

Prenatal Diagnosis of Vein of Galen Aneurysmal Malformation with Color Doppler Ultrasonography – Report of Three Consecutive Cases and Review of the Literature

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2. Key words

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1. Abstract

1.1. Background and Purpose: Vein of Galen aneurysmal malformation (VGAM) is a rare, congenital condition consisting of pathological arteriovenous connections within the fetal brain which can prenatally lead to cardiomegaly and severe onset of congestive heart failure. Doppler ultrasound examination is sufficient to confirm the diagnosis and to determine the time of delivery and the prognosis. The aim of this paper is to discuss the pathophysiology and indicators of poor prognosis in the VGAM patients as well as to outline the crucial role of prenatal diagnosis in terms of planning the treatment after delivery.

1.2. Method: Case presentation. This work presents three cases of ultrasonographic prenatal diagnosis of vein of Galen aneurysmal malformation. Fetuses' hemodynamic status was subsequently carefully monitored by serial Doppler ultrasound and echocardiographic examinations.

1.3. Results: All babies were delivered by caesarean section. Two of the presented babies, prenatally diagnosed with heart compromise and tricuspid regurgitation died in the neonatal period due to circulatory failure. First one was disqualified from neurosurgical embolization and died in the 12th day of life due to circulatory insufficiency. Second underwent unsuccessful two-stage neurosurgical embolization and died in the 38th day of life in the cardiac arrest mechanism. The neonate, in whom ultrasound parameters before delivery were most favorable, was hemodynamically stable after birth. Infant underwent successful two-stage neurosurgical embolization and develops adequately in line with its age.

1.4. Conclusions: Presented cases confirm that prenatal heart insufficiency and the presence of tricuspid regurgitation (TR) to be important indicators of poor prognosis.

3. Introduction

Vein of Galen aneurysmal malformation (VGAM) is a unique intracranial condition with the incidence of 1% among all the intracranial vascular malformations [1]. Although rare, VGAM constitutes around 30% to 60% of arteriovenous malformations of childhood and infancy [2]. Anatomically VGAM is a bundle of arteriovenous shunts draining into the persistent embryonic median prosencephalic vein (MProSV), known as vein of Markowski. Malformation develops between 8th and 11th week of gestation and was primarily described (and falsely recognized as the vein of Galen) by Raybaud and Strother in 1986 [3].

Clinical implications antenatally consists predominantly of non-

immune hydrops, hydrocephalus, intracranial hemorrhage, hepatosplenomegaly, ascites, polyhydramnios, tricuspid regurgitation and cardiomegaly with congestive heart failure [1, 5-6].

Crucial facilitation of the prenatal diagnosis has been enabled by the widespread use of Doppler sonography with color flow imaging. Diagnosis of the VGAM can be done by visualizing a turbulent flow as vein of Galen aneurysmal malformation is the only cystic structure presented in the midline of the brain that shows a blood flow within it [1]. Before the onset of ultrasound examination the diagnosis was done principally, namely in 85% of the cases, by the means of postmortem examination [4]. Antenatal MRI is not necessary to confirm the diagnosis of VGAM. Notwithstanding, after

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delivery, it can provide vital information in terms of neurosurgical treatment being three dimensional visualization of the malformation with the exact data concerning the anatomy of the shunts and the eventual presence of the thrombosis within the lesion [5].

In this paper we present three cases of prenatal diagnosis of vein of Galen aneurysm and discuss the role of prenatal Doppler ultrasonography as well as fetal echocardiography in the prediction of prognosis.

4. Case Report 1

A prenatally diagnosed 33-year old gravida 3 para 3 was referred to our unit at 37 weeks gestation for fetal evaluation. Mother's medical and obstetrical history were unremarkable.

On ultrasound examination done shortly after admission to the unit we found a singleton fetus in cephalic presentation with supratentorial cystic structure located posterior to the third ventricle. Pulsed Doppler examination demonstrated a high velocity venous flow within the lesion. Additionally, cardiomegaly with heart-to-thorax ratio (Ha/Ca) of 0,55 and tricuspid regurgitation of 3m/s were revealed. All biometric parameters were in the norm for 37th week of gestation. Fetal middle cerebral artery pulsatility index (MCA PI) and umbilical artery pulsatility index (UA PI) were pathological, 0,62 and 1,02 respectively, which suggested centralisation of blood flow to the brain. Moreover, Doppler examination of ductus venosus (DV) showed absence of the A-wave which is considered to be a marker of cardiac deterioration. Promptly after, to enhance pulmonary maturation, corticosteroids were administered and two days later, at 37 weeks gestation, by elective caesarean section a 3130g female baby was born. Apgar scores were 10 and 10 at 1st and 5th minutes respectively. Directly after delivery, infant was cardiovascularly stable and did not require additional medical interventions.

During hospitalization echocardiographic examination was performed and severe symptoms of steal phenomenon from systemic circulation with right to left flow through ductus arteriosus was visualised and hiperkinetic circulation with signs of substantial right heart volume overload were identified. Nevertheless infant did not require inotropic agents. Additionally, in abdominal ultrasound examination widening of hepatic vessels was reported. Transfontanellar ultrasonography depicted large 24x26x18 mm aneurysmal malformation of vein of Galen and pathological image of brain hemispheres with abnormal echogenicity of white matter and narrowing of pallium. VGAM was the cause of mass effect and lateral ventricles displacement. In the 2nd day of life neonate was discharged in a stable condition and transferred to the reference hospital. In transfontanellar ultrasonography atrophy of the hemispheres was confirmed and MRI reported lack of normal cerebral parenchyma and pathological, blurred, hypoechogenic hemispheres;

only the cerebellum seemed to be normal. Unfortunately, due to significant central nervous system damage, girl was disqualified from the neurosurgical embolization of vein of Galen aneurysmal malformation. Infant died in 12th day of life due to circulatory failure.

5. Case Report 2

A 26-year-old primigravida was admitted to our unit at 35th week of gestation with the diagnosis of vein of Galen aneurysmal malformation, cardiomegaly, ascites and right pleural effusion in the fetus.

Ultrasound examination showed a singleton fetus in cephalic presentation with 25,5mm x 19,9mm cystic lesion located in the midline of fetal brain connected to dilated to 9mm straight sinus. Two feeding vessels ejecting from posterior cerebral arteries were visualised. Additionally, signs of steal phenomenon from anterior part of circle of Willis and low-resistance waveforms in both posterior cerebral arteries were depicted. All the biometric parameters were normal. MCA PI was 2,25. The ductus venosus pulsatility index (DV PI) was increased (1,26); UA PI was in the normal range (1,17). Echocardiography revealed numerous accompanying cardio-vascular pathologies, namely: cardiomegaly with Ha/Ca ratio of 0,46, 3rd degree holosystolic TR of 3,61m/s and mild mitral regurgitation, right ventricle overload, distention to 8mm of vena cava superior and reversed flow in the aortic arch. Due to diagnosis of fetal heart insufficiency, corticosteroids were administered to enhance pulmonary maturation and three days later caesarean section was performed. A 2100g premature female baby was born with Apgar scores of 6 in the 1st minute, 7 in the 3rd minute and 8 in the 5th and 10th minutes.

Directly after delivery, as a result of respiratory and cardiac failure, newborn required resuscitation and intubation. In the 1st day of life infant developed high output cardiac failure which was treated by the means of catecholamines and milrinone. In the physical examination child presented enlarged abdomen, peripheral edema and jugular vein distention. Because of right pleural effusion thoracentesis was performed. Shortly after, diagnosis of pulmonary hypertension was made. Due to anemia, in the 4th day of life neonate required red blood cells transfusion. In 7th day of life neonate was transferred to the Neonatal Intensive Care Unit in the reference hospital.

During further hospitalisation infant's condition was severe. Chest and abdomen X-ray performed shortly after admission reported cardiomegaly with Ha/Ca ratio of 0,66 and atelectasis of upper lobe of the right lung. Echocardiographic examination showed enlarged right ventricle and atrium, 3rd degree tricuspid regurgitation with regurgitant velocity of 4,0-4,2 m/s, pulmonary regurgitation, reversed flow in the aortic arch and pulsatile flow in the abdominal

aorta with reversed diastolic blood flow. Transfontanellar ultrasonography showed VGAM with maximal dimensions of 22,5 x 23 x 33mm and confirmed its connection to straight sinus. Left choroid plexus and left lateral ventricle were compressed by the malformation. In the 8th day of life 1st stage of neurosurgical embolisation of VGAM was performed. During procedure three from six major fistulas were successfully coiled. After intervention, infant was in severe condition and showed no signs of haemodynamic improvement. Postoperative transfontanellar ultrasonography reported VGAM of similar to preoperative dimensions with outflow to distended to 11mm straight sinus. In the following days increasing symptoms of heart and circulatory failure were observed. Echocardiography confirmed aforementioned pathologies however the severity of tricuspid regurgitation diminished from 3rd to 2nd degree with regurgitant velocity of 3,6m/s. Additional findings encompassed severe distention of vena cava superior, distention of pulmonary trunk and pulmonary arteries, right-to-left flow in the area of foramen ovale and patent ductus arteriosus with bidirectional flow. Newborn showed also symptoms of severe multiorgan failure with renal insufficiency, bowel and liver ischaemia, pulmonary congestion and respiratory acidosis. In 15th day of life infant underwent high-risk 2nd stage neurosurgical embolisation of VGAM. Two fistulas were effectively coiled, nevertheless embolisation of one remaining fistula was unsuccessful due to large vessel diameter and hyperkinetic blood flow within it. Transfontanellar ultrasonographic examination and echocardiographic assessment reported no signs of haemodynamic condition improvement. Serious perioperative complications consisting of intraventricular haemorrhage and active hydrocephalus with frontal horns of the lateral ventricles distention to 16-17mm required external ventricular drainage implementation. In echocardiography 2nd degree tricuspid regurgitation persisted with regurgitant velocity increasing to 4,2m/s and regurgitant blood flow reaching dilated coronary sinus. Additionally, flow through foramen ovale became bidirectional. Rest of the parameters were similar to previous examinations. In the following days infant suffered from intestinal ischemia, hepatic insufficiency and frequent episodes of desaturation, needed multiple blood and cryoprecipitate transfusions due to coagulopathy (bleeding from urinary and respiratory tract, intraventricular haemorrhage, bleeding from injection sites). Throughout hospitalization newborn required intensive care management (mechanical ventilation, parenteral nutrition). Child died in the 38th day of life in cardiac arrest mechanism.

6. Case Report 3

A 27-year old primigravida with undistinguished medical history presented at 39th week of gestation at the obstetric emergency ward due to prelabour rupture of membranes. The diagnosis of vein of Galen aneurysmal malformation was done outside our unit. An

ultrasound and echocardiographic examination showed a singleton fetus in cephalic presentation with anechoic intracranial 19mm x 24mm lesion situated in the midline of the brain with turbulent blood flow observed in color Doppler ultrasound. Furthermore, cardiomegaly with Ha/Ca ratio of 0,39 was detected. There were no signs of tricuspid regurgitation and structural heart anomalies. All biometric parameters were in the norm for 39th week of pregnancy. Fetal MCA PI and UA PI were normal, 1,62 and 0,75 respectively. Additionally, DV PI was 0,9 and reduced A-wave was identified.

Due to clinically apparent labour contractions which appeared shortly after the admission to the unit, caesarean section was performed. A 3540g female baby was born with an Apgar scores of 10 in the 1st minute and 10 in the 5th minute. Directly after delivery, newborn did not require additional medical interventions. In view of stable condition, neonate was discharged in 6th day of life and transferred to the reference hospital in order to plan the neurosurgical treatment.

In the reference hospital chest X-ray revealed cardiomegaly with Ha/Ca ratio of 0,67 and increased pulmonary blood flow. MRI depicted vein of Galen aneurysmal malformation with maximal dimension of 17mm and causing mild compression as well as downward displacement of vermis of cerebellum. In the 15th day of life infant underwent 1st stage neurosurgical embolisation of VGAM. Postoperative course was uneventful. 2nd stage was originally planned in the 3rd month of life, however was postponed due to viral infection of the neonate. During 2nd hospitalisation in the 7th month of life in the chest X-ray no signs of cardiomegaly were identified; pulmonary blood flow was normal. Successful 2nd stage neurosurgical embolisation of VGAM was conducted. Postoperative course was uneventful and no further neurosurgical treatment is needed. So far child shows no developmental disorders. Control MRI is planned when the infant will be 1 year old.

7. Discussion

In the vast majority of cases the diagnosis of VGAM is made in the third trimester [7]. In two of the presented cases (Case Report (CR) 1 and 3) vein of Galen aneurysm was recognized between 36th and 39th week of gestation, in the Case Report 2 an early diagnosis around 20th week of gestation was made. Differential diagnosis encompass arachnoid cyst, porencephalic cyst, choroid plexus cyst, pineal tumor, intracerebral hematoma and choroid papilloma [8,10]. The most frequent associated anomalies are cardiomegaly, ventriculomegaly and enlarged neck vessels, described by Sepulveda et al. as a pathognomonic sign occurring in 32% of the VAGM patients [7]. In the presented cases, all fetuses suffered from cardiomegaly, none demonstrated enlarged neck vessels in the perinatal period, however one presented jugular vein distention shortly after delivery (CR 2). What is more, various structural cardiac anomalies can be asso-

ciated with the vein of Galen aneurysmal malformation. The most common being: sinus venosus atrial septal defect, coarctation of aorta, partial anomalous pulmonary venous connection, ventricular septal defect and atrioventricular canal [5,9]. Two of the fetuses from described cases (CR 1 and 2) suffered from tricuspid regurgitation which is not a structural heart disease nevertheless may be an important risk factor of unfavorable outcome [6].

Pathophysiology of the vein of Galen aneurysmal malformation is crucial to understand the dynamics of the disease and carefully plan the delivery warranting best possible outcome. Numerous arteriovenous shunts implicate severe hemodynamic changes in fetal cardiovascular system which are often associated by pathologies of central nervous system. What is more, brain infarcts and leukomalacia may occur, mainly due to compression of the cerebral cortex by dilated aneurysm and to diversion of blood from parenchyma to arteriovenous malformation, known as steal phenomenon [10]. Dilated aneurysm may also cause the obstruction of aqueduct of Sylvius and subsequently hydrocephalus [10]. Another possible cause of hydrocephalus is impaired reabsorption of cerebrospinal fluid by virtue of increased cerebral venous pressure [13]. Furthermore, large aneurysm of vein of Galen can create a mass effect and result in displacement of lateral ventricles. After birth, one infant (CR 1) suffered from lateral ventricles displacement as a result of mass effect created by VGAM. Another child (CR 2) suffered from postoperative hydrocephalus with asymmetry of ventricular system due to VGAM compression and required external ventricular drainage implementation.

As far as hemodynamic changes are concerned, steal phenomenon is the cause of considerably increased cardiac preload which can lead to congestive heart failure and nonimmune hydrops. Moreover, myocardial ischaemia and heart insufficiency may occur due to reduction of coronary artery flow caused by the diastolic steal to VGAM and shortened diastole due to tachycardia [12]. Generally, fetus hemodynamic status is well compensated in the perinatal period because of low resistance of placental vascular area and often cardiomegaly is the only sign of cardiac insufficiency. Nevertheless, shortly after delivery when systemic vascular resistance increases, high-output cardiac failure may ensue [10]. All of the fetuses presented cardiomegaly, but only one (CR 2) was diagnosed with fetal heart insufficiency which is considered to be an important risk factor of unfavorable outcome [11]. Additionally, fetus with prenatal cardiac insufficiency (CR 2) presented reversed flow in the aortic arch which was the result of steal phenomenon caused by VGAM. Haemodynamic condition of this neonate was serious from the first minutes after birth with severe symptoms of steal phenomenon from systemic circulation. Subsequently, infant required catecholamines, nonetheless heart and circulatory function deteriorated. This case confirms that antenatal diagnosis of heart insufficiency

is correlated with poor postnatal outcome. Also, after delivery, fetus with cardiomegaly and accompanying tricuspid regurgitation (CR 1) developed high-output cardiac failure and presented severe symptoms of steal phenomenon from systemic circulation. In comparison, fetus with cardiomegaly without accompanying tricuspid regurgitation (CR 3) presented symptoms of right heart volume overload and subsequently was diagnosed with compensated heart failure.

Numerous authors try to identify the indicators of poor prognosis. Has et al. outline anatomical brain lesions and hydrops as correlated with the most unfavorable prognosis [10]. Gailloud et al. correlate prenatal brain atrophy and prenatal cardiac insufficiency as markers of bad prognosis [11]. Paladini et al. in their retrospective analysis of 49 prenatally diagnosed VGAM patients define three parameters associated with poor neonatal outcome; these are major brain lesions, tricuspid regurgitation and less significantly a VGAM volume $\geq 20\,000\text{mm}^3$ [6]. It is worth outlining that the occurrence of tricuspid regurgitation is an independent risk factor of the associated brain changes and VGAM volume $\geq 40\,000\text{mm}^3$ may denote a prenatal progression of the malformation [6]. The demise of two of the presented newborns (CR 1 and 2) may confirm the fact that the prenatal occurrence of tricuspid regurgitation as well as prenatal diagnosis of heart insufficiency are indicators of poor prognosis. Neonate suffering from tricuspid regurgitation without prenatal heart failure (CR 1) presented more severe cardiac problems in comparison to the neonate without tricuspid regurgitation (CR 3) and was eventually disqualified from operative treatment. Eventually child died from circulatory insufficiency. Infant diagnosed with tricuspid regurgitation as well as prenatal heart failure (CR 2) died despite two neurosurgical embolisations of VGAM. As for recommended time of delivery, in the cases of substantial VGAM volume early term delivery at 37 gestational weeks' should be considered [6]. Occurrence of another risk factors outlined by Paladini et al., namely TR or major brain lesions, do not influence the time of recommended delivery, which shall be at term [6]. However, there could be another accompanying pathologies influencing the time of birth. In the first of the presented cases (CR 1), the occurrence of pathological Doppler findings in MCA and UA lead to the decision of elective caesarean section in the 37th week of gestation. In the second case (CR 2), fetal heart insufficiency lead to the decision of preterm elective caesarean section. Neonate was born in severe condition and required resuscitation in the operating room. In the third case (CR 3), labour contractions occurred in the 39th week of gestation and caesarean section was subsequently conducted. The first and the third neonate were born in a good condition. Diagnosis and prenatal monitoring of VGAM can be conducted with Doppler ultrasound examination which is cheap and widely accessible method in the terms of fetus serial monitoring.

For the neonates with pharmacologically resistant high output cardiac failure invasive treatment might be crucial; early endovascular embolisation is a treatment of choice [5, 10]. In the Case Report 2, neonate diagnosed with prenatal heart insufficiency was haemodynamically unstable after birth and required high doses of catecholamines and milrinone. Infant underwent early 2-stage endovascular embolisation, however vessel diameter and hyperkinetic blood flow within the lesion precluded closure of all arteriovenous shunts which probably have been a cause of circulatory failure and child's demise. Albeit, if heart function can be optimized, Jones et al. suggest the delay of the embolization for several months [15]. In the Case Report 3, 2nd stage of the embolisation could be delayed as haemodynamic condition of the neonate significantly improved after 1st stage of neurosurgical treatment. Both interventions were successful, with uneventful postoperative course and improvement of haemodynamic status.

Besides, it is worth remembering that in the cases of unexplained cardiac failure in the neonates in their first week of life, vein of Galen aneurysmal malformation should always be taken into consideration to guarantee fast and effective treatment as well as reduction of mortality [15].

8. Conclusions

Presented cases confirm that prenatal heart insufficiency and presence of tricuspid regurgitation are important indicators of unfavorable outcome with TR being the most crucial factor. The infant who underwent successful neurosurgical treatment and develops adequately in line with his age did not suffer from neither prenatal nor postnatal tricuspid regurgitation. Also, early prenatal diagnosis, careful evaluation of indicators of poor prognosis and serial monitoring of VGAM patients by means of Doppler ultrasound examination create the opportunity to carefully plan the most appropriate term of the delivery at a tertiary centre where experienced teams of obstetricians as well as neonatologists, pediatric neurologists, pediatric cardiologists and pediatric neurosurgeons can ensure the highest level of medical care and the best possible outcome.

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