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Interrupted inferior vena cava in fetuses with omphalocele. Case series of fetuses referred for fetal echocardiography and review of the literature

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ABSTRACT

Objectives: Congenital heart disease is reported in 15–45% of omphalocele cases. Associated abnormalities of systemic veins have occasionally been reported in children and rarely documented in the fetus. We report a case series of interrupted inferior vena cava (Int-IVC) in association with omphalocele and review the literature.
Methods: From our fetal database we identified all cases of omphalocele referred for fetal echocardiography (FE) between 1997 and 2012. We reviewed pre and postnatal medical records and performed a literature search from 1975 to present to identify previous relevant publications.
Results: Of 9627 fetuses referred for FE, 34 had an omphalocele. Gestational age at FE was 17^{+6} to 26^{+4} weeks. Seven of the 34 fetuses were shown to have an Int-IVC with azygos continuation to a right-sided superior vena cava (SVC). The heart was structurally normal in all but one case. The abdominal wall defect was large and contained liver in all. There were three fetal demises and one neonatal death. Three cases were operated successfully. Since 1975, we identified 12 publications reporting omphalocele with systemic venous abnormalities. Abnormal IVC angulation may lead to surgical complications. Failure of IVC formation is likely to be a developmental rather than a situs abnormality. Int-IVC with a dilated azygos influences venous access and may predispose to venous thrombosis.
Conclusion: We have documented an association between large omphalocele and Int-IVC with azygos continuation to the SVC. In this small series, this did not have surgical implications. It will however, influence route of any future cardiac catheterisation and may have long-term implications.

1. Introduction

Congenital abdominal wall defects (omphalocele or exomphalos and gastroschisis) occur in approximately 1 of 2000 live births [1] and are usually detected on fetal ultrasound. With advanced technology and improved skills in prenatal medicine, diagnosis can be made as early as 12–14 weeks of gestation [2].

Omphalocele can occur in isolation but other structural defects, chromosomal abnormalities or genetic syndromes are relatively common. Additional structural defects have been reported in up to 89% of cases [3]. Trisomy 13 and 18 account for a high percentage of all karyotypic abnormalities [4]. Omphalocele is also part of many genetic syndromes, including Beckwith Wiedemann, pentalogy of Cantrell and OEIS (omphalocele exstrophy imperforate anus spinal defects syndrome) [5].

Congenital heart disease (CHD), with or without a chromosomal abnormality is common in fetuses with omphalocele, including septal defects, coarctation of the aorta and tetralogy of Fallot. Its prevalence varies in different series, being reported in up to 45% [1]. Abnormalities of the systemic veins have occasionally been reported in children with omphalocele [6–13] but only rarely have these been described in the fetus [14,15].

The aim of this study is to report our experience of prenatal diagnosis of interrupted inferior vena cava (Int-IVC) in association with omphalocele, its potential clinical implications and review the relevant literature.

2. Methods

This is a retrospective study. From our clinical fetal database, we identified all cases of omphalocele referred for fetal echocardiography (FE) between January 1997 and December 2012 and reviewed all available prenatal and postnatal records. This is not a consecutive series of omphalocele as only those referred for FE were reviewed. We

Abbreviations: Int-IVC, interrupted inferior vena cava; FE, fetal echocardiography; SVC, superior vena cava; CHD, congenital heart disease; NT, nuchal translucency; CoA, Coarctation; VSD, ventricular septal defect; Az, azygos vein.

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performed a literature search (Pubmed and Google scholar), using a combination of the following terms: exomphalos, omphalocele, azygos vein, inferior vena cava, interrupted inferior vena cava and prenatal diagnosis to identify any previously reported cases and related publications.

3. Results

During the 16-year study period, a total of 9627 fetuses were referred for FE of which 34 had an omphalocele (Fig. 1A). Of these, seven (21%, 95% CI 0.1–37%) were shown to have an Int-IVC with azygos continuation to a superior vena cava (SVC). This compares to 49 cases of Int-IVC among the 9593 cases with no omphalocele who had a cardiac scan (0.005%, 95% CI 0.004–0.007). Details for the series of seven cases are shown in Table 1. Maternal age ranged from 20 to 33 years (mean, 28 years). All were diagnosed in the first trimester at a mean gestational age of 13^{+0} weeks (range: 12^{+4} to 13^{+4} weeks). Gestational age at the first fetal echocardiogram was 17^{+6} to 26^{+4} weeks (mean, 24^{+0} weeks). Nuchal translucency (NT) was normal in five fetuses.

3.1. Cardiac findings

Fetal cardiac situs was inferred by the relative position of the abdominal vessels (aorta, IVC and azygos vein) as previously described [16]. Situs was normal (solitus, compatible with usual atrial arrangement) in 27 of the 34 cases. In seven fetuses the ultrasound findings suggested left isomerism as there was an Int-IVC with azygos continuation to a right SVC (Figs. 1 and 2). The descending aorta was to the left of the spine and the azygos, posterior and to the right of the aorta in all. The cardiac axis was rotated leftward in all seven cases. All but one case had normal intracardiac anatomy and normal great arteries. One fetus had a large ventricular septal defect (VSD) and features suggestive of coarctation of the aorta (CoA). There were no other cardiac abnormalities. Among the 27 cases without Int-IVC, the omphalocele contained liver in 12 cases. Three cases had a cardiac abnormality.

3.2. Extracardiac and chromosomal findings

Details of individual cases are shown in Table 1. The omphalocele appeared large and contained liver and bowel in all cases and stomach in five. Karyotype was available in six fetuses. One had trisomy 18 and five were normal. One child (with normal karyotype) was shown to have ectrodactyly of the right hand on postnatal examination. Four fetuses were small for gestational age.

Among the 27 cases without Int-IVC five fetuses had trisomy 18 (four cases with a prenatal diagnosis and one case with a postnatal diagnosis), 20 had normal chromosomes; two mothers declined invasive testing. One fetus was small for gestational age.

3.3. Outcome

Details are shown in Table 1. No pregnancy was terminated. There were three intrauterine deaths, including the fetus with trisomy 18 and another case that developed severe ascites in the omphalocele sac at 28^{+3} weeks and died at 32^{+3} weeks. Of four live births, one was delivered at 25 weeks of gestation due to maternal pre-eclamptic toxemia and died shortly after birth. Three fetuses were delivered at term by normal vaginal delivery. Surgery was performed at the age of two weeks, 9 months and two and a half years. There were no obvious surgical complications related to the abnormal systemic venous drainage.

Among the 27 cases without Int-IVC, there were four pregnancy termination, two fetal losses and 21 livebirths.

3.4. Review of the literature

A summary of previously reported cases of omphalocele with associated abnormalities of systemic veins, diagnosed pre or postnatally is shown in Table 2.

4. Discussion

In this study we have documented an association between omphalocele and Int-IVC with azygos continuation to the SVC, which has been rarely reported in the fetus This venous abnormality was observed in seven of 34 fetuses with omphalocele referred for FE over a 16-year period. All seven cases were examples of large abdominal wall defects, all containing liver.

Omphalocele is an anterior abdominal wall defect with herniation of abdominal contents. It may occur either as a result of an interruption in the development of the lateral folds [17] or as a failure of the intestinal loops to re-enter the abdominal cavity after the physiological umbilical herniation [18] which happens between the 6th and 10th week of development. During this physiological process, which is completed by 12 weeks, the intestines herniate into the base of the umbilical cord and are covered by the peritoneum and amnion [19]. If they persist out of the abdominal cavity, omphalocele can develop, either small (only bowel and/or stomach) or large (also containing liver).

The development of the *systemic venous system* occurs between the 5th and 11th weeks of gestation, at the same time as the development of abdominal wall defects. During this time, a variety of venous anastomosis occurs. The IVC derives from anastomosis of the right supracardinal vein, the right subcardinal vein and the right vitelline

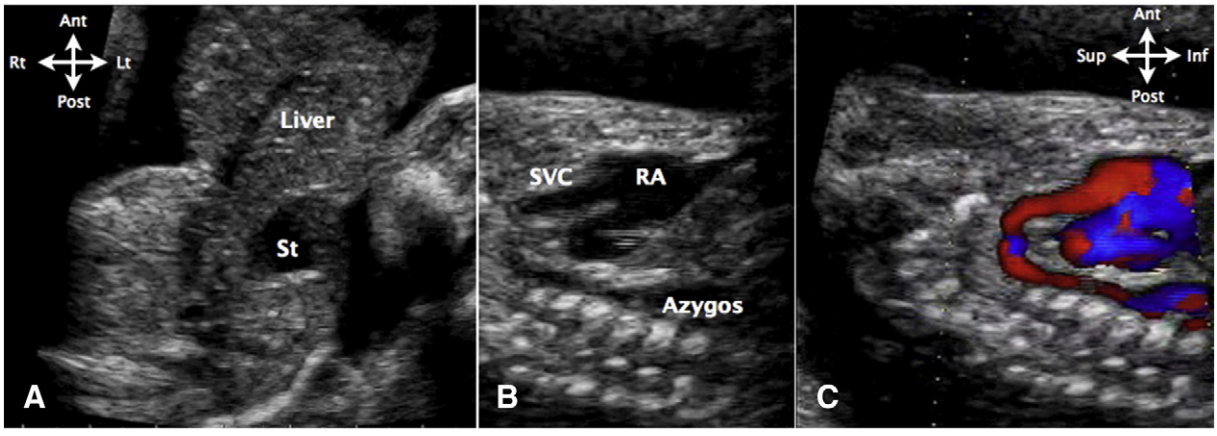

Fig. 1. Images obtained from case 4 at 24 weeks of gestation. (A) Transverse view of the fetal omphalocele with herniation of liver and stomach (St). (B) and (C) represent sagittal views of the fetus, with (B) additional power Doppler. Note the azygos vein joining the superior vena cava (SVC) before entering the right atrium (RA).