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Ductus venosus agenesis – significance, impact and management

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ABSTRACT

Introduction. The ductus venosus is a intrahepatic venous connection between the left portal vein and inferior vena cava in the fetus. Regarding agenesis of the ductus venosus (DVA) real incidence in not known.
Material and methods. In high-risk population its prevalence is reported as up to 1 in 2500 cases. Approximatively 20% of DVA may be asymptomatic. Cardiac, extracardiac and chromosomal anomalies may be associated. We conducted a review analyzing a total of 7 studies and a total of 151 cases of pregnancies with DVA.
Results. 19.2% cases were isolated incidental findings with no other anomalies associated. Overall adverse outcome was identified in 74 cases, mostly due to chromosomal anomalies, multiple malformations, and cardiac anomalies. For 40 of these cases termination of pregnancy was recommended. Although 104 of pregnancies reached postpartum life, death occurred in 19 cases after birth.
Conclusions. In cases with isolated DVA discovery, the prognosis is favorable, thereby counseling should be reassuring. However, a careful assessment of the umbilical vein connections and a careful second trimester screening for cardiac and extracardiac anomalies should be performed.

Keywords: ductus venosus agenesis, prenatal ultrasound screening

INTRODUCTION

The ductus venosus Arantii (DV) is a fetal intrahepatic venous shunt connecting the left portal vein and the inferior vena cava or the left or middle hepatic vein. Its main purpose is the prenatal transport of umbilical vein blood (rich in oxygen) to the right atrium. The blood flows through the umbilical vein to the recessus umbilicalis of the left portal vein, which is connected to the DV (1). Some days after birth, the DV and umbilical vein are initially still patent and recognizable in a slightly left sagittal view using ultrasound examination. In full-term neonates, DV closes according to literature after 7 days in 60-75% of cases and after 18 days in 89-100 %. In premature neonates it would seem that DV closes with a slight delay (2,3).

The real incidence is not known, given there is no exact data regarding ductus venosus agenesis (DVA). In high-risk population after first trimester screening, the prevalence has been reported from 1:500 up to 1:2500 (4). DVA can be asymptomatic in approximatively 20% of cases, having good progno-

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sis and outcomes. DVA may be associated with multiple other pathological findings which include chromosomal anomalies, various cardiac defects, porto-caval shunts or agenesis of the portal vein (5). The possible consequences include fetal heart failure, fetal hydrops, outlining a poor prognosis including prenatal mortality or iatrogenic termination of the pregnancy.

In the cases of DVA, abnormalities of the vascular system are frequently associated, being used by the umbilical cord blood to reach the fetal systemic circulation. The umbilical vein may connect itself directly with the intrahepatic inferior vena cava and not with the portal vein's left branch. Apart from this, intrahepatic or extrahepatic portosystemic shunts may occur. Regardless of DV, congenital portosystemic shunts are reported at 1:30000 births (6).The prognosis in isolated cases of DVA is not very well known, current counseling being based on relatively small case series (5).

Currently ISUOG practice guidelines do not recommend the screening for DVA in the first trimester (11-13^{+6}weeks of gestation) ultrasound screening. Fetal Medicine Foundation recomand the DV examination to be reserved for the 15% intermediate risk population (between 1 in 51 and 1 in 1000) after combined testing (Figure 1).

Although at the mid-trimester ultrasound screening (18-22 weeks of gestation), the examination of the cord vessels is recommended, this exam does not extend to the exploration of DV (7,8).

We conducted a review including various small case series published in the literature focusing on the implications of ductus venosus agenesis in the fetal and neonatal evolution, and suggested management options of the authors.

MATERIAL AND METHODS

By analyzing Uptodate, Pubmed and Medscape databases, we conducted a systematic literature review of case reports or case series reports of ductus venosus agenesis and its screening methods, associated pathological findings (either prenatal or postpartum), management options, and outcomes of the pregnancies.

We selected 7 studies from literature published between 1998 and 2019 with a cumulative number of 151 cases of pregnancies with DVA, including isolated DVA, as well as pregnancies with chromosomal anomalies, genetic syndromes, cardiac or extracardiac anomalies, or those with multiple malformations. Given the fact that currently there is no medical practice guideline regarding the screening for DVA, we have taken into consideration all pregnancies regardless of their gestational age at the ultrasound diagnostic. We have also included any invasive testing such as amniocentesis followed by karyotyping for the suspected anomalies associated.

RESULTS

Out of 151 pregnancies with DVA (Table 1), 29 (19.2%) cases were isolated incidental findings with no other anomalies associated, but in one of these cases neonatal death occurred.

Overall adverse outcome was identified in 74 cases (49%), mostly due to chromosomal anomalies, multiple malformations, cardiac anomalies. Among these 74 cases, for 40 of them (26.49%) termination of pregnancy was opted. Although 104 of pregnancies reached postpartum life (68.87%), death occurred in 19 cases (12.58%) after birth.

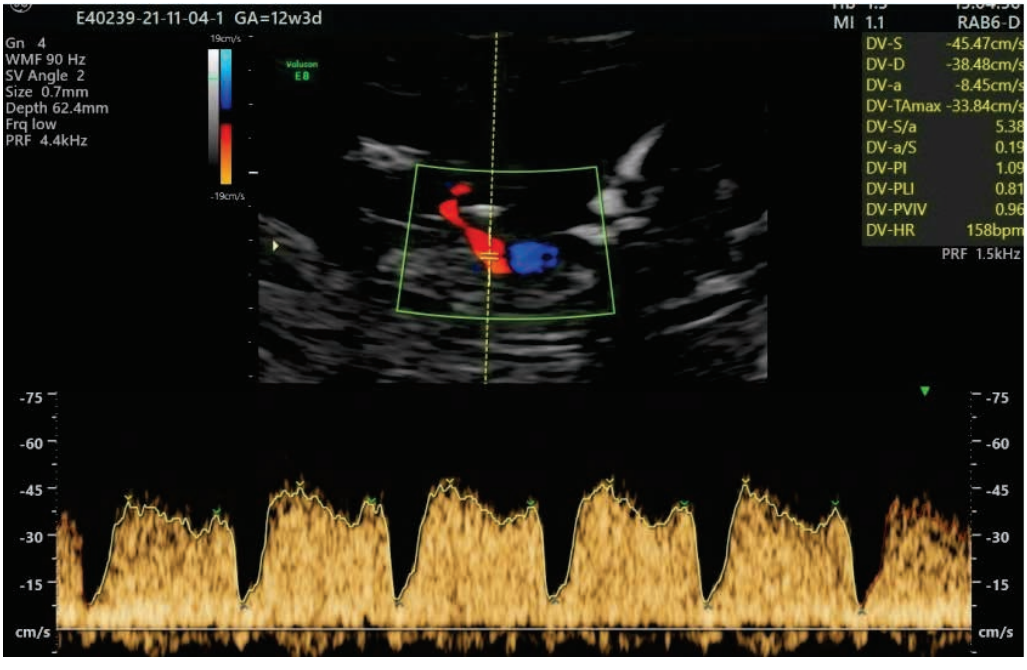

FIGURE 1. Ductus venosus flow with normal positive a-wave during first trimester screening (personal collection of Roxana Bohiltea)

TABLE 1. Patient distribution, gestational week at diagnosis and outcome, according to the studied references

AUTHORS	No. of cases	Isolated DVA (no.)	Associated conditions (no.)	GA at screening (weeks)	Outcome
Strizek et al. (5)	**119**	**24**	**95**	**11-37**	**31 TOP, 5 IUFD, 10 NND, 3 ICD, 70 survived**
Iliescu et al. (9)	**11**	**2**	**9**	**11-16**	**7 TOP, 1 ICD, 3 survived**
Contratti et al. (10)	**10**	**2**	**8**	**21-31**	**1 TOP, 1 IUFD, 1 NND, 1 LTF, 1 ICD, 5 survived**
Maruotti et al. (11)	**6**	**-**	**6**	**15-35**	**2 NND, 4 survived**
Gembruch et al. (12)	**2**	**1**	**1**	**19-36**	**2 survived**
Warner et al. (13)	**2**	**-**	**2**	**20-23**	**1 ICD, 1 survived**
Alcalde et al. (14)	**1**	**-**	**1**	**27**	**1 TOP**

TOP – termination of pregnancy; IUFD – intrauterine fetal death; NND – neonatal death; ICD – death in infancy or childhood; LTF – lost to follow-up

Several chromosomal abnormalities such as monosomy x, trisomy 21, trisomy 18, and additional ring chromosome have been revealed by the invasive tests with karyotype performed in some cases. A series of genetic syndromes was discovered in association with DVA such as Turner syndrome, Beckwith-Wiedemann syndrome, Dandy-Walker malformation, Pallister-Killian syndrome.

An important mention is that ultrasound diagnosis of DVA was performed mostly in the second or third trimester. Out of the selected studies, only one author, Iliescu et al. (9) considered as inclusion criteria first trimester diagnosis. In 94 cases intrahepatic umbilical vein drainage shunts were identified. In regard of the extrahepatic drainage shunts, the majority cases presented umbilical vein – inferior vena cava connections. Other connections described had been between umbilical vein and right atrium, iliac vein and renal vein.

The prognosis of DVA pathology is highly correlated with the type of abnormal venous circulation kindred to congenital malformations and/or chromosomal anomalies. Almost half of the cases were associated with congenital heart disease, with an important mention that more than 50% of the cases with extrahepatic drainage, either connections with inferior vena cava, either with the right atrium, presented cardiomegaly (11). Cardiomegaly in cases with intrahepatic drainage was seen only in association with other congenital anomallies (6,15).

Although our study gathers a relatively considerable cohort, a serious limitation concernig prenatal screenig must be taken into account. That is the lack of a homogenous, standardized protocol for ultrasound evaluation in first or mid trimester. Literature describes a strong association between DVA and large nuchal translucency, however, most of our cases have been diagnosed at the point of mid-trimester fetal ultrasonografic morphology screening or after (16,17). In spite of the fact that invasive testing was available, revealing chromosomal and/or genetic anomalies, an important limitation was the absences of anatomopathological informations for the cases either TOP or IUFD (5).

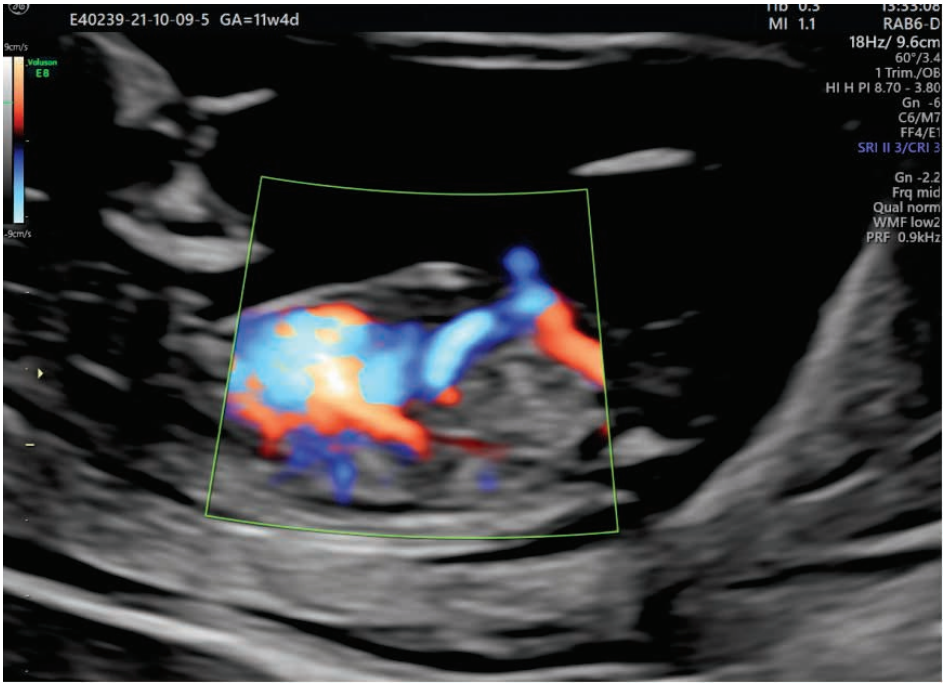

FIGURE 2. Absence of ductus venosus in color Doppler imaging (personal collection of Roxana Bohiltea)

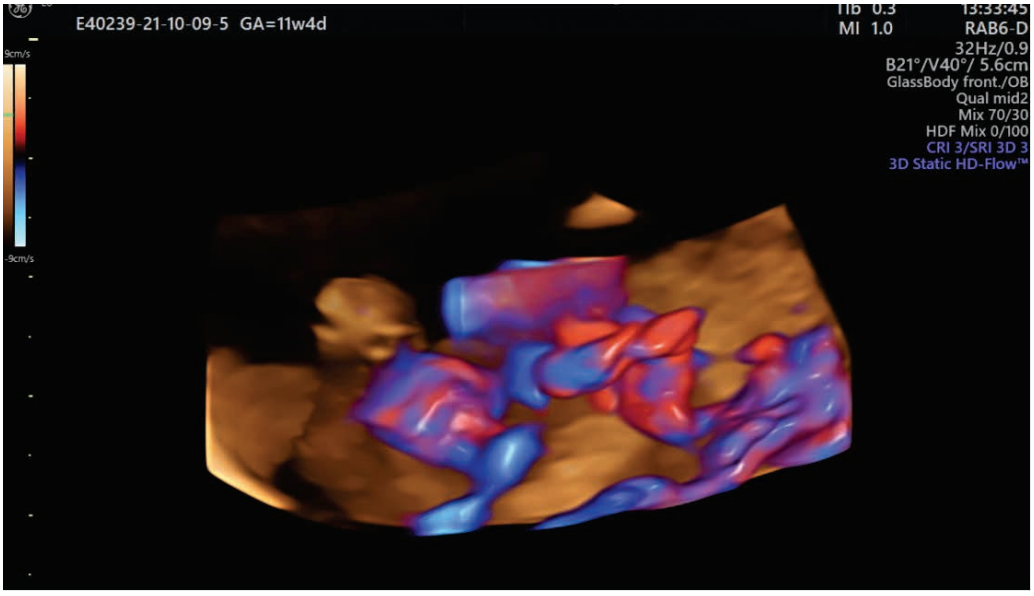

FIGURE 3. 3D static HD flow in DVA (personal collection of Roxana Bohiltea)

An issue to be stressed out is that apart from associated cardiac and extracardiac congenital anomalies, DVA may associate long therm complications related to intrauterine heart failure. Limited follow-up affects any definitive conclusions in regard to the long-term evolution of this rare congenital pathology (12). In regard of dellivery management there is no consensus, however, isolated DVA should not be a decisional criteria taken into consideration, spontaneus natural dellivery being a valid option. Cesarean section should be chosen in the case of associated malformations or any other abnormalities that threten the wellbeing of the fetal evollution (10,12).

Our experience consists in 5 cases of DVA that have been diagnosed during first trimester screening (Figures 2,3) and tested subsequently from genetical point of view, either by fetal DNA or microarray; all the results were negative for major chromosomal anomalies or monogenic syndromes, but in all the cases intrauterine growth restriction developed by the beginning of the third trimester.

CONCLUSIONS

In cases with isolated DVA discovery, the prognosis seems to be favorable, thereby counseling should be reassuring. However, taking into account that the overall adverse outcome for DVA is 49% of our included cases, the assessment of the ductus venosus should be consider as part of the routine ultrasound evaluation of the first trimester. We also consider mandatory that isolated DVA should be further assessed for the umbilical vein connections and a careful second trimester screening for cardiac and extracardiac anomalies should be performed. Invasive genetic testing should be limited for the cases of DVA associated with other findings.

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