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Research paper

Prognosis for newborns with vein of Galen malformation diagnosed prenatally based on a new scale

Maria Respondek-Liberska, Maciej Słodki

Department of Prenatal Cardiology, Polish Mother's Memorial Hospital Research Institute in Lodz, Poland

Abstract

Introduction: Vein of Galen malformation occurs rarely and accounts for 1% of intracranial vascular abnormalities, and they usually have poor outcome. Therefore, we focused on the prenatal features that might suggest favourable prognosis.

Material and methods: We analysed fetal echocardiograms and neonatal management from 10 fetuses with diagnosis of vein Galen malformations.

Results: The size of Galen malformation was mean 35 mm ×19 mm. Five fetuses had transplacental digoxin treatment. Cardiovascular profile score (CVPS) at the initial evaluation was mean 6 ±2, the minimum value was 4, and the maximum value was 10. Cardiovascular profile score at the last evaluation was mean 7.3 ±2.4, but an increase was seen only in two survivors (the third survivor had only one echo examination and did not undergo transplacental treatment). There were two intrauterine demises and eight pregnancies with live born newborns. Mean gestational time of delivery for live born newborns was in the 37th week. There were four neonatal deaths on days 1, 2, and 3 before attempted neurosurgery. Three newborns had neurosurgery procedures on day 3 (two newborns) and on day 7 (one newborn). The last one died on day 27. Based on our prenatal data we suggested a new scale to predict a prognosis for newborns with vein of Galen malformation.

Conclusions: Prenatal detection of Galen aneurysm, CVPS of seven or more before birth, transfer in utero, delivery at term, and earliest possible neurosurgical treatment might be beneficial and change the poor natural outcome known from the past in these cases. Good cooperation between members of the perinatology team might be crucial for saving lives in prenatally diagnosed AVGM.

Corresponding author:
Prof. Maria Respondek-Liberska
Department of Prenatal Cardiology
Polish Mother's Memorial Hospital Research Institute
281/289 Rzgowska
93-338 Lodz, Poland
e-mail: maria.respondek-liberska@uni.lodz.pl

Introduction

Vein of Galen malformation (VGM) occurs rarely and accounts for 1% of intracranial vascular abnormalities. It is the most common prenatal cerebral arteriovenous malformation. To date, there have been many publications about prenatal diagnoses of VGM, usually with poor outcome [1–5]. Therefore, we focused on the prenatal features that might suggest favourable prognosis.

Material and methods

We analysed fetal echocardiograms from 10 fetuses with diagnosis of VGM from our database collected from 1996 to 2017 (Table 1). They had 21 fetal echocardiographic exami-

Table 1. Clinical data and US data of 10 fetuses with Galen malformations

Case	Year of exam	Maternal age	Medical history	Low risk pregnancy	Gest age Based on LMP	Gest age based on biometry	AFI	Size of Galen (mm)	Ventriculomegy (mm)
1	1996	23	1st pregnancy	Yes	32	33	26	30 × 25	No
2	1999	31	3rd pregnancy: 1st pregnancy boy with TOF, 2nd pregnancy healthy girl		29	31	30	40 × 30	7
3	2000	27	1st pregnancy	Yes	33	34	14	47 × 16	No
4	2003	25	1st pregnancy	Yes	38	39	16	36 × 16	No
5	2006	22	1st pregnancy	Yes	27	29	24	30 × 15	
6	2007	25	2nd pregnancy, 1st miscar.		37	37	27	32 × 17	4
7	2016	24	2nd pregnancy, 1st miscar.		39	39	20	37 × 18	
8	2017	25	1st pregnancy	Yes	30	30	27	31 × 19	
9	2017	25	2nd pregnancy, 1st miscar.		28	29	15	29 × 17	16
10	2017	35	2nd pregnancy, 1st healthy boy	Yes	25	25	20	37 × 18	No
Mean		26.1			31.8	32.8	22.1	34.9 × 19.1	
SD		3.9			4.8	4.3	8	5.4 × 4.4	

nations (from one to five per fetus). We compared: maternal age, medical history, gravidity age during diagnosis, amniotic fluid index (AFI), size of VGM in prenatal US, presence of ventriculomegaly, cardiovascular profile score, presence of ascites, pericardial effusion, fetal cardiomegaly measured by Ha/Ca ratio, presence of tricuspid valve regurgitation, transplacental digoxin treatment and its timing, steroid for lung maturation, time of delivery, method of delivery, and time of the first neurosurgery procedure after delivery.

Results

Mean maternal age was 26.1 ±3.9 years (min. 22, max. 35), there were six low-risk pregnancies and four high-risk pregnancies, including three previous miscarriages, and in one family there was a previous pregnancy with congenital heart defect (tetralogy of Fallot). Nine out of 10 had normal NT measurement in the first trimester of pregnancy. There was one fetus with extracardiac malformation (no. 6), who also had a diaphragmatic hernia. Mean gestational age at the time of first targeted ultrasound and echocardiography examination in our centre was 31.8 ±4.8 weeks based on last menstrual period and 32.8 ±4.3 based on fetal biometry. The earliest gestational age was 25 weeks of pregnancy and the latest was 39. There were three fetuses diagnosed before 30 weeks of gestation and seven fetuses diagnosed later on. Mean amniotic fluid index was 22.1 ±8 (min. 15, max. 27). The size of Galen malformation was mean 35 mm × 19 mm (the smallest single diameter was 15 mm and the largest single diameter was 47 mm). Three fetuses had dilatation of ventricles (4–7 mm), including one with posterior horn up to 16 mm.

Selected echocardiographic data of 10 fetuses with Galen malformations are presented in Table 2. Eight out of 10 fetuses

Table 2. Selected echocardiography data of 10 fetuses with Galen malformations and their outcome

Case	Ha/Ca	TR (m/s)	Oedema, ascites	PE	CVPS (first)	CVPS (last)	Digoxin	Time of treatment
1	0.5	2.1	Yes	Yes	7	8	Yes	4 weeks
2	0.6	2.3	Yes	Yes	4	4	No	–
3	0.55	3	Yes		4	4	Yes	3 weeks
4	0.6	2.5	Yes	Yes	4	4	No	–
5	0.5	2	Yes	Yes	4	4	No	–
6	0.4	1.5	No	No	9	9	No	–
7	0.5	No	No	No	7		No	–
8	0.5	2.5	No	Yes	7	8	Yes	5 weeks
9	0.4	No	No	No	10	10	Yes	6 weeks
10	0.6	2	Yes	Yes	4	4	Yes	3 weeks
Mean	0.5				6	7.3		
SD	0.07				2	2.4		

Table 3. Delivery and neonatal data and follow-up

Case	IUD	CS	Gest week	Gender	Birth weight	Apgar score	Demise after birth	Demise after surgery	Alive & well
1		CS	38	F	3600	7			1
2	Yes (32nd week)	V		F					
3		CS	37	M	3500	9/9	Yes		
4		CS	38	F	3350	6	Yes		
5	Yes (29th week)	V		M					
6		V	36	M	3000	4	Yes		
7		CS	38	M	2929	10			1*
8		CS	38	M	3500	9			1*
9		CS	36	F	2950	8		1	
10		CS	36	M	2290	3	Yes		
Mean			37		3139				
SD			0.9		437				

**First embolisation on day 3.*

had cardiomegaly: Ha/Ca 0.5–0.6. Two fetuses had Ha/Ca 0.4. Eight out of 10 presented functional tricuspid valve insufficiency (1.5 m/s to 3 m/s). Five fetuses had oedema or ascites and six fetuses had pericardial effusion > 3 mm. Cardiovascular profile score (CVPS) at the initial evaluation was mean 6 ±2, the minimum value was 4, and the maximum value was 10. CVPS at the last evaluation was mean 7.3 ±2.4, but an increase was seen only in two survivors (the third survivor had only one echo examination and did not undergo transplacental treatment).

Five fetuses had transplacental digoxin treatment based on standard protocol in our institution (two days i.v. 0.25 mg every eight hours and then orally 2–3 times daily with serum digoxin level monitoring). In three pregnancies the duration of transplacental digoxin treatment was at least four weeks.

Neonatal follow-up is presented in Table 3 and Figure 1. There were two intrauterine deaths and eight pregnancies with live born newborns: seven caesarean sections and three vaginal deliveries. Mean gestational age at the time of delivery for live born newborns was 37 weeks. There were six males and four females, mean birth weight was 3139 ±437 g (min. 2290 g, max. 3600 g), and mean Apgar score was 7 ±2 (min. 3, max. 10). There were four neonatal deaths on day 1, 2, and 3 before attempted neurosurgery. Three newborns had neurosurgery procedures on day 3 (two newborns) and on day 7 (one newborn). The last one died on day 27.

The two survivors had a total of seven procedures of pathologic brain vessel closing, and each of them spent more than two months in the hospital. We observed also a newborn (case no. 1) who was in congestive heart failure in our intensive care unit for more than three weeks, later with gradually improvement, and discharged from the hospital after six weeks, who later had abnormal platelet number (700,000–900,000/ml), and at the age of three months a transfontanelle scan did not show any pathological flow or ventricle dilatation. She had normal paediatric check-up at the age of 12 months and at two years old.

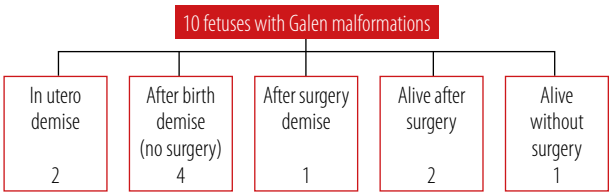

Figure 1. Follow-up of 10 fetuses with Galen malformations from our presented series of cases

Based on the analysed data from our series of patients as well as from publications, we created Table 4, which shows possible positive prenatal features for Galen vein aneurysmal malformation and good outcome.

Discussion

Vein of Galen malformation is a complex arteriovenous malformation, which is of multiply communications between of the vein of Galen and the cerebral arteries. It represents less than 1% of all cerebral arteriovenous malformations.

The first report of prenatal diagnosis of VGM was published in 1986 by Vintzileos, and five years later Evans (in 1991) reported the role of colour flow Doppler in Galen malformation [3, 4]. Usually detection of VGM takes place prenatally in the third trimester of pregnancy, but Hartung (2003) reported of such finding in the 22nd week of pregnancy, and Yukhayev in 2017 reported second trimester VGM before cardiac manifestation [5, 6]. Usually it comprises a hypoechogenic structure located in the midline of the brain, with turbulent flow in colour Doppler ultrasound. It is caused by the presence of arteriovenous fistulas directing blood flow toward the dilated, persistent proximal median prosencephalic vein. This abnormal flow prevents involution of the embryonic vein and subsequent development of the vein of Galen. Usually VGM causes volume overload of the heart, and fetal cardiomegaly or even congestive heart failure might be the first ultrasound abnormalities [5]. The current diagnosis in addition to ultrasound and Dop-

Table 4. Possible positive prenatal features for fetal Galen vein aneurysmal malformation and good outcome – survival based on presented series of 3 survivors (bold) and 7 non-survivors: positive outcome in score 8 ±1.4 points, negative outcome in score 5 ±2.8 points. Each feature present has one point

Case	Size of Galen < 4 cm	CVPS > 6	Ascites/ oedema	Ha/Ca < 0.6	Digoxin treatment	Time of transplacental digoxin treatment > 3 weeks	Delivery > 37 weeks	Caesarian section	Neurosurgery in first 3 days of life	Summary
1	**1**	**1**	**0**	**1**	**1**	**1**	**1**	**1**	**0**	**7**
2	0	0	0	0	0	0	0	0	0	0
3	0	0	0	0	1	0	0	1	0	2
4	1	0	0	0	0	0	1	1	0	3
5	1	0	0	1	0	0	0	0	0	2
6	1	1	1	1	0	0	0	0	0	4
7	**1**	**1**	**1**	**1**	**0**	**0**	**1**	**1**	**1**	**7**
8	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**1**	**9**
9	1	1	1	1	1	1	0	1	0	7
10	1	0	0	0	1	0	0	1	0	3

pler may include fetal MRI and 3D ultrasound. Most of the publications as case reports, but also series of cases, confirm that the outcome for fetuses with VGM is poor [1, 2].

Therefore, the aim of this analysis was to focus on prenatal and postnatal findings that might suggest a favourable outcome, which is rare. It might be important for future parents for whom termination of pregnancy is not a good option or late pregnancy termination is not possible due to legal aspects.

From neurosurgery publications, we can see that there is an increase in the number of survivors after introduction of the latest methods of treatment (arterial rather than venous access to endovascular therapy, coils, or adhesive substances) with good neurological development from 32% to 74% [1, 2, 7–9]; however, in these publications there is little information about prenatal assessment.

Based on our series of cases, the "positive" sonographic and echocardiographic features are presented in Table 4. These features sum up the team approach effect: fetal cardiology team, obstetrical team, in utero transfer, good cooperation with neonatology team, and early neurosurgery approach. This is like a well prepared and organised "team" in sports activities, and it seems to be a more reasonable approach compared with the analyses of Yuval et al. and Paladini et al. [2, 10]. These teams looked for in utero prognostic factors underlying prenatal ultrasonographic indices. The indices included mapping of intracranial feeding arteries, assessment of the width of the straight sinus, assessment and measurement of flow in the straight sinus, existence of 'steal' retrograde aortic flow, volume of the AVGM (on ultrasound and MRI), ventriculomegaly, and other major brain abnormalities. Also, Statile et al. and Godfrey et al. focused on cardiac findings suggesting an adverse outcome in cases of congestive heart failure [11, 12]. From our point of view, the prediction of neonatal outcome is more than high-output fetal cardiac state.

For the very first time in an analysed group of fetuses with VMG we indicate the value not only of third-trimester echocardiography but also of fetal echocardiography monitoring. The importance of "late" echocardiography was also stressed by us in other prenatal conditions such as unexpected newborns with HLHS, who had normal four-chamber and mediastinum view in midgestation [13].

Although fetal cardiac symptoms are usually bad indicators for prognosis, we report for the first time the value of transplacental digoxin treatment in these cases as early as possible and for as long as possible. Digoxin is usually well accepted by pregnant woman; it was proven in several other fetal cardiac conditions [14]. In this series of cases with AVGM an improvement in CVPS was seen in two survivors and no improvement was observed in non-survivors (Table 2). The numbers are small; however, in this unique group of fetuses it is worth mentioning the value of prenatal longitudinal observations by echocardiography.

It is important to notice that in our case from 1996, despite the presence of prenatal signs of cardiac insufficiency (Ha/Ca ratio 0.5, massive tricuspid valve regurgitation), a spontaneous cloth in the Galen vein was observed in early infancy, but with no need for neurosurgery. There are cases reports about spontaneous cloth in VGM during fetal life as well as in postnatal life [15, 16].

Neonatal and paediatric neurosurgery are also evolving all the time, and, as shown by experience from Toronto, neonatal VGMs can be treated successfully with a strategic approach integrating antenatal diagnosis, endovascular surgery, treatment at intensive care facilities, and the cooperative efforts of different specialties [17].

Based on the presented data we believe that neurosurgery in neonates with VGM should be performed as early as possible; however, in babies delivered in term, such a strategy might be beneficial, as was shown in two of our cases; this was also stressed by others [18–20]. It is worth stressing the beneficial role of prenatal diagnosis to reduce the time for postnatal treatment, which is in contrast to the recommendation from 20–25 years ago.

In this analysis we focused on survival in the presence of prenatal cardiac insufficiency and brain ventricular chamber dilatation. We did not analyse prenatal or postnatal MRI, and we did not focus on possible additional brain abnormalities such as ventriculomegaly, hydrocephaly, polymicrogyria, cortical thickening, porencephaly, schizencephaly, periventricular leukomalacia, or intracerebral haemorrhage. All these problems were mentioned in a publication by Deloison et al., which reported a series of 22 fetuses with AVGM and only three cases with good outcome [1]. Therefore, our data (Table 4) and conclusions might add a new green light for the medical society regarding this nightmare condition.

Conclusions

Prenatal detection of VGM, CVPS of seven or more before birth, transfer in utero, delivery at term, and earliest possible neurosurgical treatment might be beneficial and change the poor natural outcome known from the past in these cases. Good cooperation between members of the perinatology team might be crucial for saving lives in prenatally diagnosed AVGM.

Conflict of interest

The authors declare no conflict of interest.

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Division of work:
Maria Respondek-Liberska (ORCID: 0000-0003-0238-2172): research concept and design, collection and/or assembly of data, data analysis and interpretation, writing the article, critical revision of the article, final approval of article
Maciej Słodki (ORCID: 0000-0002-0160-8013): data analysis and interpretation, writing the article, critical revision of the article, final approval of article