

Radiological and Clinical Features of Vein of Galen Aneurysmal Malformation in Newborn Infants and, the Results of Endovascular Interventional Treatment: 10-Years Experience

Keywords: Vein of Galen aneurysmal malformation; Neonate; Endovascular therapy; High outflow heart failure

Abstract

Aim: To assess the clinical features, diagnosis, treatment and prognosis of newborn infants with a diagnosis of Vein of Galen Malformation (VGAM) during a 10-year period.

Method: Eight patients with a diagnosis of VGAM in the neonatal period were assessed retrospectively in terms of clinical signs, diagnosis, treatment strategies and follow-up. Three of four patients who survived had neurological assessment whereas one was lost to follow-up because of moving to another city.

Results: Seven of 8 patients had an antenatal diagnosis. In all cases severe heart failure and pulmonary hypertension were present from the first day of life and hypotension, multiorgan failure, hydrocephaly and seizures developed in the following days. VGAM and its feeder arteries were mapped by cranial magnetic resonance imaging and magnetic resonance angiography. Transarterial embolization therapy was performed on 7 patients, of whom four babies survived and three babies died, while one patient died before any intervention.

Conclusion: The mortality and morbidity rates of VGAM is high because of its mixed anatomy, pathophysiology and characteristic features leading to severe neurological sequelae in the survivors. Prognosis in high risk neonates can be improved with aggressive medical support and early endovascular embolization therapy.

Introduction

Vein of Galen Aneurysmal Malformation (VGAM) composes 1% of all vascular malformations and 30% of vascular malformations in childhood. The patients usually present with severe heart failure in the neonatal period. VGAM is a small, deep venous internal cerebral vessel with a thin wall. The conjunction of choroidal and thalamostriate veins in the interventricular foramen creates internal cerebral veins. VGAM is generated between the 6th and 11th weeks of gestation by the connections between primitive choroidal vessels and median prosencephalic vein (Markowski) [1].

The two widely used classifications of VGAM have been defined by Lasjaunias and Yasargil [2-6]. Lasjaunias classified VGAM in two types: Choroidal type (Type I), which is the most common and the most complicated type, is usually seen in the early stages of life. Multiple supplying arteries penetrate the median prosencephalic vein usually through the anterior wall. All choroidal arteries and



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their inter connections, anterior cerebral artery, pericallosal artery, thalamoperforating artery and quadrigeminal arteries also support the blood supply. Mural type (Type II), has a single or multiple arteriovenous fistulas (AVF) which drain the median prosencephalic vein at the inferolateral mural side. The shunt is usually fed by collicular and posterior choroidal arteries. The resultant AVF leads to an abnormal flow which prevents the regression of the embryonic vein, generating VGAM. There are also mixed types of VGAM carrying the characteristics of both choroidal and mural types. Yasargil classification has four types. In types I, II and III, all lesions have direct fistulous connections with the vein of Galen. In type IV, there is a paranchymal arteriovenous malformation which drains into the vein of Galen. In Type I, there is an AVF between vein of Galen and pericallosal branches of leptomeningeal arteries and/or any branch of posterior cerebral artery. In Type II, vein of Galen is fed by two branches of posterior cerebral artery and thalamoperforating vessels. Type III is a mixture of type I and type II and is the most common form. Type IV is known as the secondary type and has three subtypes: In Type IVA an aneurysmal dilatation develops in the vein of Galen by the neighbouring thalamic arteriovenous malformation. Type IVB is similar to type IVA, but arteriovenous malformation is mesencephalic rather than thalamic. In Type IVC thalamomesencephalic or mesodiencephalic plexiform malformation drains into the vein of Galen by a nearby and different cisternal AVF. Yasargil classification is helpful when an open surgery is indicated, whereas Lasjaunias classification is helpful if endovascular intervention is the treatment option [4].

Prenatal diagnosis is made by color Doppler ultrasound examination in the third trimester of pregnancy. Aneurysmatic dilatation localized at the midline and posterior to the third ventricle, venous and arterial turbulent blood flow in hypochoic structures can be shown [7]. Fetal magnetic resonance imaging (MRI) is needed both to confirm VGAM and to exclude the diagnosis of arachnoidal,

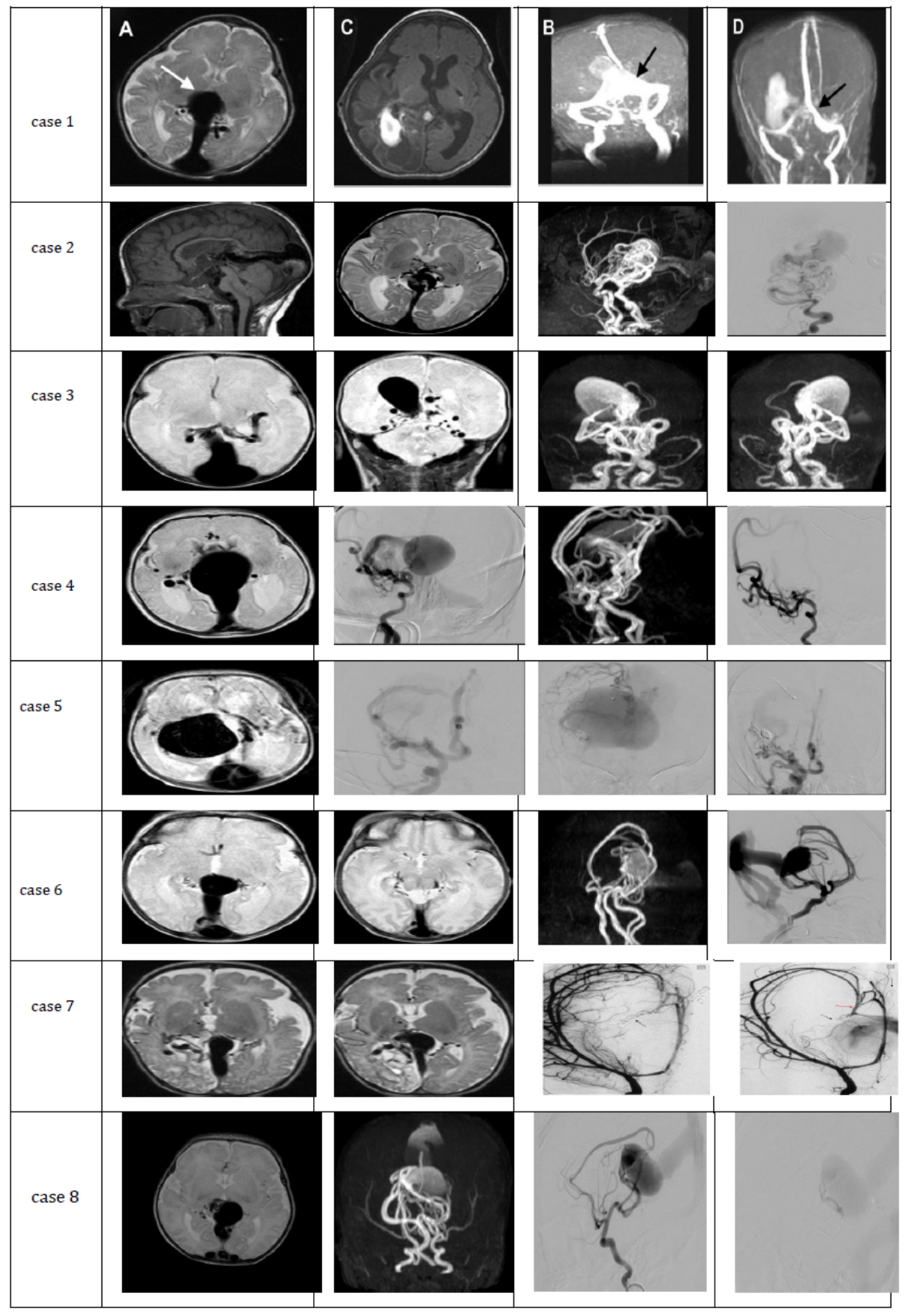


Figure 1: Enlarged precursors of VGAM and large feeder arteries at the posterior side of the third ventricle are shown by MRI, MR angiography and DSA imaging.

Table 1: Bicetre scoring system (13).

Points	Cardiac function	Cerebral function	Respiratory function	Hepatic function	Renal function
5	Normal	Normal	Normal	Not scored	Not scored
4	Overload, no medical treatment	Subclinical isolated electroencephalo-graphic abnormalities	Tachypnea, finishes bottle feeding	Not scored	Not scored
3	Failure-stable with medical treatment	Non-convulsive intermittent neurological signs	Tachypnea, does not finish bottle feeding	No hepatomegaly; normal function	Normal
2	Failure-unstable with medical treatment	Isolated seizures	Assisted ventilation; normal saturation FiO ₂ <25%	Hepatomegaly; normal function	Transientanuria
1	Ventilation necessary	Seizures	Assisted ventilation; normal saturation FiO ₂ >25%	Moderate or transient hepatic insufficiency	Unstable, diuresis with treatment
0	Resistant to medical treatment	Permanent neurological signs	Assisted ventilation; desaturation	Coagulopathy; Elevated enzymes	Anuria

Maximum score, 5 (cardiac)+5 (cerebral)+5 (respiratory)+3 (hepatic)+3 (renal)=21.
Score>12=delayed embolisation; score 8-12=urgent embolisation; skor<8=no embolisation.

Table 2: The demographic, clinical and echocardiographic features of cases with Vein of Galen malformation.

Feature	CASE 1	CASE 2	CASE 3	CASE 4	CASE 5	CASE 6	CASE 7	CASE 8
GW ¹	37 ^{4/7}	41 ^{1/7}	36 ^{3/7}	38	38	39 ^{3/7}	39	39 ^{4/7}
Gender	male	female	male	male	male	male	male	male
Birth weight (kg)	3.29	3.2	3.1	3.8	3.5	2.77	3.25	3.015
Time of prenatal diagnosis (GW ¹)	35	37	33	26	26 ^{5/7}	38	N/A	37
ECHO findings	1.PHT ² 2.PFO ³ 3.TR ⁴ 4.CM ⁵	1.PHT 2.RVD ⁶ / RAD ⁷ 3.R-L ⁸ shunt 4.ASS ⁹ , CM 5.left aorticarch, TR 6.VSD ¹⁰	1.PHT 2.TR 3.CM	1.PHT 2.TR 3.CM 4.RVD/ RAD	1.PHT 2.CM 3.RVD/ RAD 4.TR	1.PHT 2.CM 3.RVD/ RAD 4.TR 5.PDA	1.PHT 2.CM 3.PFO 4.TR	1.PHT 2.CM 3.RVD/ RAD 4.TR
Major cardiac findings	Severe heart failure	Severe heart failure	Severe heart failure	Severe heart failure	Severe heart failure	Severe heart failure	Severe heart failure	Severe heart failure
VGAM Type	mixed	choroidal	mixed	mixed	mixed	mixed	mixed	mixed
Bicêtrescore	9	13	5	11	7	12	12	12
Other clinical features	1.seizure 2.hydrocep. 3.hyperten. 4.V-P shunt	1.hypotens. 2.sepsis	1.seizure 2.GI bleeding 3.MOF ¹¹ 4.hypotens	1.SVT ¹² 2.seizure	1.hypotens. 2.seizure 3.MOF	1.cholestatas 2.hypotens. 3.ventriculomegaly	1.seizure 2.hydroceph. 3.VP shunt 4.sepsis 5.hypotensio 6.ARF ¹³	1.seizure 2.sepsis 3.hypotension 4.MOF
Duration MV ¹⁴ (days)	26	9	4	14	4	17	2	3
Neurological outcome	Normal	Normal	Death on 4 th day	Death on 55 th day	Death on 4 th day	Normal	Significantimpairment	Death on 5 th day

¹GW: Gestational Weeks
⁴TR: Tricuspid Regurgitation
⁷RAD: Right Atrial Dilatation
¹⁰VSD: Ventriculer Septal Defect
¹³ARF: Acute Renal Failure

²PHT: Pulmonary Hypertension
⁵CM: Cardiomegaly
⁸R-L: Right-Left
¹¹MOF: Multiple Organ Failure
¹⁴MV: Mechanical Ventilation

³PFO: Patent Foramen Ovale
⁶RVD: Right Ventricule Dilatation
⁹ASS: Atrial Situssolititus
¹²SVT: Supra Ventricular Tachycardia
N/A Not Available

prosencephalic and choroid plexus cysts, pineal tumor, choroid papilloma and intracerebral hematoma [8]. The aneurysm leading to a cerebral shunt flow, increases blood return to the right ventricle,

which may lead to congestive heart failure. Cardiomegaly, tricuspid regurgitation, polyhydramnios, pericardial/pleural effusions, edema and ascites are predictive of a high outflow anomaly which is usually

Table 3: The feeding vessels and the embolizing agents used in endovascular treatment of the cases.

Case	Postnatalage at intervention	Feedingvessels	Embolizingagent
1	3. day	-right ACA ¹	NBCA ⁹
2	2. day 9. day 4. year	-right ACA, -left PCA ² , right PMCA ³ , right PLCA ⁴ -embolised in the another centre because of moving to another city.	NBCA
3		MOF ⁸ , nointervention	
4	18. day 27. day	-right ACA -right ACA, right PCA, right PCLA ⁵ .	NBCA
5	1. day	-right ACA	EVA ¹⁰
6	2. day 4. day 8.day	-right ACA -right PCA, MCA ⁶ -left ACA	EVA
7	25. day 40. day 9.5 month	-right ACA -left PCA -left ACA	NBCA
8	3. day	-left ACA, left TMPA ⁷	NBCA

¹ACA:anterior choroidalartery²PCA:posterior choroidalartery
³PMCA:posteromedial choroidalartery⁴PLCA:posterolateral choroidalartery
⁵PCLA:pericallosal artery⁶MCA:median choroidalartery
⁷TMPA:thalamoperforating artery⁸MOF:multi organ failure
⁹NBCA:N-butyl cyanoacrylate¹⁰EVA:ethylene vinylalcohol

refractory to treatment and carries a poor prognosis [6].

In this report we reviewed 8 cases of newborn babies with an antenatal diagnosis of VGAM with an emphasis on clinical features, transarterial endovascular treatment and prognosis. There are many case reports about VGAM published previously; but this is the first report of a case series from our country.

Method

The newborn patients who were hospitalized in our Neonatal Intensive Care Unit (NICU) between 2005 and 2015, with a diagnosis of VGAM were included. Data about the NICU care, neuroradiological interventions and follow-up were collected from the hospital records retrospectively. Every patient had a cranial MR angiography/venography prior to endovascular intervention, for mapping of the vessels and revealing the type of malformation. Decision for endovascular intervention was made according to the patients cardiovascular and respiratory status. The large feeder vessels were identified and appropriate cases underwent endovascular intervention. The embolizing agents used were N-butyl cyano acrylate (NBCA) (5 patients) and ethylen vinyl alcohol (EVA) (2 patients). During endovascular intervention, maximal doses of radiocontrast material were not exceeded and intervention was stopped when the dose reached maximum values. Except the third case in whom embolization could not be applied, femoral arteries were used in 6 patients whereas umbilical artery was used in one patient for the procedure.

The care of all the patients was carried out in the NICU. High frequency oscillation ventilation (HFOV) was used in cases unresponsive to conventional ventilation. According to the International Pediatric Organ Failure criteria, a patient having more than one system dysfunction was defined as having multiorgan failure [9]. All patients were evaluated by the Division of Pediatric

Cardiology on the first day of life with a close follow-up thereafter. Long term neurologic prognosis of the babies who survived to discharge, were assessed by the Division of Pediatric Neurology. Neurological outcomes were classified as normal (no neurological and cognitive deficit), mild impairment (neurological and cognitive deficits which do not affect age-appropriate functions) and severe impairment (neurological and cognitive deficits which affect age-appropriate functions). Bicetre score, which is used to select patients who can benefit from endovascular intervention, was assessed retrospectively (Table 1).

Results

Seven out of eight patients were males. All patients were full term except one, who was born at 36 3/7 weeks of gestational age and all were born with cesarean section. Seven of these patients were diagnosed antenatally except one who was referred from another hospital.

All patients developed severe heart failure in the early days of life. Respiratory failure, tachycardia, hyperdynamic precordial activity, 2-4/6 systolic or continuous murmur heard through the anterior fontanel were the common physical examination findings in all patients. Posteroanterior chest X-rays showed cardiomegaly. Echocardiografic findings were tricuspid regurgitation (TR), cardiomegaly (CM), severe pulmonary hypertension (PH) in all patients and severe right atrium and right ventricle dilatation in five patients. Additionally one patient had atrial situs solitus (ASS), left aortic arch, small ventricular septal defect and one other patient had hemodynamically significant patent ductus arteriosus. Cranial ultrasound imaging showed wide VGAM in all patients.

All patients needed ventilatory support due to respiratory failure on the first day of life, either conventional or high frequency oscillatory ventilation. Fluid restriction, digoxin, dobutamine and/

or dopamine perfusions and furosemid were used for cardiac failure. Sildenafil (n=3) and inhaled nitric oxide therapy (n=1) were given for severe pulmonary hypertension in 4 patients. Six patients developed refractory hypotension and three of these died because of multiorgan failure. Bicetre scores of 4 patients who died were 5, 11, 7 and 12 respectively. Seizures developed in six patients (one of them without embolization treatment) and ventriculoperitoneal shunt was needed in two patients with hydrocephaly. Upper gastrointestinal bleeding (n=1), supraventricular tachycardia (n=1), acute renal failure (n=4), cholestasis (n=1) and sepsis (n=3) were the other morbidities. The demographic characteristics, clinical and echocardiographic features, prognosis and neurodevelopmental outcomes are summarized in Table 2.

Vascular mapping of VGAM by cranial MRI and MR angiographic images were assessed by the Department of Neuroradiology (Figure 1). Data about the interventional therapies are shown in Table 3.

Discussion

The incidence of VGAM is reported to be 1 in 25,000 live births [10]. The total number of births between the years 2005-2015 in our hospital was 19,835 and the number of cases with VGAM was 7, with a resultant incidence of 1 in 2833 live births. This figure is much higher than the reported incidences which is probably due to the fact that our hospital is a tertiary perinatal-neonatal referral center in Istanbul.

It has been reported that VGAM is seen more frequently in males. In our case series seven out of eight patients were males also. However the reason of this male gender dominance is unknown [11].

VGAM can be a lifethreatening situation in newborn infants, especially when it causes severe heart failure. Choroidal and mixed types of VGAM may lead to mild to severe heart failure, cerebral atrophy, and seizures in the early days of life. In infancy, macrocrania and hydrocephalus, asymptomatic cardiomegaly or moderate heart failure; in older children mild heart failure, asymptomatic cardiomegaly, headache and intracranial hemorrhages can be seen. The severity of heart failure in newborns with VGAM differs according to the type and size of the aneurysm [12]. In neonatal patients with choroidal and mixed types of VGAM, severe heart failure and hypotension refractory to treatment, may lead to multiorgan failure which cause ischemia of vital organs [3,8,10,13]. In our patient group, mixed type VGAM was the most frequent type and all the patients had severe heart failure. Three of six patients with refractory hypotension who developed multiorgan failure died.

Bicetre scoring system has been developed to identify those babies with heart failure who may benefit most from endovascular treatment. The scoring system is performed in patients with high output heart failure looking at the presence or absence of multiorgan failure. This system is beneficial in the decision of early interventional therapy but is not reliable in the early days of life [14]. We did not use the Bicetre scoring system for treatment decisions in our patient group; however when evaluated retrospectively Bicetre scores and the therapeutic management strategies were found to be compatible.

An association between VGAM and congenital cardiac anomalies like sinus venosus type atrial septal defect and coarctation of the aorta had been reported [15]. Mc Elhinney et al. also reported the presence

of partial pulmonary venous return abnormalities, ventricular septal defect and atrioventricular channel defect in association with VGAM [16]. In our patients ventricular septal defect, patent ductus arteriosus, patent foramen ovale, atrial situs solitus and left aortic arch anomalies were the associated cardiac findings.

The treatment options for VGAM are open surgery, endovascular therapy and stereotactic radiosurgery, of which endovascular therapy is the most preferred method. The aim of this therapy is to selectively catheterize the feeder arteries and to close the fistulae with liquid (NBCA, EVA) or coil, in order to reduce the high flow in this vascular malformation [17,18]. After multiple embolization procedures, systemic cardiovascular load also decreases with the decreasing flow in the malformation. This intervention in the neonatal period should be done under optimal conditions by an experienced team and risk-benefit ratio should always be kept in mind. The interventional therapy should be delayed to decrease the risks and increase the success of the procedure as long as the baby tolerates the condition. However, early intervention is necessary if there is severe and intractable respiratory or cardiac failure.

The advances in interventional neuroradiology resulted in a more favorable prognosis in VGAM cases [19] in recent years. However mortality and morbidity is still high. Severe heart failure can progress quickly to multiorgan failure and death; can also lead to cerebral venous hypertension, vascular leak, cerebral ischemia and infarction. The patients with high outflow, choroidal and mixed type malformations carry a worse prognosis than the patients with mural type and/or those who can tolerate later intervention. Fullerton et al. reported the mortality rate in 27 children with VGAM (21 newborns) as 15% in 2003. Four of their patients died, all of whom developed symptoms in the neonatal period [20]. Geibprasert et al. reported the mortality rate as 36% in 25 children (20 newborns) in 2010 [21]. Excluding one patient, who died without having a chance of any intervention, mortality rate in our patients after endovascular treatment was 43%. This high mortality rate was thought to be the result of the type of the malformations (choroidal-mixed type, with multiple feeder vessels) and severe and very early clinical presentation in the newborn period.

Neurological sequelae can be seen in 37-50% of VGAM patients. When the patients who survive after embolization are assessed neurologically, 66% was found to be normal, 11.5% had moderate neurological problems and 8.5% had irreversible neurological deficits [22]. Patients who develop multiorgan failure, develop cerebral infarction more frequently and has a poorer neurodevelopmental outcome in the long term [10]. In our case series, three out of four patients who survived had a normal neurological development whereas one patient had severe impairment.

In conclusion, in neonatal patients with a high output cardiac failure without a cardiac origin, VGAM should always be considered in the differential diagnosis. Prenatally diagnosed patients should be born in a tertiary level perinatal-neonatal center, with experienced neuroanesthesiology and neuroradiology clinics. Although mortality and morbidity is high, endovascular interventional treatment of VGAM in the neonatal period may result in a favorable outcome.

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