

PERSISTENT PULMONARY HYPERTENSION IN A NEONATE WITH VEIN OF GALEN MALFORMATION

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PERZISTENTNA PLUĆNA HIPERTENZIJA KOD NOVOROĐENČETA SA ANEURIZMOM GALENOVE VENE

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ABSTRACT

The vein of Galen aneurysmal malformation (VGAM) is a rare congenital vascular malformation which can present in a newborn as high-output congestive heart failure and rarely as neonatal persistent pulmonary hypertension (PPHN).

The objective of our study was to describe the clinical course and management of a newborn with VGAM, presenting as refractory PPHN, with an adverse short-term outcome. Following an urgent caesarean section, the newborn was admitted to our hospital's neonatal intensive care unit due to prematurity and signs of respiratory distress. Echocardiography excluded congenital heart disease, but revealed PPHN with near systemic pulmonary pressures. Sildenafil and a low-dose diuretic were started. After a brief improvement, the child's condition deteriorated, revealing suprasystemic PPHN, global ventricular dysfunction, and right-to-left shunting at the ductal and atrial levels. Anticongestive medications and inotropes were given in addition to sildenafil. A cranial ultrasound revealed a midline cystic formation measuring 13.7 x 13.2 mm with colour Doppler showing turbulent blood flow in the vein of Galen area, which was diagnostic for the vein of Galen malformation. Treatment of our patient included mechanical ventilation and other supportive measures, management of heart failure, and PPHN. However, the neonate remained in critical condition, and even though endovascular embolisation was considered, the transfer to a neurosurgical centre was impossible, and the baby succumbed to her disease.

Even though the association of VGAM with PPHN is not common, in cases of systemic PPHN and heart failure refractory to treatment, AV malformations in the liver and brain should be ruled out.

Key words: vein of Galen malformations; intracranial aneurysm; hypertension, pulmonary; infant, newborn.

INTRODUCTION

It has been well established that the vein of Galen malformation (VGAM) represents a rare congenital vascular malformation that develops from an arteriovenous connection between primitive choroidal vessels and the median prosencephalic vein of Markowski

SAŽETAK

Aneurizma vene Galene (VGAM) retka je kongenitalna vaskularna malformacija, koja se može manifestovati već u novorođenačkom periodu kao kongestivna srčana insuficijencija, a u manjem broju slučajeva i kao perzistentna plućna hipertenzija novorođenčeta (PPHN).

U ovom radu prikazujemo klinički tok i lečenje novorođenčeta sa VGAM koja se manifestovala teškom PPHN i nepovoljnim kliničkim tokom. Usled prematuriteta i znakova respiratornog distresa, novorođenče je hospitalizovano na odeljenju neonatalne intenzivne nege naše bolnice. Ehokardiografskim pregledom je utvrđeno postojanje PPHN, sa očuvanom globalnom srčanom funkcijom, te je započeta terapija sildenafilom i niskim dozama diuretika. Nakon inicijalnog kliničkog oporavka usledilo je naglo pogoršanje opšteg stanja, kada je utvrđeno postojanje PPHN sistemskog nivoa, sa globalnom ventrikularnom disfunkcijom i reverzijom šanta na nivou ductus arteriosusa i foramen ovale, u desno-levi. Sildenafilu su dodati antikongestivna terapija i inotropi. Ultrazvučnim pregledom centralnog nervnog sistema uočeno je postojanje hipoehogene, cistične formacije u medijalnoj liniji, dimenzija 13,7 x 13,2 mm, u kojoj se kolor doplerom prikazao turbulentan protok krvi, što je odgovaralo postojanju arteriovenske malformacije po tipu VGAM. Dalji tretman novorođenčeta podrazumevao je primenu mehaničke ventilacije i ostalih suportivnih mera, nastavak lečenja kongestivne srčane insuficijencije i PPHN. Razmatrana je endovaskularna embolizacija VGAM, ali zbog kritičnog stanja deteta transport do neurohirurškog centra nije bio moguć, tako da je novorođenče preminulo.

Uprkos činjenici da je udruženost VGAM sa PPHN u neonatalnom periodu retka pojava, u slučajevima PPHN sistemskog nivoa udružene sa kongestivnom srčanom insuficijencijom refraktorne na lečenje, treba isključiti postojanje arteriovenskih malformacija u mozgu i jetri.

Cljučne reči: malformacije Galenove vene; intrakranijalna aneurizma; plućna hipertenzija; odojče, novorođenče.

(1). In 40-50% of cases, VGAM presents during the newborn period, usually as high-output congestive heart failure and less frequently as persistent pulmonary hypertension of the newborn (PPHN) (2). Congestive heart failure in newborns is usually caused by congenital heart defects; a less common cause is the vein of Galen malformation. However, if this arteriovenous

malformation is not recognised on time, with consequent delay in treatment, heart failure becomes difficult to manage with associated high mortality (3, 4).

CASE PRESENTATION

A female neonate was born at 31 weeks and 1 day gestation via urgent caesarean section (CS) due to hypertension in the mother and imminent placental insufficiency. She was the second child to a mother whose pregnancy was complicated by a urinary tract infection diagnosed at the start of the 3rd trimester; otherwise, no abnormal signs were detected on antenatal ultrasound. Before antibiotic treatment for the urinary tract infection (UTI) could be started, the mother went into premature labour, and an emergency caesarean section was performed.

At birth, the baby girl's body weight was 1540g (25-50th percentile), body height was 40 cm (25th percentile), and head circumference was 29 cm (75th percentile). The Apgar score was 4/7 at 1 and 5 minutes, respectively. The infant's mother had a history of hypertension diagnosed years earlier. She was on methyldopa during pregnancy. The mother was a gravida 2, para 2, this being her second child. Apart from the mother's hypertension, the family history was uneventful.

Following CS, the infant cried on extraction, but subsequently became breathless, bradycardic, and cyanotic, not responding well to stimulation. Suctioning and bag-mask ventilation were performed with added supplemental oxygen, after which there was an increase in heart rate with irregular respirations. The newborn was transferred to the Pediatric Clinic, Nis, Serbia, neonatal intensive care unit in the 14th hour of life. Her initial vital signs were: blood pressure of 49/22 mmHg, body temperature of 35.9 °C, pulse rate of 150 beats/min, respiratory rate of 65 breaths/min, and oxygen saturation of 65% with supplemental oxygen FiO₂ of 50%.

The initial physical examination revealed lethargy, tachypnea, chest retractions, peripheral cyanosis, normal heart sounds and no cardiac murmur, diminished breath sounds on lung auscultation, and no hepatomegaly. She was supplemented with 10% dextrose and 100% oxygen was administered. Capillary blood gas revealed mixed respiratory and metabolic acidosis (pH 7.06; pO₂ 35 mmHg; pCO₂ 54 mmHg; lactate 6), and mechanical ventilation (MV) was started with PC-SIMV mode (FiO₂ 85%). Antibiotics were administered empirically for early-onset neonatal sepsis (Ampicillin, Gentamycin), and the low albumin level was corrected.

On the 5th day of life, there was a deterioration in the patient's condition, with a rise in inflammatory parameters (C-reactive protein: 117, platelets: 90), and antibiotic therapy was modified empirically (Meropenem,

Vancomycin) for late-onset neonatal sepsis. Coagulopathy was treated with fresh frozen plasma. Blood culture revealed *Klebsiella pneumoniae* ESBL+.

On the 8th day of life, a cardiac murmur was noted, and a cardiology consultation was obtained. Echocardiography excluded critical congenital heart defects; the heart was structurally normal, but significant tricuspid regurgitation was observed (a high systolic velocity jet of 3.2 m/s, suggesting an elevated right ventricular pressure of 40 mmHg), left-to-right shunting at both atrial and ductal levels was appreciated. The finding was suggestive of persistent pulmonary hypertension of the newborn (PPHN) with near systemic pulmonary pressures. Sildenafil and low-dose furosemide were started. Following treatment, there was an overall improvement in the general condition of the patient, and weaning from mechanical ventilation commenced at a slow pace.

However, the patient's condition deteriorated on day 15 of life, with a second rise in inflammatory parameters (blood culture revealed *Acinetobacter baumannii*, which required the addition of one more antibiotic (colistin). The patient was still on mechanical ventilation (MV) with FiO₂ 70%, and weaning was not possible. Physical examination revealed tachycardia, tachypnea, with marked chest recessions, an overactive precordium, a loud systolic murmur over the tricuspid area, hepatomegaly and cardiomegaly on the chest X-ray. Abdominal ultrasound (US) revealed ascites. Repeat echocardiography revealed suprasystemic PPHN (estimated pulmonary pressure around 60 mmHg), with right ventricular dysfunction, ductal flow shunt reversal was noted at the level of the aortic isthmus as well as flow reversal at the atrial level (right-to-left). There was volume overload of the right

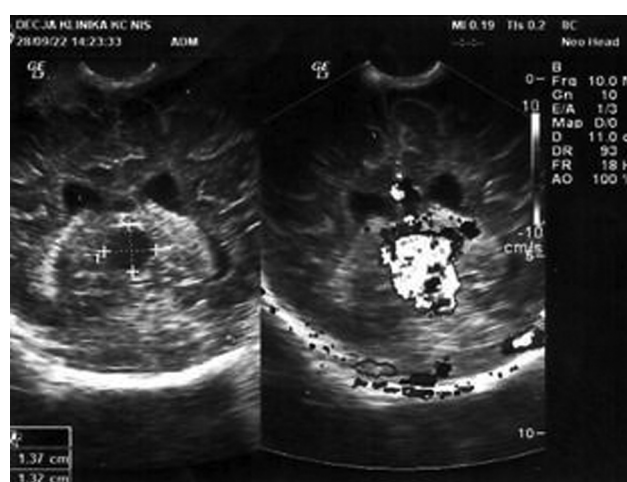


Figure 1. Vein of Galen Malformation. Ultrasound examination of the head (coronal views) shows dilated lateral ventricles with a midline anechoic structure (13.7 mm x 13.2 mm) with turbulent flow on application of colour Doppler imaging (Radiology Department, Pediatric Clinic, Clinical Center, Nis, Serbia).

heart resulting in right heart failure. Anticongestive medications (angiotensin-converting-enzyme inhibitor and diuretics) were given in addition to sildenafil. As it had not been previously performed, a cranial ultrasound was ordered, revealing a midline anechoic formation measuring 13.7x13.2mm with colour Doppler turbulent blood flow, in the vein of Galen area, suggesting VGAM (Figure 1).

Due to the general poor condition of the child and third-time sepsis, markedly reduced diuresis, head magnetic resonance imaging (MRI) was not done to confirm the diagnosis of VGAM, however, the diagnosis was clear from the cranial ultrasound and clinical presentation. No head bruit could be appreciated. Further management of heart failure comprised low-dose inotropes, dopamine, and dobutamine.

Management of our patient included mechanical ventilation and other supportive measures, aggressive medical treatment of congestive heart failure and PPHN. Endovascular embolisation of the AV malformation was suggested. However, the patient remained in critical condition, and the transfer to a specialised neurosurgical centre due to the long distance was impossible, and the baby succumbed to her disease before definitive treatment was possible. Informed written consent was obtained from the parents.

DISCUSSION

The vein of Galen arteriovenous malformation is a rare vascular malformation of the embryonic choroid plexus. It develops between the 6th and 11th week of fetal life and comprises approximately 30% of childhood vascular malformations (1, 5). This VGAM most commonly

presents as high-output congestive heart failure in the newborn period, and rarely as PPHN. It can also obstruct the flow of cerebrospinal fluid and result in hydrocephalus or cause progressive neurological impairment due to mass effect. If left untreated, the vein of Galen malformation has a mortality of 42–91% (2).

During infancy, congestive heart failure is mostly the result of congenital heart disease, particularly lesions associated with large left-to-right shunting (6). On the other hand, pulmonary hypertension is a life-threatening condition in newborns. While common causes include perinatal asphyxia, meconium aspiration, sepsis, lung hypoplasia secondary to congenital diaphragmatic hernia, rare etiologies such as cerebral vascular malformations must be considered, particularly when standard therapies fail (6).

During fetal life, cardiac failure may not occur because the low vascular resistance in the cerebral arteriovenous malformation is balanced by the low resistance of the placental circulation (3). After birth, removal of low-resistance placental circulation diverts blood flow through the low-resistance arteriovenous shunt in the brain. The malformation acts as a vascular steal, stealing a great percentage of aortic blood flow, in some cases up to 80% can be diverted away from systemic circulation (3, 7).

Partial blood flow deviation to the aneurysm causes a compensatory increase in cardiac output in order to maintain systemic perfusion and subsequent enhanced pulmonary flow to improve the preload. As a result, there is increased venous return through the superior vena cava which will, in time, result in right ventricular overload, increasing pulmonary pressures and subsequently leading to severe pulmonary hypertension. This can result in right-to-left shunting at the atrial and ductal levels (8).



Figure 2. Vein of Galen Malformation. Ultrasound examination of the head (coronal view) shows dilated lateral ventricles with a midline anechoic structure (Radiology Department, Pediatric Clinic, Clinical Center, Nis, Serbia).



Figure 3. Vein of Galen Malformation. Ultrasound examination of the head (sagittal views) shows dilated lateral ventricles with a midline anechoic structure with turbulent flow on application of colour Doppler imaging (Radiology Department, Pediatric Clinic, Clinical Center, Nis, Serbia).

Alongside increased pulmonary blood flow, there is magnified pulmonary return to the left atrium, which results in high cardiac output that will be further diverted to the vacuum of low-resistance vessels in the arteriovenous malformation. The final outcome is flow reversal in the proximal and distal arch, that becomes detrimental to systemic perfusion, leads to minimal peripheral oxygenation, lactic acidosis (pseudo aortic coarctation pathophysiology), and therefore dependency on the patency of ductus arteriosus (9, 10).

Right heart strain and enlargement can impact the left side, eventually leading to left heart failure. In conjunction with right-to-left shunting, systemic hypoperfusion becomes pronounced, there is a reduction in coronary flow, with possible myocardial ischemia and if left untreated, multiple organ failure (8, 11, 12).

Our patient developed respiratory distress soon after birth, which was interpreted to be a result of prematurity and suspected perinatal infection, and was treated accordingly. However, over the first days of life, the patient showed signs suggestive of cardiac failure - tachypnea, desaturation, hepatomegaly and a systolic murmur was appreciated. Echocardiography excluded critical congenital heart disease, revealing severe pulmonary hypertension. Treatment included mechanical ventilation, inotropes, diuretics, fresh frozen plasma, antibiotics and other supportive measures.

Because of poor response to treatment, bedside cranial ultrasound was ordered. It revealed a large midline anechoic formation with colour Doppler turbulent blood flow, in the vein of Galen area, suggesting VGAM. Immediate neurosurgeon consultation was obtained, and it was decided that a brain MRI be performed and that once the baby is stable, endovascular embolisation should be attempted in our referral pediatric neurosurgery center 250 km away. Data shows that if cranial US is performed according to strict criteria, a normal US excludes severe lesions on later MRI in 99% of cases (13).

Literature states that infants with VGAM present with severe cardiorespiratory symptoms at birth or shortly after, as was the case with our patient; the majority of cases (94%) have high output cardiac failure (8, 14). Pulmonary hypertension of the newborn (PPHN), refractory to treatment, may be a complicating factor (15).

There are a few case reports on VGAM presenting in the neonatal period with PPHN, such as the case reported by Seher et al (16), who described a baby presenting at 24 h of age with cardiac failure who had VGAM and died at 22 days of age. Farhat AS et al (4) presented a case of VGAM, in a term neonate who succumbed to her illness on day 3 of life, diagnosed at 37 weeks of gestation during intrauterine life.

The dominant clinical feature in our patient was PPHN. PPHN is a syndrome characterized by an elevation in pulmonary vascular resistance, right-to-left shunting at the levels of the patent foramen ovale and ductus arteriosus with subsequent hypoxemia. Its prevalence is 2–6/1000 live-births. Diagnosis of PPHN is confirmed by echocardiography. The cardinal findings include abnormal right ventricular dilatation, right-to-left shunting at the levels of the patent foramen ovale and ductus arteriosus, and severe tricuspid regurgitation, suggesting raised pulmonary pressure, which can be quantified based on the velocity of tricuspid valve regurgitation jet (4, 6, 10).

Despite brain MRI being the definitive diagnostic procedure as it has the advantage to accurately demonstrate the location of the lesion, vascular architecture, and vessel drainage in the VGAM; it also helps exclude other lesions which can be in our differential diagnosis such as arachnoid cysts, choroid plexus cysts, pineal tumours, choroid papilloma, hemangiomas, and pial arteriovenous malformations (17), initial diagnosis can be made by colour Doppler cranial ultrasound, as the VGAM is the only lesion that displays blood flow within (18).

Significant hemodynamic instability and multiple organ failure despite optimisation of treatments were the main reasons why transport was not undertaken. Unfortunately, the newborn succumbed despite all supportive measures due to refractory PPHN.

In conclusion, the vein of Galen malformation (VGAM) is a rare congenital arteriovenous malformation. Although the classical clinical feature in neonates is heart failure, this study highlights the need for providers to consider VGAM in the presence of PPHN. There is usually a delay in diagnosis because the clinical picture might mimic critical congenital heart disease. Echocardiography represents a useful diagnostic tool in such cases. Even though the association is not common, consideration of VGAM in a newborn with PPHN refractory to treatment may help with early diagnosis, which can in turn guide management strategies and improve outcomes.

ABBREVIATIONS:

- CS - Caesarean section
- MRI- magnetic resonance imaging
- MV - mechanical ventilation
- PPHN - neonatal persistent pulmonary hypertension
- US - ultrasound
- UTI - urinary tract infection
- VGAM - vein of Galen aneurysmal malformations

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