in the newborn secondary to multiple high-flow fistulas with little outlet restriction.

In Type II, the mural type, there are single or multiple fistulas at the inferolateral margin in the wall of the median prosencephalic vein (Fig. 4B). Arterial feeders arise from the collicular or quadrigeminal arteries and/or the posterior choroidal arteries and may be unilateral or bilateral. Due to the smaller number of fistulas and more outflow obstruction, they are associated with more severe dilation of the median prosencephalic vein and manifest later in infancy as macrocephaly, hydrocephalus, or failure to thrive. Cardiac failure, if present, is mild and cardiomegaly may be asymptomatic.

Yaşargil Types

In his classification, Yaşargil divided these malformations into 4 types. The distinctions in Yaşargil’s classification are whether the malformation is a pure AVF (Types I–III) or an AVM with or without associated AVF (Types IVA–C), and the exact origin of the feeding arteries. Type I is a pure AVF between the leptomeningeal arteries such as pericallosal branches and/or feeders from the P3 segments of the posterior cerebral arteries and vein of Galen (Fig. 5). Type II has feeders from the thalamoperforating vessels and from the P1 and P2 segments of the posterior cerebral arteries (Fig. 6). Type III, which is the most common type, is a mixture of Types I and II. In this type, there are not only leptomeningeal shunts to the vein of Galen, but also participation of perforating arteries from the posterior communicating arteries and from the P1 segment of posterior cerebral arteries (Fig. 7). Type IV, also known as the secondary type, has 3 subtypes. Type IVA is an aneurysmal dilation of the vein of Galen resulting from shunting from an adjacent thalamic AVM (Fig. 8). Type IVB is similar to Type IVA but with the AVM being mesencephalic instead of thalamic (Fig. 9), and Type IV C is a thalamomesencephalic or mesodiencephalic plexiform malformation along with an adjacent and separate cisternal AVF to the vein of Galen (Fig. 10).

Besides an enlarged vein of Galen, there are enlarged median atrial vein, internal cerebral vein, and basal vein of Rosenthal. Pathognomonic for this type are enlarged distal pericallosal feeding arteries (A1) or distal feeding arteries from the posterior cerebral arteries (P2) on angiograms. A comparison of Litvak and Yaşargil’s classifications shows that Yaşargil’s Types I–III are comparable to Litvak’s Type A, Yaşargil’s Types IVA–B to Litvak’s Type B, and that Yaşargil’s Type IV C falls into Litvak’s Category C. These 2 classifications are important when considering open surgery, whereas Lasjaunias’s classification is relatively more suitable for endovascular management. The important venous differences in the Yaşargil types are that the internal cerebral veins remain invisible on angiograms in Types I–III, and that in Type IV the internal cerebral and mesencephalic veins are dilated and visible in the early phase of angiograms synchronically filling with the dilated vein of Galen, the straight sinus, or the fetal parietooccipital vein.

Secondary Enlargement of Vein of Galen

In contrast to VGAMs, in this group the true vein of Galen and not its embryonic precursor is enlarged and receives drainage from an AVM. In contrast to VGAMs, in this group the true vein of Galen and not its embryonic precursor is enlarged and receives drainage from an AVM. Dilation of the vein of Galen may occur secondarily to an adjacent vascular malformation, fistula, or venous outlet obstruction. This group can be divided into 2 entities: the vein of Galen dilation and the vein of Galen varix.

Vein of Galen Dilation

Vein of Galen dilations are a group of malformations that drain pial or dural shunts into the true vein of Galen or its tributary associated with dilation of the vein of Galen. The degree of dilation is variable and depends on the extent of venous stenosis or thrombosis. The frequency of vein of Galen dilations in neonates and infants is low, and patients with these malformations often present in late childhood, with intracranial hemorrhage and focal neurological deficits, and at a very young age, with delayed psychomotor development. Dural AVMs with vein of Galen dilations are acquired lesions that present in the 4th or 5th decades of life, in which AV shunts are located in the wall of the vein of Galen itself.
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Dilation of the vein of Galen may be secondary to straight sinus stenosis or thrombosis. Reflux into afferent cerebral veins from the vein of Galen is noted. The clinical presentation is similar to that of other dural AVMs draining into cerebral veins. The arterial supply of the dural AVM is predominantly from dural falcorientorial arteries of the carotid or vertebral systems and from the vasa vasorum to the wall of the vein of Galen, which arise from pial arteries. Epilepsy is not common in patients with vein of Galen dilations, due to the deep location of the lesions, and heart failure is also uncommon because of the presentation in older children.2,14

Vein of Galen Varix

Vein of Galen varices are dilations of the vein of Galen in the absence of an AV shunt.2 Two types have been encountered in children. One is a transient dilation of the vein of Galen in neonates presenting with cardiac failure from a cause other than VGAM. This dilation is usually found on ultrasound studies and disappears within several days following improvement of cardiac conditions. The dilation is asymptomatic. The second type of vein of Galen varix occurs as an anatomical variation when venous drainage of the brain converges toward the deep venous system. It is asymptomatic, but the lack of compliance of this type of venous drainage may lead to cerebral venous thrombosis.3

Clinical Presentation

Patients can be divided in neonatal, infantile, and juvenile/adult age groups.4 In the neonatal age group, these malformations usually lead to heart failure secondary to AV shunting. In the infantile form the malformations tend to cause hydrocephalus and head enlargement,5 and in the juvenile/adult group hydrocephalus, headaches, and developmental delay are often present.

Cardiac Failure

Patients with VGAM diagnosed in the neonatal period almost always present with high-output cardiac failure. Cardiac failure in the fetus is rare but is associated with a poor prognosis.6 One series of 18 patients with prenatally diagnosed VGAM showed that the presence of cardiac enlargement on prenatal ultrasound was not compatible with life.7 Symptoms usually develop as a result of changes in the circulation from the fetus to the newborn. In the fetus, as a result of high pulmonary re-
sistance, most of the output from the right heart bypasses the left heart and flows directly into the aorta through the pulmonary artery and ductus arteriosus. With the presence of a high-flow AVF, there is volume overload of the right ventricle without significant volume surplus of the left ventricle. With delivery of the newborn, several circulatory changes occur. A decrease in pulmonary resistance results in an increase in pulmonary blood flow, increased pulmonary venous return, and an elevation of left atrial pressure and closure of the foramen ovale and the ductus arteriosus. Under these circumstances, the existence of a high-flow fistula leads to volume overload in all 4 heart chambers. Elevated pressure in the right atrium and increased pulmonary blood flow from the fistula maintains right-to-left shunting through a patent foramen ovale and the ductus arteriosus. Coronary perfusion is compromised due to reduction of end-diastolic pressure in the aorta in the presence of an AVF, increase in end-diastolic ventricular wall pressure from increased preload, and reduction in the duration of diastole with tachycardia. Diversion of blood flow to the fistula results in diastolic flow reversal in the descending aorta.32 Low perfusion leads to liver, kidney, and multiple organ failure.4

Diuretics and volume restriction to reduce preload are the mainstay of medical treatment for neonatal high-output cardiac failure. Administration of inotropic agents to increase cardiac contractility can improve cardiac output. Digitalis, dopamine, and dobutamine have been used for this purpose. Digitalis therapy in neonates is challenging because it affects liver and kidney function and the clinical benefits of digitalis to increase contractility further in an already hyperfunctioning heart are unclear. Digitalis therapy through the mother for the fetus with a prenatally diagnosed VGAM facilitates control of digitalis levels in comparison with beginning this therapy after birth.4 Nitric oxide is used as a treatment for the resultant pulmonary hypertension. Unless medical treatment is insufficient to control heart failure and emergency embolization in the neonatal period is indicated, the neonate will be discharged home to allow for weight gain and scheduled for treatment of the VGAM at 5 months of age.4

**Hydrocephalus**

Malabsorption of CSF and venous hypertension caused by an intracranial AV shunt usually occur in infants and young children. Several different mechanisms lead to CSF malabsorption in this age group. Arachnoid granulations, the main mechanism of CSF reabsorption in the mature brain, are not recognized until the 35th week after birth and develop thereafter. Instead, medullary veins located in proximity to the ventricular wall are
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Fig. 10. Yaşargil Type IVC malformation—mesodiencephalic AVM. A: Note the feeders from posterior communicating artery and P1 segments, and drainage to the dilated vein of Galen. There is also a separate fistulous connection from the pericallosal and P2 segments to the dilated vein of Galen. B: Note thalamomesencephalic AVM as well as a separate fistulous connection between the distal pericallosal artery and the vein of Galen. The internal cerebral vein is usually dilated. (Figure and original illustration by P. Roth in Microneurosurgery, Volume IIIIB by M. G. Yaşargil, published by Thieme Verlag in 1988. Illustration modified by C. J. Griessenauer and M. M. Mortazavi. Reprinted with permission.)

thought to be responsible for CSF absorption in neonates and infants. Neonatal venous drainage into the torcula occurs because connection to the cavernous sinuses is delayed and occurs several months after birth. Venous hypertension in the presence of an AV shunt results in CSF malabsorption, which is further aggravated by pulmonary hypertension and premature closure of the ductus arteriosus and foramen ovale. An AV shunt also inhibits proper maturation of the jugular bulb and results in persistent patency of embryonic sinuses draining from the torcula. This in turn prevents maturation of the sigmoid sinus. With closure of the embryonic sinuses, venous hypertension, and occlusion of the sigmoid sinus and jugular bulb, drainage relies on alternative routes through the cavernous sinus. If extracranial venous connections are established at that time, symptoms are mild. Without these connections, symptoms of venous hypertension such as hemorrhage and seizures from cortical venous reflux develop.2

Direct compressive obstructive hydrocephalus from VGAMs is rare although compression of the aqueduct by the malformation is possible. With occlusion of the transverse and sigmoid sinuses or the jugular bulb, the superior and inferior petrosal sinuses are the only venous drainage pathways of the posterior fossa. If the cavernous sinuses are underdeveloped, venous congestion of the cerebellum can lead to tonsillar herniation. This phenomenon is potentially reversible if endovascular embolization is used early. Since the tonsillar herniation under these circumstances is not a reflection of globally increased intracranial pressure, ventricular shunt insertion is not indicated. Ventriculomegaly without increased intracranial pressure occurs with subependymal atrophy. Continued progressive destruction of surrounding brain parenchyma, mainly affecting the white matter, is referred to in advanced stages as “melting brain syndrome,” which consists of rapid destruction of the brain (mostly the white matter), with secondary enlarged ventricles.2,21 It occurs as a result of decreased venous blood flow with venous hypertension in the presence of any form of AVF. It is only observed in fetuses, neonates, and infants and is indicative of a poor prognosis. Because it is rapidly progressive and irreversible once it starts, emergency treatment should be undertaken.20

Endovascular embolization to decrease venous hypertension is the preferred modality for prevention or treatment of hydrocephalus. Ventricular shunt placement is a less favorable option in the treatment of hydrocephalus because it will reverse the pressure gradient between the ventricles and the brain parenchyma, thus aggravating the venous congestion and brain edema. This can result in calcification of the white matter and subependymal atrophy, which will clinically manifest as seizures or mental retardation.

Treatment and Outcome

Endovascular therapy has emerged as the treatment of choice. Prior to the advent of endovascular therapy, direct clipping of some AVFs was performed. Currently, surgery is only indicated in exceptional cases as a complement to endovascular therapy (Fig. 12).

Surgery

Surgery has played some role prior to the advent of endovascular therapy. Via craniotomy and an occipital paramedian transcalfine-transientorial approach, access to the bilateral aspects of the VGAM has been possible. The pericallosal and posterior cerebral artery feeders as well as thalamoperforators have been able to be occluded, with good long-term results (Yaşargil Types I, II, and III).39 These types can be microscopically explored and the feeding arteries eliminated using bipolar coagulation. The additional occurrence of mesodiencephalic plexiform AVM (Types IV A–C) is not amenable to surgical
therapy due to involvement of the thalamic or eloquent mesencephalic circulation. The appearance of the dilated internal cerebral veins on cerebral angiograms should be seen as a warning sign. Open surgery of Type IV malformations without previous embolization has turned out to be hazardous in Yaşargil’s experience, keeping in mind that preoperative selective embolization of the perforating vessels from posterior communicating arteries and P2 segments was unavailable in Zürich before 1985. Microsurgical devascularization can be performed in children with moderate clinical conditions or in patients with residual feeders following endovascular management (Fig. 13). (See Table 1 for a summary of Yaşargil types and a treatment proposal.)

Endovascular Therapy

Today the mainstay of therapy is transarterial embolization of VGAM in patients who survive, to achieve as normal a neurological development as possible.23 Patient selection and timing are critical factors in the management of this condition. It is more important to restore normal growth conditions than a normal morphological appearance, with the primary therapeutic objective being normal development of the child. Most authors would
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**TABLE 1: Angiographic findings and treatment proposal for VGAMs according to Yaşargil**

<table>
<thead>
<tr>
<th>Angiographic Findings &amp; Proposed Treatment</th>
<th>VGAM Type</th>
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<tbody>
<tr>
<td><strong>pericallosal arteries, P&lt;sub&gt;1&lt;/sub&gt;-P&lt;sub&gt;2&lt;/sub&gt; arteries, &amp; anterior &amp; posterior choroidal arteries</strong></td>
<td>present</td>
</tr>
<tr>
<td><strong>perforators from posterior communicating arteries, P&lt;sub&gt;1&lt;/sub&gt; perforators</strong></td>
<td>absent</td>
</tr>
<tr>
<td><strong>like Type II, plus accompanied by intrinsic thalamic or mesencephalic plexiform AVM or both</strong></td>
<td>absent</td>
</tr>
<tr>
<td><strong>internal cerebral veins, atrial vein, &amp; lat mesencephalic veins are visualized on cerebral angiogram</strong></td>
<td>absent</td>
</tr>
<tr>
<td><strong>surgery</strong></td>
<td>yes</td>
</tr>
<tr>
<td><strong>embolization before or after surgery</strong></td>
<td>yes</td>
</tr>
<tr>
<td><strong>embolization alone</strong></td>
<td>yes</td>
</tr>
<tr>
<td><strong>Gamma Knife surgery</strong></td>
<td>no</td>
</tr>
</tbody>
</table>

* Personal correspondence, 2012.

also agree that patients at the far ends of the presentation spectrum, those with profound symptoms and multisystem failure, and those with asymptomatic lesions may be followed expectantly. Lasjaunias has reported the largest series of patients with transarterial embolization, which we will refer to in later sections of our paper. Of the 216 cases reported, death occurred despite or because of embolization in 10.6%. Of the survivors, 74% were neurologically normal, 15.6% had moderate retardation, and 10.4% had severe retardation. Age appears to be an important prognostic factor; the death rate in the neonatal group was 52% compared with 10.6% for the whole cohort.

**Treatment in Neonates (birth–1 month)**

Of the 216 patients reported by Lasjaunias et al., 23 were classified as neonates. Prenatal diagnosis is not by itself an indication for termination of pregnancy, early delivery, or cesarean delivery. Only 2 prenatal manifestations have shown prognostic value and represent an indication for abortion: in utero cardiac failure and cerebral damage. These findings are associated with severe, irreversible multiorgan failure at birth. When the diagnosis of VGAM is suspected, a pretherapeutic evaluation should be performed including the following information: (1) clinical evaluation, including height and weight; (2) evaluation of renal and liver function; (3) ultrasound to evaluate for encephalomalacia; (4) cardiac ultrasound; (5) brain MRI; and (6) electroencephalogram if the infant is in an ICU, intubated, and sedated. Lasjaunias and colleagues have developed a scoring system to best predict the degree of cerebral tissue impairment not evident on imaging in an effort to facilitate treatment decisions (Table 2).

The Bicêtre neonatal evaluation score assesses cardiac, cerebral, respiratory, hepatic, and renal function. A score of less than 8 of 21 is associated with a poor outcome and may be an indication for not treating. A score of 8–12 indicates emergency endovascular treatment. A score of greater than 12 of 21 indicates medical management until the child is at least 5 months old. At 5 months of age, endovascular treatment may be offered. Lasjaunias et al. reported that treatment at 5 months of age provides the optimal balance of maximum efficacy of embolization while minimizing the risk of cerebral maturation delay. The optimal treatment strategy involves transarterial embolization of the AV shunt in an effort to reduce flow and recreate conditions enabling further maturation of the vascular system. Venous embolization in neonates has been associated with greater morbidity and should not be used when an arterial route is available. Glue is the preferred agent of embolization due to its resistance to recanalization. A complete angiographic cure is not necessary for clinical improvement, and the end point of partial embolization is usually a reduction of 30%–50% of the AV shunt expected to result in significant systemic impact. Death occurred in 52%. Of the survivors, 36.4% were neurologically normal, 54.5% had moderate retardation, and 9.1% had severe retardation (Table 3).

**Treatment in Infants (1 month–2 years)**

Of the 216 patients reported by Lasjaunias et al., 153 were classified as infants. In this group the immediate goal is to preserve the hydrovenous equilibrium, to preserve normal brain development, and to exclude the lesion. Hydrocephalus in patients with VGAMs is due to intracranial venous hypertension and frequently responds to treatment of the lesion. Insertion of a CSF shunt should be postponed until after endovascular treatment of the lesion for two reasons. First, CSF shunting procedures can be problematic in this patient population, contributing to vasocongestive brain edema, and can carry a risk of subdural hematoma development. Second, less than 50% of patients with hydrocephalus will require a shunt. Today, endoscopic third ventriculostomy offers an acceptable alternative to shunt placement after embolization in patients with symptomatic hydrodynamic disorders. Developmental delay is a part of the natural history of untreated VGAMs, due to long-term intracranial venous hypertension and hydrocephalus. Although elevated intracranial pressures are well documented in patients with VGAM, some authors are unwavering in their belief that
embolization should be performed to normalize venous pressure and treat hydrocephalus prior to CSF shunting procedures. These patients were treated with transarterial embolization in which glue was used. Death occurred in 7.2%. Of the survivors, 78.9% were neurologically normal, 11.3% had moderate retardation, and 9.8% had severe retardation (Table 3).

**Treatment in Children (2–16 years)**

Of the 216 patients reported by Lasjaunias et al., 40 were classified as children (nonneonates/noninfants). In this subgroup no deaths occurred, 67.5% were neurologically normal, 20% had moderate retardation, and 12.5% had severe retardation (Table 3).

**Complications of Embolization**

In the 12-year experience of Lasjaunias and colleagues the following complication rates were reported: 1.5% risk of death related to embolization, 1.6% risk of transient neurological disability, 2.1% risk of permanent neurological disability, 5.6% risk of hemorrhage, and 6.7% risk of a nonneurological complication.

**Alternative Approaches—Transvenous Embolization**

Some centers treating VGAM use both transarterial and transvenous approaches, depending on the angioarchitecture of the lesion. However, many centers reserve the transvenous approach for those cases in which transarterial embolization has either failed or is not feasible. When the transvenous approach is used, occlusion of the VGAM is usually obtained by packing the venous pouch with materials such as coils, balloons, or nylon. If transvenous embolization of the VGAM is performed without careful consideration of the arterial and venous anatomy, complications may occur. Blind occlusion of the vein can impair venous drainage of the brain, resulting in venous hypertension, infarction, and hemorrhage. Although some small series report favorable outcomes with no major complications following percutaneous transvenous embolization of VGAM, there remains a preponderance of evidence suggesting that the venous route is associated with increased morbidity and should only be used when an arterial route is not available.

**TABLE 2: Bicêtre neonatal evaluation score**

<table>
<thead>
<tr>
<th>Points</th>
<th>Cardiac Function</th>
<th>Cerebral Function</th>
<th>Respiratory Function</th>
<th>Hepatic Function</th>
<th>Renal Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>normal</td>
<td>normal</td>
<td>normal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>overload, no med.</td>
<td>subclinical, is. EEG abnormalities</td>
<td>tachypnea, finishes bottle</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>failure, stable</td>
<td>nonconvulsive, intermittent neurologic signs</td>
<td>tachypnea, does not finish bottle</td>
<td>no hepatomegaly, normal hepatic function</td>
<td>normal transient anuria</td>
</tr>
<tr>
<td>2</td>
<td>failure, not stable</td>
<td>isolated convulsion</td>
<td>assisted ventilation, normal saturation FIO2 &lt; 25%</td>
<td>hepaticmegaly, normal hepatic function</td>
<td>unstable diuresis with treatment</td>
</tr>
<tr>
<td>1</td>
<td>ventilation n.</td>
<td>seizures</td>
<td>assisted ventilation, normal saturation FIO2 &gt; 25%</td>
<td>moderate or transient hepatic insufficiency</td>
<td>abnormal coagulation, elevated enzymes</td>
</tr>
<tr>
<td>0</td>
<td>resistant to med. therapy</td>
<td>permanent neurological signs</td>
<td>assisted ventilation, desaturation</td>
<td>normal</td>
<td>anuria</td>
</tr>
</tbody>
</table>


**TABLE 3: Therapeutic results in the embolized group, 1981–2002**

<table>
<thead>
<tr>
<th></th>
<th>Neonates</th>
<th>Infants</th>
<th>Children</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>neurologically normal (BOS 3–5)</td>
<td>36.4% (4/11)</td>
<td>78.9% (112/142)</td>
<td>67.5% (27/40)</td>
<td>74% (143/193)</td>
</tr>
<tr>
<td>moderate retardation (BOS 2)</td>
<td>54.5% (6/11)</td>
<td>11.3% (16/142)</td>
<td>20% (8/40)</td>
<td>15.6% (30/193)</td>
</tr>
<tr>
<td>severe retardation (BOS 1)</td>
<td>9.1% (1/11)</td>
<td>9.8% (14/142)</td>
<td>12.5% (5/40)</td>
<td>10.4% (20/193)</td>
</tr>
<tr>
<td>death despite or because of embolization</td>
<td>52% (12/23)</td>
<td>7.2% (11/153)</td>
<td>0% (0/40)</td>
<td>10.6% (23/216)</td>
</tr>
</tbody>
</table>

* BOS = Bicêtre outcome score. Total of 216 patients, 193 surviving. Note that nearly 50% of neonates referred for management died. Many of these represent earlier cases that today would be scored below eight and, thus, would fall into the nontreatment group. Reprinted with permission from Lasjaunias PL, Chng SM, Sachet M, Alvarez H, Rodesch G, Garcia-Monaco R: The management of vein of Galen aneurysmal malformations. Neurosurgery 59 (5 Suppl 3):S184–S194, 2006 (Table 7). [Note a relatively low overall mortality rate of 10.6%, a significantly high mortality rate for the neonatal group, and no deaths in the children group. M. M. M.]
Vein of Galen aneurysmal malformations

Gamma Knife Treatment for VGAM

The literature is scarce on Gamma Knife treatment for VGAM. Payne et al. reported on a series of 8 patients including individuals with Yaşargil Types I–IV. Although 1 of the patients failed to undergo a final angiogram, among the other 7 there was no residual filling in 4, residual fistula in a nonirradiated fistula that was initially missed in 1, and marked reduction in filling in 2. Therefore, it appears that use of the Gamma Knife can be complementary in selected cases.

Challenges in the Management of VGAM

Cardiac manifestations include high-output congestive heart failure due to the intracranial AV shunt. In most cases there is a brief period of stabilization, after which the congestive heart failure worsens during the first 3 days of life, then stabilizes again and improves with appropriate medical management. Severe congestive heart failure requiring mechanical ventilation is usually associated with poor outcome. The congestive heart failure encountered in the setting of a VGAM usually resolves after endovascular treatment of the lesion. The cardiac status usually improves even if complete occlusion of the VGAM is not achieved.

Macrocrania and hydrocephalus are additional challenges caused by VGAM. They result from abnormal hemodynamic conditions present at the confluence of the sinuses, the posterior convergence of the venous drainage of the brain, and the immaturity of the granulation system. Endovascular treatment of the VGAM followed by shunt insertion or third ventriculostomy, if necessary, provides the best option for treatment of these disorders. Dural sinus occlusion with subsequent supratentorial and infratentorial reflux can produce venous infarction and tonsillar prolapse, respectively. Both situations are best managed by endovascular embolization. Late sequelae include seizures and mental retardation, and these are the main symptoms if correction of the AV shunt has not been performed in time.

Discussion

Since 1937 when Jaeger coined the term “vein of Galen aneurysm,” the understanding of this entity has evolved substantially based on significant advancement in understanding its embryological development. In 1960, Litvak et al. took another pioneering step when they presented a case series of 10 patients and divided them into aneurysms, AVMs, and a mixture of the two, as well as other vascular malformations. The next landmark step was taken by Yaşargil when he broke away from the term “aneurysm” and moved toward the use of “aneurysmal dilation” in describing the vein of Galen as a secondary feature of an AVM or AVF. This was the first time that the fistulous nature of this entity was brought into focus. Yaşargil, furthermore, made extensive descriptions of common arterial feeding vessels and the draining vein patterns. He categorized surgical routes to treat these entities based on the aforementioned delineation of the vascular anatomy. However, the literature is relatively scarce in regard to surgical management of this group of malformations with acceptable results.

Lasjaunias made another crucial step in describing this condition. He emphasized more the arteriovenous nature of this entity, the location of the shunting, and the volume of the shunting. Surprisingly, he reported that the amount of shunting had no impact on the outcome.

The change of nomenclature of this entity over time entails the change from a descriptive to a more functional terminology. Initially, the malformation was described as an aneurysmal dilation of what was thought to be the vein of Galen. With further research, we now know that it is a pathological persistence of the fetal median prosencephalic vein of Markowski along with its fetal arterial tributaries, and it is the secondary shunting within it that makes the functional basis of the term VGAM. To emphasize the fetal origin of this term is crucial because there are conditions with vein of Galen dilations that are secondary to other acquired lesions, venous stenosis, and AVFs.

Along with a better understanding, better treatments have emerged. Litvak’s classification had only a short popularity because it was not easily applied and did not have a practical association with clinical syndromes, treatment, and outcome. The current 2 classifications by Lasjaunias and Yaşargil, although relatively different in their view, are more helpful. The fact that both classifications continue to be used indicates the lack of a uniform classification system. Both are descriptive of the functional and angiographic findings but do not incorporate the associated clinical findings and outcomes. The Yaşargil classification is probably the most descriptive one so far proposed, with application toward open neurosurgery, whereas the Lasjaunias system is more applicable to endovascular approaches. However, few have reported on results after craniotomies for VGAM, and with the advent of endovascular treatment open surgery has become much less common.

A new more translational classification is needed. The problem is that the clinical picture does not always follow the angiographic findings; complete angiographic resolution is not needed to get a good clinical outcome. Another problem is that this is a complex anatomical abnormality with multiple vascular variations. With the emergence of endovascular surgery, the treatment of VGAM has changed substantially. Both transarterial and transvenous embolization are now possible. The goal of treatment is to reach a steady neurophysiological and hemodynamic state with as little risk of neurological sequelae as possible, even though this may entail only a partial embolization of the lesion. Equally important is to postpone shunt insertion until all the available endovascular armamentarium has been used, allowing the venous pathophysiology to alter to a more normal state, avoiding shunt placement as well as secondary encephalomalacia.

New Classification System

Although it is not validated, we propose a new classification scoring system combining the previous ones and including the 2 most important parameters affecting outcomes reported so far: heart failure and age (Table 4).
Arterial Feeders. It has been shown that distal pericallosal and posterior cerebral arteries can be sacrificed without major sequelae to the deep structures. Sacrificing P1–2 feeders, thalamoperforators, choroidal and direct feeders from the basilar artery has so far not been possible without major neurological deficit. Therefore, it appears that sacrificing those feeders is a limiting factor for successful treatment of the malformation, and inclusion of those into the treatment would entail worse outcome. Occurrence of any of these feeders is therefore given 1 point, and lack of them is given 0 points.

Clinical Symptoms. Heart failure is clearly the condition that carries the highest risk for a poor outcome. Data show that heart failure diagnosed prenatally carries the highest risk for a poor outcome. Other clinical syndromes including seizure and hydrocephalus are generally treatable. One series of 18 patients with prenatally diagnosed VGAM showed that the presence of cardiac enlargement on prenatal ultrasound was not compatible with life. We propose that patients with heart failure get 1 point and those without get 0 points.

Age. The venous system matures within the first 6 months of postnatal life. For instance, the cavernous sinuses are immature at birth and the cerebral venous outflow is mostly dependent on the posterior venous circulation. Younger age has more of a negative impact than older age. Because 5 months of age has been used as a cutoff in Lasjaunias and colleagues’ large series, for treatment of these entities we believe it is reasonable to give a higher score to patients younger than 5 months of age compared with those who are 5 months or older. Therefore, patients 5 months or older get 0, and those younger than 5 months of age get 1 point. The ratio of risk and benefit of treatment appears to be in favor of treatment at 5 months and thereafter, prior to the development of irreversible sequelae. Thus, symptomatology requiring early treatment before 5 months of age is less favorable and carries a higher risk.

Arteriovenous Malformations. Although AVMs have been included in VGAM classifications by Litvak and Yaşargil previously, we think that these lesions should be excluded. The fact that the vein of Galen is dilated in the vicinity of a thalamic or mesencephalic AVM might be a secondary process, and the vein of Galen dilation does not need to be primarily involved in the pathology. The fact that the vein of Galen is significantly dilated in Yaşargil Type IV malformations compared with the enlargements secondary to an adjacent AVM described earlier can have to do with the amount of shunting and not be a primary pathological process. We agree, however, that the vein of Galen itself usually appears malformed in Yaşargil Type IVA and B malformations, but the main pathological process in Type IV is the mesodiencephalic AVM, and in Type IVC again it is the mesodiencephalic AVM, despite being associated with a separate AVF. Therefore, we suggest that AVMs should be completely excluded from this group. The degree of AV shunting was not considered in this classification proposal. Although lowering the amount of shunting has been a partial goal of therapy, previous evidence does not demonstrate a correlation between symptomatology and characteristics of the AV shunting.

Proposed New Treatment Recommendations

Table 5 shows the following treatment recommendations (Table 5): endovascular (no urgency, treat in 1 stage) for patients with 0–1 points; endovascular (urgency, treat in multiple stages) for patients with 2 points; and consider endovascular or palliative treatment (treat in multiple stages) for patients with 3 points.

Comparison of the Classification Systems

A comparison of the previous 3 classification systems with our proposed new classification system is shown in Table 6.

Conclusions

The optimal management of VGAM hinges on a correct understanding of the anatomy and pathophysiology of these entities. Transarterial embolization is the treatment of choice. Although each case is unique, CSF shunting procedures should be reserved until the outcome of previous embolization has been fully evaluated. Direct

**TABLE 4: New classification system proposed by Mortazavi et al.*

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>arterial feeders</td>
<td>0</td>
</tr>
<tr>
<td>any feeders other than P1–2, thalamoperforators, choroidal, basilar</td>
<td></td>
</tr>
<tr>
<td>clinical symptoms</td>
<td>0</td>
</tr>
<tr>
<td>no heart failure</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>0</td>
</tr>
<tr>
<td>≥5 mos</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>1</td>
</tr>
<tr>
<td>&lt;5 mos</td>
<td></td>
</tr>
</tbody>
</table>

* The distinctive difference of this system is inclusion of clinical symptoms and correlation to treatment. Note exclusion of AVM and inclusion of heart failure and age as important prognostic factors.

**TABLE 5: Treatment related to new proposed grading**

<table>
<thead>
<tr>
<th>Points</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–1</td>
<td>endovascular (no urgency); treat in 1 stage</td>
</tr>
<tr>
<td>2</td>
<td>endovascular (urgency); treat in stages</td>
</tr>
<tr>
<td>3</td>
<td>consider endovascular treatment or palliation; treat in stages</td>
</tr>
</tbody>
</table>

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TABLE 6: Angiographic comparison of all the existing and new classification systems*

<table>
<thead>
<tr>
<th>Litvak</th>
<th>Yaşargil</th>
<th>Lasjaunias</th>
<th>Proposed Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>I</td>
<td>Type II (mural)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>II</td>
<td>Type I (choroidal)</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td>excluded</td>
</tr>
<tr>
<td>B</td>
<td>IVA–B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>IVC</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Note the exclusion of true AVM in the new proposed classification system. Note also that there is no perfect comparison available between the new proposed classification system and the 3 older classification systems, which do not include any clinical symptoms, age, treatment, and outcome. Only the angiographic component of our proposed classification system is shown in this table.

surgery of the malformation itself has little role when safer endovascular therapies exist. We propose a more descriptive scheme for these malformations and would favor a more descriptive term for the entities, such as median proencephalic vein aneurysmal AVF or simply “Markowski malformations.” We also suggest that AVMs should be excluded from this group. A new classification scoring system combining angiographic and clinical presentation is proposed. The utility of this system can be confirmed after validation among users.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: Mortazavi, Tubbs. Acquisition of data: Mortazavi, Greissener, Foreman, Shahripour, Shoja, Tubbs. Analysis and interpretation of data: Mortazavi, Greissener, Shoja, Rozzelle, Tubbs, Fisher, Fukushima. Drafting the article: Mortazavi, Tubbs. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Administrative/technical/material support: Tubbs. Study supervision: Mortazavi.

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