Vein of Galen malformation in neonate: A lesson learned

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SUMMARY

Vein of Galen Malformation (VGM) is a rare arteriovenous anomaly that presents a unique clinical challenge, particularly due to its association with heart failure and hydrocephalus. We report a case of a full-term male neonate diagnosed antenatally with the choroidal form of VGM, confirmed through pre- and postnatal magnetic resonance imaging. Arrangements were made for delivery at a tertiary centre with a multidisciplinary team, including an interventional radiologist; however, due to logistical constraints, this could not be accomplished. Clinical deterioration ensued on day 4 of life, marked by worsening heart failure necessitating aggressive ventilatory and hemodynamic support. The patient's condition progressed to severe pulmonary hypertension, multiorgan impairment, and disseminated intravascular coagulation (DIVC), resulting in a Bicêtre score of 1, signifying poor prognosis and high risk for endovascular intervention. The patient passed away on day 28 of life. This case adds to the limited literature on VGM management in Malaysia by illustrating the challenges of managing such a complex condition in resource-limited settings. It underscores the importance of coordinated delivery planning and timely referral to specialised centres with endovascular specialties.

INTRODUCTION

Vein of Galen malformation (VGM) is a severe and rare congenital intracranial anomaly characterized by arteriovenous fistulas between various arterial feeders and the median prosencephalic vein of Markowski.[1] The prevalence of VGM has increased over the past decade, with an estimated incidence of 1:58,100 live births.[2] Typically presenting in neonates with high-output heart failure and severe cardiopulmonary distress, VGM is often complicated by pulmonary hypertension, neurological, hepatic, and renal dysfunction. Historically, neurosurgical management yielded poor outcomes with a mortality rate around 90%. However, the advent of endovascular techniques has markedly improved prognosis, reducing mortality to approximately 50%.[3] This case report illustrated the critical role of prenatal diagnosis, the challenges of postnatal management, and the impact of timely delivery and treatment on outcomes.

CASE PRESENTATION

A full-term infant was admitted to the Neonatal Intensive Care Unit (NICU) at birth due to respiratory distress requiring support. The infant, delivered via caesarean section to a 40-year-old primigravida mother who is Human Immunodeficiency Virus (HIV) positive and on Highly Active Antiretroviral Therapy (HAART) with a low CD4 count, was conceived through in vitro fertilization using an ovum donor. Prenatal assessments revealed a Vein of Galen aneurysm, with associated dilated internal jugular veins, right atrial enlargement, and cardiomegaly, confirmed by foetal magnetic resonance imaging (MRI) (Figure 1). Despite recommendations for delivery at a tertiary centre due to potential postnatal complications, logistical challenges led to delivery at a secondary hospital.

At birth, the infant had Apgar Score of 7 at 1 minute and 9 at 5 minutes. Physical examination showed a weight of 2000g (<3rd centile), a length of 45 cm (10th centile), and a head circumference of 40cm (>97th centile), with a thrill palpable over his anterior fontanelle. Other anomalies include low-set ears, microtia, a receding chin, and a left preauricular tag, and signs of heart failure were present (hyperactive precordium, displaced apex beat, grade 4 ejection systolic murmur, and hepatomegaly extending 4 cm below the right costal margin).

Chest radiograph revealed cardiomegaly and plethoric lung fields (Figure 2). An echocardiogram identified pulmonary hypertension with dilated right heart chambers, a dilated superior vena cava (SVC) with reversed flow, increased blood flow through the aortic arch, and a small patent ductus arteriosus (PDA) with a right to left shunt. Postnatal MRI of the brain showed the choroidal variant of a vascular malformation, with multiple enlarged arterial branches originating from the posterior cerebral artery and bilateral posterior communicating arteries supplying a dilated prosencephalic vein of Markowski resulting in obstructive hydrocephalus (Figure 3a, 3b and 3c).

Upon NICU admission, the infant was started on non-invasive respiratory support and anti-heart failure medications, including intravenous Furosemide and oral Spironolactone. The initial Bicêtre score of 21 indicated a stable condition. However, on day 4, the infant's condition rapidly deteriorated, showing signs of cardiac decompensation further complicated by severe pulmonary hypertension, necessitating invasive mechanical ventilation and inhaled nitric oxide (iNO). Multiple inotropes including dopamine, dobutamine, and noradrenaline were initiated for cardiovascular support. The Bicêtre score dropped to 8,

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Table I: Bicêtre Score at Presentation and at Clinical Deterioration

Points	Clinical status	Points	Birth	Day 4	Final
Cardiac function	Normal	5	√		
	Overload, no medical treatment	4			
	Failure, stable with medical treatment	3			
	Failure, not stable with medical treatment	2			
	Ventilation necessary	1		√	
	Resistant to medical therapy	0			√
Respiratory function	Normal	5	√		
	Tachypnoea, finishes bottle	4			
	Tachypnoea, does not finish bottle	3			
	Assisted ventilation, normal saturation FiO2 <25%	2			
	Assisted ventilation, normal saturation FiO2 >25%	1		√	
	Assisted ventilation, desaturation	0			√
Cerebral function	Normal	5	√		
	Subclinical, isolated EEG abnormalities	4		√	
	Nonconvulsive intermittent neurologic signs	3			
	Isolated convulsion	2			
	Seizures	1			√
	Permanent neurological signs	0			
Renal function	Normal	3	√		
	Transient anuria	2			
	Unstable diuresis with treatment	1		√	
	Anuria	0			√
Hepatic function	No hepatomegaly, normal hepatic function	3	√		
	Hepatomegaly, normal hepatic function	2			
	Moderate or transient hepatic insufficiency	1		√	
	Abnormal coagulation, elevated enzymes	0			√
Total scores			21	8	1

reflecting significant clinical deterioration which rendered the infant too unstable for transfer to a centre with endovascular intervention capabilities.

In addition to developing clinical seizures, the patient experienced progressive multiorgan dysfunction. Renal function significantly declined (urea 5.9 mmol/L, creatinine 279 µmol/L), resulting in anuria and severe oedema. Liver function was also severely compromised, as evidenced by elevated transaminase levels (AST 934 U/L, ALT 834 U/L) and unconjugated hyperbilirubinemia (total bilirubin 766 µmol/L). Other laboratory workup showed (PT 67 sec, APTT >180 sec, INR 5.35) suggestive of disseminated intravascular coagulopathy (DIVC) refractory to cycles of fresh frozen plasma, cryoprecipitate, platelet transfusions, and vitamin K therapy. A reassessment revealed a Bicêtre score of 1, indicating a high risk for interventional embolization, leading to a decision for conservative management. Despite all efforts, the infant ultimately succumbed on day 28 of life (Table I).

DISCUSSION

VGM is the most common type of arteriovenous malformation in neonates and infants. Although endovascular embolization has improved outcomes, the complexity of VGM cases continues to present significant mortality risks.[2] The exact aetiology of VGM remains unclear but it is believed to stem from abnormal embryonic vessels development in the prosencephalon.[1] Although the exact genetic basis of VGM remains incompletely understood, emerging evidence suggests involvement of mutations in genes regulating vascular development and angiogenesis, including chromatin-modifying genes and those within the Ephrin signalling pathway.[4] Facial dysmorphism is not a typical feature of VGM; however, its presence in our patient raises the possibility of an underlying syndromic diagnosis. Unfortunately, due to resource constraints, further genetic evaluation could not be pursued. This underscores the pressing need to improve access to genomic diagnostics, especially in patients presenting with atypical or syndromic features. Meanwhile, maternal HIV infection and in utero exposure to HAART have been associated with a modest increase in congenital anomalies, though current evidence does not indicate an increased risk of intracranial arteriovenous malformations such as VGM in exposed infants.[5]

VGM is anatomically classified into choroidal and mural types. The choroidal type (Type 1) is the most common and severe, characterised by multiple feeding arteries entering the prosencephalic vein of Markowski, leading to high-output failure. Conversely, the mural type (Type 2) involves fewer arterial feeders, resulting in greater outflow resistance and less severe cardiac failure, with symptoms emerging later in infancy.[6] Although maternal HIV infection and in utero exposure to HAART have been associated with a mild increase in congenital malformations generally, studies have not demonstrated an elevated risk of intracranial arteriovenous anomalies such as VGM in exposed infants.

Prenatal diagnosis of VGM is typically achieved through colour Doppler ultrasonography during the third trimester. However, foetal MRI provides a more detailed evaluation of VGM's size and location, offering superior diagnostic clarity.[7] Early detection facilitates planning for delivery at a tertiary

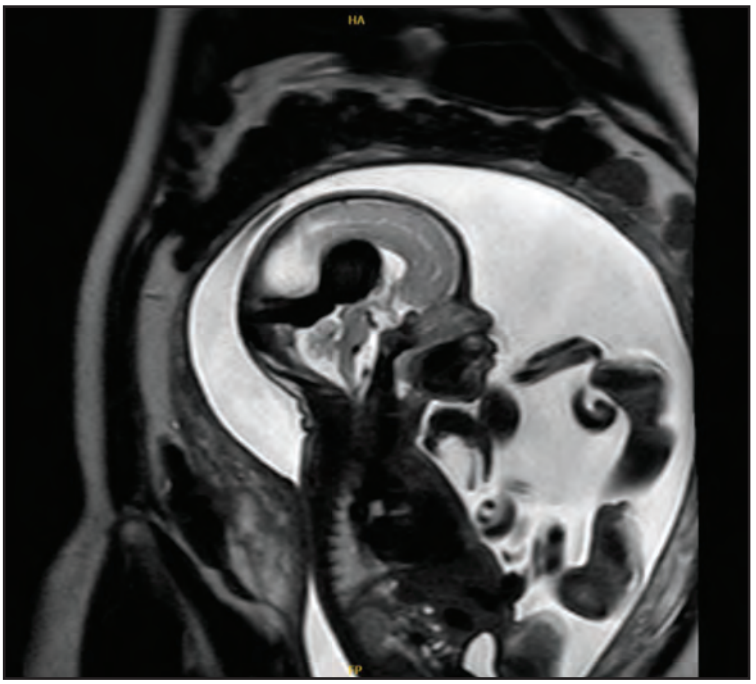

Fig. 1: Maternal T2-weighted magnetic resonance at 32 weeks of gestation showing a Vein of Galen malformation in the foetus, characterized by a dilated flow void structure in the posterior midline

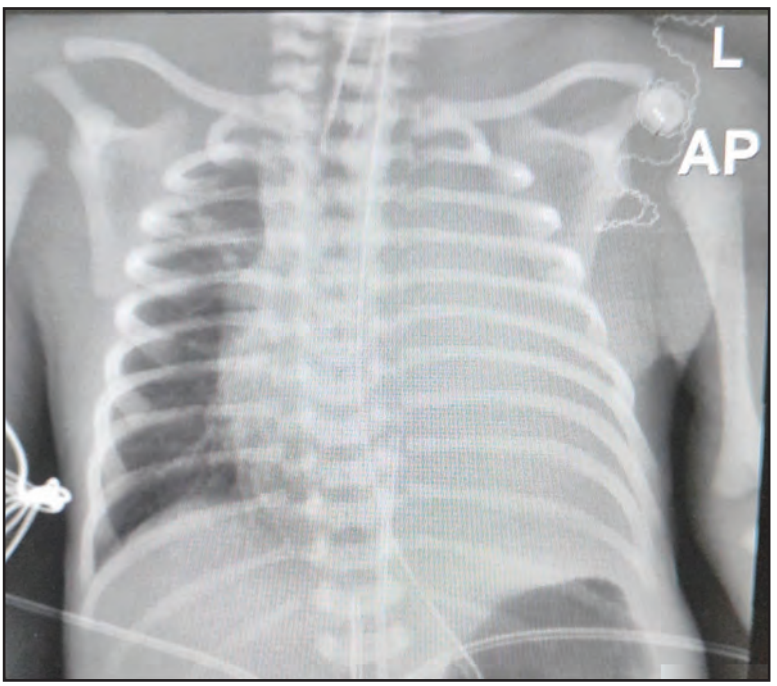

Fig. 2: Chest X-ray of the neonate showing cardiomegaly with an enlarged cardiac silhouette and pulmonary vascular congestion

centre equipped with a multidisciplinary team. In our case, logistical constraints led to delivery at a secondary hospital, adversely affecting the outcome. The high-flow nature of the choroidal type placed immense strain on the infant's heart exacerbated haemodynamic instability. The cerebral arteriovenous shunt diverted significant cardiac output from systemic circulation, leading to myocardial ischaemia, lactic acidosis and multiorgan failure despite aggressive interventions.[8] The inability to transfer the patient for further intervention highlights the critical need for delivery at a facility with the appropriate capabilities and expertise.

The timing and method of endovascular embolization depend on the clinical presentation, with the Bicêtre score

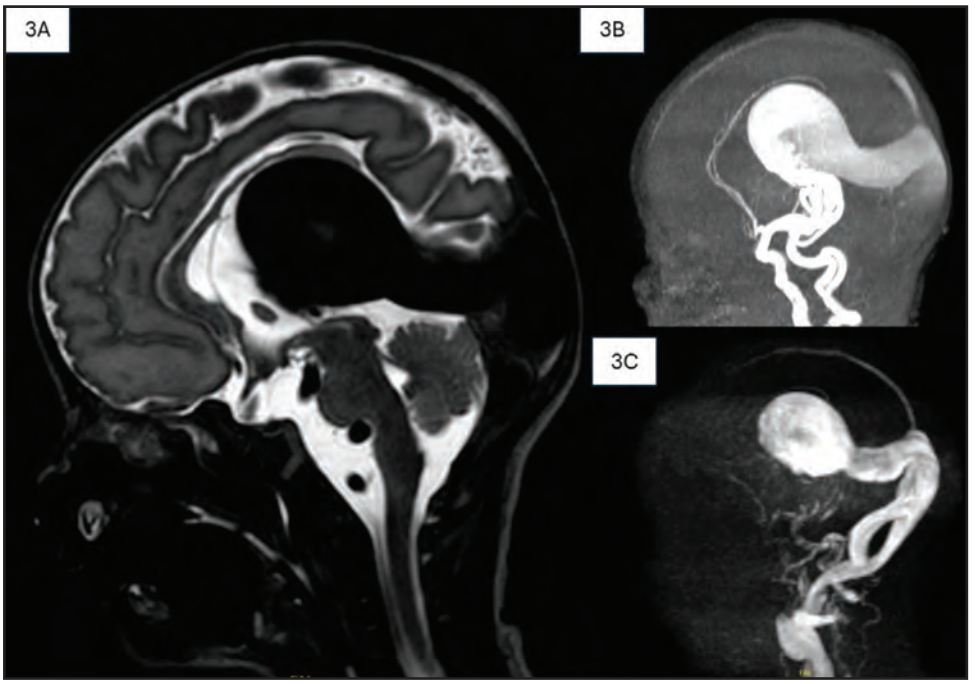

Fig. 3: A) Sagittal T2-weighted magnetic resonance image showing a choroidal-type Vein of Galen Malformation with dilated prosencaphalic vein of Markowski and persistent falcine draining sinus. B) Sagittal T2-weighted magnetic resonance angiography image showing enlarged branches of the anterior and posterior cerebral arteries coalescing to the dilated recipient vein. C) Sagittal T2-weighted magnetic resonance angiography image showing a Vein of Galen aneurysmal malformation in continuity with the dilated straight sinus, torcula herophili, and transverse sinus

guiding treatment decisions. Scores <8 suggest conservative management, scores between 8 and 12 warrant emergency intervention, and scores >12 allow for delayed treatment after 5 months, permitting the infant to grow and better tolerate the procedure.[9] Our patient's rapid clinical deterioration highlights the importance of monitoring Bicêtre score fluctuations, which affect risk stratification and intervention timing, particularly in centres lacking endovascular expertise. Recent reviews suggest that aggressive cardiac management and early neuro-endovascular intervention can achieve high survival rates with low morbidity, even with a Bicêtre score below 8.[2] Consequently, many referral centres have adopted a more nuanced approach, moving beyond rigid score cutoffs to make individualized care decisions based on evolving clinical circumstances.

Managing heart failure in VGM remains challenging, particularly due to the complexities involved in choosing the appropriate timing for intervention. Medical management primarily focuses on stabilizing the patient to allow for sufficient growth before considering more invasive procedures. This stabilization involves early cardiovascular interventions aimed at enhancing systemic output by reducing both systemic and pulmonary vascular resistance while improving myocardial function. Diuretics, such as furosemide, should be administered shortly after birth to manage fluid overload and reduce the workload on the heart.[10] Prostaglandin E1 is recommended to maintain adequate systemic circulation by promoting right-to-left ductal shunting, which is crucial in sustaining oxygen delivery. Inodilators, including milrinone and levosimendan, are also used to improve cardiac output by providing inotropic support while simultaneously dilating blood vessels.[11] Low doses of catecholamines like dopamine and noradrenaline are added to further support cardiac function.[9] Although previous guidelines advocated for the use of milrinone in combination with inhaled nitric oxice (iNO) for treating VGM-related pulmonary hypertension, recent evidence advises against relying solely on iNO. The potential ineffectiveness of iNO and its risk of exacerbating pulmonary oedema make it less favourable option.[9,11] Therefore, treatment strategies now focus on a more comprehensive approach, incorporating various pharmacological agents to optimize patient outcomes.

CONCLUSION

Despite advancements in endovascular embolization improving VGM prognosis, the condition remains associated with significant mortality. A multidisciplinary approach in intensive care, combined with early diagnosis, is crucial for optimizing outcomes. Ideally, intrauterine transfer or early postnatal transfer to a specialised centre with endovascular capabilities is essential. This case highlights the critical importance of prenatal diagnosis and meticulous planning for the delivery and care of neonates with VGM.

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COMPETING INTERESTS

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

1. Raybaud CA, Strother CM, Hald JK. Aneurysms of the vein of Galen: embryonic considerations and anatomical features relating to the pathogenesis of the malformation. Neuroradiology 1989; 31(2): 109-28.
2. Brevis Nuñez F, Dohna-Schwake C. Epidemiology, diagnostics, and management of vein of Galen malformation. Pediatr Neurol 2021; 119: 50-5.
3. Hansen D, Kan PT, Reddy GD, Mohan AC, Jea A, Lam S. Pediatric knowledge update: Approach to the management of vein of Galen aneurysmal malformations in neonates. Surg Neurol Int 2016; 7(Suppl 12): S317-21.
4. Duran D, Karschnia P, Gaillard JR, Karimy JK, Youngblood MW, DiLuna ML, et al. Human genetics and molecular mechanisms of vein of Galen malformation. J Neurosurg Pediatr 2018; 21(4): 367-74.
5. Williams PL, Crain MJ, Yildirim C, Hazra R, Van Dyke RB, Rich K, et al. Congenital anomalies and in utero antiretroviral exposure in human immunodeficiency virus-exposed uninfected infants. JAMA Pediatr 2015; 169(1): 48-55.
6. Lasjaunias PL. Vascular diseases in neonates, infants and children: interventional neuroradiology management. Interv Neuroradiol 1997; 3(Suppl 1): 37-119.
7. Saliou G, Vraka I, Teglas JP, Elie C, Alison M, Baugnon T, et al. Pseudofeeders on fetal magnetic resonance imaging predict outcome in vein of Galen malformations. Ann Neurol 2017; 81(2): 278-86.
8. Hendson L, Emery DJ, Phillipos EZ, Bhargava R, Olley PM, Lemke RP. Persistent pulmonary hypertension of the newborn presenting as the primary manifestation of intracranial arteriovenous malformation of the vein of Galen. Am J Perinatol 2000; 17(8): 405-10.
9. Cory MJ, Durand P, Sillero R, Morel B, Delcour C, Harroche A, et al. Vein of Galen aneurysmal malformation: rationalizing medical management of neonatal heart failure. Pediatr Res 2023; 93(1): 39-48.
10. Frawley GP, Dargaville PA, Mitchell PJ, Tress BM, Loughnan P. Clinical course and medical management of neonates with severe cardiac failure related to vein of Galen malformation. Arch Dis Child Fetal Neonatal Ed 2002; 87(2): F144-9.
11. Buratti S, Mallamaci M, Tuo G, Giordano L, De Rosa G, Cicenia M, et al. Vein of Galen aneurysmal malformation in newborns: a retrospective study to describe a paradigm of treatment and identify risk factors of adverse outcome in a referral center. Front Pediatr 2023; 11: 1193738.