Ductus venosus reversed flow in omphalocele: Could it be a prognostic factor for long-term neurological impairment?

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ABSTRACT

Omphalocele (exomphalos) represents one of the most frequent congenital abdominal wall defects. It presents as a defect of inconstant size and is located on the midline, at the base of the umbilical cord, the skin, fascia, and abdominal muscles being absent at this level. Omphaloceles are classified as liver-containing or non-liver-containing, the latter containing primarily bowel loops. We present the case of a 37-year-old pregnant woman with an early diagnosis of liver-containing omphalocele associating ductus venosus reversed flow, with the aim to highlight the importance of the first-trimester morphology scan and to develop a pilot study regarding the neurological development of infants after surgical repair of giant omphaloceles. The particularity of this case consists of a fetus with a positive diagnosis of a giant liver-containing omphalocele but with a small abdominal wall defect during the first-trimester morphology scan at 13 weeks and 3 days of gestation which associated ductus venosus reversed flow, presenting a normal karyotype postabortum. With a small defect, we can speculate the risk of strangling besides the mechanical traction exercised on the ductus venosus generating fetal distress, specifically fetal hypoxia at an early gestational age. In conclusion, the main issue, in this case, was if the fetal omphalocele and ductus venosus reversed flow indicated fetal hypoxia, what was the obstruction effect on the oxygenated blood pathway caused by the abdominal defect, and which were the long-term effects on infants with this complex pathology with an unknown outcome.

KEYWORDS: omphalocele, congenital abdominal wall defects, ductus venosus reversed flow, neurological impairment.

ABBREVIATIONS: OEIS complex – omphalocele, exstrophy of the bladder, imperforate anus, spinal defects complex; AFI – amniotic fluid index; AC – abdominal circumference; C-section – Cesarean section.

INTRODUCTION

Omphalocele (exomphalos) represents one of the most frequent congenital abdominal wall defects. It presents as a defect of inconstant size and is located on the midline, at the base of the umbilical cord, the skin, fascia, and abdominal muscles being absent at this level [1]. Omphaloceles are covered by the amnion, Wharton's jelly, and peritoneum. The apex of the sac presents the umbilical cord insertion; the sac usually contains herniated abdominal organs: midgut, liver, spleen, or even gonads [2]. Omphaloceles are classified as liver-containing or non-liver-containing, the latter containing primarily bowel loops. The size of the omphalocele is between 2–10 cm, and 40–80% of cases have a minimum of one associated anomaly [3]. Furthermore, giant omphaloceles are described as omphaloceles that contain more than 75% of the liver or a defect size more than 5 cm [3].

Omphaloceles have an incidence of 2 per 10,000 live births in the United States and 2.6 per 10,000 births worldwide [4]. Women at the extreme reproductive ages (<20 years old and >40 years old) have a twofold higher risk of delivering a newborn with omphalocele than the general reproductive population [5, 6], and women of color present a higher prevalence than white women (1.91 *vs.* 1.47 per 10,000 live births) [7]. Omphaloceles also have a higher prevalence in male newborns and are associated with multiple births [6]. The risk associated with in utero exposure to selective serotonin reuptake inhibitor (SSRI) of omphalocele has been controversial [8, 9].

We present the case of a 37-year-old pregnant woman with an early diagnosis of liver-containing omphalocele associating ductus venosus reversed flow, with the aim to highlight the importance of the first-trimester morphology scan and to develop a pilot study regarding the neurological development of infants after surgical repair of giant omphaloceles.

CASE REPORT

A 37-year-old woman presented to our medical unit for early diagnosis of pregnancy and pregnancy monitoring. We noted nothing abnormal from the physical, ultrasonographic examination, and the patient's medical and obstetrical history. At 10 weeks of gestation, the patient returned for an ultrasonographic examination in which a physiologic hernia was observed. During the fetal morphology scan at 13 weeks and 3 days of gestation, a 1,02 cm abdominal wall defect was detected: a liver-containing omphalocele (Figure 1 and 2). The ductus venosus flow was evaluated during the morphology scan, and the fetus presented ductus venosus reversed flow (Figure 3). No other morphological abnormalities were detected when transvaginal ultrasonography was performed. The patient was recommended to undergo a non-invasive prenatal screening test, but she refused. The patient was informed about the risks of neonatal complications, and the reconstruction possibilities implied, and she decided to terminate the pregnancy. A karyotype evaluation of the conception product was performed, and the result was negative for chromosomal abnormalities.

DISCUSSION

Over 90% of cases of omphalocele are diagnosed prenatally during a standard obstetric ultrasonographic examination [10]. Usually, non-liver-containing omphalocele can be properly diagnosed after 12 weeks of gestation, thus diagnosing correctly the cases of a small omphalocele, which can be easily mistaken for physiologic midgut herniation. On the other hand, liver-containing omphaloceles can be diagnosed earlier using transvaginal ultrasonography at 9 or 10 weeks of gestation due to the well-known fact that the liver does not herniate physiologically [11, 12]. The ultrasonographic findings include a midline defect of the abdominal wall in the umbilical area, of varying size, a membranous sac usually containing bowel, livers, stomach, or even bladder [12]. The sac comprises the amnion representing the exterior layer and Wharton's jelly in the middle and peritoneum – the interior layer. The fetus might present ascites in the abdominal cavity or the sac. The sac could contain ductus venosus that can be evaluated using color Doppler [11]. Small omphaloceles, non-liver-containing, are usually correlated with fetal aneuploidies, while omphaloceles with the liver in the sac are commonly affiliated with euploid fetuses [13]. The most frequent pathologies we should consider while making a differential diagnosis are represented by: gastroschisis, umbilical cord hernia, ectopia cordis, cloacal exstrophy, limb-body wall complex, Pentalogy of Cantrell or urachal cysts [10].

Omphaloceles are in a proportion of 35% to 70% associated with structural anomalies such as tetralogy of Fallot, dextrocardia, malrotation, intestinal atresia, ventricular septal defect, bladder or renal agenesis, ureteral stenosis orofacial clefts, diaphragmatic and neural tube defects [14–16]. 60% of non-liver-containing omphaloceles are linked to fetal aneuploidies such as trisomy 13, 18, or 21, triploids, Turner syndrome, and rare chromosomal deletions [17, 18]. One-third of pregnancies with omphaloceles present polyhydramnios after the 20th gestational week; fetal growth restriction is also associated with omphalocele [17, 19]. Regarding syndromes, omphalocele is encountered in Beckwith-Wiedemann syndrome, Schisis association, Pentalogy of Cantrell, OEIS (omphalocele, exstrophy of the bladder, imperforate anus, spinal defects) complex, Donnai-Barrow syndrome, and Shprintzen-Goldberg omphalocele syndrome [20].

After a positive diagnosis of omphalocele, complementary investigations should be recommended: microarray, given the high risk of aneuploidy, fetal echocardiogram due to elevated incidence of associated cardiac abnormalities, and testing for Beckwith-Wiedemann syndrome due to its increased risk in euploid fetuses presenting omphalocele, but only after a negative microarray test for aneuploidies [21].

Figure 1. Crown-rump length (CRL).

The next step after the positive diagnosis of omphalocele is to counsel and inform the parents about the implications of omphaloceles associated or not with congenital syndromes or congenital abnormalities. Also, the parents might choose to terminate the pregnancy, and a pathology report will be realized to establish the omphalocele's etiology and avoid recurrence in future pregnancies. Cases implying omphalocele associated with trisomy 13, 18, triploidy, or pulmonary hypoplasia from Pentalogy of Cantrell have an obscure prognosis [22–24].

The pregnancy monitoring consists of ultrasonographic examinations to follow the fetal growth every three to four weeks and non-stress test or biophysical profile monitoring starting with the 32nd week of gestation in the cases with normal growth and adequate amniotic fluid index (AFI). Intrauterine growth restriction appears frequent in pregnancies with omphalocele and associated abnormalities, presenting an elevated risk of unfortunate neonatal outcomes [25]. The standard biometry measurements include abdominal circumference (AC), biparietal diameter, head circumference, and femur length. In case of inconsistent or diminished AC, the other parameters (femur length, biparietal diameter) and AFI should be closely evaluated. A specific formula to assess the fetal weight in case of abdominal wall defects was elaborated by Siemer *et al.* [26], which estimates the fetal weight using the occipitofrontal diameter,

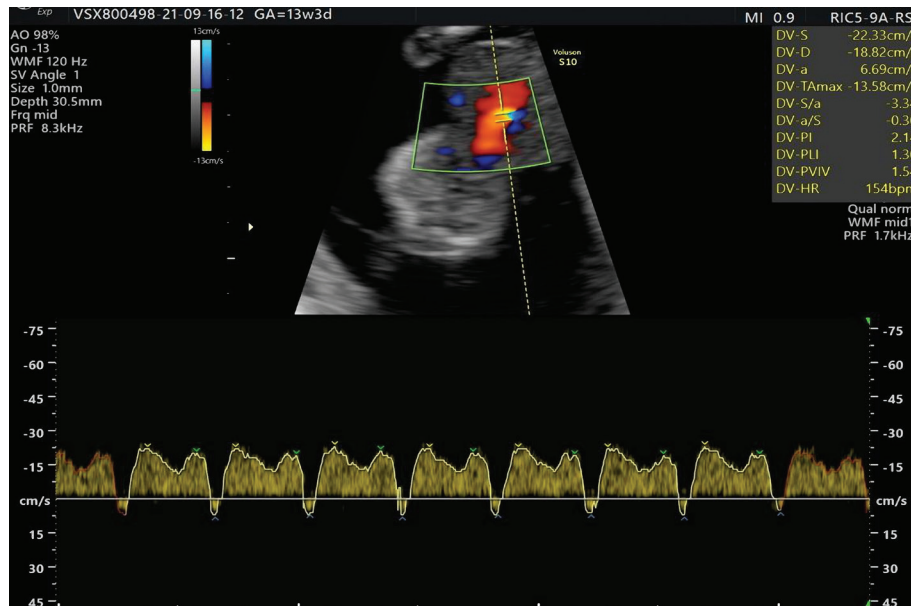**Figure 2. Omphalocele containing bowel, liver and stomach.**

Figure 3. Ductus venosus reversed flow.

biparietal diameter, and femur length measurements. Regarding the location, the newborn should be delivered at a tertiary care center, vaginal delivery should be attempted, in the absence of standard indications for C-section; cesarean delivery is recommended in cases of fetuses with giant omphaloceles [27–29].

When the newborn is delivered, it is essential to avoid clamping the umbilical sac to prevent accidents of bowel injury. Further, the newborn with omphalocele requires immediate care in order to be placed in a thermoneutral environment. The surgery is discussed: for small abdominal wall defects measuring 2 to 3 cm, the surgery occurs in the first 24–72 hours of life and consists of primary closure of the fascia and skin [30]. Larger defects usually benefit from silo placing over the defect in the first 24 hours of life, and the closure is delayed. After three to seven days, the silo is reduced progressively in the intensive care unit, and the definite closure of the abdominal wall defect occurs in the operating room [30]. Reducing liver-containing omphaloceles should be done under Doppler ultrasound guidance to ensure that silo reduction does not damage the vena cava and hepatic outflow [30].

Regarding giant omphaloceles, the management could include acellular dermal patch, silo, and skin graft or sclerosing solution (topical povidone-iodine) application, which aids in amniotic sacs eschar formation, followed by delayed hernia repair [30]. The infant might need prolonged mechanical ventilation to manage compression of the vena cava and respiratory difficulties due to omphalocele reduction. Moreover, postoperative surveillance must include urine output, blood pressure, and pulse rate monitoring [31]. Multiple reconstructive procedures may be mandatory in the cases of a newborn with large liver-containing omphaloceles, which could have a role in the long-term morbidity [31].

Regarding the consequences of ductus venosus reversed velocity, Caradeaux *et al.* [32] reported an 11.6 odds ratio for fetal death for fetuses with absent ductus venosus or reversed end-diastolic velocity. Alves *et al.* [33] associated fetuses with absent or ductus venosus reversed flow with the following postnatal outcomes: low birth weight, lower Apgar scores at 1 and 5 minutes. These newborns with absent or ductus venosus reversed flow present a higher incidence of orotracheal intubation, pH at birth less than 7.2, pulmonary hemorrhage, thrombocytopenia, intracranial hemorrhage, hypoglycemia, and postnatal death.

Besides being a marker of fetal cardiac malformations, many authors [34–36] have associated ductus venosus reversed flow with fetal hypoxia in cases of a poorer perinatal outcome as well as intrauterine growth restriction. The TRUFFLE study by Visser *et al.* [37] concluded that fetuses delivered prematurely based on the first appearance of an abnormal ductus venosus waveform have a better neurological development at the 2-year follow-up than those delivered due to an abnormal cardiotocography. Therefore, we can hypothesize that the ductus venosus reversed flow is an early marker of fetal hypoxia.

CONCLUSION

The particularity of this case consists of a fetus with a positive diagnosis of a giant liver-containing omphalocele but with a small abdominal wall defect during the first-trimester morphology scan at 13 weeks and 3 days of gestation which associated ductus venosus

reversed flow, presenting a normal karyotype post abortum. With a small defect, we can speculate the risk of strangling besides the mechanical traction exercised on the ductus venosus generating fetal distress, specifically fetal hypoxia at an early gestational age.

In conclusion, the main issue, in this case, is if the fetal omphalocele and ductus venosus reversed flow indicate fetal hypoxia, what is the obstruction effect on the oxygenated blood pathway caused by the abdominal defect, and which are the long-term effects on infants with this complex pathology with an unknown outcome.

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