Case Report

Current Opinion in Gynecology and Obstetrics Ductus Venosus Agenesis and Fetal Malformations: Report of Four Cases

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Abstract

Background: The agenesis of the ductus venosus (DVA) is a rare condition with a variable prognosis that relies partly on the presence of associated conditions. Therefore, the prenatal evaluation should include a careful examination of fetal circulation, particularly the umbilical and portal venous malformations.

Methods: In this study we describe four cases of DVA diagnosed at our institution. For each case, we access the patient's files in order to extract the following information: gestational age, umbilical vein connection, pre-natal imaging findings, gestational age at delivery or at pregnancy termination, fetal outcomes, post-natal imaging findings, post-mortem findings and karyotype.

Results: From the four cases included, two were diagnosed in the first trimester and the other two cases in the second trimester of gestation. Prenatal ultrasound studies revealed an intrahepatic shunt in one case and an extrahepatic shunt in three cases. In one case, the karyotype was not performed, whereas the other three had a normal karyotype. Cardiac anomalies were found in three of the four fetuses. All but one case presented with extracardiac abnormalities. None of the cases developed hydrops. Two cases are currently alive and well, one termination of pregnancy occurred at 25 weeks of gestation and one case died at 14 days during surgical correction of a complex cardiac malformation.

Conclusions: Clinicians should be aware of different and important findings during the fetal examination, which can be indicative of a DVA, and, when suspected, serial revaluations should be scheduled in order to identify any malformation.

Keywords: Ductus venosus, Agenesis, Fetal malformations, Outcome

Background

The agenesis of the ductus venosus (DVA) is a rare anomaly first published in 1826 by Mende who reported a case of direct drainage of an umbilical vein into the right atrium during an autopsy of a stillborn infant [1]. Paltauf in 1888, describes the second case of DVA in an infant born with severe hydrops and portal congestion without the ductus venosus. This information was only obtained

in the post-mortem examination [2]. Nowadays it is feasible to detect the DVA prenatally and even in early pregnancy. With the widespread use of ultrasonographic techniques and their improvement over the years, a more careful examination of the fetal circulation, particularly the umbilical and portal venous malformations, is now performed prenatally which led to the increase number of DVA cases published in the literature.

When the ductus venosus is absent, the umbilical blood flows from the umbilical vein through an aberrant vessel that may be extrahepatic, bypassing the liver or intrahepatic via the portal venous system [3-5]. Findings of cardiac malformations, hydrops and non-chromosomal malformation syndromes has been described as predictive of in-utero or neonatal demise, whether drainage is intra or extrahepatic [6].

The interest in the investigation of the DVA has become even more relevant now that the systematic DV evaluation by color Doppler in the first trimester screening has become part of the daily clinical practice.

Previously it was easier for the DVA to go unnoticed.

However, in spite of the new and better technologies, this is still a rare condition with a reported prevalence of 1 in 2532 [7] and 1 in 556 fetuses [8], and with a variable prognosis that relies partly on the presence of associated conditions.

Methods

In this study, we describe four cases of DVA diagnosed at our institution. For each case, we access the patient's files in order to extract the following information when

Table 1: Main findings of the four cases of DVA diagnosed at our institution.

Case	GA	UV connection	Prenatal sonographic findings/associated anomalies	Karyotype	Outcome	Postnatal/ Post-mortem findings
1	13+0	PV	Apparent retrognathia. No other obvious changes in echoanatomy.	NP	VD at 39w	Male, 3285gr, 50cm, Apgar 9/10/10.
2	13+6	RA	Congenital heart defect with cardiac chambers disproportion with a smaller LV, hypoplastic aortic arch, great arteries disproportion, moderate to severe VSD, small aortic valve. Bilateral pyelectasis.	46,XY	VD at 39w+6d NND	Male, 3300gr, 53cm, Apgar 8/10/10. Corrective cardiac surgery at 14d, died in the intra-operative period. Autopsy: hypoplastic LV, hypoplastic aortic valve (bicuspid), ascending aorta and aortic arch, RA and RV hypertrophy, large ventricular meso-septal defect. Bilateral pyelectasis. Lymphangiectasis.
3	22+5	RA	Mild cardiomegaly, no usual vascular pattern of the portal system is observed, suspected portal vein agenesis, Blake's pouch cyst with normal cerebellar vermis, IUGR.	46,XY	CD at 34w+5d	Male, 1700gr, 41cm, Apgar 9/10/10, no dysmorphic features.
4	14+5	RA	SUA, tetralogy of Fallot with hypoplastic pulmonary artery.	46,XX	TOP at 25w	Autopsy: confirmed the DVA, biometric parameters adequate for GA, severe hypoplastic PuV (quasi-atresia), hypoplastic pulmonary trunk, abnormal RV morphology, lightly hypoplastic ductus arteriosus, sub-aortic VSD and SUA.

GA, Gestational age; UV, umbilical vein; PV, portal vein; NP, not performed; VD, vaginal delivery; RA, right auricle; LV, left ventricle; VSD, ventricular septal defect; RV, right ventricle; IUGR, intrauterine growth restriction; CD, caesarean delivery; SUA, single umbilical artery; TOP, termination of pregnancy; DVA, ductus venosus agenesis; PuV, pulmonary valve.

available: gestational age, umbilical vein connection, pre-natal imaging findings, gestational age at delivery or at pregnancy termination, fetal outcomes (intrauterine fetal death, neonatal death or survival), post-natal imaging findings, post-mortem findings and karyotype.

The study was approved by the ethics committee of our hospital. The confidentiality was guaranteed as the participants were only referred as case numbers. Furthermore, no information regarding the patient's identification or identifying details were used in the study.

Case Series

The four cases of DVA diagnosed at our institution and the main findings are listed in table 1. As we can observe, 2 cases were diagnosed in the first trimester and the other 2 cases in the second trimester of gestation. Prenatal ultrasound studies revealed an intrahepatic shunt only in case 1 and extrahepatic shunts in the other three cases. All the 3 fetuses with an extrahepatic shunt of the umbilical vein drained into the RA (figure 1 and 2).

Figure 1: Ultrasound images from case 2 performed at 16 weeks + 2 days: (A) Depiction of the umbilical venous circulation obtained by Color Doppler showing a large vascular structure with a discrete aliasing, establishing a continuum between the umbilical vein and the right atrium, (B) Blood flow waveform obtained by pulsed Doppler showing a highly pulsatile flow without any retrograde waveform.

Figure 2: Ultrasound images from case 4 performed at 16 weeks + 4 days: (A) Depiction of a large vessel, without any funnelling, connecting the umbilical vein to the right atrium, (B) Blood flow waveform obtained by pulsed Doppler from a region with aliasing, showing higher velocities than those normally obtained from the umbilical vein and no retrograde flow.

In case 1, the karyotype was not performed, whereas in the other three cases the amniocentesis showed a normal karyotype.

Cardiac anomalies were found in three of the four fetuses and ranged from mild cardiomegaly (case 3) to complex cardiac malformations (case 2 and case 4). Case 1, case 2 and case 3 presented extracardiac abnormalities such as retrognathia, urinary tract (pyelectasis), and nervous system findings (Blake's pouch cyst). Case 4 presented also a single umbilical artery. None of the cases developed hydrops.

Case 1 was a male infant born at 39 weeks of gestation by vaginal delivery. At birth, the infant had no apparent anomalies, and is currently alive and well.

Case 2 was a male fetus with a complex cardiac malformation diagnosed during prenatal evaluation.

Parents decided to continue with the pregnancy. The infant was born at 39 weeks of gestation and required corrective surgery at 14 days of age. Death was declared during surgery due to severe ventricular dysfunction. The autopsy showed: hypoplastic left ventricle; hypoplastic aortic valve (bicuspid), ascending aorta and aortic arch; right atrium and right ventricle hypertrophy and large ventricular meso-septal defect (figure 3). It also showed bilateral pyelectasis.

Figure 3: Macroscopic images from necropsy examination of an infant with 14 days with a normal karyotype showing hypertrophy of the right atrium (RA) and right superior vena cava (RSVC) (case 2).

Case 3 was a male infant born by cesarean delivery at 34 weeks and 5 days. At birth, the infant had no apparent dysmorphisms. Due to the preterm labour and lower weight (1700 gr) the infant was admitted in the neonatal intensive care unit. He is currently alive and well.

In case 4, parents decided to terminate the pregnancy at 25 weeks of gestational age. The autopsy confirmed the DVA and showed an aberrant course of the umbilical vein running anterior to the liver and leaving a marked groove in its surface until reaching the atrium (figure 4). The autopsy also showed biometric parameters adequate for gestational age, severe hypoplastic pulmonary valve (quasi-atresia), hypoplastic pulmonary trunk, abnormal right ventricle morphology, lightly hypoplastic ductus arteriosus, sub-aortic ventricular septal defect and a single umbilical artery (SUA).

Discussion

The ADV results from a failure of the 'critical anastomosis' between the portal-umbilical venous system and the hepatic-systemic venous system. When

the ductus venosus is absent, the umbilical blood flows from the umbilical vein through an aberrant vessel that may be extrahepatic, bypassing the liver, or intrahepatic, via the portal venous system [3-5].

Regarding the extrahepatic shunt, there are different possible connections between the umbilical vein and the venous system: (1) right atrium (RA), left atrium or through a dilated coronary sinus. The connection to the RA is considered the most common as described by Moaddab and colleagues which reported a prevalence of 68:153 (44%) [9]; (2) inferior vena cava. This is the second most common connection [9]; (3) superior vena cava; (4) left, right or internal iliac vein. The connection to the iliac vein was first described in 1996 [10]; (5) renal vein; (6) right ventricle.

Figure 4: Macroscopic images of the umbilical venous circulation from necropsy examination of a fetus with 25 weeks with a normal karyotype (case 4). (Liv, Liver; UV, umbilical vein; RA, right atrium; SUA, single umbilical artery).

In the intrahepatic umbilical venous drainage without liver bypass, the umbilical vein connects to the portal sinus as usually but without giving rise to the DV [4].

In our study we found an extrahepatic shunt in three cases, all of which with direct connection to the RA, and an intrahepatic shunt in one case. Gembruch and colleagues reported, in 1998, the first two cases of intrahepatic drainage diagnosed prenatally [11]. Since then, the intrahepatic umbilical venous drainage was less often reported in comparison to the extrahepatic. One possible explanation is pointed by Berg and colleagues, that although the extrahepatic connection is much rarer its assessment is easier, while the intrahepatic shunt may occur more frequently, but often escapes diagnosis [6].

Regarding the time of diagnosis, two cases were diagnosed in the first trimester whereas the other two were diagnosed in the second trimester of gestation. The DVA can be accurately detected by early scan during first trimester [8]. This demonstrates the need for a careful and effective evaluation in early pregnancy as the detection of DVA is possible and may have an impact on the follow-up and care needed during pregnancy.

The DVA has been related to congenital cardiac, genitourinary and/or gastrointestinal anomalies with or without associated chromosomal abnormalities. Although the malformations found in our cases occurred in association with the DVA we cannot conclude that they are disease-specific.

The DVA has also been associated with syndromic diseases such as Turner or Noonan syndromes [7,12]. In our study, three cases presented with a normal karyotype while in one case amniocentesis was not performed. When the DVA is associated with other findings it is much easier to diagnose the DVA as the fetus needs a more accurate evaluation.

The outcome of fetuses with DVA has been related with the type of umbilical venous shunt along with the presence of other abnormalities. If the venous drainage is extrahepatic the likelihood of a poorer outcome is much higher comparing to the presence of an intrahepatic shunt [6,9].

Although the trigger is not yet fully understood, the umbilical venous drainage with liver bypass is often associated with fetal cardiac compromise, a characteristic that typically is not found in the intrahepatic pattern [12-

14]. It has been suggested that the probable mechanism responsible for triggering heart failure might be the increased cardiac preload, increased cardiac work and progressive cardiac decompensation [13]. The macroscopic images from necropsy examination of case 2 (figure 3) represents hypertrophy of the right atrium and right superior vena cava which might be explained by the volume overload from the umbilical vein in the absence of the DV.

The direct drainage of the umbilical blood flow into the heart, that becomes unrestricted in cases of absent ductus venosus, can lead to high central venous pressure [14,15]. This increase in central venous pressure is most likely due to the volume overload as a result of the DV regulatory mechanism loss [14,16]. This chronic volume overload may lead to an increased stress on the fetal myocardium with the risk of high-output heart failure, leading to fetal hydrops [12,15]. Although hydrops has also been related to DVA, in our study none of the cases developed this condition.

In conclusion, the clinicians should be aware of different and important findings during the fetal examination according to different steps in developmental biology, which can be indicative, although not disease-specific, of a DVA, and, when suspected, serial reevaluations should be scheduled in order to identify any malformation.

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