Abstract

Arteriovenous fistulae between the embryonic vessels situated in the midline are often associated with aneurismal dilatation of the great cerebral vein. These fistulae occur in the telencephalic, diencephalic, and mesencephalic segments of the primitive brain. The evolution of these malformations is described.

INTRODUCTION

The term Vein of Galen malformation (VGM) includes a variety of vascular abnormalities. Various authors make a distinction between those that have an arterial component and those that are primarily venous dilatation of the vein without any arterial component. The origin of the VGA appears to be speculative in many instances.

The classical work by Padget indicate that the process of development of cerebral arteries and veins is very methodical and the basic segmental pattern of the primitive brain is retained even in the adult in spite of complex changes [1,2]. The present review highlights the drawbacks of forcing the adult anatomy to explain a complex developmental process that occurs in the embryo.

The interpretation of the angiograms is often difficult due to the complex anatomy. There are many classifications based on the radiological appearances. The management of these problems are based on the clinicians understanding of the embryology and interpretation of the flow pattern in these lesions. There are many studies to determine the flow characteristics based on experimental studies in the laboratory and dynamic interpretation of dynamic MR angiograms.

This paper reviews the recent concepts of embryology, classification, radiological interpretations, and flow patterns of the lesion. The author’s interpretation of the developmental anatomy and flow studies are also included. Without a clear understanding of the embryology speculating the process based on the features in the adult would result in poor treatment modalities.

CLASSIFICATION

The following are some of the types of classification that are popular at present.

Mortazavi et al classified based on: Arterial feeders - presence or absence of Thalamo perforators of the P1-2 segments Posterior Cerebral arteries, Chroidal and Basilar arteries, heart failure and age {5mos} [3].

Lasjaumas classified as Type 1- choroidal and Type 2-mural [4]. This classification is based on the concept that there are normally multiple capillary shunts in the early stages of development and they disappear as the development progresses. Vascular malformations occur due to persistent shunts. This interpretation is based on the findings in chick embryo by Streeter [5].

Sheth indicated that choroidal type of arteriovenous malformation is distinct from an arteriovenous malformation with venous drainage into a dilated, but already formed, vein of Galen (VG) [6]. The basis for this opinion is not made clear. Perhaps it stems from the publication by Streeter that in the normal developing brain there are multiple arterio venous connections which disappear in course of development. Streeter was unable to distinguish between arteries and veins in chick embryos. Therefore, the validity of this opinion by Sheth is questionable.

Galliod and Knipe and Khosla et al. indicate that persistent embryonic prosencephalic vein of Markowski drains into the VG [7-9]. These authors suggest that the VGMs are uncommon intracranial anomalies that tend to present dramatically.
Markoski’s description of the median procencephalic vein is not supported by later publication by Padget [1,2].

Kosla et al. suggest that in VGM with dilated median porencephalic vein the venous dilatation is the primary pathology [9]. They do not explain how a venous dilatation occurs spontaneously. There is no evidence to support the presence of a median procencephalic in the early embryo. Procencephalon is not drained by a single vein. There is only an anterior venous plexus at the stage when the authors indicate the presence of procencephalic vein. At 10mm stage procencephalon develops into telencephalon and diencephalon. It is at this stage one can identify segmental veins. The median proencephalic vein is not identified in any classical work on the anatomy of cerebral veins. Their classification of Pseudo-VGMs suggests that Vein of Galen dilatation is not VGM. They contend that the latter occurs with a component from arterio-venous malformation. The third group is said indicate that vein of Galen aneurysm occurs without the arterial component. This classification does not recognize arterial element in all VGMs.

Yasargil [10] classified as

Type I: small pure cisternal fistula between the VG and either the pericallosal arteries (anterior or posterior) or posterior cerebral artery.

Type II: multiple fistulous communications between the VG and the thalamic perforating vessels.

Type III: high flow mixed type I and II.

Type IV: parenchymal arteriovenous malformation (AVM) with drainage into the vein of Galen.

This classification is based on the angiographic findings. Yasargil classification accepts that all VGMs are due to arteriovenous fistula. His classification is based on the angiographic features.

Quisling and Mickle classified into three types based on the complexity of the nidus, afferent supply and efferent drainage patterns [11]. Their observations on the venous pressure provided the basis for treating the high output lesions via the venous route.

Raybaud et al. in a series of 23 patients identified arterial feeders from posterior choroidal, anterior cerebral and anterior thalamo perforators [12]. While they accept the embryonic origin of the VGM, they do not make any reference to the segmental locations of these vessels. The authors also suggest that the dilatation of the VG is due to the dilatation of median prosencephalic veins. They indicate that VGM develops late and does not have connections with the choroidal branches of the anterior cerebral artery. These theories are difficult to interpret in terms of embryology.

Amachar and Shillito have classified based on the clinical presentation in the neonates. The group 1 consists of neonates with cranial bruits and severe heart failure [13]. Group 2 consists of those with mild heart failure and craniomegaly within 6 months. Group 3 includes children up to 12 months with craniomegaly and no heart failure. This classification does not include visual problems, seizures and developmental retardation.

**DIAGNOSTIC TECHNIQUES**

Over a period of time various diagnostic studies have been used to evaluate the VGAs.

**Ultrasound**

During the intrauterine and early neonatal period, this procedure is favored because it is noninvasive and can be repeated. The color Doppler is useful in studying the blood flow within the malformation when evaluating the results of therapy [14].

**Computed Tomography**

The value of this investigation is limited to identifying thrombosis of the vein and presence of calcification.

**Magnetic Resonance Angiography**

This noninvasive technique is very valuable in identifying the anatomy of the lesion in axial, coronal and sagittal planes. Often this avoids invasive angiography. Flow features of the lesion is not reliable by this method. Angiography by injection techniques is still the standard study to evaluate the anatomy in great detail, particularly when a surgical option is considered [9,15,16].

Zivadinov et al. published recommendations for a multimodal protocol that includes both noninvasive and invasive screening procedures for evaluating these abnormalities [17]. Color Doppler ultrasound study to evaluate the chronic cerebral venous insufficiency has been suggested as a very effective method. Unfortunately, this is operator dependent and has problems in consistency. The 3-D MR venography map is operator independent and has a distinct advantage, because this method also provides good standard vascular images. The availability of such sophisticated techniques is very limited. These investigations are possible only after birth. Intrauterine diagnosis of this malformation provides only very basic information.

Fetal MRI evaluation [Wagner 18], is useful in identifying important prognostic factors such as cardiomegaly, hydrocephalus, severe dilation of jugular veins and injuries to the brain. This examination provides very little information regarding the flow characteristics of the malformation.

**CLINICAL PRESENTATION**

**Congestive cardiac Failure**

The VGM is established around 80mm stage of development. The clinical manifestation is dependent on the size of the fistula. Congestive cardiac failure is the major cause in infants and
neonates. Because of the shunt up to 80% of the left ventricular output is lost to the general circulation. There is overload on the right ventricle leading to myocardial ischemia [19]. Even in severe cases this problem does not occur in utero because the low vascular resistance of the placenta compensates for the volume lost by the shunt. Less severe shunts will manifest as proptosis, seizure, mental retardation. In lesser shunts the lesion may remain silent or present in adult life as intracranial hemorrhage or seizures. The reason for late presentation is because of subtle changes in the diameters of the feeding artery or the fistula or changes in systemic arterial pressure [20]. This concept is addressed in detail by Casikar.

**Hydrocephalus**

Hydrocephalus is generally due to obstruction to the aqueduct by the enlarged VGM. Problems with trans ependymal movement of the cerebrospinal fluid and cerebral atrophy are other possibilities [4,11,21].

**TREATMENT**

The primary goal of treatment is to control the congestive cardiac failure in the initial stages. Clear evidence of brain damage in radiographic studies is considered a contraindication for any treatment [4]. This is a controversial opinion because the degree of brain damage is difficult to quantify. In a clinically stabilized condition surgery may be an option. Jager tried bilateral carotid ligation. There was no evidence to support a favorable outcome following this procedure.

Microsurgical approaches to obliterate the feeding arteries have been reported [22-25]. There is a significant complication due to perfusion pressure break through resulting in brain swelling. Hemorrhage and seizures [26]. Occlusion of some of the feeding vessels to reduce the flow often results in steal phenomenon [20,25]. The experimental findings by Casikar and Ramaswamy identified the causes for the steal and have explained the reasons for this phenomenon. Bhagwat following CFD studies have further confirmed the conditions when steal is likely to occur [27].

Endovascular treatments by embolization and glue occlusions are more recent approaches to this problem. Bernstein et al. have suggested pre-operative occlusion of surgically inaccessible vessels followed by surgical ligation of major arterial feeders [28]. Trans torcular embolization is advocated by Mickle and Dowd as a better form of treatment [29,30]. The CFD studies by Bhagwat have suggested that venous pressure plays a critical role in the flow across the fistula [27].

**DISCUSSION**

It is a common practice to describe the anatomy of the Arteriovenous malformations (AVM) regarding adult anatomy. The arterial feeders and the venous sinuses into which the arterialised blood drains are easily identifiable. However, the arterialised venous channels extending between the arteries and the Dural sinuses are just described as "abnormal venous channels". These AVMs occur due to developmental anomalies in the embryos. It is possible to identify these vessels. These structures normally disappear during development, as they become atretic due to diversion of blood away from them. In the presence of an AVM, these vessels persist because of the abnormal flow created by the fistula [1,2]. This publication demonstrates the method of identification of these segmental vessels in VGM. It is possible to deduce the anatomy if the formations of these malformations are followed through the various stages of the development of the embryo.

The term vein of Galen aneurysm includes diverse group of vascular abnormalities. The anatomy of the VGMs in adult appear very complex. There are many attempts to classify these lesions based on the features in the adult. There is no common agreement on the definition of these lesions.

Sheth et al. and Kosla et al. indicate that dilatation of the vein of Galen can occur without an arterial component [6,9]. This opinion is based on embryology of Median Proencephalic vein described mercowski. There is no single vein draining the proencephalon. It is drained by Anterior venous plexuses. These authors indicate that this vein of Merkoski is the precursor of internal cerebral vein. Internal cerebral vein occurs around 24mm stage when the proencephalon is already subdivided into telencephalon and diencephalon with corresponding segmental veins [31].

As in other parts of the body, AVMs of the brain occur when there is a direct pathological communication between arteries and veins, without the intervention of a capillary system. Although trauma is responsible for many of the arteriovenous fistulae, cerebral arteriovenous malformations manifest in the intrauterine period because of defective development of the vessel walls in certain critical regions of the brain.

Since in the brain the pathological process occurs in an immature system [primitive brain], the severity of the lesions is more extensive when compared with those in other regions of the body. The way the primitive cerebral vascular system adjusts to the abnormal circulatory condition is governed by certain general principles of embryology. The complex variations seen in the post-natal period follow a definite predictable pattern.

The primitive brain [notochord] is segmental in origin. Each segment has a pair of arteries and veins. The segmental veins drain laterally into longitudinal channels. This pattern is repeated in every segment. Around the 40mm stage, these arteries and veins (pia-arachnoidal vessels) cross each other at right angles. If, at their points of intersection, the development of their vessel walls is defective, creating potential weakness, arteriovenous fistulae result.

The development of the arteries progress at a faster pace, compared with that of the veins [29]. At the 40-mm stage, the arterial system is nearly complete. The effects of an arteriovenous fistula on the arterial system, therefore, tend to be localised to the embryonic segment.
On the contrary, the venous system lags in its development. The influx of abnormal quantities of blood creates severe circulatory problems in the immature veins. The effects often extend to the regions distant from the primary lesion. The extent of these changes is related to the size of the shunt and the capacity of the venous channels that receive the excess flow. If there is a small shunt in a large vein, the latter accommodates the overflow easily. If, on the other hand, there is a large shunt in a relatively small vein, the adjacent venous channels are also used to accommodate the influx.

During the development, the cerebral venous system constantly adjusts its anatomy to suit the changing needs of the developing brain. Inefficient and roundabout routes are replaced by efficient and direct channels. When there is an arteriovenous fistula, the vascular channels that normally undergo atritic process are retained to assist in the drainage. The embryo does not produce any new vessels exclusively to deal with the fistula. Existing channels are used to the best advantage. In cerebral AVMs, the abnormal venous channels represent these persistent embryonic veins Vidyasagar. The segmental pattern is retained in the adult and can be recognised in spite of complex anatomy. Recognition of this segmental pattern is fundamental for the interpretation of the anatomy of the AVMs. This logic is applicable to VGMs also.

Pathophysiology

Septal and terminal veins form the origin of internal cerebral vein. The two ICVs join to form the great cerebral vein of Galen (GCV) and join the straight sinus. Segmental veins initially drain laterally into the tentorial sinus. There is a backward swing of the brain around 80mm stage. The lateral drainage by the tentorial sinus become less efficient. The drainage occurs into the straight sinus which is a more direct route. If a A-V fistula occurs between the segmental arteries and veins a high volume of arterial blood drains directly into the great cerebral vein. At this stage, the GCV is unhindered by the developing brain and dilates to a large size. This is the basis for formation of VGM. The dilation of the vein is not the primary pathology. It is the effect of large volume flow under high pressure directly into the vein. The capillaries which modulate the pressure are absent in these malformations.
In some instances, in the angiograms in the adult do not easily demonstrate the arterial component in the VGMs. This has led to the concept that VG can dilate without an arterial component and probably due to occlusion of venous sinuses. There is no basis to support this concept based on the embryological studies. Venous channels in the embryo do not occlude, they become atretic if there is no flow through them. This is the normal mechanism.

**Development of fistula**

Despite the complex developmental changes, it is possible to identify the early segmental pattern. Understanding the concepts of segmental anatomy is necessary to interpret the anatomy in the adult.

**Telencephalon**

In the region of the telencephalon (Figure 1) the segmental pial vessels are represented by the medial striate artery and the anterior striate vein. These cross each other at right angles [1,2].

If an arteriovenous fistula occurs (between 20mm and 40mm stage) between medial striate artery and the anterior striate striate vein the direction of flow of blood would be through inferior striate vein, deep telencephalic vein, superficial telencephalic veins, tentorial sinus, and finally into the transverse sinus.

Between 60-80mm stage, there is a backward swing of the developing brain. This stretches the tentorial sinus, reducing the size of the lumen. The shunt now changes into more medially situated a more direct channel – the basal vein – and drains into the great cerebral vein.

Sometimes in the embryo the inferior striate vein anastomoses with the caudate tributaries of the terminal vein. On such occasion, the shunt is directed into the anterior end of the internal cerebral vein via the terminal vein.

In this angiogram (Figure 2A) the feeding artery – Medial striate Artery entering the dilated internal cerebral vein can be clearly seen.

Yasargil in his classification of Vein of Galen aneurysms, type IV labelled the vein, [marked by 2 arrows], as the septal vein [4]. The author would like to suggest that this is an embryonic inferior striate vein. The fistula has occurred between medial striate artery and anterior striate vein at 40-80mm stages of development. In the embryo, the septal vein does not cross the medial striate artery, and therefore, it is unlikely to be involved directly in the formation of the fistula.

Therefore, an arteriovenous fistula between the medial striate artery and anterior striate veins can either shunt along the basal vein into the great cerebral vein, or along the terminal vein into the internal cerebral vein (Figure 2B). The latter usually dilates more as it is mainly extracerebral till 80-mm stage. It has no restraints of the surrounding brain. Many examples of the so-called aneurysms of the vein of Galen belong to this category (Figure 2C).

**Diencephalon**

In the region of the dienencephalon (Figure 3A & Figure 3B) the segmental pial veins are dorsal and ventral diencephalic veins, crossed by the corresponding pial arteries Posterior cerebral and posterior choroidal arteries respectively.

For instance, if we look at the combination of posterior cerebral artery and dorsal diencephalic vein producing an arteriovenous fistula, at 20mm stage the shunt is into the tentorial sinus and transverse sinus. At 60mm there is a backward shift with the rest of the brain. This shift compresses the tentorial sinus. The flow is diverted to basal vein around 80 mm because the basal vein is more direct route and later into internal cerebral vein (Figure 3B). Venous system continuously keeps modifying in response to the flow.

The ventral diencephalic vein crosses posterior choroidal artery. If there is a fistula between them the drainage occurs into the primitive cerebral vein. If the flow of the fistula is high AVG can occur. Posterior choroidal artery secondarily migrates to the posterior cerebral artery. This malformation would be classified as a posterior fossa lesion if the embryological migration is not recognised [30].
Mesencephalon

The mesencephalic segment the mesencephalic artery and vein cross each other. The initial drainage into the tentorial sinus is later shifted to the great cerebral vein. The mesencephalic vein is shown in green. The mesencephalic artery at 20-mm stage arises independently in the mesencephalic segment which is gradually incorporated into the posterior cerebral artery. This is often not appreciated and is classified under posterior cerebral malformation (Figure 1).

The following is an example borrowed from the post-mortem report by Alpers and Forrester (Figure 4) [32]. The original pictures were of poor quality for reproduction. This is a reformatted illustration. The point or origin of the mesencephalic artery on either side is clearly seen. The mesencephalic vein is represented by means of venous channels draining into the vein of Galen.

It is perhaps relevant to quote the authors’ original description here: ‘The basilar artery divided normally into two posterior cerebral arteries, but a branch from each posterior cerebral vessel could be followed coursing around the mesencephalon sending branches into the aneurysm. On the tectum of the midbrain lay a large mass of vessels connected with the posterior cerebral artery sending many branches into the wall of the aneurysm.

Figure 3C is an example borrowed with permission from Radiopaedia illustrating the contribution from Mesencephalic artery.

Metencephalon and Myelencephalon

In the metencephalic [the cerebellum] and the myelencephalic [medulla oblongata] segments the segmental pial veins drain directly into the transverse sinus. They are therefore unaffected by the developmental changes in the embryonic tentorial sinus seen in other segments.

Therefore, persistent embryonic veins in the arteriovenous malformations of these segments drain into the transverse sinus in the adult [33-36]. It is exceptional for these to drain into the cerebral vein.

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Clear understanding of any developmental abnormality is essential when planning the treatment. Often multiple arterial feeders are seen in VGMs. Unless the primary feeder is identified occlusion of secondary feeders will lead to very poor outcome. Identification of the primary feeder is possible by relating to the embryonic segmental anatomy. Occlusion of secondary feeders alone can produce catastrophic out flow abnormalities. Casikar and Ramaswamy have published flow patterns in experimental conditions in dogs by inserting multiple accurately machined acrylic shunts between the femoral vessels [20]. Their data indicate the relationship between flow pattern and changes to volume of flow with changes in vessel diameter.

Marcotti et al. have used an electric circuit design where flows are modelled as currents, vessel resistance as impedance and pressure difference as voltage changes [39]. They have used Poiseuille’s law and used standard linear relation between pressure drop and flow rate. This assumption does not reflect AVM where two fluid systems with varying pressures are interconnected. Their opinion that increased venous pressure can damage blood brain barrier is an accepted pathology of white matter damage.

The mathematical models developed by Urisino and Muller have extrapolated the flow characteristics in a linear tube to evaluate the flow patterns in AVMs [40,41]. The experimental findings of Casikar have indicated that in an AVM two fluid systems of different pressures are interconnected and assumptions based on flow in a linear tube are not applicable [20]. Computational fluid dynamic studies by Bhagwat have indicated that the observations made by the experimental studies by Casikar are consistent with CFD data [26,20]. This study has also indicated the importance of venous out flow in an AVM. This data will further the treatment options and in particular retrograde venous route treatment in VGMs. Interfering with the VGM without proper understanding of the flow dynamics will lead to poor outcome if the management decision is based on angiographic features alone.

CONCLUSION

If the course and termination of the embryonic pia-arachnoidal veins are known, the anatomical and radiological features of arteriovenous malformations can be easily predicted. The dilations of the VG occur because at the period in the embryo when the fistula occurs there are no structures restraining the dilatation. The primary pathology is not the aneurysm. It is the effect of the arterio-venous fistula. The concept that VGM can dilate without an arterial component is not supported by data on the development of blood vessels in the brain. This article provides a frame work of the pathology. It would be impossible to cite all the possible variations. The reader can use the model (Figure 1) to understand the anatomy and plan the surgery.

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DISCLOSURE

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