VEIN OF GALEN MALFORMATIONS: STUDY ON NATURAL HISTORY AND FACTORS PREDICTING INITIAL CLINICAL PRESENTATION AND TREATMENT OUTCOME

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled "VEIN OF GALEN MALFORMATIONS: STUDY ON NATURAL HISTORY AND FACTORS PREDICTING INITIAL CLINICAL PRESENTATION AND TREATMENT OUTCOME" *for the degree of* ***DM NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY*** *has been carried out by* ***DR. DEV PRAKASH SHARMA*** *under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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DECLARATION

I hereby declare that this thesis titled "VEIN OF GALEN MALFORMATIONS: STUDY ON NATURAL HISTORY AND FACTORS PREDICTING INITIAL CLINICAL PRESENTATION AND TREATMENT OUTCOME" *has been prepared by me under the supervision and guidance of Dr. Santhosh Kumar K (Additional Professor) , Dr Jayadevan E R (Additional Professor), Dr Mathew Abraham (Professor), Dr Soumya Sundaram (Associate Professor) and Dr Deepa S Kumar (Associate Professor) Department of Imaging Sciences and Interventional Radiology, Sree Chitra Institute for Medical Sciences and Technology, Trivandrum.*

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CONTENTS

INTRODUCTION

Vein of Galen malformations (VOGM or VAGM) are rare intracranial vascular anomalies. About 30 % of the intracranial vascular malformations presenting in the paediatric age group consist of Vein of Galen Malformation. In this pathological condition there is a midline venous structure called Median Prosencephalic Vein, which is aneurysmally dilated and fed by abnormal communication between the arteries and the veins. Raybaud and co-workers postulated that the ectatic venous structure that is characteristically seen in these lesions represented the median prosencephalic vein and not the vein of Galen itself, challenging the traditional concept prevalent at that time. The median prosencephalic vein lies free in the subarachnoid space and balloons out due to the high flow across the AV fistula. Persistence of the falcine sinus as well as persistence of the other embryonic structures may be associated.

The preservation of the embryonic pattern of the vascular system may explain the existence of several vascular anomalies associated with these lesions.

The presenting complaints vary from being asymptomatic incidentally noted lesion to patients with severe cardiogenic shock and multi organ failure. Timing of intervention, type of intervention, single or multiple sittings of embolizations, co-existing heart failure or other systemic factors can predict the outcome in a given case. A patient's clinical presentation dictates the timing of endovascular management.

Endovascular embolization of VOGM has become the standard of care for this patient population; however, long-term outcomes after endovascular embolization and predictors of good neurological outcomes remain less explained.

With a comprehensive multidisciplinary approach in the intensive care units, has significantly improved the prognosis of patients with VOGM.

Recently with advancement in endovascular therapy few centers have published their results of VOGM treatment. One last study was from Indian subcontinent in 2016. (1)To our knowledge, there are not many systematic studies on the Vein of Galen Malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome.

AIMS & OBJECTIVES

To study, prospectively and retrospectively, all VOGM cases presenting to Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), spanning a period from 2009 to 2021. The study tried to delineate the natural history of the VOGM who presented to our institution and either underwent embolization if indicated or were kept on follow up. Study also aimed to evaluate clinical and radiological factors affecting initial clinical presentation and factors predicting treatment outcome.

REVIEW OF LITERATURE

Introduction:

Steinheil in 1895 was possibly the first one to describe the vein of Galen aneurysmal malformation (VOGM) and cited by Dandy in 1928. (2)

The beginning of the last century witnessed the first attempt to treat the VOGM, the index patient being an infant who presented with intracranial hypertension and subsequently underwent bilateral internal carotid artery ligations.

Litvak in 1960, Raimondi in 1972, Clarisse in 1978, and Diebler in 1981 made an attempt to separate the true VOGMs with its mimickers. With gaining of knowledge, anatomic and embryologic evidence allowed to categorize a VOGM as a specific choroidal malformation that is different from a cerebral AVM draining into a dilated but not malformed vein of Galen. (3)

In 1964 in a review of 34 patients, Gold (4) described the three consecutive clinical stages in patients with VOGMs: The clinical stages suggested by Gold et al. were: (1) Cardiac insufficiency in neonates (2) Hydrocephalus and seizures in infants & young children (3) Headaches and Subarachnoid haemorrhage in older children or adults

One more group was added by Amacher in the year 1978, that included neonates and infants with macrocephaly and minimal cardiac symptoms.

In an excellent review, Johnston and colleagues analysed in an exhaustive fashion the clinical presentations of VOGMs in 82 infants. In 82 patients with VOGM the frequency

(in percentage) of the symptoms reported were as follows: Cerebro Spinal Fluid (CSF) disorders in 70 %, neurologic deficits in 31 % and neurocognitive delay in 12 %. (5)

In a study evaluating cases between October 1984 and 2002, 317 children less than 16 years of age with VOGMs, 233 patients were treated with endovascular embolization. Of the 216 patients, 23 died despite being treated with embolization or due to procedure-related complications (10.6%). Out of the total 193 surviving patients, severe retardation was noted in 10.4 % (n=20) of the patients, moderate retardation in 15.6 % (n=30) and remaining i.e., 74 % (n= 143) were neurologically normal on follow up. (6)

Currently, VOGM is considered a sporadic congenital disorder. Few cases of VOGM in which genetic study was performed it was found that the Mendelian disorders including instances of autosomal dominant capillary malformation-AVM syndrome type 1 caused by RASA1 mutations and of autosomal dominant capillary malformation-AVM syndrome type 2 caused by EPHB4 mutation could be associated with this rare intracranial malformation. Loss-of-function mutations in EPHB4 should be responsible for VGAM, associated or not with capillary malformations, in more than 10% of patients.(7) (8)

Anatomy and Embryology:

The vein of Galen aneurysm lies in the subarachnoid space between the foramina of Monro anteriorly and the confluence of the free margin of the falx and tentorium posteriorly (where the confluence of the straight sinus and inferior sagittal sinus is also located). This space corresponds to the cistern of the velum interpositum and

quadrigeminal plate cistern. The venous pouch is classically round or oval-shaped, with its long axis in the sagittal plane. Occasionally, wall calcifications can be seen and represent calcified mural thrombus. When large, this abnormal venous structure extends beyond the quadrigeminal plate above the roof of the third ventricle.

The development of the human embryo is very interesting and passes through various stages incorporating changes in the future brain parenchyma as well as its associated vascular structures. To start with, at approximately 6 weeks of gestation when the crown rump length is 5 mm, the developing brain is surrounded by the meninx primitiva. The meninx primitive coalesces into the anterior, middle and posterior plexi which correspond to prosencephalon, mesencephalon and rhombencephalon which are drained by longitudinal primary head sinuses which are paired structures. To start with, there are no deep cerebral veins. Once the growing embryo progresses into the 7 th week (CRL of approximately 18 mm), the primitive sagittal sinus forms in the midline formed by the paired marginal veins (one each for telencephalic lobe). The superior sagittal and straight sinuses develop from a meshwork of anastomotic channels called the sagittal plexus, which are contained within the primitive falx cerebri. Persistence of the one or more of the channels of the caudal anastomotic loops of this sagittal plexus results in persistent falcine sinus which are classically posteriorly located, though few anterior interhemispheric variants have been reported in the world literature. (9) Persistent falcine sinus can not only be seen as a variant of normal development but also act as alternative drainage channel which get reopened in the event of the thrombosis of other Dural sinuses.

8 th week of embryological development is characterised by the appearance of the median prosencephalic vein of Markowski, which is nothing but the important venous connection between the choroid plexi and the forming sagittal sinus. The median prosencephalic vein of markowski can be considered as having two parts: the anterior portion and the posterior portion. The anterior portion of the vein of markowski, under normal circumstances, lies in the roof of the third ventricle and subsequently atrophies. The internal cerebral veins developing with the growing choroid plexus, basal ganglia and thalami- drain into the posterior portion of the median prosencephalic vein of Markowski. When abnormal arterial connections remain, it results in non-involution and hypertrophy of the median prosencephalic vein of markowski, which was previously called vein of Galen aneurysmal malformation and is still being commonly used in the clinical practice. (10)

The dominant venous drainage of the brain which is initially centrifugal (inside to outside) changes to centripetal (outside to inside) via the Internal Cerebral Veins with development of the Choroid plexus.

This persisting peculiar venous arrangement pattern allows one to establish the time (before the 12th week of gestation) at which the malformation developed, and one may consider a VOGM to be the result of an error in the early phase of vasculogenesis. Prenatal diagnosis of VOGM may be made as early as the second trimester of intrauterine life by sonography or MR imaging.

The venous aneurysm is usually drained by the straight sinus and/or a persistent falcine Dural sinus. Abnormalities of the straight sinus, including stenosis, absence, duplication,

and fenestration, are common. The straight sinus is frequently absent, with venous blood being drained from the venous pouch through a falcine sinus, and courses superiorly or posterosuperiorly in the falx cerebri to the posterior third of the superior sagittal sinus. An unusual route of venous drainage, described by Raybaud et al, is the “falcine loop.” (3) It corresponds with drainage of the aneurysmal sac into the superior sagittal sinus through a falcine sinus, with partial diversion of flow anteriorly through the superior sagittal sinus into a second falcine sinus. The second falcine sinus runs parallel to and crosses the first falcine sinus in the Dural reflections of the falx without communication. It drains into the torcula or the transverse sinus opposite the one that drains the first falcine sinus.

The arterial supply of a VOGM usually involves all of the choroidal arteries, including anterior choroidal contributions. It may also receive significant contributions from the subependymal network originating from the posterior circle of Willis. These arteries should be differentiated from trans mesencephalic ones, because the involvement of the latter excludes the diagnosis of VOGM and indicates a tectal and not a choroidal AVM. The subependymal arteries after piercing the floor of the third ventricle, run under the ependyma and join the choroid fissure, where they contribute to the blood supply of the Vein of Galen Malformation. Due to the sump effect of the venous drainage the accessory supply is obtained from the subependymal and thalamo-perforating arteries which usually disappear following proper occlusion of the most prominent shunts. Cerebellar arteries do not supply a VOGM except indirectly through their dural branches, which can be enlarged because they may participate in the supply to the vasa

vasorum at the venodural junction. In approximately 50 % of the cases of neonatal VOGM, a persistent limbic arterial arch, is noted. The persistent limbic arch bridges the cortical branches of the anterior choroidal artery and the posterior cerebral artery. This limbic arch should be distinguished from subcallosal and subforniceal supply to the choroidal shunts. The arch regresses (matures) after obliteration of the VOGM by means of embolization. (11)

The nidus of a VOGM is usually located in the midline and has supply from both sides of the cerebral hemispheres. The most common types of angioarchitecture described in VOGM are the Choroidal and Mural types. The choroidal type of VOGM corresponds to a primitive condition involving all the choroidal arteries and an interposed network before opening into a venous pouch which is usually large. The most neonates with severe symptoms have choroidal VOGM. The mural type of VOGM corresponds to direct arterio venous fistula within the wall of the median vein of prosencephalon. The fistula may be single, or multiple (more often) and converge into either a single venous chamber or into the multiple venous chambers. The mural form has been found to be better tolerated than the choroidal form. Mixed forms may occur, such as those with a choroidal nidus and high-flow fistulas located in the wall of the venous pouch.

In the description of the angioarchitecture of the VOGM, the arterial feeders can be described as being the primary or the secondary arterial feeders.

Primary arterial feeders (12): Primary feeders of the aneurysmal sac include the anterior & posterior choroidal arteries as well as the anterior cerebral arteries, all situated in the cistern of the velum interpositum. The medial and lateral posterior choroidal arteries are

the most common primary feeders of the malformation. The medial posterior choroidal arteries originate from the cisternal segments of the posterior cerebral arteries, are 1 to 3 on each side, and principally supply the tela choroidea. The lateral posterior choroidal arteries originate from the posterior cerebral arteries, more distally than the medial posterior choroidal arteries. They are 1 to 6 on each side and principally supply the choroid plexus of the lateral ventricle. The anterior cerebral arteries are the second most common primary arterial feeders and typically provide a bilateral supply to the vein of Galen aneurysm through the pericallosal branches. The anterior choroidal artery originates from the supraclinoid internal carotid artery and supplies the choroid plexus of the temporal horn of the lateral ventricle. It is a common arterial feeder only in neonates, usually unilaterally. Quadrigeminal arteries located in the quadrigeminal plate cistern are also frequent primary arterial feeders. The main quadrigeminal artery is the collicular or the long circumflex artery, which originates from the crural or ambient segment of the posterior cerebral artery. Accessory quadrigeminal branches that originate from the superior cerebellar artery and medial posterior choroidal arteries and commonly supply the venous pouch classically form an attenuated network over the quadrigeminal plate.

Secondary Arterial Feeders. An arterial supply from the middle cerebral arteries (distal branches) is only occasionally seen in neonates and is usually unilateral. The anterior thalamoperforate arteries (arising from the posterior communicating arteries), posterior thalamoperforate arteries, and distal cortical branches of the posterior cerebral arteries are common secondary feeders. Occasionally, an arterial supply from meningeal arteries

is seen. In particular, arterial feeders from the posterior temporoparietal trunk of the middle meningeal artery follow a recurrent course from the posterior midline and forward along the wall of the venous pouch to supply the venous pouch at its anterior aspect.

Persistence of embryonic venous structures is common (13), including persistent occipital, tentorial, and marginal venous sinuses in the posterior fossa. Persistence of the primitive marginal sinuses, which are embryonic precursors of the superior sagittal sinus, was also described (14). They represent bi- or unilateral prominent parasagittal Dural sinuses that connect the proximal segment of the superior sagittal sinus or the median vein of the prosencephalon to the junction of the transverse and sigmoid venous sinuses. The venous drainage of the choroidal shunt is always via a median prosencephalic vein and has traditionally considered to have no communication with the deep venous system. However the communication with deep venous system is now being reported by many of the authors in the recent literature. (1) (15) (16) (17)

The choroidal veins are the embryonic tributaries of the median vein, and, potentially, the choroidal nidus may drain into the choroidal veins before they join the median Ponto mesencephalic vein. The connection between the medial Ponto mesencephalic vein and the choroidal veins may result in reflux into the pial venous system due to communications between the choroidal and striate veins. Intraventricular bleeds and cerebral venous infarctions may occur after complete occlusion of a VOGM via the venous route if the lesion drained into the choroidal, subependymal, or striate venous systems. Reflux into the pial venous system increase the risks of seizures and bleeds.

Dilatation of the median Ponto mesencephalic vein is variable and is unrelated to the architecture of VOGM. This vein opens into a large falcine sinus most commonly. Sometimes, stenoses at the veno-sinus junction may be encountered, the presence of which may increase the cerebral venous pressure. Conversely, the heart function may improve due to reduction of the overload on the cardiovascular system.

The VOGM uses the posterior sinuses as a route of drainage and drains into the straight sinus. The alternative pathways are utilised by the deep cerebral venous system. The alternative pathways are via thalamic and sub temporal or lateromesencephalic veins. This arrangement is demonstrated on the lateral angiogram (venous phase) as the typical epsilon shape (Epsilon sign). The presence of the epsilon sign on the internal carotid arteries injections during the angiogram is a favourable sign. It has been found to be associated with a good neurologic prognosis. Apart from these, other alternative routes of the cerebral venous drainage are the cavernous sinuses. There is no communication between the cavernous sinuses and the cerebral veins during the antenatal period and during the first months of life. During the period of initial growth and development, the cavernous sinuses mature and are able to ‘‘capture’’ blood from the sylvian veins. The cavernous sinus capture offers the brain a potential drainage pathway through the orbits, pterygoid plexuses, or the inferior petrosal sinuses.(2)

Consequent to the cerebral venous drainage via the ophthalmic veins, the facial and scalp veins become more prominent and are visible clinically. Dilated facial veins in infants indirectly implies cavernous sinus capture and is associated with better

outcomes. Nasal mucosal swelling and mild epistaxis may result from the facial venous congestion, though very uncommon the clinical practice.

Perinatal and postnatal periods are the time periods in which the maturation of the jugular bulbs and of the venous sinuses at the base of the skull occurs.

It encompasses regression of the embryonic occipital and marginal sinuses, remodelling of the torcula and the definite formation of the jugular bulbs. The maturation may be disturbed by the shunt across the VOGM as well as by the presence of the macrocephaly. High-flow pial arteriovenous fistulas in new-borns and infants are also associated with impaired venous maturation at the base of the skull.

Maturation or the absence of it (in its various stages of the evolution) of the Sino-jugular junctions have been found to be associated with the prognosis in infants with VOGM. Cerebral venous hypertension results in cases of severe stenosis of the jugular bulb or in cases of the thrombosed jugular bulb. The VOGM and the brain use the cavernous sinuses to drain, in these situations. (18)

Narrowing and occlusion of the posterior fossa dural sinuses are common in patients with vein of Galen malformations and seem to be acquired. They are believed to be secondary to the increased blood flow at the malformation site, referred to as high-flow angiopathy. This results in progressive enlargement and tortuosity of the primary arterial feeders and draining veins. There are associated histopathologic changes in the vessel walls, including, in particular, marked intimal hyperplasia in the venous walls with

venous intimal tears, which results in the accumulation of mural thrombi and, ultimately, mural fibrosis. (19)

Narrowing and occlusion of the Dural venous sinuses typically develop in the infantile period in patients with hydrovenous disorders, and, if left untreated, result in worsening of the hydrovenous disturbance, with accelerated brain damage secondary to venous congestion and ischemia.

Classification: Vein of Galen aneurysmal malformation

Litvak Categories (20)

Category A, B, C

Category A, also known as "Aneurysms of the great vein of Galen," refers to presence of a singular dilation of the great cerebral vein of Galen contiguous with a dilated straight sinus and torcula. The shunting lesion is fed by the anomalous anterior and posterior circulation branches.

Category B, also known as "Racemose conglomerations of blood vessels deep in the cerebral structures with dilated deep venous structures," refers to a vermiform cluster (Angiomas and haemangiomas) of arteries and veins located in the midline and deep cerebral structures draining centripetally into dilated deep veins and sinuses that may not include the vein of Galen itself, even though it might be displaced or engorged.

Category C, which is named “Transitional types of midline arteriovenous shunts” (thus lesions that would not belong to either category). It includes 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 the venous sinuses which are usually deformed and dilated.

Yaşargil Types (21)

In his classification, Yaşargil divided these malformations into 4 types.

Yasargil classification:

Type I: small pure cisternal fistula of vein of Galen with either the anterior or posterior pericallosal arteries or posterior cerebral artery

Type II: Single VOG with multiple fistulous communications with multiple thalamoperforate vessels

Type III: Mixed type I and II high flow fistula

Type IV: Vein of Galen receiving Parenchymal arteriovenous malformation (AVM) drainage

The distinctions in Yaşargil’s (Types I–III) or an AVM with or without associated AVF classification are whether the malformation is a pure 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 -perforating vessels and from the P1 and P2 segments of the posterior cerebral arteries. 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. 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. Type IVB is similar to Type IVA but with the AVM being mesencephalic instead of thalamic, and Type IVC is a thalamomesencephalic or mesodiencephalic plexiform malformation along with an adjacent and separate cisternal AVF to the vein of Galen. 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 (A5) or distal feeding arteries from the posterior cerebral arteries (P4) 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 IVA–B to Litvak's Type B, and that Yaşargil's Type IVC falls into Litvak's, Category C. These 2 classifications are important when considering open surgery, whereas Lasjaunias 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.

Lasjaunias Classification of VOGM (22)

The classification of Lasjaunias into 2 types of VOGM, choroidal and mural, is the most commonly used classification because it is the most relevant for endovascular treatment.

Choroidal type: This is the most common (more than 90%) and most complex type, where multiple arterial feeders enter the anterior aspect of the median prosencephalic vein. The arterial feeders include choroidal arteries (posterior and anterior choroidal arteries, anterior cerebral arteries), with a frequent supply from thalamoperforating and quadrigeminal arteries. These feeders converge into a fistulous site at the anterior aspect of the median prosencephalic vein. Choroidal-type VOGMs frequently present with high-output cardiac failure in the neonate due to multiple high-flow fistulas and no outlet restriction.

Mural type: There is a single fistula or several fistulas at the inferolateral wall of the median prosencephalic vein. Arterial feeders are uni-or bilateral from the quadrigeminal arteries and/or the posterior choroidal arteries. Because there is more outflow obstruction, there is more severe dilatation of the median prosencephalic vein. These patients typically present later in infancy, with hydrovenous complications, including macrocephaly, hydrocephalus, and failure to thrive. Cardiac failure is usually mild or absent. Location of the fistulae are in the wall of the median prosencephalic vein within

the subarachnoid space. Many cases are associated with either absence or stenosis of the dural sinuses or the stenosis at the level of the jugular foramen.

Secondary Enlargement of Vein of Galen

In contrast to VOGMs, 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 (10)

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 haemorrhage 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. This describes a range of situations in which a pial arteriovenous fistula or nidal arteriovenous malformation uses the mature vein of Galen in its major drainage pathway and dilates it as a result.

Vein of Galen aneurysmal dilatation (VGAD) which develops later in the embryonic life than the vein of Galen malformation, has mature vein of Galen in contrast to that seen in the Vein of Galen malformation.

VGAD very rarely presents before the age of 3 years and tends to present later in childhood. The common clinical manifestations of VGAD are neurological deficits, intracranial haemorrhage or delayed development. Usually, the VGAD regresses after treatment of the underlying AVM.

Vein of Galen Varix (10)

It has been recently classified as a primary venous malformation.

A. Primary venous varix: Primary isolated cerebral varix is rare and may pose a diagnostic challenge. It is speculated that this phenomenon is due to the persistence of embryonic venous drainage and the inherent weakness of the venous wall. Most of the cases are asymptomatic. In rare cases, patients experience headaches or epilepsy secondary to the mass effect, thrombosis, or haemorrhage. A comprehensive imaging evaluation of the cerebral venous anatomy, including digital subtraction angiography (DSA), should be performed to determine the importance of variceal segment in overall brain damage to in turn predict the relative risk of its occlusion. Occasionally, asymptomatic incidental venous varices are usually followed by serial imaging studies. Isolated cerebral varices are isodense masses on CT, usually located extra axially and show significant post contrast enhancement. Osseous erosions or thinning results from the lesions

underlying the bone. On MRI, the varix may appear as a flow void or as an isointense lesion, with uniform contrast enhancement that can mimic meningioma. MR venography can help confirmation of the venous origin. Thrombosed varices show T1 and T2 signals based on the age of the clot/thrombus. Symptomatic varices may require treatment with endovascular or surgical occlusion.

B. Secondary venous varix: Focal venous dilatation is secondary to increased venous pressure from shunting vascular malformations (including pial AVFs and nidal AVMs). As such, VGAD is a type of secondary varix. Alternatively, secondary venous varices can occur without arteriovenous shunting, in the context of developmental venous anomalies (DVA).

Mortazavi et al classification: (23)

	SCORE	
Parameter	0	1
Arterial feeders	any feeders other than P1 P2 PCAs, Thalamoperforators, choroidal, basilar	Any of the following feeders: P1-2 PCA, thalamoperforators, choroidal, basilar
Clinical symptoms no heart failure		Heart failure
Age > or equal to 5 months	< 5 months	

Treatment recommendations: endovascular (no urgency, treat in 1 stage), for patients

with 0–1 point; 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.

Litvak	**Yaşargil**	**Lasjaunias**	**Mortazavi**
A	I	Type II (Mural)	0
	II	Type I (Choroidal)	1
	III		
B	IV A B		Excluded
C	IV C		

There was exclusion of true AVM in the proposed classification system by Mortazavi et al. Note should be made that there is no perfect comparison available between the latest proposed classification system by Mortazavi et al. and the 3 older classification systems, which do not include any clinical symptoms, age, treatment, and outcome.

Recently Mankad et al. have classified cerebral venous malformations, including VOGM, as appended below:

Classification of venous disorders (10)

Pathophysiology	**Grouping**	**Subtypes**
Arteriovenous shunting-related disorders	Dural arteriovenous shunts (DAVS)	• Dural sinus malformation • Infantile Dural arteriovenous shunts • Adult-type DAVS in children
	Cerebral arteriovenous shunt	• **Choroidal or mural VOGM** • Vein of Galen aneurysmal dilatation • Pial arteriovenous fistula • Pial arteriovenous malformation
	Calvarial or scalp arteriovenous shunt	• Soft tissue scalp AVM with sinus pericranii • Intraosseous Calvarial AVM
Primary malformations	Venous varix	• Primary • Secondary

Pathophysiology	Grouping	Subtypes
	Developmental venous anomaly (DVA) Sinus pericranii (SP) Sturge-Weber syndrome (SWS) and cerebrofacial venous metameric syndrome Hereditary haemorrhagic telangiectasia Diffuse venous malformation	
Veno-occlusive disorders	Thrombotic	• Cerebral sinovenous thrombosis (CSVT) • Deep medullary venous pathology
	Non-thrombotic	• Craniosynostosis and venous outflow obstruction • Achondroplasia and venous outlet obstruction • Transverse sinus stenosis in idiopathic intracranial hypertension

Vein of Galen aneurysmal malformation: Pathophysiology (6)

These malformations are congenital arteriovenous fistulas draining to the median vein of the prosencephalon that is the vein of Galen embryonic precursor.

The choroidal type is more common (more than 90% of malformations) and includes a nidus like network located in the anterior wall of the median prosencephalic vein, supplied by the choroidal, pericallosal and the thalamoperforating arteries. They are usually high- volume shunts, manifesting as congestive heart failure in the neonatal period, and the prognosis is relatively poor.

Mural type of the VGAM consists of a limited number of direct fistulous connections, usually in the inferolateral wall of the median prosencephalic vein, without an intervening network. These patients often present with symptoms related to hydrovenous symptoms in late childhood, such as developmental delay, hydrocephalus, or seizures. However, they can be detected as asymptomatic entities on prenatal imaging.

VOGM should be distinguished from aneurysmal dilatation of the true vein of Galen caused by an adjacent brain AVM (vein of Galen aneurysmal dilatation) which has a higher risk of haemorrhage.

Neonatal and antenatal clinical presentation

VOGM are occasionally detected on antenatal ultrasound scans (from about 25 weeks' gestation). (24) (25)Antenatal MRI will confirm the diagnosis and allow assessment of any pre-existing damage to the brain. (26) (27) It will help in treatment planning and pooling of resources at designated centres of excellences having facilities of

Interventional Neuroradiology, Neurosurgery, paediatric cardiology, paediatric neurology, neonatology and comprehensive child development assessment along with neurocognitive assessment. Though the antenatal diagnosis of the VOGM has increased, still it is diagnosed after birth more commonly. Usually, the peripartum period and 1 st 24 hours of birth are unremarkable.(6) However, larger shunts may then show rapid deterioration with progressive congestive cardiac failure. (28)

VOGM acts as left to right shunt. Commonest manifestation in the neonatal group and possibly low cardiovascular volume of these patients can explain it. The prognosis of the neonate with VOGM is related to the severity of heart failure and in many cases, the diagnosis of VOGM is obtained only after an investigation for congestive heart failure. Many of the severely affected patients have progression to pulmonary hypertension with respiratory distress and multiorgan failure, which is why the Hospital Bicêtre group have introduced a scoring system to gauge the severity of the clinical presentation based on the assessment of multiple organs. (6)

In the infantile age group, clinical presentation with hydrodynamic disorders such as hydrocephalus and macro crania are more common. Increased venous pressure results in straight sinus and the torcula due to the high- flow arteriovenous shunting. Till the time cranial sutures are not fused, adaptation to the increased pressure occurs by expansion of the intracranial volume, resulting in macro crania. (29)

This expansion of the upper part of the skull, i.e., cranial vault together with the presence of high-flow shunts, interferes with the normal development of the skull base and can lead to secondary jugular foramen stenosis. Furthermore, intimal hyperplasia

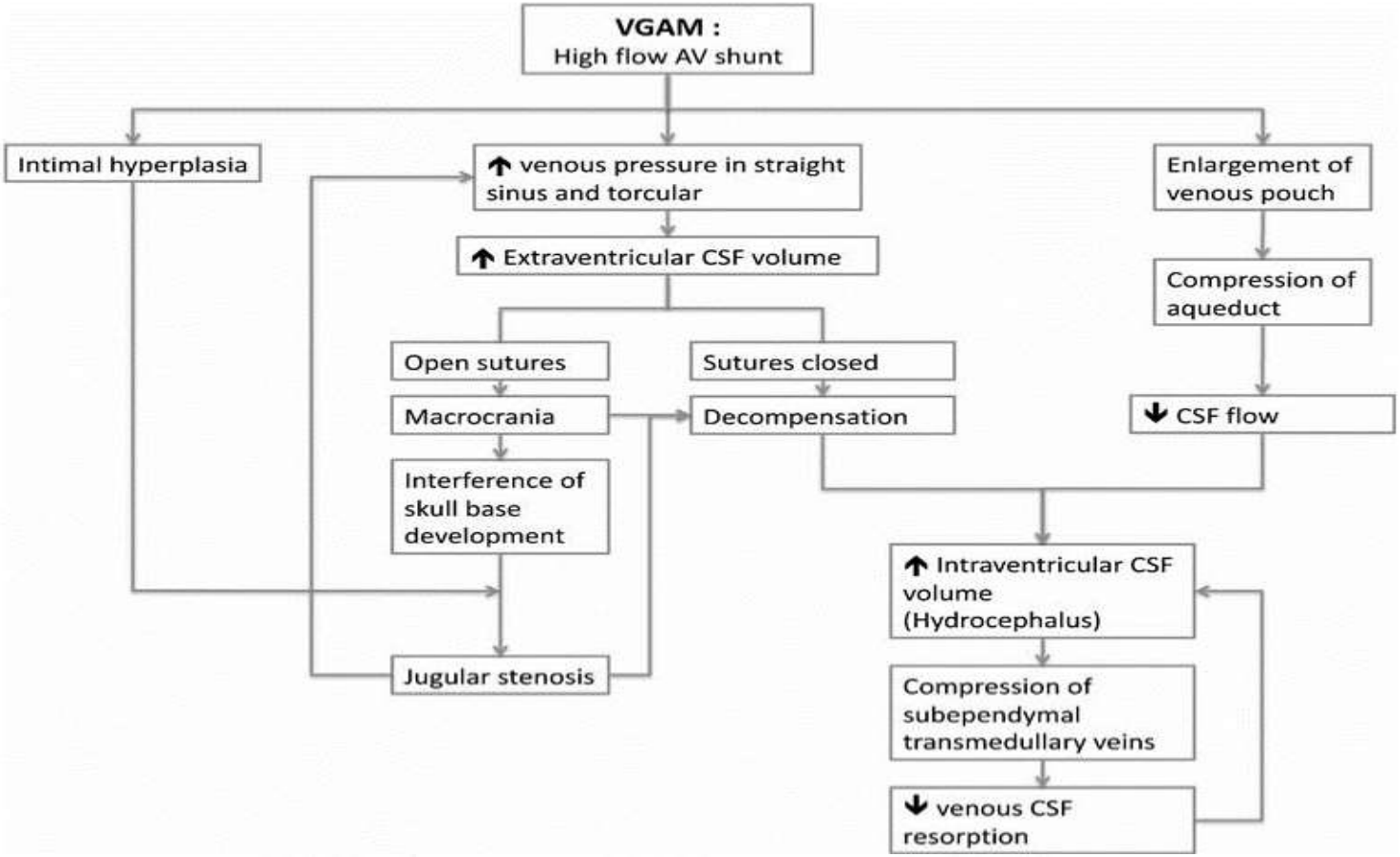
caused by increased shear stress of the vein wall due to high-flow shunt may also play a role in the so-called jugular vein immaturity/dysmaturation, and is also seen in changes in peripheral veins in patients with haemodialysis grafts. A combination of these two factors will result in varying degrees of jugular bulb stenosis, which will lead to improvement of the cardiac overload (and, therefore, a paradoxical amelioration of cardiac symptoms) but will also lead to further increased intracranial venous pressure.

Similar to the pathophysiology observed in cases of severe craniosynostosis, if in these patients the cranial vault fails to expand, decompensation occurs. In combination with the compression of the aqueduct by the enlarged venous pouch, subsequent ventricular dilatation will ensue.

Compression of the medullary veins happens due to hydrocephalus which further decreases reabsorption of cerebrospinal fluid and further worsens the hydrocephalus and increases intracranial pressure. As a result, tonsillar herniation can occur.

Most patients with significant jugular bulb stenosis have associated hydrocephalus, proving the role of increased venous pressure in the pathomechanism of hydrocephalus. Management of hydrocephalus should be directed at reducing the arteriovenous shunt as the underlying cause. Clinical presentation in children is related to long-standing venous hypertension, caused by the hydrovenous disorder described above, and will lead to neurocognitive delay since there will be interference with normal myelination. In deep hydrovenous watershed failure, which can occur when the compliance of the medullary veins loses their normal ventricular–cortical gradient, calcifications occur that will lead to epilepsy.

These calcifications are usually bilateral and symmetrically located, preferentially in the frontal region. Calcifications in the striatum and in particular the caudate and putamen bilaterally are an expression of the subacute ischemia in the region of the prominent collateral circulation system, after the cortical veins become unable to drain the cerebral white substance, or when the persisting thalamic pathways are overloaded with the drainage of the parieto-occipital regions. The calcifications are not produced by arterial steal.



A simple diagrammatic representation of the pathogenesis of the development of hydrocephalus in VOGM patients (30)

Depending on the degree of obstruction of cerebral venous outflow, the occurrence of cerebral venous and water congestion leads to the development of macro crania, enlarged ventricles, hydrocephalus, tonsillar prolapse and the so-called melting brain syndrome. This condition is the result of chronic hypoxia, accelerated white matter destruction and secondary hydrocephalus caused by venous hypertension. If left untreated this can quickly become fatal and so urgent intervention is required. Venous hypertension is assumed to cause WMI and is also a major factor in the "brain melting" syndrome, which suggests that earlier embolization regimens can prevent brain damage. (31)

Cerebral tonsillar herniation can result from the sinus occlusion. It is usually secondary to the cerebellar pial congestion and is only seen in its presence. This condition is reversible provided the condition is treated early. Peculiarity of the neonatal and infant CSF physiology is that the pacchionian granulations are not functional during the first months of life, adding to the burden of the medullary veins. The immature pacchionian granulations and venous hypertension arising from stenoses at the skull base results in an unbalanced hydrovenous state, leading eventually to hydrocephalus. The cerebral aqueduct is patent in almost all patients. Hence, the mechanical compression should not be considered to be the primary cause of the ventriculomegaly.

Subcortical white matter calcifications and subependymal atrophy with ventricular dilatation results in untreated VOGMs. These are supposed to be due to the chronic venous ischemia.

Deep hydrovenous watershed failure is usually suggested to be the cause of these calcifications. These white matter calcifications (usually bilateral, symmetrical) occur when the compliance of the medullary veins loses its normal ventricular cortical gradient. These calcifications also may be asymmetrical or unilateral. The subependymal atrophy has posterior predominance, commonly affecting the occipital regions. Abnormal postnatal development of the corpus callosum may also play a role in it. Isolated cortical vein spontaneous thrombosis in untreated patients with VOGM, is also a possibility.

Venous Drainage of the Normal Brain

In the absence of a normal deep venous system, the deep venous drainage of the brain takes alternative embryonic routes, mainly the lateral mesencephalic veins, lateral pontine veins, and superior petrosal sinuses. The internal cerebral veins frequently do not communicate with the venous pouch and are drained through collateral mesencephalic veins, which gives a characteristic epsilon or Fig 3 configuration on angiography. Although it was classically held that a normal deep venous drainage is consistently absent in a VOGM, several recent publications document normal deep venous drainage through the galenic system. This has important implications on treatment planning because embolization of the venous side of the VOGM in such instances carries a risk of deep venous infarction and/or haemorrhage. Levrier et al recommend a systematic pre-treatment evaluation of the VOGM anatomy with MR imaging, MR angiography, and MR venography, with specific attention to the normal cerebral venous drainage. (32)

Pseudophlebitic appearance, suggestive of cerebral venous hypertension on angiography may be seen in cases with absent cavernous sinus capture or the obstructed venous drainage. Intracerebral hematomas or subdural or subarachnoid haemorrhage may be seen in neglected or undiagnosed cases of VOGM which usually implies the combination of jugular bulb occlusion and venous pial reflux.

Clinical manifestations

Clinical manifestations can be divided into those related to high output cardiac failure and those involving neurologic symptoms (secondary to venous congestion and abnormal CSF flow).

In the new-borns and infants, systemic manifestations and hydrocephalus are the most common signs, whereas common adult symptomatologies consist of neurological signs and symptoms and haemorrhage.

CARDIAC MANIFESTATIONS

Shunting in VOGM results in a larger volume of venous return to the right side of the heart and could possibly lead to dilatation of the right-sided chambers. Continuous shunt reduction by staged embolization of the fistula is believed to stop the progression or even sometimes recanalize the occluded sigmoid sinus and thus improve the manifestations of the hydrovenous syndrome. Patients who present with neonatal high-output congestive heart failure usually have normal sigmoid venous sinuses and jugular bulbs, and timely treatment of the vascular malformation in these patients prevents the development of venous stenosis or occlusion. Likewise, narrowing or occlusion of the

jugular bulb is very rare at birth but not uncommonly develops during the first months of life in patients with vein of Galen malformations. The etiology is unknown, but it might be secondary to venous high-flow angiopathy or abnormal skull base growth in the setting of macrocephaly. When severe, narrowing of the jugular bulb can lead to decompensation of a previously stable patient due to venous congestion with secondary cerebral venous ischemia, hydrocephalus, or cerebral haemorrhage, even when the vein of Galen shunt is completely cured. It might be accompanied by secondary narrowing of the bony jugular foramina. When treatment is considered, a CT should be obtained because the presence of jugular foraminal stenosis does not allow angioplasty and stent placement, and is an indication for surgical bypass. A reduced diameter of the superior sagittal sinus can also be observed in patients with vein of Galen malformations and correlates with poor clinical outcome because it might be a reflection of the arterial steal to the vascular malformation or compression of the superior sagittal sinus due to intracranial hypertension. (18)

CEREBRAL SEQUELAE OF VOGM

Brain Injury

The arterial steal phenomenon and chronic venous congestion result in progressive brain atrophy, referred to as melting brain syndrome. Melting brain syndrome typically occurs in a subependymal pattern, with predominant destruction of the white matter and secondary ex vacuo ventricular enlargement. It can be associated with parenchymal calcifications, most commonly in the white matter and basal ganglia, secondary to

chronic venous congestion. Brain atrophy is a very poor prognostic sign and is progressive. It constitutes an indication for emergency treatment. Chronic venous ischemia can also lead to pseudophlebitic congestion of the cortical veins. Congested medullary veins and cortical veins are well depicted on Susceptibility Weighted Imaging (SWI). (33) (34)

Hydrocephalus/Ventriculomegaly (35)

Venous hypertension caused by the high-flow arteriovenous shunt is the main etiology of hydrocephalus in VOGM. During the first 2 years of life, the pacchionian granulations are not yet developed and CSF drainage depends on a centrifugal pathway through the ependymal, periventricular, and trans medullary veins to the Dural venous sinuses. Elevation of the venous pressure impairs CSF resorption and results in hydrocephalus. These patients characteristically present with enlargement of the subarachnoid spaces, which precedes any significant ventricular enlargement. When the cranial sutures are still patent, macro crania accommodate the increased extra ventricular CSF volume, and ventricular enlargement is usually mild. Conversely, when the cranial sutures are closed, the intraventricular CSF volume increases and results in ventricular dilatation.

Ventriculoperitoneal shunt surgery in incompletely embolized VOGM results in a poor outcome and can be associated with brain edema and subdural hematomas. Ventriculoperitoneal shunt surgery reverses CSF drainage into a centripetal flow from the trans medullary veins to the ventricles. Early embolization and a significant reduction of the arteriovenous shunt (more than 90%) are the best treatments of

hydrocephalus because the decreased venous pressure results in improvement or resolution of hydrocephalus. A third ventriculostomy is an alternative treatment option, although the presence of dilated arteries and veins in the CSF cisterns increases the risk of haemorrhagic complications of this procedure. Compression of the aqueduct by the dilated venous pouch of the VOGM or by the coil mass after embolization is a less common etiology of hydrocephalus. Embolization of the VOGM is the treatment of choice in the first instance. Compression of the aqueduct by the coil mass can be treated by a third ventriculostomy or alternatively high valve pressure ventriculoperitoneal shunt surgery. Post haemorrhagic hydrocephalus due to subarachnoid or intraventricular rupture of the VOGM is uncommon. These critical situations require external ventricular drainage. (36)

Reversible Tonsillar Prolapse

Venous congestion of the cerebellum can result in tonsillar herniation, which is reversible with endovascular embolization.

Prevalence of VOGM:

Though the current prevalence of the VOGM is not well documented and is considered to be rare condition few literatures cite it being 1 of 25,000 deliveries. (37) The long-term outcome and the natural history of the VOGMs is often taken as very poor with many patients succumbing to complications related to the brain parenchymal injury, hydrocephalus and Congestive Heart Failure (CHF). Exact prevalence in India has not been reported till date.

NATURAL HISTORY OF VOGM

The natural history of VOGM is difficult to discern from reports documented in the literature. Natural history of surviving children comes from case series that include patients who had undergone shunting procedures. (38)

With a male to female ratio of 3:1, many VOGMs present in the neonatal period and with estimated incidence of 1: 25000. (10)

In the late phase of the VOGM the onset of seizures can ensue even after shunting. Through management of VOGM patients, the predictability of certain evolutions and the various clinical tools developed over the years have helped to determine the optimal timing for treatment (therapeutic window). The therapeutic window outlines the optimal moment for the endovascular approach. To achieve normal cerebral development does not require, in all cases, rapid morphological disappearance of the AV shunt or rapid shrinkage of the ectasia. An understanding of the clinical and the anatomical and pathophysiological features of VOGM has reversed the former poor prognosis, as was indicated by Johnston et al. in 1987. (5)

Few reported cases of spontaneous thrombosis of a VOGM are available.(6) (39) Thrombosis usually occurs late, when permanent damage has already occurred. Antenatal diagnosis and referral to a centre with facilities for advanced neonatal cardiac care as well as for interventional neuroradiological therapy can go a long way in improving the prognosis in these children. Development delay is part of the natural history of most patients with untreated VOGMs. Careful evaluations of neurocognitive

performances show that most children with increasing head size present with some degree of mental retardation. In infancy, assessment of neurocognitive delay is not easy and requires collaboration with a specialist. Consistent and uniform well-established grading scales should be used. The major aim of such tests should not be to compare children but are intended to act as an aid to follow one child's ongoing development. From the point of view of management, it is important to recognize irreversible brain damage and potentially treatable or preventable situations.

The presence of venous infarcts or calcifications as well as encephalomalacia would suggest irreversible brain damage, while presence of hydrovenous disorders and hydrocephalus are potentially treatable conditions. As mentioned above, treatment of hydrovenous disorders should be achieved with eradication of the fistula itself, rather than placement of a shunt. With increasing head size, obstruction of venous outflow by narrowing of the jugular veins tends to become apparent.

Chronic vein of Galen aneurysm malformations with patent sinuses: A patient who does not undergo decompensation, either because of the presence of congestive cardiac failure at neonatal age or the presence of cerebrospinal fluid hydrodynamic disorders, will subsequently enter into a stage of chronicity. At this stage, the clinical manifestation as well as the prognosis is primarily dependent on the patency of the draining Dural sinuses. If there is patency of draining sinuses, the prognosis is generally good. Seizures and mental retardation are the main symptoms if the correction of the arteriovenous shunt is not done in time. Morphological sequelae express themselves in the form of calcifications, subependymal atrophy, and eventually the stigmata of previous acute

accidents, with cortical and subcortical atrophy. Since in classical VAGM there cannot be any pial or subpial reflux, focal venous infarcts or parenchymal haemorrhages are not common. The insult to the brain is a slow and permanent one and is usually demonstrated in the form of calcifications and atrophy. The timing of intervention is, therefore, important, and most of these sequelae can be prevented by early occlusion of the shunt. However, it is important to realize that the clinical outcome of children with patent sinuses is relatively good compared with those with secondary occluded sinuses.

Dural sinus occlusion and supratentorial congestion and reflux (19): Evolution of a VOGM to dural sinus occlusion and supratentorial congestion and reflux is very common and presumably related to abnormal skull base growth and maturation caused by increased head size, as well as by venous high-flow angiopathy. It is usually progressive and may develop slowly without symptoms over a long period of time. The development of jugular bulb stenosis protects the heart but it exposes the brain to congestion, venous infarcts, and haemorrhagic manifestations. The capture of the sylvian veins by the cavernous sinus would have a significant positive influence in the overall course of events. Overall, there is little understanding at present of the cause of occlusion of the dural sinuses. Neither has it been possible to precisely predict the patients who are going to evolve toward this occlusive phenomenon. Subsequent to the occlusion, the overall prognosis remains guarded and little can be done in terms of management. Hence identification of the therapeutic window prior to the onset of this occlusive phenomenon is important.

The infratentorial impact and consequence of the dural sinus occlusion is tonsillar prolapse. It is secondary to posterior fossa venous congestion and usually disappears with correction of the arteriovenous shunt. Syringomyelia has also been described as a consequence of this tonsillar prolapse. The stenosis of the jugular foramina and the timing of capture of the cavernous sinus affect the overall prognosis. At present, these cannot be predicted. Stenosis of the jugular foramina after capture of the cavernous sinuses allows an alternative route of drainage for the brain. However, if it occurs prior to capture of cavernous sinuses, the outcome is dismal. (18)

Complications of VOGM

Dural arteriovenous fistulas represent a rare and poorly documented complication of VOGM. (40)The anatomic location of the aneurysmal sac is favourable to the development of dural arteriovenous fistulas due to the surrounding dura of the tentorium, falx cerebri, and falx cerebelli.

Lasjaunias et al. (6) reported on a series of 233 patients, in which the endovascular embolization of the VOGM via a transfemoral approach was used. There was 10.6% (23 of 216 patients) general mortality rate, whereas the neonatal mortality rate was 52% (12 of 23 patients).

Non-neurological complications related to the embolization procedure and the technical difficulties of injecting glue are rare; Lasjaunias et al. found a 4% complication rate. This was related to glue causing an asymptomatic occlusion of the internal iliac artery or

the microcatheter getting glued in place. Repeated punctures of the femoral artery do not seem to cause any significant problems. The risk of venous passage of glue is obvious, particularly in inexperienced hands. The malformations are typically high flow and usually operators use a very high concentration of glue during embolization in these patients. Tantalum powder is typically added to the mixture to increase opacification. The injection can be made under induced hypotension. Care must be taken with catheter positioning, which should ideally be against the vessel wall in order to have a slower flow and a shorter polymerization time. Venous infarction as a consequence of venous passage of glue has been described but is rare. The phenomenon of perfusion breakthrough has not occurred in our experience or that of Lasjaunias et al. Acute closure of these high-flow fistulae does not, therefore, seem to cause any problems if performed by arterial embolization. Also, in the experience of Lasjaunias et al., consumption coagulopathy has not been observed.

Overall, in experienced hands with a staged procedure approach to VOGMs, arterial embolizations can be performed with a low complication rate. (41) An untreated vein of Galen arteriovenous malformation results in chronic venous ischemia with secondary development of dystrophic subcortical white-matter calcifications and subependymal atrophy with ventricular dilatation. (42)

- Calcifications: (43) and subependymal atrophy could result during the natural history of the VOGM.

Procedural complication (44)

Neurological

- Deep haemorrhagic venous infarct
- Nontarget arterial glue embolization
- Intraprocedural arterial perforation

Non-neurological

- Glue embolization to lungs
- On-table cardiac arrest
- External iliac artery occlusion

In general, it is accepted that contrast toxicity with iodinated contrast agent such as Iohexol 240 equivalent ensues in dosage at or above 3-5 ml/kg. Operators are worried about Contrast Induced Nephropathy (CIN), defined as > 25 % increase in creatinine from the baseline. However, no evidence of contrast limit not more than 5 ml/kg, if kidneys were right, as cited in cardiology literature hold true as per the latest experiences. Among the Liquid Embolic Agent (LEA) such as Onyx: safe DMSO dose suggested is < 2 ml/kg (adult) and < 0.33 ml/kg (paediatric).

Radiological diagnosis of VOGM:

- Plain radiography:

Skull radiographs may demonstrate a rim of calcification within the wall of the aneurysmal sac. Usually, obsolete. Not to be used in clinical practice for diagnosis or follow up of the cases of VOGM.

Features of congestive heart failure may be seen on the Chest radiographs.

- Ultrasound:

Venous sac of the VOGM is seen as a sonolucent mass located posteriorly to the third ventricle on the antenatal ultrasound.

Pulsatile blood flow within VOGM helps in differentiating vein of Galen arteriovenous malformations from other midline cystic lesions.

Associated venous anomalies are often visualized.

Evidence of hydrocephalus and cardiac dysfunction may be obtained.

On antenatal US, VGAMs are identified by the presence of a large tubular or spherical midline mass (the varix) which is hypoechoic or slightly echogenic, with arterialised Doppler flow. (10) Ancillary findings include presence of hydrocephalus, hydrops foetalis and cardiac dilatation. The main intracerebral arteries may demonstrate significantly variable impedances (with different pulsatility indices) due to the steal phenomenon. In the postnatal period, cranial ultrasound features are similar to those on antenatal scans.

- Plain and Contrast-enhanced CT:

Well-defined, multilobulated, intensely enhancing lesion located within the cistern of the velum interpositum.

Dilatation of the ventricular system, periventricular white-matter hypodensities and calcifications, and diffuse cerebral atrophy will be seen.

On CT, in non-contrast studies, varix is generally isodense to hyperdense relative to the brain, and in the case of partial thrombosis or wall calcification it is of the mixed attenuation.

- MRI:

  The dilated feeding and draining vessels appear as flow voids on T2-weighted imaging.

  MRI can demonstrate the location of a fistula, presence of any nidus, arterial components, venous sac, and the status of venous drainage.

  Allows adequate depiction of thrombosis of the venous sac.

On MRI, due to phase incoherence, feeding vessels of the varix appears as flow voids in and around the ambient cistern. Thrombosis is well appreciated, with T1 and T2 signal differing based on the age of the thrombus. MRI also depicts parenchymal lesions, usually bleed or ischemia. Identification of irreversible brain damage is exceedingly important. Changes in the apparent diffusion coefficient with restriction on diffusion-weighted MRI should mitigate against any kind of management as it indicates arterial steal, which often triggers apoptotic cascades (melting brain syndrome).

- Angiography:

  Gold standard for the evaluation of vein of Galen arteriovenous malformations. Allows catheterization and visualization of small feeders supplying the fistula.

  Allows evaluation of the dynamic aspects of the venous drainage of the normal brain and also the hemodynamic relationships with the venous drainage of the arteriovenous shunt.

Imaging modalities for evaluation of the cerebral venous system (10)

Imaging modality	Overview	Advantages	Disadvantages
Doppler ultrasound (US)	Excellent correlation of anatomy with MR venography. High specificity for Dural venous sinus thrombosis in neonates	Portable, Non-invasive, and non-ionising	Operator dependent, cannot be used in relatively older age groups, limited to use in infants with a good acoustic window and pregnant women.
Computed tomography (CT) venography	Multiplanar cross-sectional imaging.	Good availability, fast, may be done without requiring anaesthesia.	Radiation risk with its associated likely complications, limited skull base visualisation due to streak artefacts. Needs iodinated contrast which itself can lead to contrast related side effects, including encephalopathy and even death.

Imaging modality	Overview	Advantages	Disadvantages
Magnetic resonance venography (MRV) - 2D time of flight MRV - 3D phase contrast MRV - Contrast-enhanced 3D MRV	Flow-related enhancement utilised in 2D TOF MRV resulting from differences in magnetisation between nuclei in moving blood and stationary tissues	Shorter scan time and even slow flow can be detected	Thrombus can be mimicked by saturation effects from in-plane flow. vessel mis-registration caused by patient motion and structures with intrinsically short T1 (fat, gadolinium, blood, proteinaceous material, melanin) can mimic blood flow on maximum intensity projection (MIP) images
	velocity-induced phase shifts in 3D PC MRV Spins that move through a magnetic field experience a phase shift proportional to their velocity.	Flow quantification and direction possible	Longer scan times and need to predict the optimal velocity encoding variable (VENC). Not routinely being used in the clinical diagnostic studies

Imaging modality	Overview	Advantages	Disadvantages
	T1 shortening effects of gadolinium utilised in Contrast-enhanced 3D MRV	Better anatomical assessment, background signal which is unwanted is better suppressed and also there is near elimination of saturation effects seen with TOF techniques	High cost, Intravenous cannulation leading to patient discomfort and its associated potential complications. Long term safety of gadolinium and its deposition, especially in paediatric population not proven and is still area of active research.

Imaging modality	Overview	Advantages	Disadvantages
Digital subtraction angiography (DSA)	highest spatial resolution among all the modalities, considered gold standard technique	same sitting for pre-operative planning and intervention, during follow up to look for residual sac as well as need for further treatment (however non-invasive modalities are preferred here).	Invasive, ionising and not widely available due to training and expertise required for performance specially in the developing and underdeveloped countries like India

Recently T2WI MRI without flow compensation and presence of MCA pseudo feeders on fetal MRI are advocated for assessment of angioarchitecture and management decision respectively. (45) (46)

TOF MRA and 2 mm thin axial T2WI TSE sequences without flow compensation by 1.5 T MRI has been reported to be a good modality for assessment of angioarchitecture pre-embolization. Standard T2WI TSE sequences are not well suited for characterizing the angioarchitecture of VOGMs. An axial slice thickness of 5 mm and even 3 mm is insufficient for detecting fine vessels. (45)Now if MCA pseudo-feeders are seen on MRI, few authors are recommending to deliver early if the fetus is expected to weigh more than 2500 grams, so that the fetus can be given drugs to improve his cardiac failure. (46) Indeed, there is some controversy regarding the efficacy and safety of maternal treatments to limit heart failure in the fetus.

TREATMENT OF VOGM

Due to the poor results of VOGM, all authors agree that these malformations should be actively treated. However, authors have found that the contraindications are manifested as pre-treatment proof of brain tissue damage or uncontrollable systemic failure, so this treatment aims to compensate for previous (or even partial) heart failure that has responded to medical treatment. Second, the appearance of subcortical calcification, drug resistance or clinical deterioration can also lead to emergency treatment.

The main goal of treatment is to achieve normal development of the child and control the hydrovenous consequences of the shunt rather than attain a complete morphologic disappearance of the arteriovenous shunt. Patient selection and timing of treatment are critical. The Biceˆtre neonatal evaluation score developed by Lasjaunias (6) assesses the cardiac, cerebral, respiratory, hepatic, and renal functions of the neonate with VOGM

and facilitates treatment decisions. This stood the test of the time but has been recently challenged by few authors who have highlighted its inadequacy in treatment decision making. (47) (48)

Lasjaunias recommends that patients who present with neonatal high-output cardiac failure and can be adequately controlled with medical treatment of the cardiac failure should be treated at 5 months of age to allow for weight gain before treatment. Patients inadequately controlled by medical treatment undergo emergency embolization. More recent meta-analyses and cohort studies recommend emergency treatment of neonates with VOGM who present with cardiac failure because their cardiac failure cannot be effectively controlled with medical treatment, and early treatment protects the brain from white matter injury secondary to venous hypertension. (49) (50)

Emergency management should be limited to a few situations, such as non-resolving congestive cardiac failure that cannot be stabilized by medication, growing head circumference because of altered cerebrospinal fluid hydrodynamics, and impending occlusion of jugular veins without sufficient rerouting of blood to the facial venous system.

Goals of treatment (more pertinent to EVT of VOGM): (1) (51) (6) (49) (43)

Endovascular management of VOGM is clearly beneficial over other forms of treatment. The trans arterial approach with undiluted N-butyl cyanoacrylate (NBCA/Glue) as the embolic agent is the typical classic approach. Limited case reports exist in the literature of using a transvenous approach to reach the dilated sac. Conceptually, the aim of

treatment is to exclude the malformations from the circulation. Hence, theoretically, the ultimate result should be similar whether the arterial or the venous route is used to achieve this. However, the limited experience of intervention using the venous route and the lack of published outcome analysis data do not seem to support this and most of the authors, therefore, feel that the results are better using the trans arterial route. Possible reasons for poor results from the venous approach may be related to poor overall understanding of the anatomy and pathophysiology. In a mural type of VOGM with a single hole, excellent results should be possible by either of the two routes. However, if there is a possibility of reflux into secondarily recruited arteries of the brain parenchyma, created as a consequence of the sump effect, the venous approach may lead to complications, such as haemorrhage. We also strongly believe that for the choroidal type of VOGM, the venous approach would not be suitable given the interspersed nidus, which will lead to haemorrhage when occluding only the dilated venous sac.

Staged embolization of the fistula site of the VOGM is the standard treatment. Staging treatment in multiple embolization sessions allows a more controlled devascularization and prevents adverse events such as a normal perfusion pressure breakthrough phenomenon or massive venous thrombosis. Proximal feeder occlusion is avoided because it leaves the fistula site open and eliminates future access to the fistula.

Most reported series use a trans arterial approach. Arterial coiling has been performed in some rare favourable cases with single high-flow mural types. The fistulous point had been reached either through arterial or venous approach retrogradely. Trans arterial balloon occlusion of the fistula's feeder was also advocated in the past; however, the

lack of long-term clinical results, unreported failures, and complications supported our technical choices.

Patients who present in infancy usually manifest with hydrocephalus or mild congestive heart failure and are classically treated electively. Patients with very low scores due to severe multiorgan failure and/or brain injury are not treated because the prognosis remains very poor despite treatment. (6)

OTHER TECHNIQUES

Transvenous treatment of VOGM has been described. (52) Exclusive transvenous or transtorcular approaches have a higher complication rate. Combined trans arterial and transvenous techniques have also been used. Reduction in arteriovenous shunting is achieved by packing the venous pouch with a variety of materials, including coils, balloons, and nylon. Transvenous dural sinus angioplasty and stenting have also been performed in patients with progressive sigmoid sinus-jugular occlusion. The long-term results of these anecdotal dural sinus stenting procedures are unknown at this point. Transvenous occlusion of the venous pouch carries the risk of venous infarction and haemorrhage. Consumptive coagulopathy after transvenous treatment has also been reported. A number of centres use a combination of both trans arterial and transvenous approaches, tailoring the technique according to the angioarchitecture of the lesion and response to previous treatment attempts.

Stereotactic radiotherapy has a limited role in the treatment of VOGM. (53)The effectiveness is uncertain and the time required to achieve results is unacceptably long

for the developing brain. The introduction of large coils in the venous pouch to slow down the flow so that glue may be used has also been proposed by others. However, series and clinical outcome are still missing. The time required by stereotactic radiotherapy to achieve a significant result is too long for developing and maturing brain and may not prevent the negative effects of the lesion, mainly in regard to hemo- and hydrodynamic disorders (atrophy, subcortical calcifications etc.) created by the VOGM, thus leading to irreversible mental retardation.

Primary surgical treatment for this vascular malformation is not practiced currently; few old reports are there in the literature with discouraging results. Endovascular methods are currently the best treatment method with overall low mortality rate (13%) and the technical morbidity rate in children of 0%. The surgical treatment on the other hand has 91 % mortality in new-borns and 38 % in infants.

In a series involving 43 patients with true vein of Galen aneurysmal malformations were reported by Lasjaunias et al. 34 cases of trans arterial embolization were done with isobutyl cyanoacrylate or n-butyl cyanoacrylate. There was no cutdown or hypotension during or after the embolization, and no balloon catheters were used. 47% of children have completely occlusive lesions, which was confirmed on follow-up angiography when the children are at least 6 months old; 52.9% were completely normal or had only mild heart failure, which could be treated with medication or moderate macrocephaly without neurological symptoms or mental retardation. 5.8% of the patients in the embolization group died due to wrong treatment (1 case) or to the inadequate timing of embolization 3 days after ventricular shunting (1 case). The total neonatal mortality rate

(embolization group and non-embolization group) was 27.7% and the total mortality rate for all age groups was 18.6%. (22)

Lasjaunias et al again came up with increased number of patients and described the management of 179 cerebral arteriovenous malformations (CAVMs) in children and infants. (39)

77 cases were true Galen venous malformations (VGAM), and 102 cases were pial AVM (PAVMs), which developed in the subpial space. 50% of children with pial AVMs had bleeding as the first symptom, but there is no bleeding in any case of VGAM. Only 31 children were found to be unsuitable for endovascular treatment, and 124 cases (with 104 embolizations) indicated embolization as the main treatment. Only 21 children received a direct surgical approach (not in the VGAM group). In the embolization group (n = 56) who completed the treatment, 8 children died, 39 were anatomically cured, and 34 were clinically normal. In the group under treatment (n = 48), 16 people were abnormal. In the nonembolized group (n = 31), 8/13 of the pial lesions were operated on (no mortality, 2 patients with moderate neurological deficits). In the VOGM group 13/18 died and 4 had spontaneous thrombosis (only 1 was neurologically normal). In the nonembolized group 13 lesions had been completely excluded, but only *5* patients were neurologically normal. This fact again stressed the need for prognostic evaluation before treatment and a clear definition of the treatment aims. Later experience of Lasjaunias et al, based on 317 patients with VOGM who were studied in Bicetre Hospital between October 1981 and October 2002, allows to describe the angioarchitecture, natural history, and management of VOGM in neonates, infants,

and children. Of the cohort of 317 patients, 233 patients were treated with endovascular embolization; of these, 216 patients were treated in their hospital. The treatment of choice is to inject glue into the fistulous area via the femoral artery approach. Of the 216 patients, 23 died despite or because of the embolization (10.6%).

Of the 193 surviving patients, 20 (10.4%) experienced severe delays in development, 30 (15.6%) were moderately retarded, and 143 (74%) had normal neurological function on follow up.

The outcome of patients who received endovascular treatment for VOGM between 1983 and 2002 was evaluated by Fullerton et al. (54) by reviewing medical records and parental questionnaires. An adapted version of the Denver Developmental Questionnaire was used to classify development as normal, mildly delayed (initially achieving milestones slowly but without permanent disability), or significantly delayed (slow or incomplete milestones with certain permanent disabilities). Twenty-seven patients were identified: 5 prenatal (by ultrasound), 16 neonates, and 6 post-neonatal visits. The most common manifestations are congestive heart failure (CHF; 16/27) and hydrocephalus (8/27). The 16 patients with CHF all presented either prenatally or neonatally; 4 cases died acutely, 6 had significant delay, and 6 cases had no developmental delay or mild developmental delay. Of those presenting in the perinatal period without CHF, all survived, two of five were significantly delayed, and three of five had no delay. Of those presenting after the neonatal period all survived and only one of six had delay. As classified by angiography, patients with choroidal VOGM (3/13 died; 5/13 had a significant delay) had worse outcomes than patients with mural VOGM (2/10 had a

significant delay; no deaths). In the whole series, 52% of the cases (61% of the survivors) had no delays or slight delays. Fourteen of the 27 children treated for VOGM performed well. Features associated with poor results are perinatal manifestations, the presence of CHF, and choroidal angioarchitecture.

Jones et al (55) retrospectively reviewed the radiology studies, hospital charts, and outpatient clinic chart notes (when applicable) of 13 children evaluated and treated for VOGM at a single tertiary care paediatric hospital. The clinical manifestations, diagnostic methods, treatment strategies and results of each child were recorded. The present neurologic status and level of function of each patient was determined by review of the outpatient charts and direct contact with the clinicians who were conducting the follow-up. The results are scored on a 5-point scale, ranging from 0 (dead) to 4 (normal), considering only neurological and developmental characteristics.

8 new-borns out of 13 patients developed congestive heart failure. The other 5 patients were between 4 months and 13 years old at the time of presentation. All 5 patients who visited outside the neonatal period achieved normal or near-normal results.

Of the 8 patients who visited during the neonatal period, 2 had normal or near-normal results, 1 had a markedly worsened condition, and 5 patients died. Authors could not determine the significant difference in results based on differences in treatment strategies. Author's experience confirms that the prognosis of children with VOGM in the neonatal period is usually much worse than that of children in later childhood.

Rodesch et al (56) described their experience of 168 consecutive cerebral arteriovenous shunts, all antenatally diagnosed lesions were vein of Galen aneurysmal malformations. The series included 18 cases of VOGM detected by ultrasound in the third trimester. There were 12 cases of normal vaginal delivery, 5 cases of caesarean section, and 1 case of induced abortion. 16 new-borns (94%) had systemic cardiac manifestations as the first clinical symptoms; 12/16 of the patients were effectively controlled with digital diuretic therapy and 4 (25%) died shortly after birth from acute heart and/or multiorgan failure with extensive brain damage. Twelve babies underwent trans arterial embolization during infancy (2 at 2 months of age). Eight infants (67%, 3 with 6 months follow up) were completely angiographically cured.

These results highlight that even after the antenatal diagnosis of VOGM and assumed bad prognosis overall, more optimistic approach could be taken regarding the management. Endovascular treatments can be performed according to strict clinicoradiological protocols.

In another series, between 1986 and 2000, 24 consecutive neonates with heart failure who required mechanical ventilation were admitted, and all cases were evaluated for cardiovascular disease by echocardiography. The same team of three doctors applied 18 trans arterial shunt occlusions with glue. Twelve infants survived and received at least one endovascular treatment (mean age 20 days), with an average follow-up time of 63 months. Due to severe brain injury or severe hypotension, 6 of the 12 non-survivors did not undergo embolization. Cardiogenic shock occurred in all non-survivors, but it also

occurred in one long-term survivor (p> 0.0001). An echocardiogram shows signs of right ventricular failure, most commonly in babies who did not survive (p=0.005).

The pulmonary systemic arterial pressure ratio was significantly increased in the non-survival group (p = 0.031), and only significantly decreased after the first embolization in surviving patients (p = 0.01). Compared with 30% of long-term survivors, all non-survivors had patent ductus arteriosus and diastolic aortic reversed flow (p = 0.003). There was no difference in left ventricular contractility and mean cardiac output between the two groups. Vein of Galen malformation complicated by severe heart failure requiring mechanical ventilation still results in poor outcomes. Neonatal embolization seems to be beneficial only for infants without suprasystemic pulmonary hypertension.

From September, 1986, to March, 1990, the Lylyk et al (57) treated 28 children harbouring a vein of Galen vascular malformation. Eleven (39.3%) patients were neonates, 13 (46.4%) were between 1 and 2 years old, and 4 (14.3%) were more than 2 years old. Fifteen patients (53.6%) had severe congestive heart failure, 6 (21.4%) had seizures, 4 (14.3%) had hydrocephalus, and 3 (10.7%) had intraventricular haemorrhage. According to the Yaşargil classification of malformations, 10 lesions (35.7%) were type I, 7 (25%) were type II, 8 (28.6%) were type III, and 3 (10.7%) were type IV. In 11 patients (39.3%), the combined transfemoral, trans arterial, and transvenous embolization of the VOGM was performed. Eight patients (28.6%) were treated with the pure transtorcular approach and in 2 patients with refractory congestive heart failure postembolization surgical clipping of arterial feeders was performed. Thirteen patients (46.4%) achieved complete anatomical occlusion of Galenian malformation. 23 of 28

patients (82.1%) improved in their clinical status immediately after embolization, and 17 patients (60.7%) observed good long-term clinical results. Five of the 28 patients in this series died (17.9%); three (10.7%) were related to transtorcular embolization, and two (7.1%) were considered related to the natural course of the disease which remained unchanged.

Friedman et al. (41) described improvement of endovascular technique. In the early studies using transcatheter embolization techniques, in a series of 22 patients, 50% mortality rate and a 37% incidence of severe mental retardation in survivors was noted.

Improvements in the embolization techniques and neonatal care have improved the outlook in a more recent 11-patient series. 91% of cases were diagnosed within 3 days after birth. There was no death, and 6 patients were functioning normally within 30 months of follow-up. Although two patients had severe neurological deficits and/or epilepsy, only one patient may be temporally related to embolization. In another patient some developmental delays were observed. These improvements are due in part to the modification of the treatment plan, including early diagnosis, avoiding the use of digoxin, improving the application of new microcatheters and acrylic polymers (n butyl cyanoacrylate), avoiding overly aggressive neurosurgery, and the use of stable central venous access for total parenteral nutrition is accompanied by other general improvements in the neonatal care.

Between 1988 and 1994, a series of 14 vein of Galen malformations diagnosed in the paediatric population and treated at the Hospital for Sick Children in Paris was reported by Borthne et al. (58) Five of the patients were diagnosed in the neonatal period and four

of them had intractable and life-threatening cardiac decompensation and high-flow arteriovenous fistulas. The embolization was performed in 4 patients during the first week after birth. One embolization failed and the result was fatal. Of the 3 patients who were embolized, 2 died within 1 week and 1 survived with a significant improvement in cardiac symptoms. Older children have hydrocephalus and neurological symptoms. Ten patients over 1 year old were also embolized. The success rate of these procedures was 90%, with hemodynamic stabilization and improvement in clinical symptoms.

In this group, the mortality rate was 10%. The overall mortality rate is 29%. In 44% of cases, hydrocephalus was considered secondary to compression of the sylvian aqueduct. Five patients underwent ventricular drainage before embolization, followed by selective staged embolization. 11 patients received trans arterial embolization whereas transvenous route taken in 2 patients.

The study population consisted of 7 cases of the VOGM who received treatment via the percutaneous transvenous approach by Casasco et al. (52) For the approach via the transvenous route, jugular vein was accessed in 6 patients and femoral vein in 1 patient. All of the malformations had multiple pedicles and additionally, in 6 of the 7 patients there was an intervening arterial- arterial network between the posterior thalamoperforating arteries and the wall of the venous system. This fistulous network was likely purely arterial and not as an associated AV malformation. For this reason, the transvenous approach was considered justified and was performed without risk of haemorrhage caused by the retrograde venous hypertension. Measurement of the intra-aneurysmal pressure during the course of the treatment was done, which possibly

allowed better understanding of the hemodynamics of the lesion and better management, as per the authors, resulting in prevention of normal perfusion pressure breakthrough (NPPB).

In comparison to transtorcular approach, which requires surgery, transfemoral approach can be performed percutaneously and is less invasive. The authors concluded that with their favourable outcomes without any major complications, via the transvenous route, it can be considered for multipeducular VOGMs over the trans arterial embolization or the surgery.

The authors could achieve 5 complete and 2 partial occlusions of the shunts via percutaneous transvenous approach.

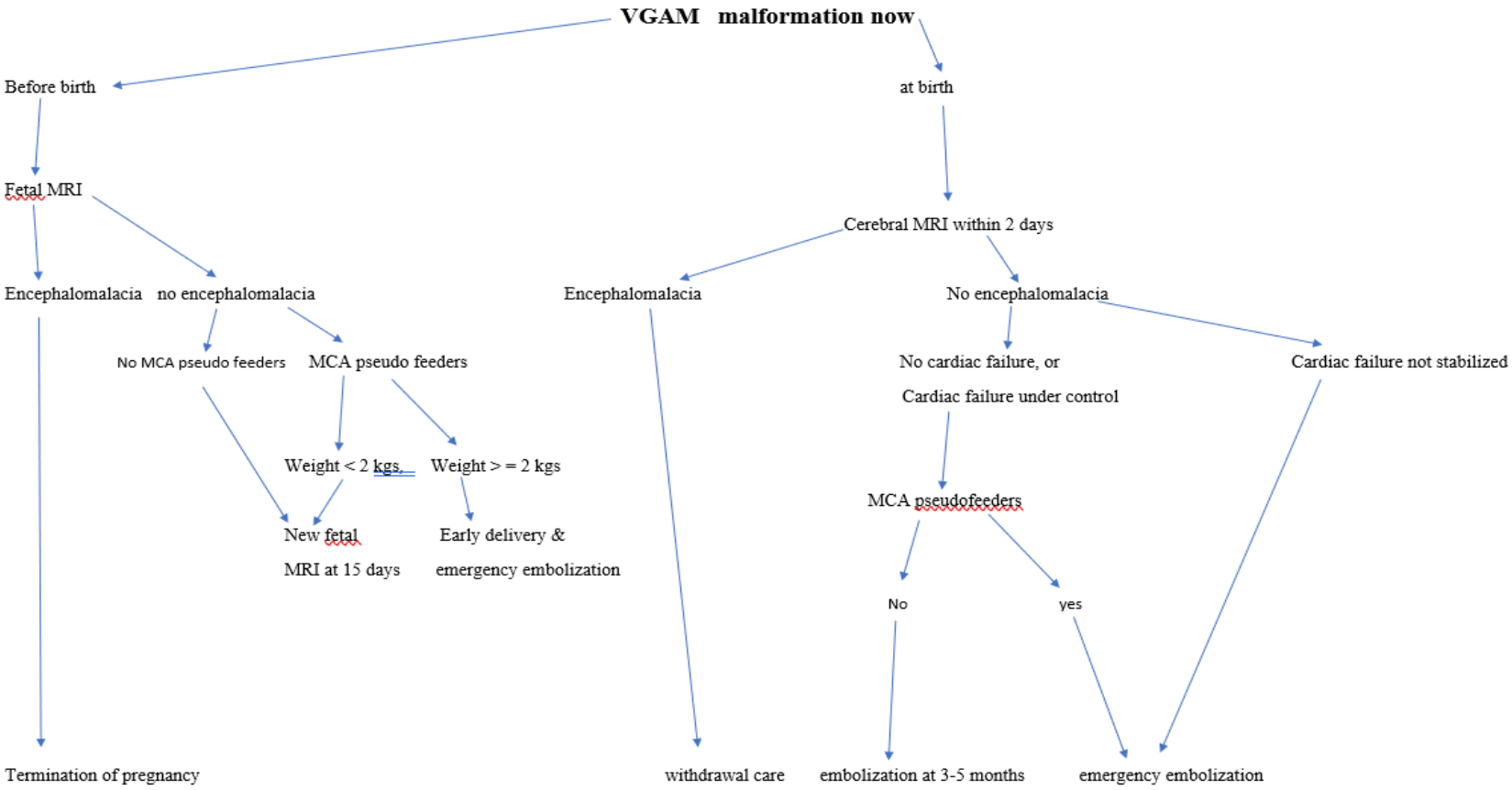
Rao et al (59) described a series from our Institute involving a cohort of 9 patients in year 1994. Percutaneous trans-arterial embolotherapy, in five patients achieved complete obliteration of the malformation in four patients and partial reduction of flow in another. While transvenous/trans-torcular approach is reserved for selected patients and direct surgery carries high morbidity, this report emphasizes the efficacy of trans-arterial embolotherapy. Gupta et al (43) from our institute reported another series in 2006. In a study period between 1983 to 2003, 25 patients with VOG malformations were referred to author's institution for evaluation and management. Age distribution of the patients in this study was as follows: younger than 2 years of age- 10 children, 2 years or older children- 11 children, adult patient- 4 patients. Younger than 2 years of age patients had rapidly increasing head size as the most common complaints. In the age groups of 2 years or older as well as the adult patients, headache was the most common complaint.

Angiographic evaluation of the lesion was performed in the 21 patients out of total 25 patients. Endovascular management was offered in 15 patients. In the presence of the high flow fistula, systemic hypotension was induced before injection of the embolic material.

Complete occlusion of the AV shunt was achieved in the 2 patients with vein of Galen aneurysmal dilation (i.e., in all the patients with this type of malformation) and in 5 of 6 patients with mural type of VOG malformation (approx. 83 %). Among choroidal type of VOGM, complete obliteration of the shunt could be achieved in 3 patients. In 3 patients with choroidal VOGM with high flow, embolization carried out in a single sitting resulted in shunt reduction of nearly 90 %.

With advent of better hardware available and feasibility of better surgical and anesthetic support, Scepter mini balloon and cardiopulmonary bypass are being attempted in overall management of the VOGM cases in case-to-case basis. (60) (61)

Based on present better antenatal detection, more frequent usage of the MRI in assessment of the VOGM and the better availability of the endovascular methods, following algorithm is suggested: (46)


VGAM malformation now
Before birth
at birth
Fetal MRI
Cerebral MRI within 2 days
Encephalomalacia
no encephalomalacia
Encephalomalacia
No encephalomalacia
No MCA pseudo feeders
MCA pseudo feeders
No cardiac failure, or
Cardiac failure under control
Cardiac failure not stabilized
Weight < 2 kgs.
Weight > = 2 kgs
MCA pseudofeeders
New fetal
MRI at 15 days
Early delivery &
emergency embolization
No
yes
Termination of pregnancy
withdrawal care
embolization at 3-5 months
emergency embolization

MATERIALS AND METHODS

All patients of VOGM who presented to SCTIMST and were followed up from 1 Jan 2009 to the 5.10.2019 were included in the retrospective arm. All patients from 5.10.2019 to 31.05.2021 formed the prospective arm of the study. Minors and neonates were included in the study as most of times these are the age groups affected by the malformation. Strict compliance with the international protocol related to the radiation protection norms were adhered to. Consent/assent obtained from guardians or appropriate persons. No inclusion of person incompetent to give informed consent, normal/healthy volunteer, Prisoner, student/staff of the institute. The patients had a baseline imaging done - either a USG or CT or MRI of the brain. Subsequently, the patients underwent a diagnostic cerebral angiogram and/or embolization in the same sitting, decided upon case-to-case basis as per the institutions protocol.

Number: 44 (minimum of 40, as per the IEC approval)

Eligibility: The inclusion and exclusion criteria are as detailed below**.**

Inclusion criteria: All patients with VOGM who visited SCTIMST from 1 Jan 2009 to 31 st May 2021 were included, irrespective of age, sex or ethnicity. Patients treated with partial or total embolization in the past who later presented in our institute were also included.

Exclusion criteria:

- Contraindication to iodinated contrast

- Patient in whom appropriate data is not available on PACS or MRD records.
- Clinical features like hydrocephalus, seizure or Congestive cardiac failure attributed to other pathologies like Brain tumour producing hydrocephalus
- Patient (parents/legal guardians) denying participation in the study

The recruitment of subject for the retrospective arm was done by the principal investigator by reviewing the patient records of the institute. The retrieval of data from the electronic data base was done using key search words like “vein of Galen malformation” and “VOGM/VAGM”. Subjects for the prospective arm were recruited by the principal investigator from the respective out patient department (OPD) & in-patient services (Neuroradiology, Cardiac surgery Cardiology, Neurosurgery and Neurology). Patient details were anonymized and key generated to analyse the patient data.

Data Analysis:

Statistical analysis of the data was performed by using statistical software**,** R version 4.0.3. Descriptive measures were calculated for all the variables. Chi square test and t tests were applied for qualitative and quantitative variables respectively after assessment of distributions. Appropriate non-parametric tests applied for non-normal distributed variables. Correlation and regression analysed to determine predictors in the study. Statistical significance was assessed using the p value < 0.05. No specific gender, class, caste, ethnic or race bias was intended in the study. For the purpose of this study, post procedure follow-ups were obtained telephonically and on OPD visits. Due to the

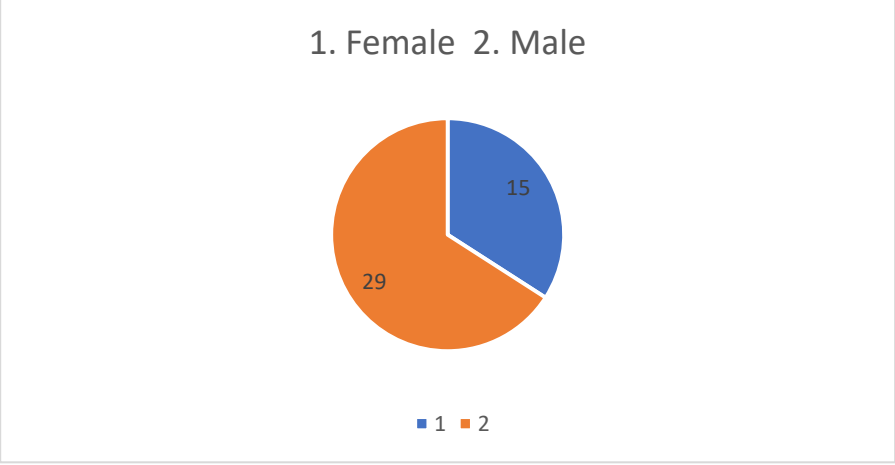
CoVID pandemic mobile consultation and follow up was encouraged. All the studies were performed on Advantx digital subtraction angiography unit (GE Milwaukee, USA) or Innova biplane flat panel digital subtraction angiography unit (GE Milwaukee, USA). A wide variety of catheters and embolic material was used for the procedures as was best suited for the individual patient depending on the angioarchitecture. Diagnostic angiographies were done under local anaesthesia when they were performed separate from interventional procedure or performed as a check angiography for follow up. The interventional procedure was done under general anaesthesia. For procedures carried out under general anaesthesia, the patient was monitored in the interventional radiology or cardiology intensive care unit. Premedication (lnj. Pethidine 25- 50mg i.m. & lnj. Phenergan l2.5- 25mg i.m.) usually was given as for all the procedures under the local anaesthesia (diagnostic DSA in young children/adults). Post procedure these patients were managed in the wards when angiography was performed under local anaesthesia. After discharge, the patients were followed up with clinical evaluation for improvement in their symptoms. Follow up imaging or angiograms were performed when required. A complete evaluation of the patient including demographic profiles (age, sex), clinical presentation, imaging features, treatment method and outcome including complications and follow up was carried out as per the proforma attached.

OBSERVATION AND RESULTS

DEMOGRAPHICS:

A total of 44 cases (age range; new-born- 28years, sex ratio; male: female =17:7) of VOGM were included.

There were 29 male (65 %), patients and 15 female (34 %) patients. The average birth weight was 2.77 kg. A total of 33 patients underwent embolization. A total of 4 patients underwent DSA only. 5 patients were kept on clinical follow up and did not undergo DSA. 12 patients out of 44 patients died during the period of study. Two patients were lost to follow up, 2 antenatally diagnosed cases who went to another centre as per their administrative convenience and 1 was lost to follow up status post embolization. There were 25 cases with choroidal (56 %) VOGM and 13 patients (29 %) with mural VOGM. In 6 patients (13.6 %), it was characterised on non- invasive imaging like MRI, USG etc and DSA was not performed or available.



One sitting was needed in 14 patients, rest 19 patients needed more than 1 sitting of embolization. On an average, 2.096 sittings of embolization were performed during the treatment. Maximum of 5 sittings of embolization were performed in 2 patients, one of which died after 5 th sitting of embolization. 20 embolized patients showed improvement post treatment. Ten out of 33 patients died during the follow up or after the embolization. 2 patients died without receiving embolization. Out of surviving children, 4 were living with major disabilities, not independent for activities of daily living while 3 patients were living with minor disabilities. Cardiac co morbidities were present in 22 (50 %) and were absent in 22 (50 %). Cardiac intervention was done in 2 patients. Heart failure at the time of presentation was seen in 14 patients (31 %), and was normal in 30 patients (68 %). Increase in head circumference was seen in 13 patients (29 %), delay in developmental milestones in 12 patients (27 %) and history of fall or imbalance was present in 4 patients (9 %). Respiratory difficulty was present in 15 patients (34 %). Headache was present in 7 patients (15 %).

Cerebellar tonsillar herniation noted in 3 patients (6 %). Ventriculomegaly noted in 30 patients (68 %). Brain parenchymal calcifications was seen in 7 patients (15 %). Parenchymal changes were present in 23 patients (52 %). Seizure was present in total of 9 patients (20 %). Two or less in Bicetre score was noted in 8 patients (18 %). First imaging performed in initial evaluation and diagnosis was USG in 22 patients (including antenatal), CT in 7 patients (15 %), MRI in 14 patients (31 %) and DSA in 1 patient (2 %).

With regards to the arterial feeders on DSA- the medial and lateral posterior choroidal arteries were the commonest arterial feeders. Lenticulostriate arteries contributed in 18 patients (40 %), and were one of the common arterial feeders. A few patients also had ACA branches like subcallosal artery and subforniceal artery as feeders. Transdural supply from meningeal arteries were noted in 3 patients (6 %). Largest venous sac size noted was: 1-3 cm in 18 patients (40 %), 3-5 cm in 21 patients (47 %), measuring 5-7 cm in 1 patient (2 %) and > 7 cm in 1 patient (2 %).

Communication between Median Vein of Prosencephalon (MVP) & deep venous system i.e., ICV noted in 6 patients (13 %), Venous drainage of the normal brain was patent in 38 patients (86 %) and not patent in 2 (4 %). Straight sinus was absent in 28 patients (63 %) and observed to be present in 12 patients (27 %). Persistent Falcine Sinus (PFS) was not seen in 3 patients (6 %), but was observed in majority of the patients numbering 37 patients (84 %). Occipital sinus was present in 27 patients (61 %) and it was absent in 10 patients (22 %). Embryonic sinus present in 37 patients (84 %) and absent in 3 patients (6 %). Cavernous sinus capture was poor in 11 patients (25 %) and it was good in 22 patients (50 %). Deep venous drainage was not present in 36 patients (81 %) whereas it was present in 3 patients (6 %). Occipital marginal sinus was not present in 12 patients (27 %) and was present in 23 patients (52 %). Diffuse bihemispheric brain injuries noted in 8 patients (18 %). Brain liquefactive or gliotic changes was present in 3 patients (6 %). 12 patients underwent embolization at 4-12 months of age. 3 patients underwent embolization < 4 months of age, 4 patients at >12 months of age. Age at 1 st embolization at <4 months was noted in 10 patients (22 %), at the age of 4-12 months in

12 patients (27 %) and > 12 months in 8 patients (18 %). 3 patients improved after embolization at < 4 months of age. 9 patients improved at embolization at 4-12 months of age, 4 patients improved after embolization at >12 months of age.

Emergent embolization was performed in 6 patients (13 %) whereas it was performed on elective or semi elective basis in the rest of the patients. Total number of sitting of Interventions performed are as follows: 1 sitting performed in 14 patients (31 %), 2 sittings performed in 7 patients (15 %), 3 sittings in 5 patients (11 %), 4 sittings in 3 patients (6 %) and total 5 sittings in 2 patients (4 %).

Reduction in shunt after 1st embolization (in percentage) achieved was as follows: < 30 % reduction in the shunt in 8 patients (18 %), 30-50 % reduction in 10 patients (22 %), reduction upto 50-70 % in 8 patients (18 %), and reduction >70 % in 2 patients (4 %). When the interval after which 2 nd sitting of embolization was performed, the following was observed:

Interval of less than 1 week in 1 patient (2 %), interval of 1-2 weeks in 1 patient (2 %), interval of more than 1 month in 9 patients (20 %), > 6 months in 3 patients (6 %), > 1 year in 2 patients (5 %).

Reduction in shunt after 2 nd sitting of embolization achieved was less than 30 % in 3 patients (6 %), upto 30-50 % in 4 patients (9 %), upto 50-70 % in 5 patients (11 %), and more than >70 % in 4 patients (9 %).

Onyx was used as liquid embolic agent in total of 3 patients (6 %), glue/NBCA in 11 patients (25 %) and squid used in total of 7 patients (15 %). In 3 patients (6 %), liquid

embolic agent and coil was used in same sitting to achieve embolization. Out of 33 patients who underwent embolization 3 patients underwent only coil embolization. Distal embolization of liquid embolic agents noted in 2 patients (4 %). Intraprocedural or post procedure haemorrhage was present in 3 patients (6 %). With respect to the final outcome, 8 (18 % of study population) females improved whereas 17 (38 % of study population) males improved. Overall, Choroidal VOGM patients who improved were 12 patients and patients with mural VOGM and showed improvement in 8 patients. All patients with non-patency of the venous drainage of the normal brain did worse. Some improvement post treatment was noted only in patients with patent venous drainage of the normal brain. 15 patients who were embolized, improved, whereas 10 patients were on the conservative management and improved.

A total of 2 patients with reduction in shunt after first embolization (in percentage) of < 30 %, showed improvement, 6 patients with upto 30- 50 % shunt reduction improved. Shunt reduction of upto 50- 70 % was noted in 7 patients who showed improvement. Only one patient with > 70% shunt reduction after first embolization showed improvement. We preferred to embolize as early as possible for the next sitting, preferably within 4 weeks, if adequate shunt reduction was not achieved in 1 st sitting of embolization.

1 patient with reduction in shunt of 30-50 % after 2 nd sitting of embolization, improved. A total of 5 patients with 50-70 % reduction in shunt after 2 nd sitting embolization improved and 3 patients with shunt reduction of >70 % after 2 nd sitting of embolization improved. In our study no patient with intraprocedural and/ or

periprocedural haemorrhage showed improvement. Total of 28 % of patients with delay in developmental milestones, showed improvement. A total of 68 % with no delay in developmental milestones showed improvement.

20 % of patients with respiratory difficulty noted to show improvement. Whereas 76 % of patients with no respiratory difficulty had shown improvement. (P= 0.06).

A total of 60 % of patients with ventriculomegaly had improved, whereas only 40 % without ventriculomegaly improved. (P=0.007). A total of 36 % of patients with parenchymal changes on imaging showed improvement. Almost 64 % of patients with no parenchymal changes on imaging showed improvement. (P=0.0007). No patient with < 2 score in Bicetre scoring in the single category improved and it was strongly statistically significant with P value of 0.00058. Overall VOGM who improved were 48 % for the choroidal type and 32 % for the mural type.

In our study the analysis of the venous sac(largest) showed following results: No patient with sac size more than 5 cm showed improvement. 48 % of patients with largest single venous sac size of 1-3 cm showed improvement. 52 % of patients with largest venous sac size of 3-5 cm showed improvement. The largest venous sac size of 1-3 cm showing improvement was statistically significant with p value of 0.01.

Statistical significance was noted for patients in whom there was no communication between the MVP and ICV vis a vis in whom there was communication between MVP and deep venous system e.g., ICV. Patients with communication with deep venous system who improved were approximately 12 % and without communication with the

deep venous system who improved were 88 % with P value of 0.01834. All the patients who had improved had patent normal venous drainage of the brain. None of the patients without the patent venous drainage of normal brain improved. Non patency of the venous drainage of the normal brain with poor outcome was statistically significant with P value of 0.01. 36 % of patient with presence of straight sinus showed improvement whereas 64 % of patients with absence of straight sinus showed improvement. Presence of straight sinus with improvement was statistically significant with p value of 0.03. Presence of Falcine sinus noted in 92 % of patients who showed improvement whereas absent falcine sinus with improvement in patient was noted in approximately 8 % of the patients. This association was tending towards statistical significance with p value of 0.054.

Only approximately 8 % of the patients with absent embryonic sinus showed improvement whereas 92 % of the patients with presence of the embryonic sinus showed improvement. This association was found to be statistically significant with a P value of 0.05. With reference to number of sittings of the intervention/embolization and patient improvement, 1 sitting with patient improvement noted in 32 % of patients, 2 sittings with improvement in 16 % of the patients, 3 sittings in 16 % of the patients and 4 sittings in 4 % of the patients. None of the patients with 5 sittings of embolization showed improvement.

8 % of the patients with reduction in shunt after 1st embolization (in percentage) of less than 30 % showed improvement. 24 % improved with reduction of approximately 30-50 % of the shunt, almost 28 % with 50-70 % shunt reduction, 4 % with more than 70 %:

shunt reduction. More than 70 % shunt reduction after 1 st sitting of embolization with patient improvement was not statistically significant with P value of 0.06. In 24 % of patients 2 nd sitting was planned after 1 month and patients showed improvement. In 8 % of patients, it was planned after 6 months and patients improved, whereas in 4 % of patients it was done after a year and patients showed improvement.

4 % of patients with reduction in shunt after 2 nd sitting of embolization with reduction in shunt of 30-50 % showed improvement. Approximately 50-70 % shunt reduction after 2 nd sitting showed improvement in 20 % of the patients >70 % shunt reduction in 2 nd sitting in 12 % of patients with improvement. There was statistical significance noted between the 2 nd sitting embolization and shunt reduction of >70 % and 50-70 % with P values of 0.04. Approximately 92 % of the patients without any diffuse bihemispheric brain injuries improved, whereas only 8 % of the patients with diffuse bihemispheric brain injuries could show improvement. This association was statistically significant with P value of 0.001. Again, the brain liquefactive or gliotic changes were found to be predictive of the final outcome. Approximately, 96 % of patients improved in absence of brain liquefactive/gliotic changes, however only approximately 4 % of the patients with presence of Brain liquefactive or gliotic changes could improve. This association was statistically significant with P value of 0.01.

12 % of the patients with age of less than 4 months at 1 st embolization showed improvement. Patients with age group of 4-12 months at 1 st embolization who improved were approximately 36 %. Approximately 16 % of the patients who showed

improvement were more than 12 months of age at the time of 1 st sitting of embolization.

No patient with emergent embolization improved (0 %), however elective or semi elective embolization produced patient improvement in 68 % and this association is statistically significant with P value of 0.009 (for elective or semi elective embolization). Patients with cardiac co morbidities showed improvement in 9 patients, and without cardiac co morbidities showing improvement in 16 patients however this association was statistically not significant ($p = 0.06$).

Patients with heart failure at the time of initial presentation showed improvement in 4 cases whereas without heart failure at presentation showed improvement in 21 patients and this association is significant with p value of 0.02.

Coming to the treatment decision for the patients- it was taken on case- to- case basis and ranged from conservative management to embolization to withholding the treatment(embolization) due to poor general condition and prognostic factors based on Bicetre scoring.

No significant relationship was found between the type of liquid embolic agent (LEA) used and the outcome. Out of all patients, 1 had puncture site minor complication. There were 2 patients with distal embolization (extracranial) of the liquid embolic agent not affecting the final outcome. 3 patients (all were mural VOGMs) underwent only coil embolization. The clinical follow up available in our study ranged between a maximum

period of 13 years to a minimum period of 6 months. Average duration of follow up available in our study is approximately 4.72 years.

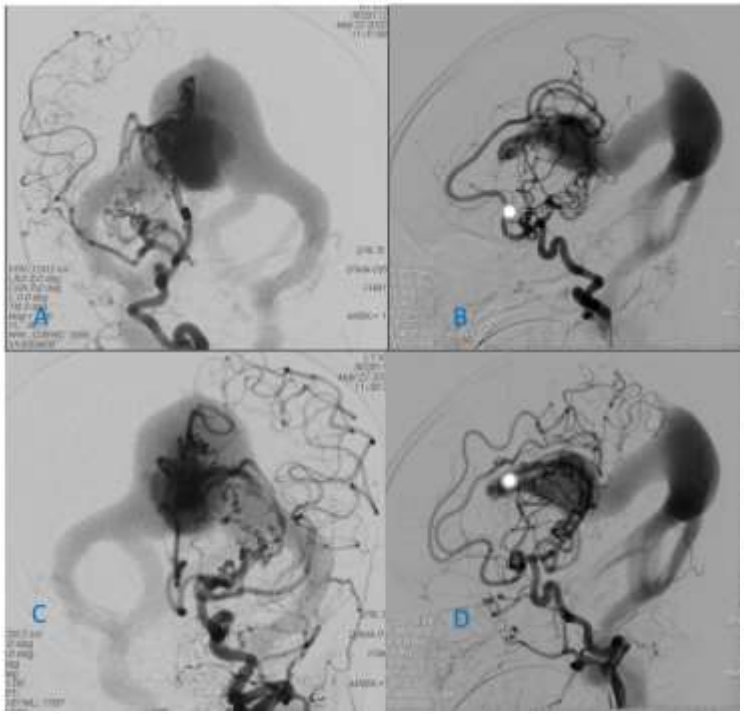
OTHER OBSERVATIONS

One patient with choroidal VOGM also had right TS dAVF which was also embolised with glue. This patient had choroidal type of VOGM. One patient with choroidal VOGM also had a small saccular aneurysm arising from the origin of right lateral lenticulostriate branch, which was not treated.

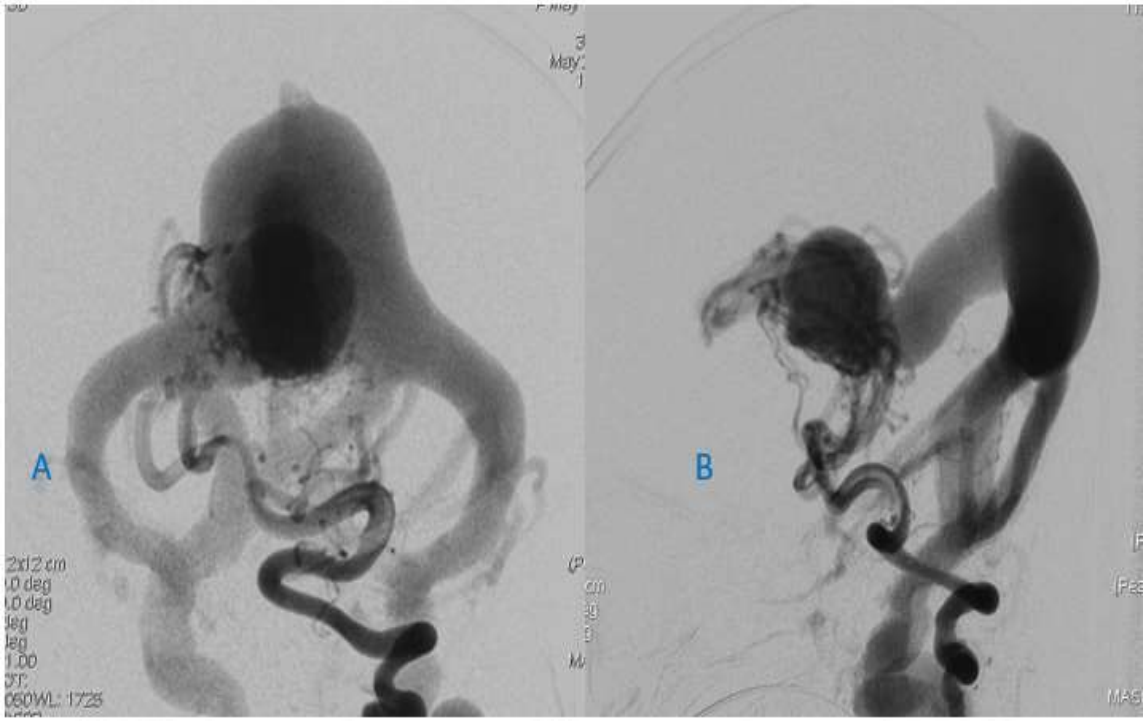
One patient with mural VOGM had suspicious right parietal AVM remained unchanged between two embolization sessions. There was severe (> 90 %) stenosis of the jugular bulb in this patient.

ILLUSTRATIVE CASES

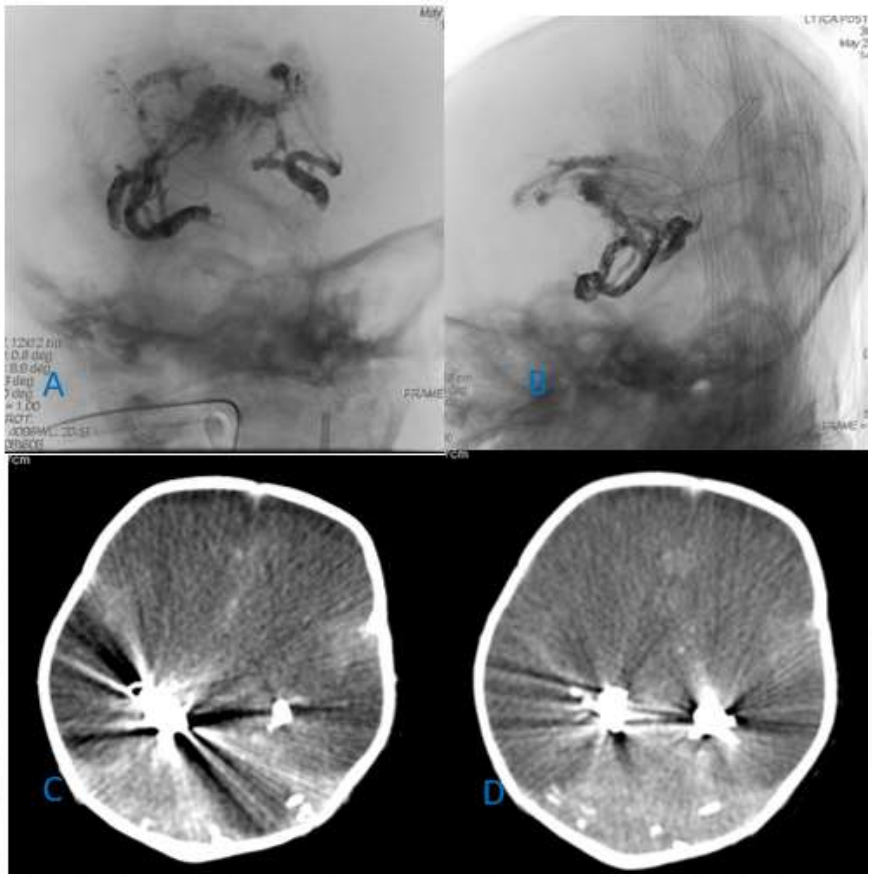
CASE 1:



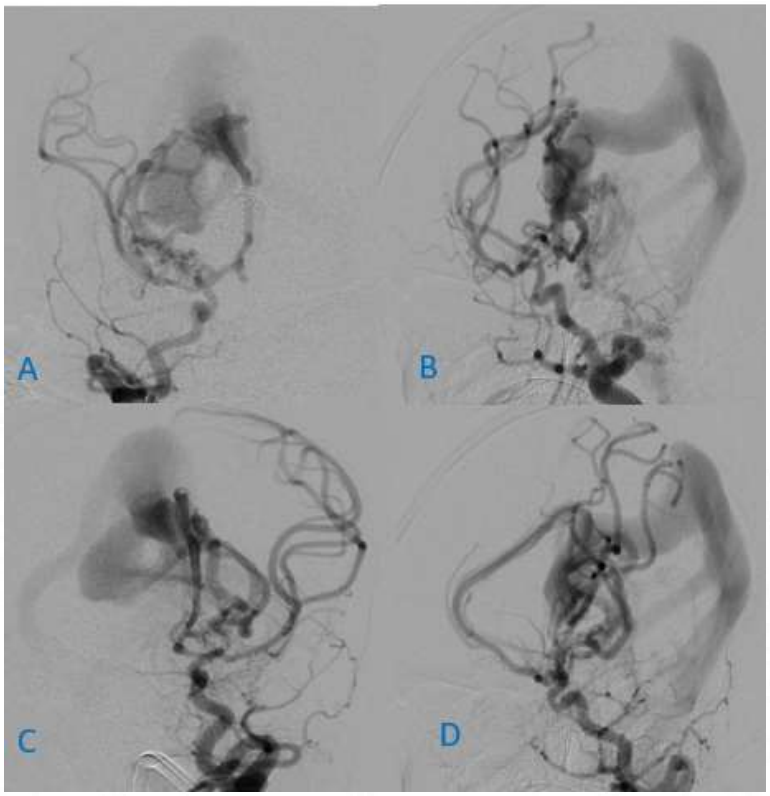
Case 1: Fig 1: 2day old baby, Bicetre score-11 Endovascular embolization of VOGM with approx. 50% reduction in shunt. Choroidal type VOGM, predominant supply from multiple hypertrophied PCA feeders (bilateral medial & Lateral posterior choroidal arteries). ACA- pericallosal branches, and few prominent thalamoperforator branches. Venous sac measured 21 x 19 x 23 mm.



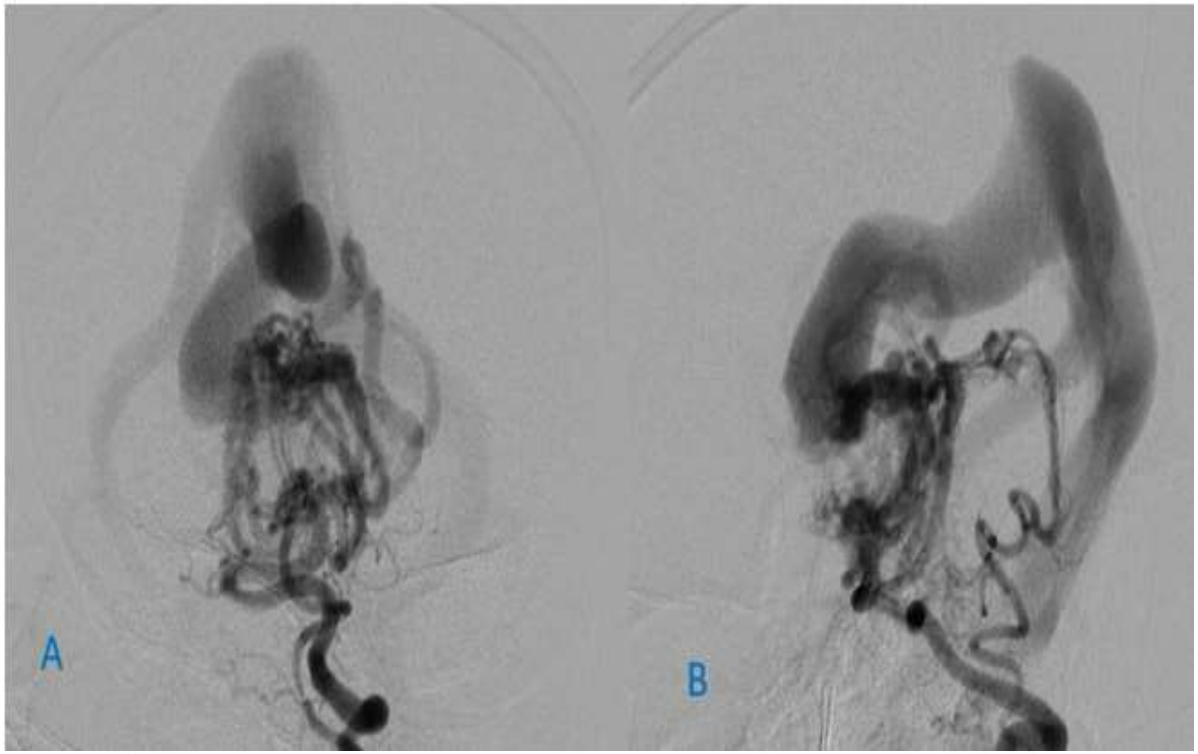
Case 1 Fig 2. VA AP VA Lateral



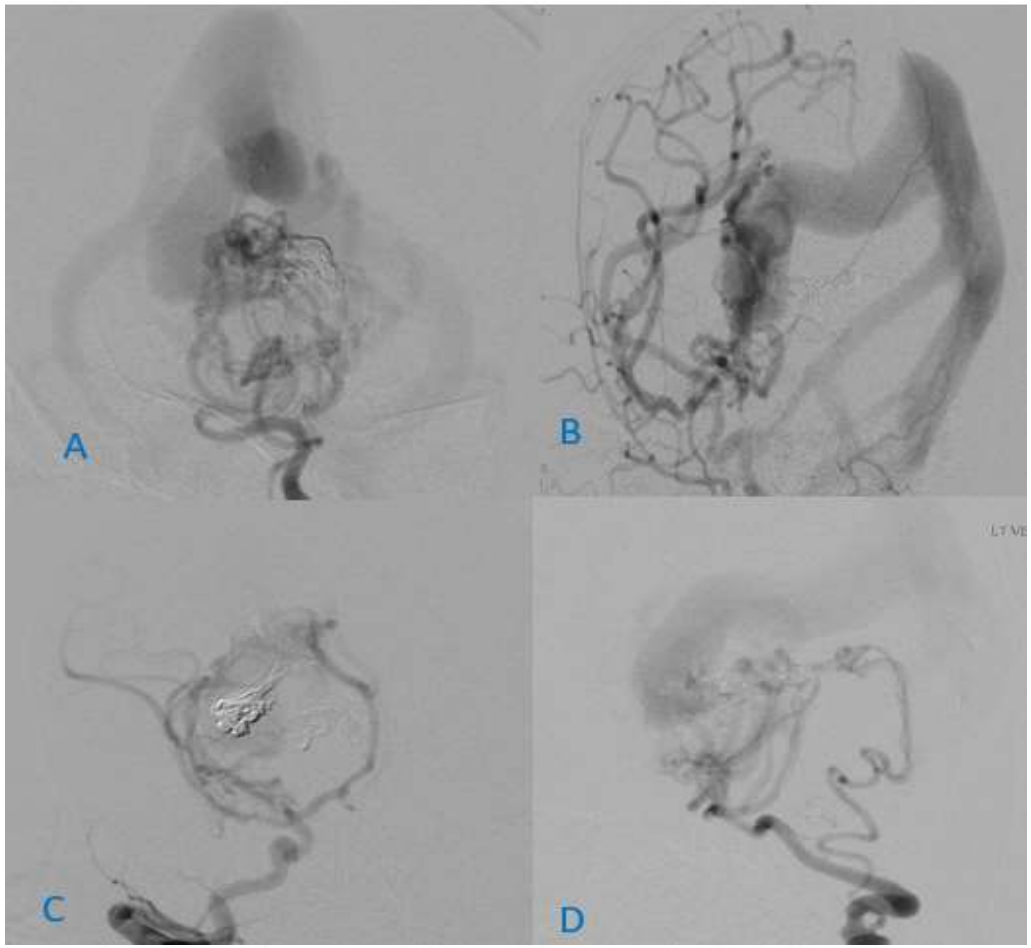
Case 1 fig 3: A & B: Post embolization NBCA cast AP view Post embolization NBCA cast Lat view C & D: CT Scan post embolization 1 CT Scan post embolization 2



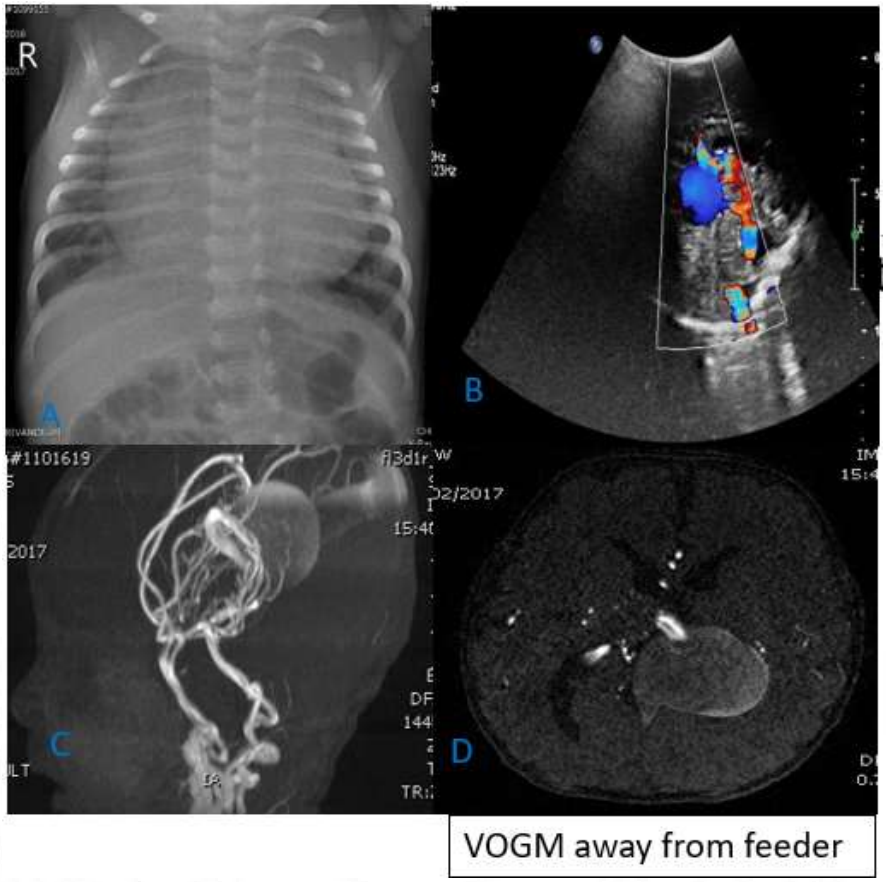
Case 2: Fig 1: Choroidal VOGM Bicetre score 8/21, A & B: Rt ICA AP Rt ICA Lateral C & D: Lt ICA AP, Lateral Choroidal type VOGM multiple hypertrophied PCA feeders (bilat medial and lat posterior choroidal branches) ACA- pericallosal br, bilateral few prominent lenticulostriate br, bilateral anterior choroidal A, and thalamoperforator branches. Contribution also from bilateral MCA distal cortical pial collaterals Venous sac 26 x 15 x 16 mm



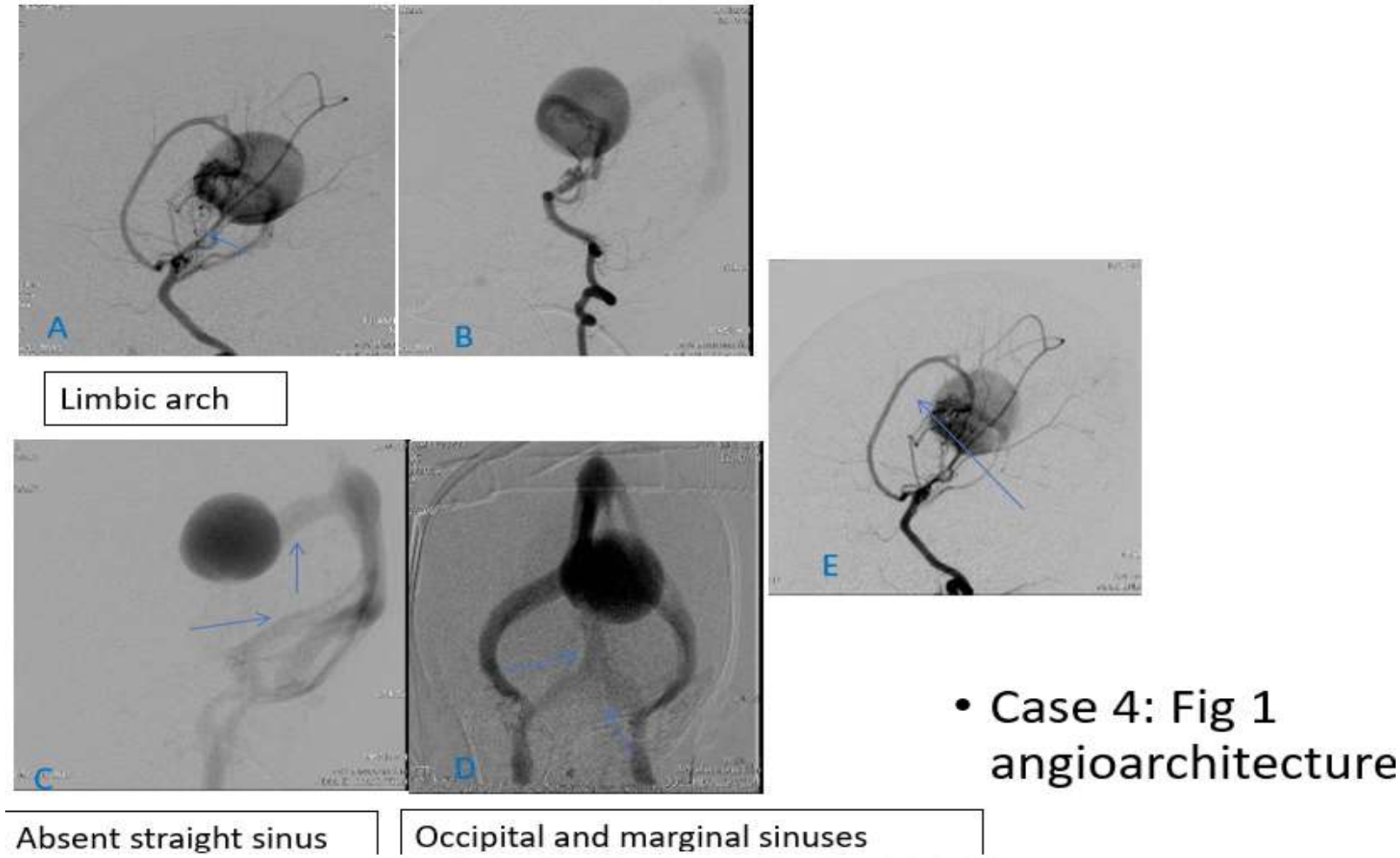
Case 2: Fig 2: A & B: Lt VA AP Lateral



Case 2: Fig 3: Rt ICA AP and Lateral post embolizationLt VA AP Lateral post embolization, Check angio – significant reduction- persistent flow - br of bilateral distal ACAs- (Lt > Rt) feeders- superior part of the network



Case 3: Fig 1: Choroidal VOGM 9 month- Antenatally diagnosed. Fetal Echo- Cardiomegaly. ECHO- Severe PAH with small ASD. HC- 34 cm to 38 cm (after 2 month).2 episodes of apnoea. Choroidal Type. DSA + Squid embolization (after 2 months)-50% reduction. Extubated next day.



- Case 4: Fig 1 angioarchitecture

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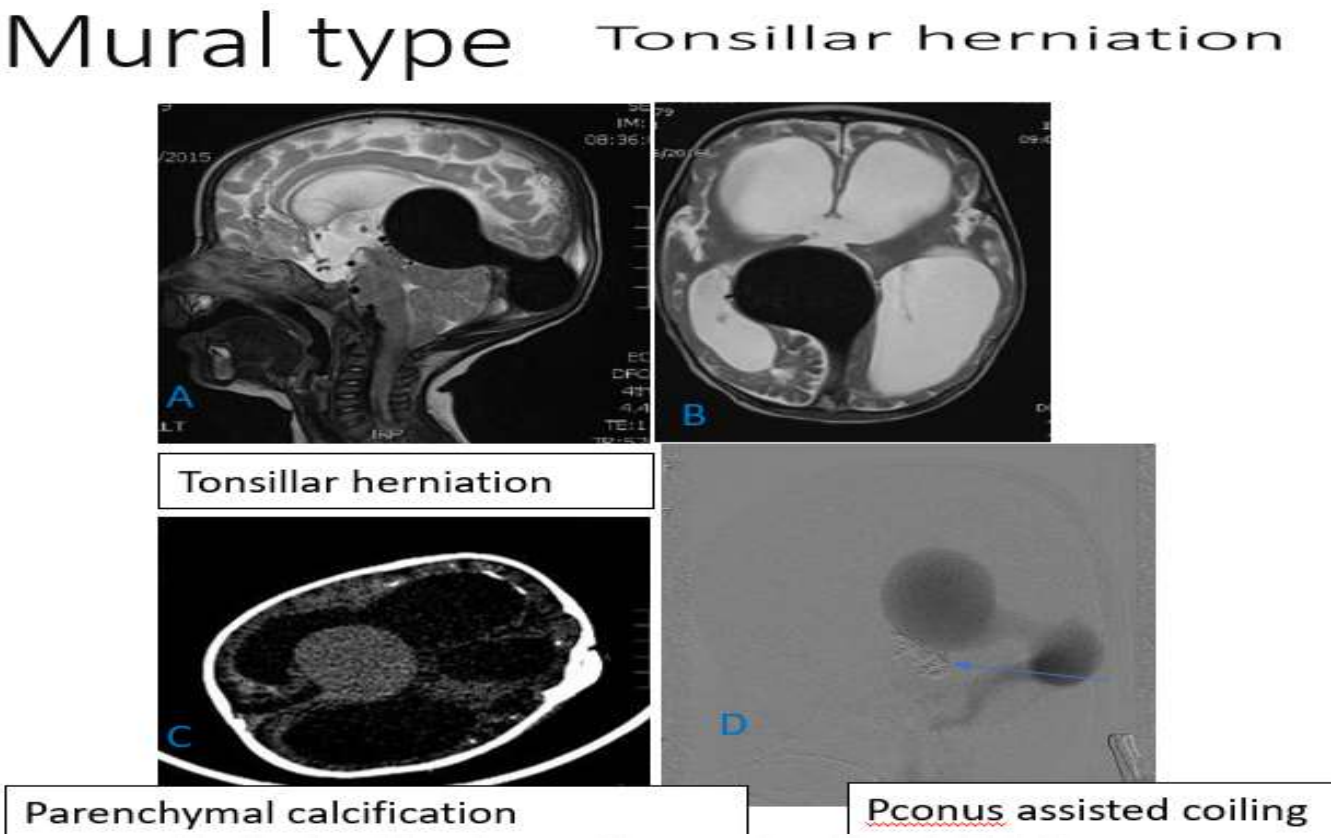
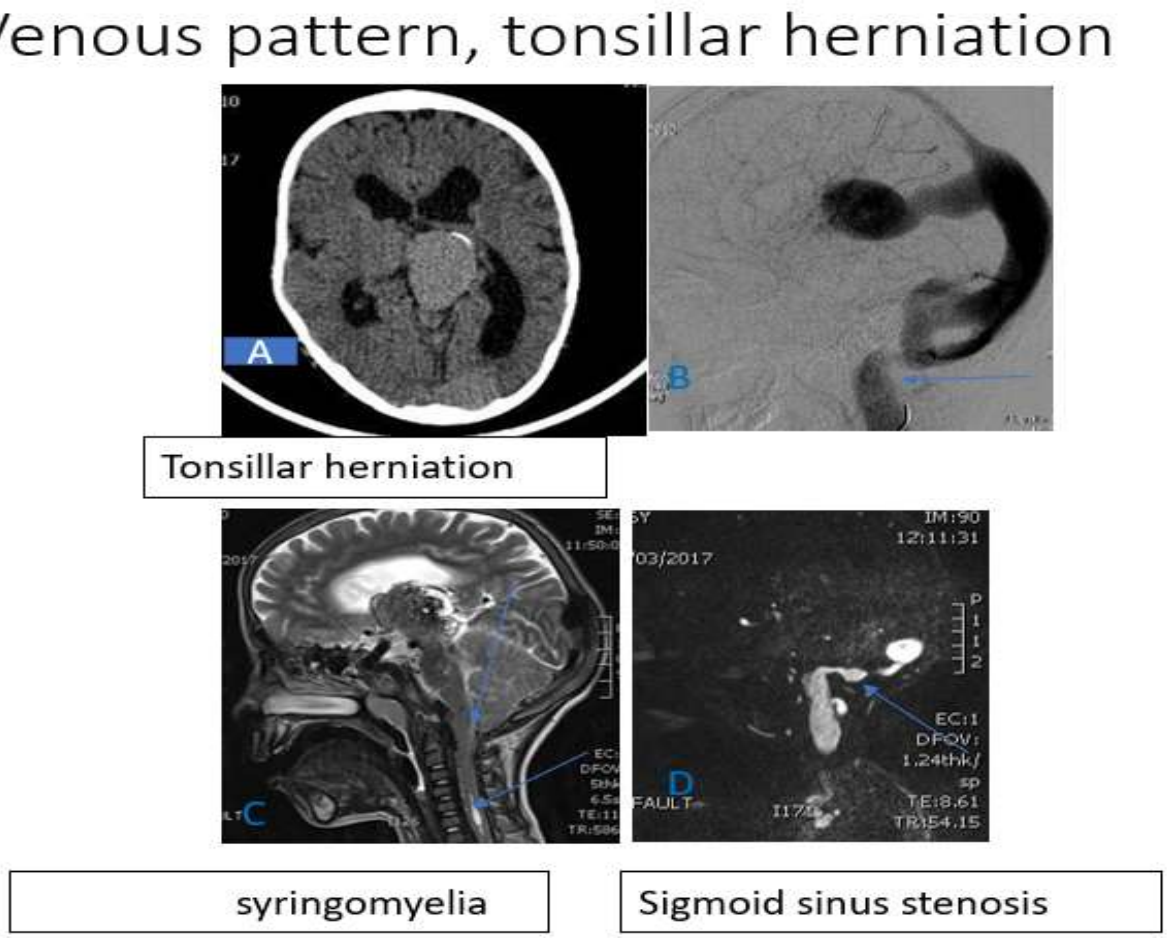
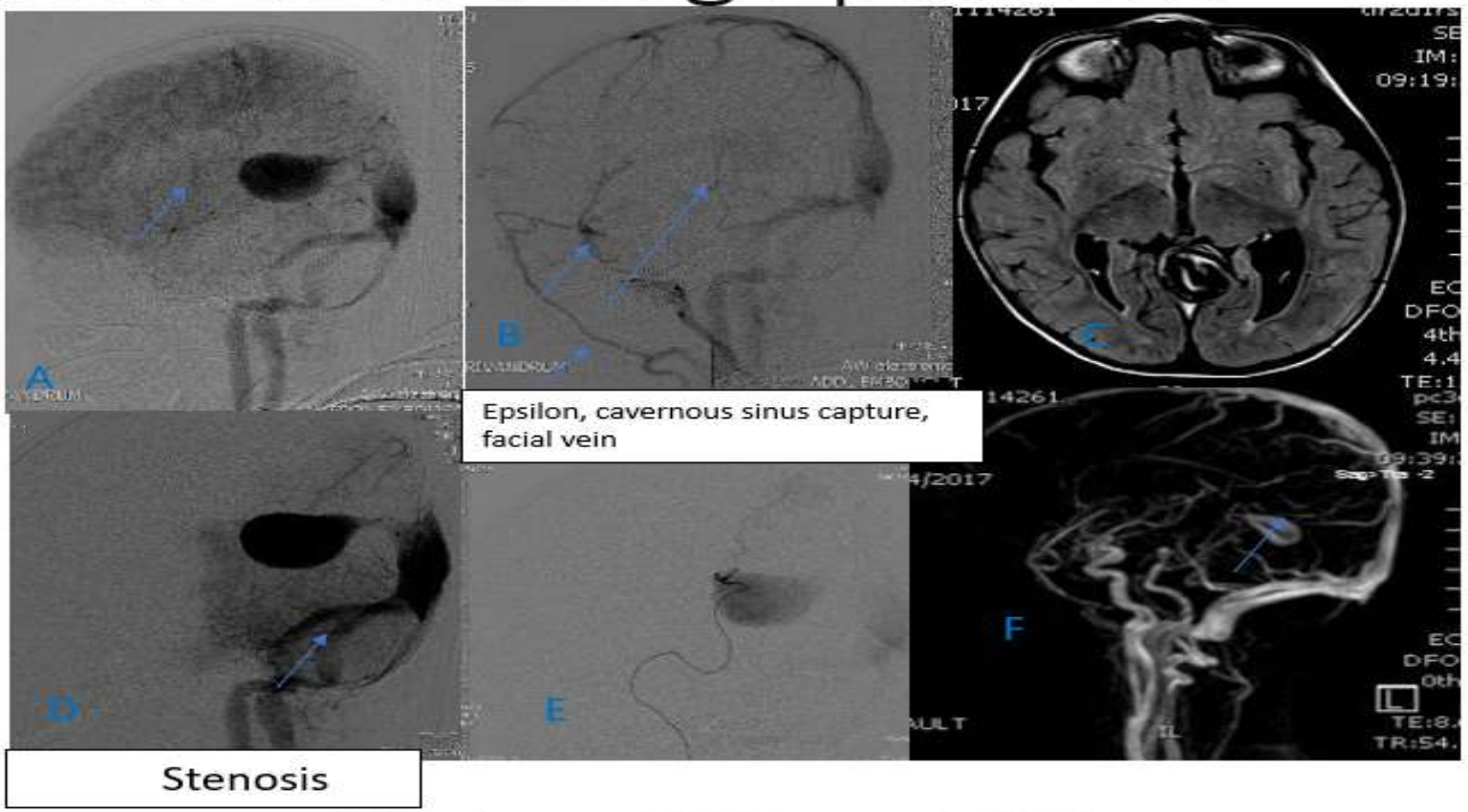


Case 5: Fig 1: No CHF. 4months- macrocephaly, stiff limbs, seizures, delayed milestones. Dec 2015, Jun 2016-coil+squid. 1 year 5 months-Global developmental delay. Jan 2017-Pconus (4x20) +3 coils-Right posterior choroidal artery. Stent assisted coiling



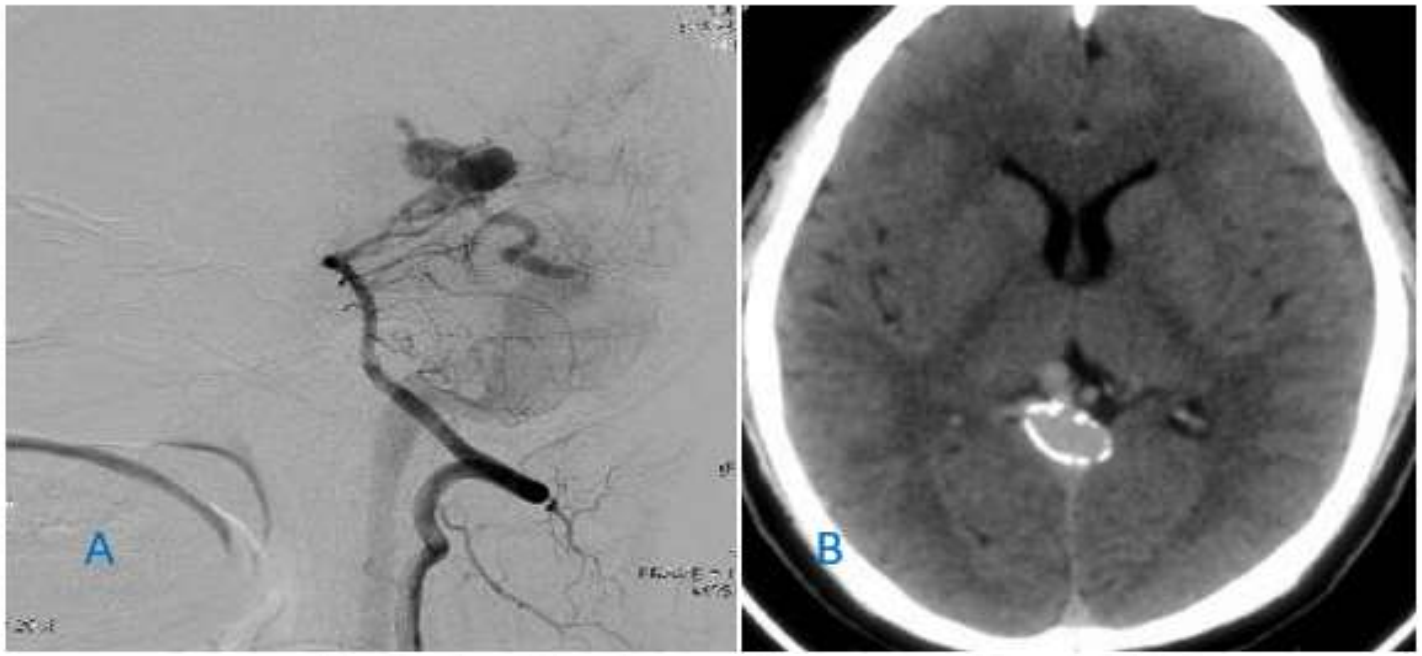
Case 6: Fig 1: Slurring of speech and paraesthesia. Squid embolization

Venous drainage patterns



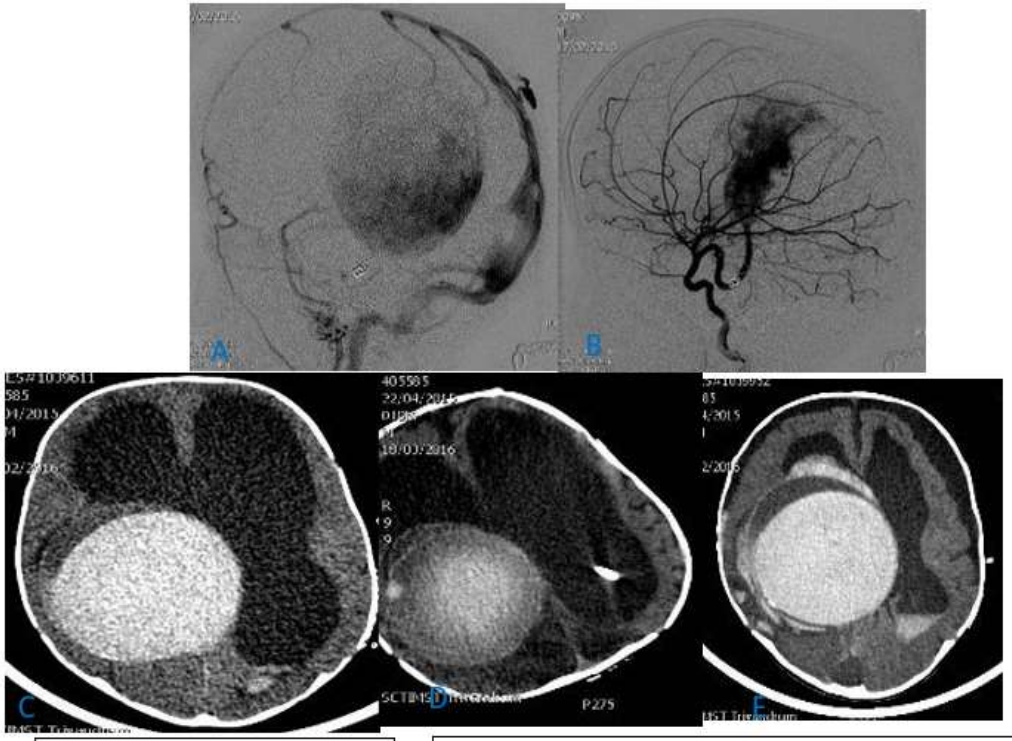
Case 7: 2 years. Mural Type. Seizures. Good milestones

Adult presentation: VOGM



Case 8:Fig 1: 20 years adult. Headache x 8 months. Mural type

Endovascular treatment complication



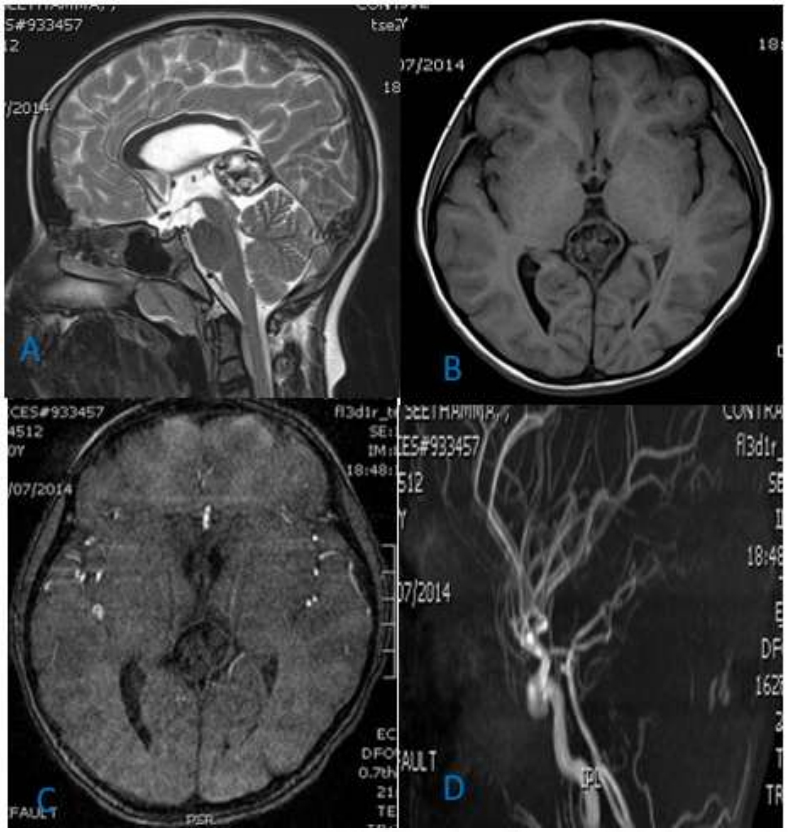
Thrombosis+
consumptive coagulopathy

Thrombosed sac

EVD- subdural collection, bleed

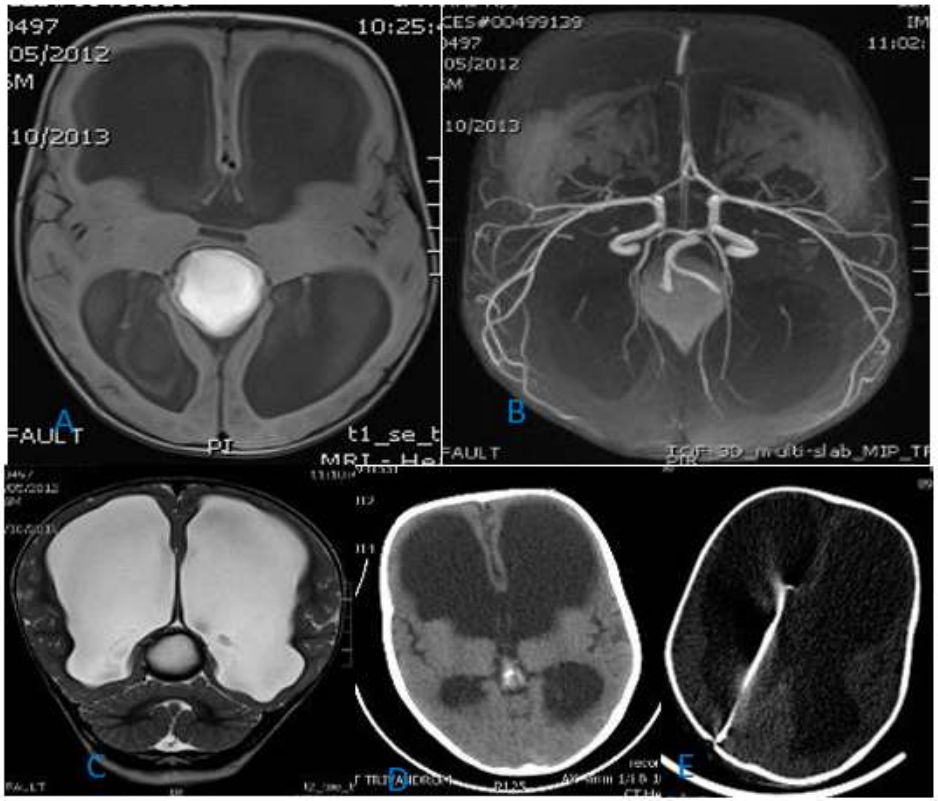
Case 9: Mural type. Single fistula.7 month-Delayed milestones. No cardiac symptoms. 9 months

Spontaneous thrombosis with good outcome



Case 10: At birth-no cry. Imaging-VOGM. Developmentally normal. Headache -2 months. Now 17 years. MRI+DSA.

Spontaneous thrombosis-need not good outcome



Case 11: 2 years. Increased head size since 4months age with CT and trans cranial USG-VOGM. Spontaneous thrombosis.

Developmental milestones delay Gross Ventriculomegaly

DISCUSSION

Our study tried to evaluate the natural history of vein of Galen malformation and factors predicting the final outcome. The main clinical presentation related to VOG malformation was either due to high output cardiac failure secondary to venous congestion or neurologic symptoms due to abnormal CSF flow. Cardiac failure was the most common clinical manifestation in the neonates and was rarely the presenting symptom in infants or children because these patients often have fewer severe cardiac symptoms. The study included a total of 44 patients, including 14 antenatally diagnosed patients. It is in contrast to previously reported low incidence of antenatally diagnosed cases from the Indian subcontinent. (1) (43) We had 5 patients in age group > 6 years of age, eldest among them being 21 years at presentation, who presented with headache. This age group comprised 11.3 % of our cases, which is lower than the study by Agarwal et al. (1)

In Bicetre hospital series they had 29.3% of cases diagnosed as fetus, 37.5% in neonatal age, 25.9% as infant and 7.3% after 2 years of age. This matches with our patients' demographic profile. Presentation in adults is also rare but has been reported in literature.

This proportion is also matching with the findings of Johnston, et al. (5), who found that, of 232 cases collected from literature, only 18% of the patients presented at an age older than 5 years. In our series 11% patients were older than 5 years at presentation.

Sex ratio in our series was in accordance with literature. 65 % of our patients were males and 35 % females with a male: female ratio of 1.93:1. Bhattacharyya et al reported it to be 3:1 in a review, similar to ours. (37)

Presentation of vein of Galen malformation patients can be varied. Our series had 13 (30 %) with increased head size, 7 (15%) with headache, 12 (27 %) with delayed milestones, 4 (9 %) with history of fall or imbalance, 15 (34 %) patients with respiratory difficulty and 14 (31 %) with different manifestations of mild to severe cardiac failure.

Other most common manifestations were asymptomatic antenatally diagnosed cases. Increasing head size as the chief complaint was reported by 11 patients in the infantile age group, 1 case who was diagnosed antenatally and later presented with increase in the head circumference as the chief complaints and 1 patient presented with this complaint in > 6 years age group. Eight children in this group also had delay in achieving developmental milestones.

Although fifteen children had a history of respiratory distress at birth or symptoms related to cardiac cause, on examination, 12 had associated cardiac co morbidities. 9 of these patients had choroidal type of malformation, five were of mural type. 8 of the patients with heart failure at presentation were of choroidal type of VOGM. 3 had mural type of VOGM and in 3 types of VOGM was uncertain type. This is in contrast to the evidence from literature which states that choroidal type is usually associated with cardiac failure and not the mural type. (28) (62)

Among 11 patients who were more than 1 year of age or older, the most common presenting symptom was chronic headache. Chronic headache is the complaint offered by most of the patients presenting late in the life, who harbour VOG malformation. Headache was present in 6 among those 7 patients and interestingly headache was complained by 1 patient in infantile age group.

Presentation with intracranial bleed was not noted in our patient cohort.

Deep venous connection: The fact that we noted deep venous reflux in six cases indicates the presence of a deep venous connection with the venous sac in VOGM. Similar findings were also reported by Levrier et al (32) and Iizuka et al.(63) and Agarwal et al.(1) Lasjaunias et al denied the possibility of a deep venous connection of the venous sac. However, Raybaud (13) in his description of the embryology of VOGM emphasized that deep venous connections could occur in certain cases in which timing of the insult is relatively delayed. Thus, our findings support the notion that insult to the developing neurovasculature can lead on to a spectrum of morphologic features depending on the timing of the insult.

Adult angioarchitecture: 3 out of 5 patients presenting > 6 years of age had patent straight sinus. This matches with study by Agarwal et al. (1) Out of 12 patients with patent straight sinus, 6 were choroidal type of VOGM, 3 were of mural type and 3 were indeterminate. (45)

Straight sinus was found more frequently in the adult patients in our series. These could, in fact, be the very factors which permitted their uneventful survival to adulthood. The

significance of predominantly choroidal type in these patients needs to be explored because, according to Lasjaunias et al, choroidal is the more severe malformation found commonly in neonates; however, they did not include patients above 16 years of age in their large series.

Dural arterial recruitment was another feature in our patients. We had total of 3 patients with dural supply, all of them had presented at > 6 yrs of age. As a matter of fact, one case out of these three was diagnosed antenatally but kept on conservative follow up. At the age of 6 yrs. this patient presented with focal seizures. This patient later underwent 5 sittings of staged embolization and unfortunately succumbed to IVH post 5 th sitting of embolization.

We had 3 patients with intraprocedural or periprocedural haemorrhage. Out of these 2 were of choroidal type and 1 was mural type of VOGM. One patient survived with deficits, 2 had fatal outcome. Lenticulostriate feeders were found in total of 18 patients (40.9 %). These were commoner in choroidal type of VOGM (n= 15) than the mural type of VOGM (n= 3).

Berenstein et al (64) also found that seven out of 71 patients with VOGM had dural arterial feeders and they were older than the other patients at the time of their initial angiogram. They attribute the dural supply to non-sprouting angiogenesis due to sump effect.

Analysis of echocardiography revealed associated cardiac manifestations in total 25 patients (56 %), 10 with choroidal and 7 with mural malformation. Among those with

echocardiographic abnormality, clinical cardiac failure was present in 11 of these patients. 7 patients with cardiac co morbidities had mural type of VOGM and 1 of them had heart failure at the time of presentation, stressing the fact that choroidal type VOGM with heart failure is much commoner than the mural type of VOGM with heart failure. Atrial septal defect (ASD) alone was the commonest cardiac co morbidity, present in 10 patients (40 %). Ventricular septal defect (VSD) along with ASD present in 8 patients (32 %). Patent ductus arteriosus (PDA) present in 7 patients (28 %), 1 patient had ASD and PDA and 2 patients had ASD with VSD and PDA. Out of 14 patients initially presenting with cardiac failure, 3 had fatal outcome. 2 neonates had severe cardiac failure at birth necessitating intensive care monitoring and died before endovascular intervention.

Cardiac manifestations are known in Vein of Galen malformation, constitutes an important component in the pathophysiology of the disease process and also has been prenatally diagnosed. In contrast to the cardiac failure observed in large haemangiomas, where they occur in infancy at the proliferative phase of the disease, the congestive cardiac failure in VOGM can be present during the neonatal period.

In his series of 18 antenatally diagnosed VOGM patients, Rodesch (56) noted that 17 were born with cardiac failure. During prenatal ultrasound examination, some cardiac enlargement was noted in four out of 17 patients. In all the four patients the neonatal score was low (<8/21) either because of the significant peripheral effect of systemic failure or because of an already demonstrable encephalomalacia. Treatment was withheld in those four patients and they soon died. The others were medically managed,

followed, embolised between 2 and 13 months trans arterially. A total of 30% of them had slight retardation (less than 20%), which resolved in a few months after embolization.

Therapeutic termination of pregnancy can be discussed in cases in which cardiac failure and or brain damage is demonstrated in utero.

As per the spontaneous evolution of CCF, Lasjaunias et al (6) suggested that after a brief period of stabilization, in most patients the CCF worsens during the first 3 days of life, and then stabilizes again to then improve with appropriate medical management. They noticed that in none of the babies referred to them with the diagnosis of VOGM did cardiac failure develop de novo after the 2nd week of life. However, it could decompensate at 3weeks or recur later following lung infection or other concomitant diseases. In infants CCF never constituted the presenting complaint nor did it worsen at that age if already present. We also observed similar pattern with none of the patients developing de novo failure at later age nor did it worsen after neonatal period. Cardiac manifestations and degree of failure seems to be variable from one child to the other and seems independent of the characteristics of the shunt. Some obvious high flow lesions are well tolerated, while conversely some apparently smaller ones may lead to multiorgan failure. Hence the intracranial hemodynamic parameters available do not provide us with any prognostic or therapeutic information. Renal and hepatic damage may further aggravate CCF, and their function can be transiently impaired (oliguria, increase of enzyme) or become rapidly unstable despite intensive medical care. Few of

our patients had transient neonatal hyperbilirubinemia and subsided on its own and was considered as physiological neonatal hyperbilirubinemia regarding its temporal evolution pattern. The cause of CCF is not fully understood. In fetal life, the effect of heart rate on combined ventricular output suggests that heart is functioning near its maximum performance. It seems that volume loading increases output to a limited extent. The fetal myocardium has less contractile tissue, as shown by its less myofibrillar contents. Several major events change the fetal circulation at birth: removal of low-pressure placental circuit, reversal of relative pressure between two atria with closure of foramen ovale, muscular contraction of ductus, and decrease in pulmonary vascular resistance. CCF is seen more commonly with choroidal type of malformation as seen in all cases of our series. Lasjaunias et al shared same experience. They stated that severe forms of CCF are associated with persistence of fetal type of circulation. Septal communications and ductus arteriosus are often noted and they should not be considered as associated cardiac malformations, even if they increase the systemic insufficiency. Like most of the disorders encountered in these circumstances, they either disappear spontaneously or following endovascular management of the AV shunt itself. They should be followed with special attention if embolization is not planned early, and they may induce a failure to thrive condition.

In the series by Lasjaunias et al, two neonates presented with an associated cardiac malformation and an aortic coarctation for which they were first operated on: embolization was then carried out at 1 and 2 months of age. Five and ten years follow up revealed satisfactory clinical outcome. In two other patients they decided to clip a patent

ductus arteriosus before embolising the VOGM in neonates with severe CCF. 2 of our VOGM patients had undergone cardiac procedure. Out of these 2 patients, 1 patient with choroidal type of VOGM had a sinus venosus ASD for which she underwent pericardial patch closure at 6 months of age. Patients underwent endovascular management for VOGM few months later than the cardiac procedure. 2 nd patient who underwent cardiac intervention was that with a female child with mural type of VOGM and sinus venosus ASD with partial anomalous pulmonary vein, underwent cardiac intervention few years later than intervention for VOGM. On follow up complete thrombosis of VOGM sac was noted and patient is doing well on 7 years follow up.

Among twelve deaths in our series, ten had undergone embolization and two did not receive embolization. Nine out of these twelve patients had features of cardiac failure at presentation. Three patients did not have cardiac failure at the presentation. Therapeutic termination of pregnancy can be discussed in cases in which cardiac failure and or brain damage is demonstrated in utero.

All the patients irrespective of the presenting complaints had undergone imaging in the form of Transcranial USG, MRI or CT. They revealed predominant findings as ventriculomegaly 30 (68 %), followed by brain parenchymal thinning in 23 (52 %), and brain parenchymal calcification in 7 patients (16%). Among patients with ventriculomegaly 17 were having mural type and the 8 had choroidal type of malformation. All 13 patients with increase in head circumference at presentation all had ventriculomegaly.

Among 7 patients with headache 4 had ventriculomegaly and 3 did not. Among 12 patients with delayed milestones at presentation 11 had it and 1 did not. Among 4 patients with history of fall or imbalance, all had ventriculomegaly. Among 25 patients with cardiac co-morbidities, 14 had ventriculomegaly. Hence delayed socioscholastic development had good association with ventriculomegaly on imaging.

As opposed to CCF, hydrodynamic disorders can manifest themselves in foetuses, neonates and infants. Choroidal and mural types almost equally give rise to this type of manifestations. They constitute the primary revealing factor at infant age if the diagnosis has not been made before. They result from the abnormal hemodynamic conditions present at the torcular venous sinus confluence, the posterior convergence of the venous drainage of the brain, and the immaturity of the granulation system of arachnoid villi. (29)

For many years, the mechanical compression of the mesencephalic aqueduct was considered to be the primary factor behind hydrocephalus. Actually, aqueduct is usually present and patent in all cases and this observation was consistently made in our patients as well.

Macro crania, while resulting in an increasing head circumference, is associated with slightly enlarged ventricles and a generous increase in perivascular spaces. The water dysfunction combines intracerebral retention with an increase in cerebrospinal fluid volume. Both phenomena have little or no effect on the brain itself as long as the suture enlarges, since they tend to continually adapt to intracranial pressure vs the resistance by

the cranial vault. On the other hand, in VOGM infants the lack of macro crania is even more worrisome than its presence. The cerebrofugal medullary veins constitute a gradient that will induce absorption of most of the intracerebral water. If the suture stops growing, if the medullary vein resorption decreases (or if the pial venous pressure increase), or if for any other reason the compliance of the venous system fails, hydrocephalus and intracranial hypertension occur. (35)

At infant stage, persistence of the situation leads to clinical manifestations in the form of irritability, altered level of consciousness and neurological status, developmental delay, decreased brain volume with increased fluid space. Before ventricular enlargement occurs, intracranial pressure is not as high because of macro crania, and therefore shunting is not required. Spontaneous stabilization of enlarging head phenomena can occur with cavernous capture of the sylvian veins. The progression of macro crania to hydrocephalus is thus not inevitable. Going with this explanation all our patients with enlarged head size did not have ventriculomegaly.

Developmental delay is part of the natural history of untreated VOGM. (6) Careful evaluation of neurocognitive performance shows that most children with macro crania present some degree of mental retardation. In view of the poor prognosis of the disease, specialists and parents tend to accept as normal a child with mild retardation (up to 20% of normal for chronological age). This level of delay allows the child to attend a normal school albeit with some support. Delayed socioscholastic development had consistent association with hydrocephalus on imaging. As opposed to CCF, hydrodynamic disorders can manifest themselves in foetuses, neonates and infants. (29) (65) Choroidal

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Although there is no direct relationship between the degree of macro crania and the severity of developmental delay (the head enlargement actually protects the children's brain), there is an obvious link between the hydrodynamic disorder and the delay. Any

event that creates a loss in compliance has an impact on brain maturation, e.g., intracranial hypertension, spontaneous decrease in head circumference and ventricular shunting. Eleven out of total twelve children with either developmental delay or poor scholastic performance had ventriculomegaly in our series, this attests to the association. Similar results were obtained in the patients managed and followed up at other centres. (54) (47)

Cerebral morphological sequelae express themselves in calcifications, subependymal atrophy (pseudo ventriculomegaly), and eventually the stigmata of previous acute accidents with cortical. and subcortical atrophy. The insult to the brain is a slow and permanent one.

We had seven patients with parenchyrnal calcification (excluding the calcifications of sac noted either at presentation or on the follow up imaging).

Spontaneous thrombosis of the VOGM is rare.(6,39) In the experience of Lasjaunias, 2.5% patients showed spontaneous thrombosis, but only Approximately half of the patients with spontaneous thrombosis of the VOG malformation were neurologically abnormal, which is less than what is achieved by proper treatment. In addition, this thrombosis is mostly unpredictable, although the tentorial edge compression of the arterial feeders together with the secondary intralurninal thrombosis in the stenosed draining vein might be an indication of such a development. In any event this thrombosis tends to occur late, when cerebral damage is already irreversible. It is possible to make a retrospective diagnosis of a completely excluded VOGM. Two (4.5 %) of our patients had spontaneous exclusion of shunt by thrombosis.

Cerebral angiography showed predominance of feeders from posterior cerebral artery branches in our patients, consistent with the existing literature. All patients had posterior cerebral contribution in their malformation.

None of our patients had contributions from the cerebellar arteries.

Analysis of angiographic results also showed associated venous anomalies in the form of persistent fetal type of circulation. Persistent falcine sinus noted in 37 patients (84 %).

There was persistent occipital-marginal sinus in 24 patients (54%) patients. Absent/Atretic straight sinus noted in 33 patients (75 %). The high flow across the arteriovenous fistula may result in the retention of fetal patterns of venous drainage. Persistence of the falcine sinus, which is a transient embryonic structure that connects the straight sinus to the superior sagittal sinus, is one such association. Persistent occipital sinus connecting torcula to sigmoid-jugular by marginal sinus is another connection. Retention of fetal patterns of venous drainage could prevent development of other sinuses such as the straight sinus and transverse sinus. Since there is aberation in the embryogenesis leading to VOG malformation, there are associated intracranial vascular malformations and sometimes retained embryonic intracranial vasculature.

Patent communication with ICV noted in 6 patients (13.6 %). This is in support of the other studies revealing patency with deep venous system in vein of Galen malformation. (1) (15)

Largest venous sac size was noted for a mural type of VOGM in which sac size was > 7 cm. The venous sac was anteroposteriorly elongated tubular in configuration draining

into the torcula. There was no significant difference between the sac sizes between the choroidal and mural type of the VOGMs. Sac size of 1-3 cm was noted in 13 cases of choroidal type of VOGM and 2 cases of mural type of VOGM; sac size of 3-5 cm was noted in 10 cases of choroidal and mural types of VOGM each. Sac size of 5-7 cm was noted for a choroidal type of VOGM. So larger venous sac size was associated with mural type of VOGM. This supports the observation by Agarwal et al. (1) Alvarez et al (2) stated that dilation of the venous sac is variable and is unrelated to the architecture of a choroidal or mural VOGM. Although the number of cases in our series is smaller, we feel this observation is significant. One possible mechanism is the occurrence of early venous outlet stenosis secondary to high flow jet from the usually enlarged arteries in the mural type of malformation.

At infant stage, persistence of the situation leads to clinical manifestations in the form of irritability, altered level of consciousness and neurological status, developmental delay, decreased brain volume with increased fluid space. Before ventricular enlargement occurs, intracranial pressure is not as high because of macro crania, and therefore shunting is not required. Spontaneous stabilization of enlarging head phenomena can occur with cavernous capture of the sylvian veins. (2) The progression of macro crania to hydrocephalus is thus not inevitable. Going with this explanation all our patients with enlarged head size did not have ventriculomegaly.

Cerebral morphological sequelae express themselves in calcifications, subependymal atrophy (pseudo ventriculomegaly), and eventually the stigmata of previous acute

accidents with cortical. and subcortical atrophy. The insult to the brain is a slow and permanent one.

According to Gupta et al.(43), Calcifications are of three types. mural, in lesion itself where the calcification is a result of partial or complete thrombosis, at the subcortical level in the white matter where they reflect hydrovenous failure. The latter occurs where the medullary vein loses its ventriculocortical gradient and its activity is shifted from subpial to medullary level. These calcifications are usually bilateral and symmetrical, located preferentially in the frontal region. The occipital lobe region is often affected earlier with atrophy and thinning of splenium of corpus callosum. Calcifications can be asymmetrically located, mostly in unilaterally shunted children and often on the side opposite to the shunt. They are not caused by arterial steal. Any transient episode of hydrocephalus may give rise to calcifications, since it expresses the loss of compliance of the fragile hydrovenous system functioning in infant. A third type of calcification is located in the striatum and caudate and putamen bilaterally and symmetrically. They express subacute ischemia in the region of the prominent trans cerebral collateral circulation system for telencephalic veins. Striate vein congestion occurs after the cortical veins can no longer drain the cerebral white substance or when the persisting thalamic pathway are overloaded with the drainage of the parietooccipital system. The calcifications indicate both the mechanism and specific vulnerability of this area at the infant stage. The clinical manifestations do not parallel the intensity of these calcifications. Some of them demonstrated during infancy after a brief episode of increased intracranial pressure may be absent or remarkably reduced on follow up. It

happened like this with one of our patients with parenchymal calcification. Therefore, although indicative of the previous ischemic insult, the calcifications do not have the predictive value for neurological outcome in a treated VOGM. They rarely produce abnormal movement disorders that are most often seen with more posteriorly located damage. We had two patients with parenchyrnal calcification and 1 with mural calcification in the wall of the sac.

In combination with faulty embryogenesis, there is high flow AV shunting in the VOG malformation. Oftentimes it leads to retained fetal pattern of the venous drainage. Persistence of the falcine sinus, which is a transient embryonic structure that connects the straight sinus to the superior sagittal sinus, is one such association. Persistent occipital sinus connecting torcula to sigmoid-jugular by marginal sinus is another connection. Retention of fetal patterns of venous drainage could prevent development of other sinuses such as the straight sinus and transverse sinus. Retention of the embryonic pattern of vasculature can explain the presence of several vascular anomalies that are associated with these lesions.

The consequences of a shunt in the developing brain are different from those in an adult, principally because of the immature cerebral venous system. (37) The arachnoid granulations by which cerebrospinal fluid will be returned, to the cerebral venous. sinuses are not fully matured until 16-18 months of age. In infancy, cerebrospinal fluid is reabsorbed across the ventricular ependyma and brain parenchyma into the medullary veins. The presence of VOGM may raise venous sinus pressure, which is transmitted in tum to the cortical and finally the medullary veins. This may result in congested

neuroparenchyma and reduced oxygenation leading to subependymal atrophy and in severe cases a progressive "melting brain Syndrome". Reduction of the arteriovenous shunt by partial embolization may promote further thrombosis and result in complete obliteration of the fistula without the need for a second procedure. Decisions regarding continuation of conservative management or timing of further embolization can be made on the basis of clinical follow up and periodic transcranial Doppler ultrasonography.

We routinely use vasodilator-induced hypotension during the injection of glue. This technique helps in the setting of glue at the site of the fistula. In the postprocedural period we maintain mean blood pressure 10 to 15% below baseline to avoid haemorrhagic complications. Maintenance of blood pressure below baseline also helps to reduce the flow within any residual shunts and, aids in progressive thrombosis of the lesion, as we have seen in our cases. Postprocedural systemic hypotension also prevents normal perfusion pressure breakthrough, which can be associated with abrupt cessation of large arteriovenous shunts. However, induction· of hypotension before closure of the fistula may be best avoided in children who have presented with congestive heart failure. The large shunt across the intracranial arteriovenous fistula significantly reduces the diastolic pressure within the aorta, causing reduced coronary artery flow. Induction of hypotension in these children may further reduce the subendocardial blood flow and result in myocardial infarction.

Total of 33 (75 %) embolized patients out of 44 patients with VOGM, 3 patients underwent only coil embolization. Few studies have shown good result with coil embolization alone. (66) Out of embolized patients 22 were choroidal type, 10 were

mural type and 1 was not certain, probably choroidal type, as patient underwent treatment at the outside centre. One sitting was needed in total of 14 patients rest of 19 patients needed more than 1 sitting of embolization. On an average, 2.096 sittings of embolization were performed during the treatment. Maximum of 5 sittings of embolization were performed in a total of 2 patients one of which died after 5 th sitting of embolization. Patients needing 5 sitting of embolization, 1 was of choroidal type and 1 was of mural type of VOGM. Out of 10 patients with mural type of VOGM, total 21 sittings of embolization were performed (Average sitting: 2.1). out of 21 patients embolizations on whom were performed for choroidal type of VOGM at our institution, total of 44 sittings were performed on an average of 2.1 sittings.

Out of 14 patients requiring one sitting of embolization, 5 were mural type of VOGM and 9 were of choroidal type. After 1 st sitting of embolization 8 patients showed approx. < 30 % reduction in shunt, 11 patients showed 30-50 % reduction in shunt, 10 patients showed 50-70 % reduction in shunt, and 2 patients showed > 70 % reduction in shunting across the fistula.

A total of 20 embolized patients showed improvement post treatment. A total of 10 out of 33 patients died during the follow up or after the embolization. 2 patients died without receiving embolization. Overall, 12 out of 44 patients had fatal outcome. Out of surviving children 4 were living with major disabilities, not independent for activities of daily living whereas 3 patients were living with minor disabilities. 1 had puncture site minor complication. There were 2 patients with distal embolization (extracranial) of the liquid embolic agent not affecting the final outcome.

Lasjaunias et al reported 100% occlusion in 82 of 193 patients, 95% in 8, 90% in 16, approximately 50% in 75 and less than 50% in 12 patients (among surviving children). So in their series among surviving children approximately 42.49% had complete, 12.44% had near total, 38.86% partial and 6.22% had incomplete embolization. In our series, the number of sittings of embolization were nearly same for both choroidal as well as mural type of VOGM. This is in contrast to previous literatures citing significantly more sittings of embolization for the choroidal type of VOGM in comparison to the mural type of VOGM. (1) (6)

Outcomes were better for mural malformation with all malformations (100%) of mural type undergoing total or near total occlusion in one or more sittings of embolizations. None of the patients with mural malformation expired whereas 12 patients with choroidal malformations died., with or without embolization. (10 patients with embolization, 2 patients without undergoing embolization).

In the study by Lasjaunias et al, in surviving children, transient neurological complication was reported in 1.55%, permanent neurological complication in 2%, non-neurological complication in 6.7%, haemorrhage after embolization in 5.7%. There was death in 23 out of 216 embolised patients (10.6%). In the series by Fullerton et al, embolization in 27 patients resulted in 61% having no or mild developmental delay and a 15% mortality rate during hospitalization. (54)

In our series death was in 12 out of 44 patients, among which 1 death was post 5 th sitting of embolization. Duration of clinical follow up ranged from 6 months to 13 years (mean 4.72 years). It is greater than the recently published literature studying the

complications and long term outcome of VOGM patients. (44) Once embolized no case showed opening up of the feeders or growth in the size of the sac on follow up imaging/DSA. Decisions regarding continuation of conservative management or timing of further embolization can be made on the basis of clinical follow up and periodic transcranial Doppler ultrasonography.

In a study by Gupta et al (43) twenty of the 24 patients treated by embolization had complete or near complete obliteration of the fistula, as demonstrated by angiographic studies immediately after the procedure. Four patients underwent partial or incomplete embolization (all four patients with choroidal malformation). In seven of eleven patients with choroidal malformations, complete or near complete obliteration of the shunt was achieved. In three patients with high-flow choroidal malformations, embolization carried out resulted in partial shunt reduction of nearly 90%. These patients received clinical follow up. Two of them expired; the third patients improved and follow up imaging showed near total obliteration. One patient with incomplete embolization which was done recently has been called for a second sitting. Among 13 patients with mural type of malformation, all showed total or near total obliteration on immediate post embolization check angiogram.

Lasjaunias et al reported 100% occlusion in 82 of 193 patients, 95% in 8, 90% in 16, approximately 50% in 75 and less than 50% in 12 patients (among surviving children). So, in their series among surviving children approximately 42.49% had complete, 12.44% had near total, 38.86% partial and 6.22% had incomplete embolization. In our series, the results are similar.

Among the all case with VOGM, 23 patients underwent USG as the first imaging modality, 7 as CT as first imaging modality and 14 as MRI as primary diagnostic modality. Average cross- sectional imaging (CT/MRI) per patient for diagnosis as well as follow up performed was 3.40 investigations per patient. The usage of imaging modalities specially the cross-sectional imaging in the diagnosis and follow up of the patients has not been reported by any of the previous studies.

STRENGTH AND LIMITATIONS

Strength: A relatively good number of cases with good average follow up done for the purpose of the study. The study has prospective arm, which has not been reported recently in the world literature, as per our knowledge.

Limitations: Our data is based on a single-centre study. Also, it may not be a true indicator of demographic factors as it is based on a single centre study with possibility of referral bias. Interrater variability was an entity not assessed in this study, which would have assessed the reliability in assessment of angio morphology in each of these modalities.

CONCLUSIONS

Our study demonstrates that there could be a wide range of demographic, clinical, and angiographic spectrum in VOGM/VAGM. Child with low neonatal score is destined to have a bad prognosis and this score needs to be calculated in all patients at the time of presentation.

Mural malformation has relatively better prognosis than the choroidal type. The mural type of malformation tends to have giant venous sacs. Trans arterial approach for reduction of shunt is a favourable option. Endovascular embolization of VOGMs can be successfully performed; however, complications are not negligible. Patient selection and timing of treatment are key to achieving good clinical outcomes. Management of VOGM/VAGM should be individualized based on clinical, brain parenchymal, and angiographic features. Good outcome after embolization can be seen in selected neonates and in most infants, children, and adults.

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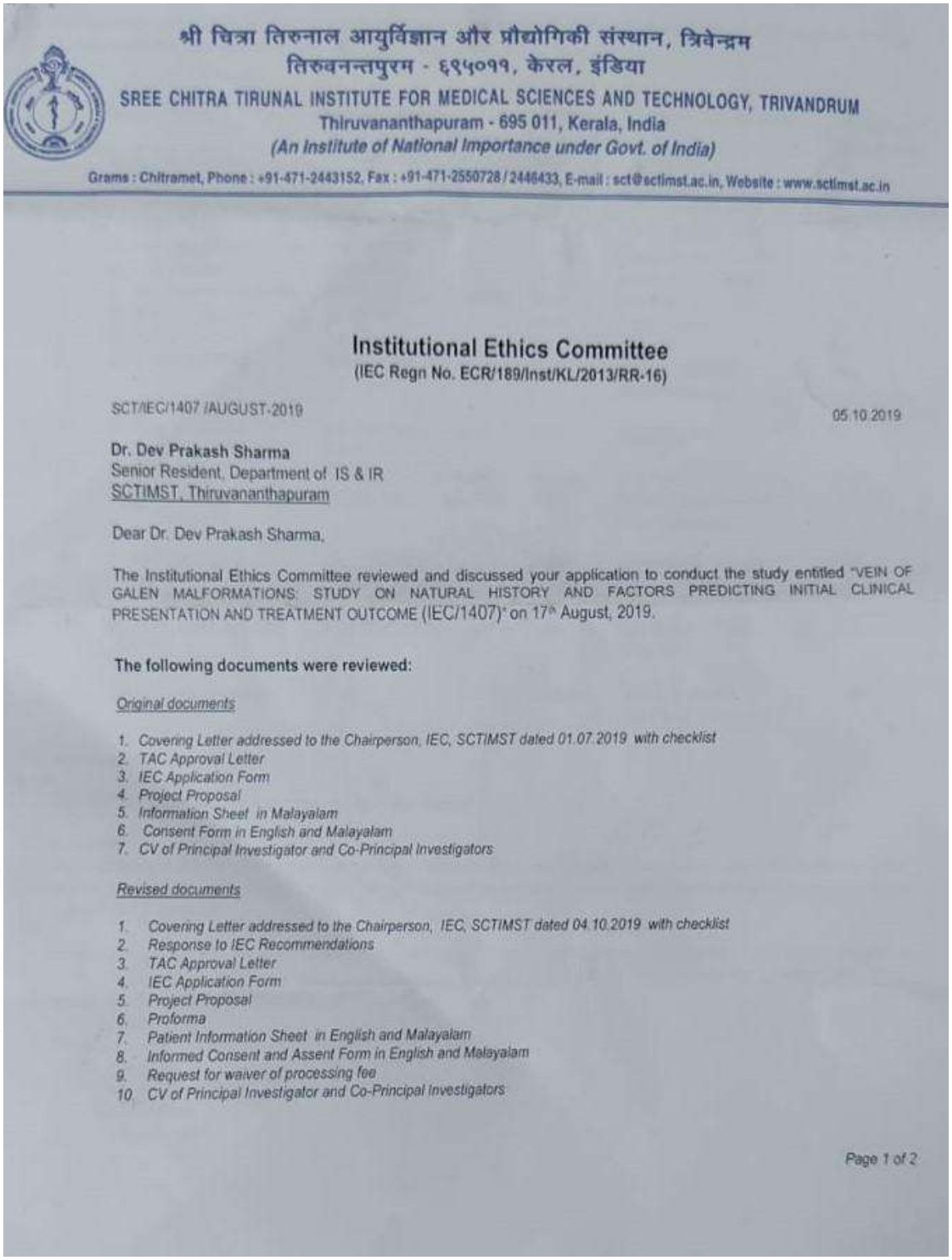
ANNEXURES

Appendix A:



श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया

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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1407 /AUGUST-2019 05.10.2019

Dr. Dev Prakash Sharma
Senior Resident, Department of IS & IR
SCTIMST, Thiruvananthapuram

Dear Dr. Dev Prakash Sharma,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "VEIN OF GALEN MALFORMATIONS: STUDY ON NATURAL HISTORY AND FACTORS PREDICTING INITIAL CLINICAL PRESENTATION AND TREATMENT OUTCOME (IEC/1407)" on 17th August, 2019.

The following documents were reviewed:

Original documents

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 01.07.2019 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Information Sheet in Malayalam*
6. *Consent Form in English and Malayalam*
7. *CV of Principal Investigator and Co-Principal Investigators*

Revised documents

1. *Covering Letter addressed to the Chairperson, IEC, SCTIMST dated 04.10.2019 with checklist*
2. *Response to IEC Recommendations*
3. *TAC Approval Letter*
4. *IEC Application Form*
5. *Project Proposal*
6. *Proforma*
7. *Patient Information Sheet in English and Malayalam*
8. *Informed Consent and Assent Form in English and Malayalam*
9. *Request for waiver of processing fee*
10. *CV of Principal Investigator and Co-Principal Investigators*

Page 1 of 2

The following members of the Ethics Committee were present at the meeting held on 17th August, 2019 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
3.	Dr. Kala Kesavan. P	MBBS, MD	Female	Basic Medical Scientist	No
4.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
5.	Dr. Harikrishna Varma PR	Ph.D(Materials Science)	Male	Medical Technology	Yes
6.	Dr. S S Giri Sankar	LL.M. Ph.D.	Male	Legal Expert	No
7.	Dr. Anand Kumar A	MD, DM	Male	Clinician	No
8.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
9.	Dr. Aneesh V Pillai	BA. LLB (Hons.), LLM, Ph. D, SET (Law)	Male	Legal Expert	No
10.	Smt. Sathi Nair	MA (English Literature)	Female	Lay Person	No
11.	Dr. P. Manickam	BSMS, MSc (Epid).,PhD	Male	Health Science Expert/ Social Scientist	No
12.	Dr. Harikrishnan S	MD, DM (Cardiology) DNB (Cardiology)	Male	Clinician	Yes
13.	Mr. Satheesh Chandran	MSW, PGDPM	Male	Lay person/ NGO/ Social Scientist	No
14.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:
The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC

Appendix B: INFORMATION SHEET

TITLE OF THE STUDY: Vein of Galen Malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome

Study number:

Participant's name: Date of Birth / Age (in years): son/daughter of _____

You have been informed that there is an abnormally dilated vein with abnormal communication between the veins deep within your brain (which is called Vein of Galen malformation), for which, you have undergone or will be undergoing a digital subtraction angiography (DSA) test and embolization. The desired result may not be achieved in one sitting and so multiple sittings may be required to achieve the best results.

The vein of Galen malformation is a disease of blood vessels in the brain where there is abnormal development of the vein/blood vessel of the brain which results in pressure on adjacent brain structures. The problem exists since the baby is in the womb and normally presents at birth or later. Abnormal mixing of blood and flow pattern may result in heart failure which may not respond to conventional/usual treatment.

You are being requested to participate in a study based on Vein of Galen Malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome Participating in this study, in which only data from the investigations you have undergone for your treatment will be used, will in no way influence treatment decisions.

What is DSA/embolization and does it have any harmful effects?

DSA is an advanced imaging technique where the blood flow to your brain will be evaluated by injecting a dye into the arteries to the brain through a small tube which will be inserted through the artery in your groin. X Rays will be obtained during the procedure which will clearly show the abnormal connections between arteries and veins if they exist. It will show abnormally dilated vein if present. You will not experience much pain as an injection will be given on your groin prior to the procedure to make it numb. You will not feel any pain during the rest of the procedure. In rare cases some people may have allergic reaction to the dye. There is also a very

small risk of injury to the blood vessel and slight chance of bleeding at site of puncture. This test is vital in diagnosis of your condition and is also the means of treatment if planned subsequently.

If you take part what will you have to do?

- For this study, we'll be using some of the data like history and other clinical details, Imaging details (CT/MRI/ CTA /MRA), Angiograms (DSA), treatment technique, outcome of the procedure, delayed follow up clinical and radiological regarding your disease and treatment which you undergo in this hospital.
- No additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research.
- Analysis of these data may or may not be useful for you later, but this is likely to give more understanding of this disease and treatment, for the benefit of future generation. You understand that strict confidentiality will be maintained.

Can you withdraw from this study after it starts?

Your participation in this study is entirely voluntary and you are also free to decide to withdraw permission to participate in this study. If you do so, this will not affect your usual treatment at this hospital in any way.

What will happen if you develop any study related injury?

This study only analyzes the results of your investigation and treatment details and thus we do not expect any injury to happen to you but if you do develop any side effects or problems due to the study, these will be treated at this institute by the experienced team of medical professionals. We are unable to provide any monetary compensation, however.

Will you have to pay for the study?

The study will only analyze the results of the investigations and treatment which you will undergo in natural process of your treatment at this institute and no extra cost will be borne by you for this particular study.

What happens after the study is over?

You may or may not benefit from this study, after the study we will be able to predict the timing, mode and methods of intervention in a patient with vein of Galen malformations and its clinical outcome post treatment; it may thus benefit other patients with similar illness.

Will your personal details be kept confidential?

The results of this study may be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

If you have any further questions, please ask Dr Dev Prakash Sharma (tel: 9496453003)

or email: devprakash@sctimst.ac.in or contact IEC member secretary

(tel: 0471-2524263)

Appendix C:

CONSENT FORM

TITLE OF THE STUDY: Vein of Galen Malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome

Study number:

Participant's name: Date of Birth / Age (in years):

I_____ _____,

Son/daughter of _____ (Please tick boxes)

Declare that I have read the above information provide to me regarding the study: 'Vein of Galen Malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome' and have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights. [ ]

• I also understand that study investigators will be using some of the data like history and other clinical details, Imaging details (CT/MRI/ CTA /MRA), Angiograms (DSA), Embolisation technique, outcome of the procedure (Immediate angiographic and clinical), delayed follow up clinical and radiological regarding the disease and treatment which I undergo in hospital. [ ]

• I also understand that no additional cost will be incurred /no additional drugs will be used and there are no additional risks as a part of the research. [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access. [ ]

• I understand that my identity will not be revealed in any information released to third parties or published. [ ]

• I voluntarily agree to take part in this study. [ ]

• I received a copy of this signed consent form. [ ]

Name:

Signature:

Date:

Name of witness:

Relation to participant:

Date:

(Person Obtaining Consent) I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____

Name and Signature of Person Obtaining Consent

Principal Investigator.

Informed Consent
(Assent form)
Participant's name:

Date of Birth / Age (in years):
I_____
_____,
son/daughter of _____ (Please tick boxes) •
declare that

• I have read the above information provide to me regarding the study: Vein of Galen malformations: study on natural history and factors predicting initial clinical presentation and treatment outcome and have clarified any doubts that I had. [ ]

• I also understand that my participation in this study is entirely voluntary and that I am free to withdraw permission to continue to participate at any time without affecting my usual treatment or my legal rights [ ]

• I understand that the study staff and institutional ethics committee members will not need my permission to look at my health records even if I withdraw from the trial. I agree to this access [ ]

• I understand that my identity will not be revealed in any information released to third parties or published [ ]

• I voluntarily agree to take part in this study [ ]

• I received a copy of this signed consent form [ ]

Name: Signature:

Signature of the Father/Mother/Relative:

Name of the Father/Mother/Relative:

Date:
I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged the participant to ask questions and that all questions asked were answered.

_____ _____
Name and Signature of Person Obtaining Consent

Appendix: D

PROFORMA

Title: Vein of Galen Malformations: Study on natural history and factors predicting initial clinical presentation and treatment outcome.

Anonymized patient key:
CLINICAL:
Age:
Sex:
Chief complaints/duration of symptoms:
History of presenting complaints: Seizure: Neurodeficits:

Past history/treatment history:

Examination:

General examination:

System examination:

CVS

Respiratory

GIT/GUT

CNS:

Higher mental function

Speech

Cranial nerve

Motor system

Sensory system

Cerebellar assessment

Tandem Gait

Other /Local examination:

IMAGING REVIEW

MRI/USG/CT:

Location of lesion –
Flow within the sac
Brain parenchyma
Ventriculomegaly
Calcifications
Type of feeders and major arterial feeders
Haemorrhage –

Others-

DSA

- Image identification number:
- Study: DSA
- Date of Image analysis:
  - Visualization of the type of VOGM.
  - Predominant feeders
  - Size of the venous sac
- Findings:
  - Lesion type: Choroidal/Mural/Mixed
  - Size of largest venous sac
  - Status of rest of the venous sinuses
  - Co- existing any other pathology, if any

Therapeutic decision and follow up:

KEYS TO MASTER CHART

S No	birth weight in kg	Age at diagnosis 1. prenatal 2. Neonate (0-6 weeks) 3. Infant (6 weeks- 12 months) 4. toddler (12-36 months) 5. Young child (36-72 months) 6. > 6 yrs	Sex 1. Female 2. Male	Cardiac comorbidities: 1. yes 2. No	Cardiac intervention: 1. Done 2. not done 3. Not applicable	Heart failure at the time of initial presentation: 1. yes 2. No	size of heart defect in mm	cardiac co morbidities : 1. ASD 2. VSD 3. Both 4. Miscellaneous 5 PDA	Location state	Location District	Symptom 1 asymptomatic 2. Symptomatic	Symptom increase in head circumference 1. yes 2. no	symptom delay in developmental milestones 1. yes 2 no
1	2.65	3	1	1	2	2	9	1	kerala	kollam	2	1	1
2	3	1	2	1	2	2	5	1	kerala	trivandrum	9	9	9
3	2.6	3	2	2	3	2	0	9	kerala	malapuram	2	1	1
4	3.18	1	1	2	3	1	0	3	kerala	trivandrum	2	2	2
5	2.8	2	1	1	2	1	0	5	kerala	idukki	2	2	2
6	2.3	1	1	1	2	1	4.5	3,5	kerala	malapuram	2	2	2
7	9	6	1	1	2	2	0	1	kerala	pathanamthitta	2	2	2
8	2.24	1	1	1	2	1	4	1,5	kerala	trivandrum	2	2	2
9	9	3	2	2	3	2	0	9	tripura	west bhuban ban	2	1	1
10	9	2	1	1	2	1	2.3	5	kerala	malapuram	2	2	2
11	9	5	2	2	3	2	0	9	kerala	palakkad	2	2	2
12	9	1	2	1	2	1	2	4	tamilnadu	coimbatore	2	1	1
13	3.23	1	2	1	2	1	6	1	kerala	idukki	2	2	2
14	3	3	1	1	2	1	2	5	kerala	kozhikode	2	2	1
15	3.2	1	2	1	2	2	1	1	kerala	palakkad	2	2	2
16	9	3	1	2	3	2	0	9	kerala	thrissur	2	1	1
17	9	6	2	2	3	2	0	9	kerala	ernakulam	2	2	2
18	2.2	3	2	2	3	2	0	9	kerala	kannur	2	1	1

symptom history of fall or imbalance 1. No 2. yes	Symptom Respiratory difficulty 1. no 2. yes	Symptom headache 1. no 2. yes	tonsillar herniation 1. No 2. Yes	Ventriculomegaly 1. yes 2. No	calcifications on imaging 1. No 2. Yes 3. information not available	parenchymal changes on imaging 1. no 2. yes	two or less in a single category of bicetre score 1. no 2. yes	neonatal score 1. 8-12 2. > 12 3. < 8 4. Not available	first imaging: 1. ultrasound 2. MRI 3. CT 4. DSA	type of VOGM 1. Choroidal 2. Mural 3. Mixed 4. uncertain	Date of first DSA	symptom seizures 1. no 2 yes	DSA feeder1- posterior lateral choroidal A 2- medial lateral choroidal A 3- Unilateral thalamoperforating A 4- Bilateral thalamoperforating A	DSA feeders more lenticulostriate 1. yes 2. No	DSA feeder more 1. ACA branches like subcallosal artery subfornical artery 2. Basilar
1	1	1	1	1	1	1	1	3	1	1	13.01.21	1	1, 2,3		1
9	9	9	1	2	1	1	1	3	1	2	9	9	9		9
1	1	1	2	1	1	1	1	4	1	1	11.12.20	1	1,2,3	1	0
1	2	1	1	2	3	1	1	1	1	4	22.5.20	1	1,2,4	1	1
1	2	1								1		1	1,2,3	1	1,2
1	2	1								1		1	1,2,3,4	1	1,2
1	1	2	1	2	1	1	1	4	3	2	02.07.20	1	1	1	0
1	2	1										1			
1	1	1	1	1	2	2	1	2	2	1	25.3.19	2	1,2,3	1	2
1	2	1						1		1		1			
1	1	2								1	16.08.18	1	1,2,3,4	1	1,2
1	1	1								1	01.09.17	1	1,2,4	1	1,2
1	2	1								2	30.11.17	1	1,2	2	2
1	2	1								2	22.02.18	1	1,2,3	2	0
1	2	1								1	09.03.17	1	1,2	1	1,2
1	1	1	1	1	1	1	1	2	2	2	18.11.16	2	1,3	2	2
1	1	2	1	2	1	1	1	4	2	2	24.10.16	1	1,2,4	1	2
1	2	1								2	17.02.16	1	1,2	2	0

DSA feeders more Transdural supply from meningeal arteries 1. yes 0 No 9 not applicable	DSA jugular bulb stenosis 1. mild < 60 %, 2. moderate 60-90 %, 3. severe > 90 % 4. not known	venous sac size largest single dimension 1. < 1 cm 2. 1-3 cm 3. 3-5 cm 4. 5-7 cm 5. > 7 cm	communication between MVP and deep venous system eg Internal cerebral vein 1. no 2. yes	Venous drainage normal brain 1. patent 2 not patent	Straight sinus 1. absent 2. present	Falcine sinus 1. No 2 yes	occipital sinus 1. present 2. absent	Embryonic sinus 1. No 2. Yes	Cavernous capture 1. None 2. Poor 3. Good	Deep venous drainage 1. No 2. Yes	Treatment decision 1. withhold treatment 2. embolization 3. Conservative management 4. neurosurgery like shunting
9	4	3	1	1	1	2	1	2	3	1	2
9	9	9	9	9	9	9	9	9	9	9	3
0	2	3	1	1	1	2	1	2	3	1	3
0	0	2	2	1	1	2	1	2	2	1	3
9	0	2	2	1	2	2	1	2	3	1	
0	1	2	1	1	1	2	1	2	3	1	
0	0	3	1	1	1	2	1	2	3	1	3
0	2	2	1	1	1	2	1	2	3	1	2
0	0	2	1	1	1	2	1	2	3	1	
0	0	3	1	1	1	2	2	2	3	1	
0	0	3	1	1	2	2	1	2	3	1	
0	0	3	1	1	1	2	1	2	2	9	2
0	1	3	1	1	1	2	1	2	3	1	2
0	3	3	1	1	1	2	1	2	3	1	2
0	0		2	1	2	1	2	1	2	2	3
0	0		1	1	1	2	1	2	3	1	

Occipital-Marginal sinus 1 No 2 yes	distal embolism of embolic agent 1. no 2. yes	intervention: 1. one sitting 2. two sitting 3. three sitting 4. four sitting 5. Five sitting 6. six sitting 7. seven sitting	Reduction in shunt after first embolization in percentage 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Interval after which 2 nd sitting planned 1. < 1 week 2. 1-2 weeks 3. 2-4 weeks 4. > 1 month 5. > 6 months 6. > 1 year	next (second) sitting date	reduction in shunt after 2 nd sitting 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Types of Liquid embolic agent used 1 onyx 2 glue 3 squid 4. combination of more than one liquid embolic agent 5. Liquid embolic agent & coil	additional embolic agent used, if any 1 coils 2 others 3. not applicable	intraprocedure or post procedure hemorrhage 1 no 2 yes	clinical follow up available at how many years/year of diagnosis of VOGM
2	1	2	1	5	17.3.21	4	1	1	1	2
9	9	9	9	9	9	9	9	3	9	2
1	9	9	9	9	9	9	3	3	1	2
2	9	1	2	9	9	9	9	3	1	2
2										3
2										0
2	9	9	9	9	9	9	9	3	9	2
										0
1									1	3
										0.5
2										4
1		3								5
2										5
2					12.04.18					5
2										5
2		2		6	26.05.17		5	1	1	6
	9	9	9	9	9	9	9	3	9	6
2										7

improvement in heart failure after 1 st embolization 1. yes 2. no 3. not applicable	next sitting 1 no 2 yes	final outcome: 1. improved clinically 2. improved angiographically 3. static clinically 4. static angiographically 5. outcome not available, lost to follow up 6.	measurement of the mediolateral diameter of the falcine or straight sinus at its shortest point in mm 1. 1 mm 2. 2-5 mm 3. 6-9 mm 4. 10 mm or more 5. not available	diffuse bihemispheric brain injuries 1 no 2 yes	brain gliotic or liquefactive changes 1 no 2 yes	microcatheter with a distal outer diameter of more than 2.0 french 1. Yes 2. No	age at first embolization 1. < 4 months 2. 4-12 months 3. > 12 months	Embolization 1. Emergent 2. Elective or semi elective embolization	non- embolized patients 1. Palliation: multi organ failure 2. Palliation: Global parenchymal changes 3. Spontaneous thrombosis of VGOM 4. Asymptomatic 5.	remarks
3	1	1, 2	3	1	1	1	2	2	6	
3	9	3	5	1	1	9	9	9	4	
3	2	1,2	2	1	1	1	2	2	6	
1	1	1,2	3	1	1	9	9		4	
		6	3							
		6	3							
3	9	3	3	1	1	9	9	9	4	
		6								
9	2	1,2	4	1	1		2	2	6	right TS dAVF also embolised with glue
		6								
			2							
			4							
			2							Right PCA territory infarct post embolization temporal hematoma
	2		3							
3			2							small saccular aneurysm arising from origin of right lateral
3	2	1,2	3	1	1		2	2	6	suspicious right parietal AVM remained unchanged between two embolization sessions
9	9	3		1	1	9	9	9	4	
										twin pregnancy, 2 nd twin normal

S No	birth weight in kg	Age at diagnosis 1. prenatal 2. Neonate (0-6 weeks) 3. Infant (6 weeks- 12 months) 4. toddler (12-36 months) 5. Young child (36-72 months) 6. > 6 yrs	Sex 1. Female 2. Male	Cardiac comorbidities: 1. yes 2. No	Cardiac intervention: 1. Done 2. not done 3. Not applicable	Heart failure at the time of initial presentation: 1. yes 2. No	size of heart defect in mm	cardiac co morbidities : 1. ASD 2. VSD 3. Both 4. Miscellaneous 5 PDA	Location state	Location District	Symptom 1 asymptomatic 2. Symptomatic	Symptom increase in head circumference 1. yes 2. no	symptom delay in developmental milestones 1. yes 2 no
19	9	2	2	2	3	2	0	9	kerala	thrissur	2	2	2
20	2.75	1	1	1	1	2	3	1,4	gujarat	surat	2	2	2
21	9	1	2	1	2	1	9	1	kerala	palakkad	2	2	1
22	2.6	3	1	1	1	2	1.4	1	tamilnadu	villupuram	2	2	1
23	3.4	3	2	1	2	1	0.8	5	kerala	malapuram	2	1	1
24	9	3	2	1	2	2	1	1, 4	tamilnadu	coimbatore	2	1	2
25	9	5	2	2	3	2	0	9	kerala	kozhikode	2	2	2
26	9	3	2	2	3	2	0	9	kerala	palakkad	2	1	1
27	9	3	2	2	3	2	0	9	andhra pradesh	nakarikal	2	1	2
28	9	6	2	2	3	2	0	9	kerala	malapuram	2	1	2
29	9	1	2	1	2	1	8	3, 4	kerala	trivandrum	2	2	2
30	9	5	1	2	3	2	0	9	kerala	trivandrum	2	2	2
31	9	4	2	2	3	2	0	9	kerala	kozhikode	2	2	2

symptom history of fall or imbalance 1. No 2. yes	Symptom Respiratory difficulty 1. no 2. yes	Symptom headache 1. no 2. yes	tonsillar herniation 1. No 2. Yes	Ventriculomegaly 1. yes 2. No	calcifications on imaging 1. No 2. Yes 3. information not available	parenchymal changes on imaging 1. no 2. yes	two or less in a single category of bicetre score 1. no 2. yes	neonatal score 1. 8-12 2. > 12 3. < 8 4. Not available	first imaging: 1. ultrasound 2. MRI 3. CT 4. DSA	type of VOGM 1. Choroidal 2. Mural 3. Mixed 4. uncertain	Date of first DSA	symptom seizures 1. no 2 yes	DSA feeder1- posterior lateral choroidal A 2- medial lateral choroidal A 3- Unilateral thalamoperforating A 4- Bilateral thalamoperforating A	DSA feeders more lenticulostriate 1. yes 2. No	DSA feeder more 1. ACA branches like subcallosal artery subfornical artery 2. Basilar
1	2	1	1	2	2	2	1	4	2	2	02.12.15	2	1,2	2	0
1	1	1								2	03.06.15	1	1,2,3	1	2
2	2	1	1	1	3	2	1	4	1	1	25.02.15	2	1,2,4	1	1
1	2	1								1	29.12.14	2	1,2,4	1	1
1	2	1								2	10.04.15	1	1,2	2	0
1	1	1	1	1	1	2	1	4	2	2	23.08.13	2			
2	1	1	1	1	1	2	1	2	2	1	03.07.13	2	1,2,4	1	2
1	1	1	1	1	1	2	1	2	3	4	9	1			
1	1	1	1	1	1	1	1	4	2	2	19.08.10	1	1,2	0	0
1	1	2	1	1	1	2	1	2	2	1	03.09.10	1	1,2,4	1	1
1	1	1	9	9	3	9	2	2	1	4	9	1	9		9
1	1	2	1	1	3	1	1	4	2	4	23.11.09	1			
2	1	1	1	1	1	2	1	4	2	4	9	1			

DSA feeders more Transdural supply from meningeal arteries 1. yes 0 No 9 not applicable	DSA jugular bulb stenosis 1. mild < 60 %, 2. moderate 60-90 %, 3. severe > 90 % 4. not known	venous sac size largest single dimension 1. < 1 cm 2. 1-3 cm 3. 3-5 cm 4. 5-7 cm 5. > 7 cm	communication between MVP and deep venous system eg Internal cerebral vein 1. no 2. yes	Venous drainage normal brain 1. patent 2 not patent	Straight sinus 1. absent 2. present	Falcine sinus 1. No 2 yes	occipital sinus 1. present 2. absent	Embryonic sinus 1. No 2. Yes	Cavernous capture 1. None 2. Poor 3. Good	Deep venous drainage 1. No 2. Yes	Treatment decision 1. withhold treatment 2. embolization 3. Conservative management 4. neurosurgery like shunting
0	2	3	1	2	1	2	1	2	2	1	2
0	0	3	1	1	1	2	2	2	3	1	2
1	3	3	1		1	2	1	2	2	1	2
0	1		1	1	1	2	1	2	2	1	
0	0		1	1	1	2	2	2	3	1	
											2
0	2		2	1	1	2	1	2	3	2	2
											4
0	2		1	1	1	2	1	2	2	1	2
1	0		2	1	1	2	2	2	3	2	
9	9	9	9	9	9	9	9	9	9	9	9
											2
											3

Occipital-Marginal sinus 1 No 2 yes	distal embolism of embolic agent 1. no 2. yes	intervention: 1. one sitting 2. two sitting 3. three sitting 4. four sitting 5. Five sitting 6. six sitting 7. seven sitting	Reduction in shunt after first embolization in percentage 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Interval after which 2 nd sitting planned 1. < 1 week 2. 1-2 weeks 3. 2-4 weeks 4. > 1 month 5. > 6 months 6. > 1 year	next (second) sitting date	reduction in shunt after 2 nd sitting 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Types of Liquid embolic agent used 1 onyx 2 glue 3 squid 4. combination of more than one liquid embolic agent 5. Liquid embolic agent & coil	additional embolic agent used, if any 1 coils 2 others 3. not applicable	intraprocedure or post procedure hemorrhage 1 no 2 yes	clinical follow up available at how many years/year of diagnosis of VOGM
2	1	4		5	10.06.16		4,5	1	1	7
1										7
2	1	5	2	6	30.04.18	4	1,3	3	2	5
2										4
1										9
	1	1	9	9	9	9	2	1	1	0
2	1	3	1	4	15.11.13		2	3	1	6
	9	9	9	9	9	9	9	3	9	9
2	1	1	4	9	9	9	2	1	1	13
1										12
0	9	9	9	9	9	9	9	3	9	0
	1	1	4	9	9	9	2	3	1	0
	9	9	9	9	9	9	9	3	9	13

improvement in heart failure after 1 st embolization 1. yes 2. no 3. not applicable	next sitting 1 no 2 yes	final outcome: 1. improved clinically 2. improved angiographically 3. static clinically 4. static angiographically 5. outcome not available, lost to follow up 6.	measurement of the mediolateral diameter of the falcine or straight sinus at its shortest point in mm 1. 1 mm 2. 2-5 mm 3. 6-9 mm 4. 10 mm or more 5. not available	diffuse bihemispheric brain injuries 1 no 2 yes	brain gliotic or liquefactive changes 1 no 2 yes	microcatheter with a distal outer diameter of more than 2.0 french 1. Yes 2. No	age at first embolization 1. < 4 months 2. 4-12 months 3. > 12 months	Embolization 1. Emergent 2. Elective or semi elective embolization	non- embolized patients 1. Palliation: multi organ failure 2. Palliation: Global parenchymal changes 3. Spontaneous thrombosis of VGOM 4. Asymptomatic 5.	remarks
9	2	1,2	3	1	1		2	2	6	
			2							
		6	4							left jugular hypertrophic right jugular hypoplastic
		6								
	1	2		1	1		1	2	6	patient had a focus of left parietal bleed in first imaging (MRI) at presentation, images not available
3	2	6		1	2		3	2	6	history of trauma, diffuse axonal injury, right centrum semiovale bleed, T2 FLAIR hyperintensities in bilateral globus pallidi centrum semiovale periventricular white matter brainstem left cerebellar hemisphere suggestive of ? venous hypertension
3	9	1	5	2	1	9	9	9	3	
3	1	1,2		1	1		2	2	6	
2	9	6	9	9	9	9	9	9	6	images not available
3	1	2		1	1			2	6	
9	9	9	5		1	9	9	9	4	

S No	birth weight in kg	Age at diagnosis 1. prenatal 2. Neonate (0-6 weeks) 3. Infant (6 weeks- 12 months) 4. toddler (12-36 months) 5. Young child (36-72 months) 6. > 6 yrs	Sex 1. Female 2. Male	Cardiac comorbidities: 1. yes 2. No	Cardiac intervention: 1. Done 2. not done 3. Not applicable	Heart failure at the time of initial presentation: 1. yes 2. No	size of heart defect in mm	cardiac co morbidities : 1. ASD 2. VSD 3. Both 4. Miscellaneous 5 PDA	Location state	Location District	Symptom 1 asymptomatic 2. Symptomatic	Symptom increase in head circumference 1. yes 2. no	symptom delay in developmental milestones 1. yes 2 no
32	9	3	2	2	3	2	0	9	kerala	ernakulam	2	1	2
33	9	3	1	2	3	2	0	9	kerala	kollam	2	2	2
34	3.1	1	2	1	2	1	8	1,5	kerala	trivandrum	2	2	2
35	9	6	2	2	3	2	0	9	kerala	kollam	2	2	2
36	9	5	1	2	3	2	0	9	andhra pradesh	krishna	2	2	2
37	3.14	1	2	1	2	1	2.9	1, 4	andamans	south andaman	2	2	2
38	9	6	1	2	3	2	0	9	tamilnadu	theni	2	1	2
39	9	5	2	2	3	2	0	9	kerala	alappuzha	2	2	2
40	9	1	2	1	2	1	2	1,5	kerala	palakkad	2	2	2
41	9	1	2	2	3	2	0	9	kerala	palakkad	9	9	9
42	3.1	2	2	1	2	2	7	1,4	kerala	kannur	9	9	9
43	9	3	2	2	3	2	0	9	gujarat	surat	2	2	1
44	1.5	2	2	1	2	2	3	1	kerala	kozhikode	2	2	2

symptom history of fall or imbalance 1. No 2. yes	Symptom Respiratory difficulty 1. no 2. yes	Symptom headache 1. no 2. yes	tonsillar herniation 1. No 2. Yes	Ventriculomegaly 1. yes 2. No	calcifications on imaging 1. No 2. Yes 3. information not available	parenchymal changes on imaging 1. no 2. yes	two or less in a single category of bicetre score 1. no 2. yes	neonatal score 1. 8-12 2. > 12 3. < 8 4. Not available	first imaging: 1. ultrasound 2. MRI 3. CT 4. DSA	type of VOGM 1. Choroidal 2. Mural 3. Mixed 4. uncertain	Date of first DSA	symptom seizures 1. no 2 yes	DSA feeder1- posterior lateral choroidal A 2- medial lateral choroidal A 3- Unilateral thalamoperforating A 4- Bilateral thalamoperforating A	DSA feeders more lenticulostriate 1. yes 2. No	DSA feeder more 1. ACA branches like subcallosal artery subfornical artery 2. Basilar
1	1	1	1	1	1	2	1	4	1	4	30.04.08	2			
1	1	2									04.07.14	1	0	0	0
1	2	1							1	1	27.04.20	1	1,2	1	0
1	1	1									30.01.19	2	1,2	2	1,2
1	1	2					1	4	3		16.04.10	1	1,2,4	2	2
1	1	1	9	9	3	9	2		1		14.09.20	1	1,2,4	1	1
2	1	1	1	1	1	1	1	2	2	1	08.02.18	1	1,2,4	1	1
1	1	1					1				9	1	9	9	9
1	1	1							1		9	1	9	9	9
9	9	9	1									1	9	9	9
9	9	9								2	9	9	9		9
1	2	1	1	2	1	1	1	2	1	1	26.11.18	1	1,2,4	2	1
1	1	1	1	1	1	2	1	2	1	4	9	1	9		9

DSA feeders more Transdural supply from meningeal arteries 1. yes 0 No 9 not applicable	DSA jugular bulb stenosis 1. mild < 60 %, 2. moderate 60-90 %, 3. severe > 90 % 4. not known	venous sac size largest single dimension 1. < 1 cm 2. 1-3 cm 3. 3-5 cm 4. 5-7 cm 5. > 7 cm	communication between MVP and deep venous system eg Internal cerebral vein 1. no 2. yes	Venous drainage normal brain 1. patent 2 not patent	Straight sinus 1. absent 2. present	Falcine sinus 1. No 2 yes	occipital sinus 1. present 2. absent	Embryonic sinus 1. No 2. Yes	Cavernous capture 1. None 2. Poor 3. Good	Deep venous drainage 1. No 2. Yes	Treatment decision 1. withhold treatment 2. embolization 3. Conservative management 4. neurosurgery like shunting
											2
0	0			1					3	1	3
0	0	3	1	1	1	2	1	2	2	1	2
2	0		1	1	2			1	3	1	2
0	1		2	1	2	1		1	3	1	2
9	0	2	1	1	1	2	2	2	3	1	2
1	0	2	1	1	2	2	1	2	3	1	2
9	9										3
9	9										
9	9								9		3
9	4	2									3
0	0	2	1	1	2	1	1	2	2	1	2
9	9	2	9	9	9	9	9	9	9	9	3

Occipital-Marginal sinus 1 No 2 yes	distal embolism of embolic agent 1. no 2. yes	intervention: 1. one sitting 2. two sitting 3. three sitting 4. four sitting 5. Five sitting 6. six sitting 7. seven sitting	Reduction in shunt after first embolization in percentage 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Interval after which 2 nd sitting planned 1. < 1 week 2. 1-2 weeks 3. 2-4 weeks 4. > 1 month 5. > 6 months 6. > 1 year	next (second) sitting date	reduction in shunt after 2 nd sitting 1. < 30 % 2. 30-50 % 3. 50-70 % 4. > 70 %	Types of Liquid embolic agent used 1 onyx 2 glue 3 squid 4. combination of more than one liquid embolic agent 5. Liquid embolic agent & coil	additional embolic agent used, if any 1 coils 2 others 3. not applicable	intraprocedure or post procedure hemorrhage 1 no 2 yes	clinical follow up available at how many years/year of diagnosis of VOGM
	1	2					9	1	1	13
	9	0	9	9	9	9	9	3	9	8
2										0
1										13
1										0
1	9	1	1	9	9	9	2	3	1	0
2	1	1		9			2	3	1	5
	9	9	9	9	9	9	9	3	9	5
										0
	9	9	9	9	9	9	9	3	9	4
										0.25
2	1	3	3	4	23.01.19	3	4	3	1	4
9	9	9	9	9	9	9	9	9	9	2

improvement in heart failure after 1 st embolization 1. yes 2. no 3. not applicable	next sitting 1 no 2 yes	final outcome: 1. improved clinically 2. improved angiographically 3. static clinically 4. static angiographically 5. outcome not available, lost to follow up 6.	measurement of the mediolateral diameter of the falcine or straight sinus at its shortest point in mm 1. 1 mm 2. 2-5 mm 3. 6-9 mm 4. 10 mm or more 5. not available	diffuse bihemispheric brain injuries 1 no 2 yes	brain gliotic or liquefactive changes 1 no 2 yes	microcatheter with a distal outer diameter of more than 2.0 french 1. Yes 2. No	age at first embolization 1. < 4 months 2. 4-12 months 3. > 12 months	Embolization 1. Emergent 2. Elective or semi elective embolization	non- embolized patients 1. Palliation: multi organ failure 2. Palliation: Global parenchymal changes 3. Spontaneous thrombosis of VGOM 4. Asymptomatic 5.	remarks
		1,2		1	1					images not loading
9	9	1,2		1	1	9	9	9	3	only final post embo without residual angio available
		6	3							
3										
		5							6	
2	1	6	9	9	9	9	1	1	6	
3	1	1,2		1	1		3	2	6	
9	9	3	9		1	9	9	9		
		6	9							
9		3	9	1	1	9	9	9	4	
3		6								
3	2	1, 2	5	1	1	9	2	2	6	
3	9	3	9	1	1	9	9	9	4	

ABBREVIATIONS

ASD - Atrial septal defect

AV -Arteriovenous

AVF -Arteriovenous fistula

AVM -Arteriovenous malformation

CAG -Cerebral angiography

CCA -Common carotid artery

CCF -Congestive cardiac failure

CHF -Congestive heart failure

CSF -Cerebrospinal Fluid

CT -Computed Tomography

DSA -Digital subtraction angiography

ECHO -Echocardiography

EEG -Electroencephalogram

ETV -Endoscopic third ventriculostomy

IVH -Intraventricular haemorrhage

IJV - Internal Jugular vein

ICA -Internal Cerebral Artery

ICU -Intensive Care Unit

IVC -Inferior vena cava

MRI -Magnetic Resonance Imaging

MR angiography -Magnetic resonance angiography

NBCA -N butyl cyanoacrylate

PCA -Posterior cerebral artery

PDA -Patent ductus arteriosus,

PHT - Pulmonary hypertension

PICA -Posterior inferior cerebellar artery

SAH -Subarachnoid haemorrhage

SCA -Superior cerebellar artery

USG -Ultrasonogram

VA -Vertebral artery

VGAD -Vein of Galen aneurysmal dilatation

VOGM -Vein of Galen Malformations,

VAGM - Vein of Galen Aneurysmal Malformation

VP -Ventriculoperitoneal

VSD - Ventricular septal defect

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