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Coincidence of congenital left-sided diaphragmatic hernia and ductus venosus agenesis: Relation between altered hemodynamic flow and lung-to-head-ratio?

T. Klein^{a,*}, A. Semaan^a, M. Kellner^b, J. Ritgen^c, T.M. Boemers^a, R. Stressig^c^a Department of Pediatric Surgery and Pediatric Urology, Children's Hospital of Cologne, Kliniken der Stadt Köln gGmbH, Amsterdamer Straße, Köln, Germany^b Department of Pediatric Radiology, Children's Hospital of Cologne, Kliniken der Stadt Köln gGmbH, Amsterdamer Straße, Köln, Germany^c Praxis für Pränatalmedizin und Genetik Cologne, Germany

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ABSTRACT

Left-sided diaphragmatic hernia (CDH) as well as ductus venosus agenesis (ADV) are rare complex congenital malformations. We present a case of coincidence of these malformations and an abnormally high lung-head-ratio (LHR). The left-sided liver-up CDH and the ADV were diagnosed in prenatal ultrasound examination. In CDH cases lung volume is decreased due to the herniation of abdominal organs into the thorax. With 1.4 the LHR of our patient exceeded the normal ratio in liver-up CDH cases considerably. One explanation for this unusually high LHR might be an altered blood flow due to the coinciding ADV. In ADV cases less blood bypasses the lung through the foramen ovale. Consecutively pulmonary circulation is improved which may constitute as an advantage in CDH cases. Diagnosis, prognostic factors, physiology, and therapy strategy are discussed.

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We present a case report of a patient with a left-sided congenital diaphragmatic hernia co-occurring with ductus venosus agenesis. To our knowledge, it is the first report of the coincidence of both malformations.

The congenital diaphragmatic hernia (CDH) is a complex birth defect with yet unknown etiology. The malformation results from a defective differentiation of the pleural and peritoneal cavity. The failure of the diaphragm to close completely during development results in a herniation of abdominal organs into the thorax that causes a secondary pulmonary hypoplasia or pulmonary hypertension later on.

The incidence of CDH is 1 in 2000–5000 live births of which only 2% are familiar [1,2]. At approximately 84% most congenital diaphragmatic hernias are left sided. With another 13% being right sided only 2% are bilateral or complete agenesis occurs [3]. Associated malformations (AMF) are diagnosed in approximately 40% of newborns with CDH, cardiovascular malformations being the most

frequent [4]. Furthermore a variety of gastrointestinal, genitourinary or musculoskeletal defects as well as abnormalities of the central nervous and bronchopulmonary system are commonly described AMFs in CDH. Focusing on genetic background Zaiss et al. found chromosomal aberrations in approximately 3% of CDH cases [4].

The data on mortality in CDH show a wide range between 8 and 79%. This results from different degrees of diaphragmatic herniation and the great diversity in associated malformations between the study populations [5–9]. The mortality rate of newborns diagnosed with isolated diaphragmatic hernia is significantly lower than in CDH accompanied by AMF [10].

Prenatal factors that are associated with a poor prognosis are the early diagnosis of CDH (before the 25th week of pregnancy), intrathoracic herniation of the liver in left-sided diaphragmatic hernia (liver-up CDH), sonographic proof of the stomach bubble within the thorax, a low lung-head-ratio (LHR), fetal hydrops, and a hypoplastic left ventricle due to compression or reduced left-sided cardiac preload [10–14]. Recently the determination of fetal lung volume (FLV) assessed by MRI and the observed to expected FLV were recognized as a prognostic factor for postnatal outcome [15–17]. In literature the rate of successful prenatal sonographic

* Corresponding author. Tel.: +49 1717806880.

E-mail address: 7081.klein@gmail.com (T. Klein).



Fig. 1. Balanced ventricles in a fetus with left-sided liver-up CDH and ADV.

diagnosis of CDH varies between 37 and 79% depending on the expertise of the examining physician [4,10]. In a study of Zaiss et al. on the prenatal diagnosis of associated malformations in a population of 362 patients with CDH only 18.4% of associated birth defects were detected [4]. By improving the prenatal diagnosis and postnatal therapy, the mortality rate has decreased within the last decade [18].

The ductus venosus (DV) develops between the 5th – 6th week of gestation. It connects the intra-abdominal portion of the left umbilical vein with the confluence of the vena cava inferior and hepatic veins. 20–30% of the oxygen- and nutrient-rich blood coming from the placenta bypass the liver passage using this connection [19]. According to the pressure gradient the blood flow accelerates passing the smallish ductus venosus. Due to this high velocity the blood streams directly into the left heart through the foramen ovale and reaches the coronary arteries and the brain highly oxygenated [20]. In a study of Staboulidou et al. the prevalence of ductus venosus agenesis (absence of ductus venosus, ADV) was 1:2532 [21]. Acherman et al. found an incidence of ADV of 6:1000 in a high risk population for fetal heart defects that presented for prenatal echocardiography in a high risk population for fetal heart defects [22]. Literature differentiates two kinds of ADV in terms of umbilical vein drainage: an extrahepatic umbilical vein drainage bypassing the liver (rare) and an intrahepatic drainage of the umbilical vein into the portal sinus (more common) [23]. The incidence of associated malformations in ADV ranges between 24 and 78%. In particular, cardiac malformations and the agenesis of the portal vein system coincide with a ductus venosus agenesis [22–25]. Furthermore, at a prevalence between 18 and 52% the percentage of fetal hydrops is increased in ADV populations [23–25]. In this context, as the ADV incidence is rare, various authors recommended a specific examination for ADV diagnosis only in children with cardiac malformations or hydrops fetalis as well as when the umbilical vein cannot be identified regularly [22,25].

1. Case report

A 26 year old pregnant women (gravida V, para II) was referred in the 12th week because of an increased nuchal translucency of the fetus, diagnosed at standard first-trimester ultrasound screening. Apart from a nuchal edema an abnormal position of the heart and a reverse flow of the ductus venosus were detected. Karyotype was normal (46, xy). Within 23 + 4th week a left-sided liver-up diaphragmatic hernia with lung-to-head ratio of 1.4, an observed to



Fig. 2. Sagittal view with T2-weighted MRI in a fetal left-sided liver-up CDH.

expected LHR (o/e LHR) of 44% and normal baseline pulmonary blood flow were protocolled. Besides the liver the herniation included the stomach and the small intestine. Furthermore, an agenesis of ductus venosus and a mild ventriculomegaly were present (see Fig. 1). Following antenatal ultrasound examinations and prenatal MRI showed a regular development of the fetus (see Figs. 2 and 3). Especially the ventricles of the heart were constantly symmetric and the lung perfusion kept normal at all times (see Fig. 4). The pregnancy continued without any complications. After spontaneous vaginal delivery (39 + 3rd week) a 3800 g newborn was endotracheal intubated primarily. It was not possible to push the umbilical vein catheter forward more than 5 cm due to ADV.

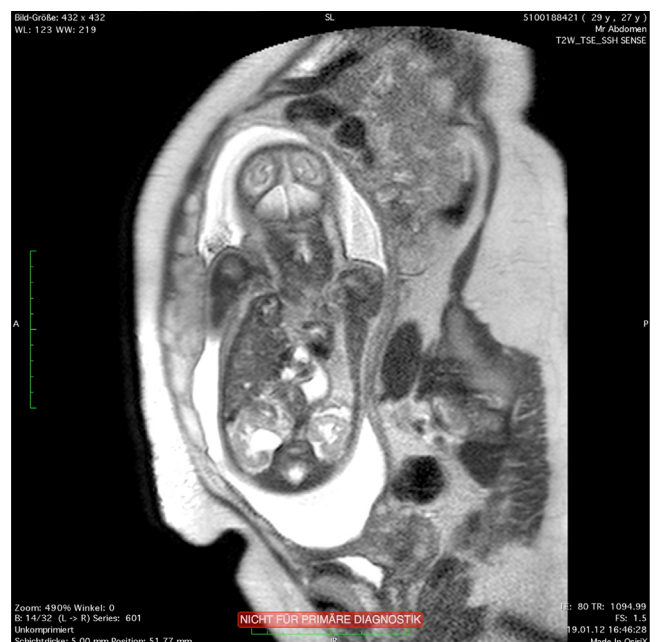


Fig. 3. Coronary view with T2-weighted MRI in a fetal left-sided liver-up CDH.

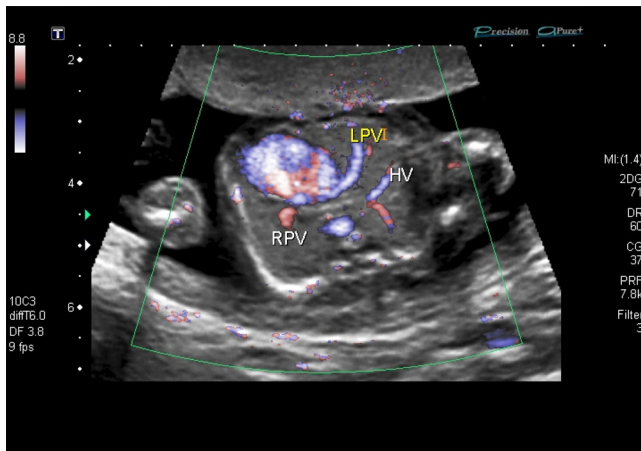


Fig. 4. Color flow mapping of intrahepatic veins in a fetus presenting with ADV (RPV = right pulmonary vein, LPV = left pulmonary vein, HV = hepatic vein).

Because of an insufficient preductal saturation during low peak pressure conventional ventilation with FiO_2 at 1.0 a nitric oxide inhalation and a high-frequency oscillatory ventilation were started. Except for a dysgenesis of corpus callosum and a mild tricuspid insufficiency no malformation was diagnosed at postnatal ultrasound and echocardiography imaging.

After stabilization of the newborn the repair of diaphragmatic hernia was performed on day 7 postpartum by a transabdominal approach using a Gore-Tex® patch. Due to the large hernia and relatively small abdominal cavity a spring-loaded silo bag was placed to reduce the risk of an abdominal compartment syndrome. On day 2 post surgery a chest tube was placed due to an increasing pleural effusion. A chylothorax was diagnosed by pleural fluid examination.

Secondary abdominal wall closure was performed 25 days after the CDH repair. After repeated weaning from mechanical ventilation the final extubation was successful on the 52nd postoperative day (POD) and the infant was respiratory stable with an intermittent need for oxygenation therapy (FiO_2 0.25–0.3).

Dysphagia and gastro-esophageal reflux complicated enteral feeding and caused repeated aspiration pneumonias. Therefore an open nissen fundoplication and a gastrostomy were performed at the age of 5 months. The following inpatient stay passed without complications and the infant was discharged home without the need for oxygen therapy at the age of 6 months.

2. Discussion

Presenting as complex malformations each for itself, pre- and postnatal prognosis of morbidity and mortality in the congenital diaphragmatic hernia and the ductus venosus agenesis is highly variable. Although cardiovascular malformations are the most common associated malformations in patients with congenital diaphragmatic hernia, so far no case of ADV associated with left-sided liver-up CDH has been described. Strouse et al. published a case of a neonate with a right-sided diaphragmatic hernia combined with an ADV with an extrahepatic umbilical vein orifice who died 90 min after birth [26].

To reduce mortality the exact prenatal diagnostic of the CDH and its associated malformations including aneuploidy and the subsequent referral to a specialist's center for diaphragmatic hernia are crucial [10,27]. In newborns that are diagnosed with a left-sided liver-up CDH before the 25th SSW and sonographic proof of the intrathoracic gastric bubble show reduced survival rates and

require a longer duration of ventilation. Two other predictive values that should be considered are the lung-head-ratio, determined from the contralateral lung volume and the head circumference, and the o/e-LHR [14].

In our patient the LHR was found 1.4 and the o/e-LHR was 44%. Both indicates a favorable postnatal prognosis. In diverse study populations of newborns diagnosed with isolated CDH an LHR greater than 1.4 was found to be associated with a 100% survival rate, whereas the prognosis decreases to nearly 0% when the LHR falls below 1.0 [28–30]. Of course these parameter only have a prognostic impact in isolated CDH cases and do not have prognostic value for other coexisting AMFs.

Despite the initial promising prognosis our patient was ventilated for 59 days and was not discharged from hospital till 6 month of age.

In a study of Jani et al. the mean ventilation time in isolated CDH cases presenting with o/e-LHR between 26 and 45% was 16 days and patients were dismissed home on average on day 44 after surgery [14].

The prolonged course in our case was probably related to the postoperative complications (chylothorax and gastroesophageal reflux disease). Both are common complications after surgical correction of CDH, which prolong the duration of ventilation and hospital stay [31,32].

In a study by Levy et al. including 1383 patients a postoperative chylothorax was diagnosed in 4.6% [31]. Patch-plastics for diaphragm closure and the ECMO (extracorporeal membrane oxygenation) treatment were identified as risk factors [31]. Usage of patch-plastics was furthermore identified as a risk factor for GERD in a study by Jaillard et al. [33].

As in CDH, the postnatal prognosis in cases presenting with ADV primarily depends on the AMF. In multiple studies the survival rate of isolated ADV was indicated with 100% [23,25]. Fetal hydrops and extrahepatic drainage of the umbilical vein increase the intrauterine and postnatal mortality rates [23,25]. The observed ventriculomegaly is a frequently described anomaly in fetuses with CVA [22–25]. The high volume load to the right atrium from vena cava inferior is believed to be the causative factor [24,25].

The LHR value of 1.4 is not consistent with values found in literature for other neonates with left-sided liver-up CDH. For example Harrison et al. found an average LHR of only 1.1 in his study population [34].

Furthermore a symmetric right and left side of the heart and a normal perfusion of the contralateral lung measured by color flow Doppler in pregnancy are valuable markers for a good neonatal outcome [35,36].

Despite above mentioned studies about the outcome of different AMF we find in our patient a great discrepancy between the poor prognosis associated with the large left-sided liver-up CDH, the early diagnosis and the intrathoracic positioning of the stomach on the one hand and the favorable prognosis of an LHR greater than 1.4 respectively an o/e LHR of 44% on the other hand. Following we will try to give an explanation for this observation.

Due to the ductus venosus agenesis less blood passes through the foramen ovale into the left ventricle and therefore the percentage reaching the lung by the right atrium and its ventricle is increased. Furthermore size and account of the pulmonary vessels seem to be increased.

It has to be considered though that increased blood flow rates into the right ventricle can as well be found in fetuses with isolated left-sided CDH and an abnormally high mouth of the ductus venosus into the V. cava inferior [35]. On the other hand the increased blood flow to the right ventricle is associated with a decreased pulmonary blood flow, a worse postnatal outcome as well as a higher rate of pre- and postnatal interventions like fetal

endoscopic tracheal occlusion (FETO) and ECMO [36,37]. The authors assume that the higher oxygenation of the ductus venosus blood might be the decisive factor decreasing pulmonary blood flow and therefore significantly elevating the intrauterine LHR. In the delineated case with ductus venosus agenesis the blood rushing into the lung has passed the liver passage, therefore is less oxygenated and the negative impact of high oxygen levels on lung perfusion is nonrelevant. This leads to a normal development of pulmonary vessels, which can be observed in prenatal ultrasound. Of course this single case is not enough to proof any of our assumptions, but might sensitize other physicians to examine positive and negative effects of these coincidence in other cases.

3. Conclusion

In prenatal consultation it is vitally important to be able to give precise information to the parents. The complexity of the malformations that can be diagnosed in utero demonstrates the great difficulty of giving an exact prognosis and makes a precise prenatal diagnosis even more important.

We point out that an interdisciplinary approach to prenatal diagnosis that results in balancing different therapeutic options and a consensus on the best possible therapy is mandatory in every individual case.

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