CASE REPORT

Concordance for hypoplastic left heart syndrome in a monochorionic twin pregnancy

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The risk of structural heart disease is significantly higher in twin pregnancies than in singleton pregnancies, but the concordance rate has been found to be relatively low, even in monochorionic pregnancies. This is the first report of a monochorionic twin pregnancy concordant for hypoplastic left heart syndrome (HLHS), the diagnosis having been made by fetal echocardiography at 15 weeks' gestation. The findings were confirmed at necropsy at 17 weeks' gestation, following termination of pregnancy. Both twins had mitral and aortic atresia, with severely hypoplastic aortic arches. This report adds weight to there being a genetic component to the cause of HLHS in some cases and illustrates how the findings from early fetal echocardiography with postmortem follow up can help to extend the understanding of the aetiology of this condition.

A 32 year old white woman was referred for fetal echocardiography at 14 weeks' gestation following the finding of increased nuchal translucency and concern about the appearance of the heart in both fetuses in her monochorionic diamniotic twin pregnancy. Chorionic villus sampling showed a normal karyotype in each twin.

Fetal echocardiography at 15 weeks' gestation showed hypoplastic left heart syndrome (HLHS) in both twins. In twin 1, a small left ventricular cavity was seen and there was retrograde flow in the hypoplastic aortic arch. The right ventricular function was good and there was no tricuspid regurgitation. In twin 2, no left ventricular cavity could be identified, and there were bright echoes in the space where the cavity would have been expected. As with twin 1, there was retrograde flow in the hypoplastic aortic arch.

In view of the potential complications of monochorionic twinning, in addition to those of HLHS, the parents elected to terminate the pregnancy at 17 weeks' gestation by induction of labour. Parental consent was given for a necropsy at which both twins were found to have pronounced residual nuchal oedema and to have soft dysmorphic features including low set ears, anteverted nostrils, and unilateral talipes equinovarus. The diagnosis of HLHS was confirmed in both twins, with mitral and aortic atresia. In twin 1, examination of the ventricular mass revealed a tiny, slit-like left ventricular cavity (fig 1) but in twin 2, no cavity was found. Instead, in its anticipated position, there was a small streak of calcification within the myocardium (fig 2).

In twin 1, the pulmonary veins were noted to be severely hypoplastic. In twin 2 the flap valve was abnormally positioned so that it lay adjacent to the posterior wall of the left atrium. Both fetuses had severely hypoplastic aortic arches, with abnormal origin of the left subclavian artery opposite the arterial duct. Additionally, both fetuses had bilateral superior caval veins, with the left sided vein in each draining to the right atrium via the coronary sinus.

Figure 1 "Four chamber" section of the heart of twin 1 showing a slit-like left ventricle. The left atrioventricular connection is absent and a persistent left superior caval vein (SCV) is present. LV, left ventricle.

Figure 2 Similar view of the heart of twin 2. The left ventricular cavity is absent and its expected location is marked by calcification. A left sided superior caval vein (SCV) is also present and the left atrioventricular (AV) connection is absent. The flap valve is deviated away from the rim of the oval foramen and attaches abnormally within the left atrium.

DISCUSSION

HLHS is readily detectable during prenatal screening because of the obvious difference between the appearance of HLHS and the normal fetal heart in a standard four chamber view. Reported data suggest that HLHS accounts for 8% of all congenital heart disease, with an estimated birth incidence of

0.1–0.25 in 1000 live births.¹ However, the true incidence is higher than this, as there is a small risk of spontaneous intra-uterine death in affected pregnancies.² Antenatal diagnosis of HLHS confers several potential advantages: it allows parents time to come to terms with the diagnosis and increases their range of subsequent choices.³ At present, the majority of parents in the UK faced with this diagnosis opt for termination of pregnancy.⁴

Most cases of antenatal HLHS are detected in low risk pregnancies at the routine 18–20 week ultrasound scan. For women considered to be at high risk, improvements in ultrasound resolution have enabled this diagnosis to be made as early as 12–14 weeks' gestation in some cases.⁵ In this situation, there may be a primary defect of left heart development. However, a normal scan at this gestation does not always exclude the diagnosis, as some forms of HLHS may develop later in pregnancy. It is well documented that aortic stenosis may progress to HLHS by term,⁶ and several animal models suggest that HLHS may be associated with decreased flow through left heart structures during intrauterine life.⁷ These findings support the idea that unobstructed flow is required for normal left heart morphogenesis. Myocyte number is initially increased in fetuses with aortic atresia and a patent mitral valve, but subsequently this proliferative response ceases, producing a hypoplastic left ventricle. The spectrum of echocardiographic appearances at different periods of gestation indicates that, although the clinical pathophysiology of HLHS is the same postnatally, during fetal life the pathogenesis of this condition is variable.

The risk of structural heart disease is significantly higher in twin pregnancies than in singleton pregnancies, but the concordance rate has been found to be relatively low, even in monozygotic pregnancies.⁸ HLHS has been previously reported in a monozygotic twin pregnancy affecting one fetus,^{9,10} but to our knowledge this is the first report of monozygotic twins concordant for this condition. This report adds weight to there being a genetic component to the aetiology of HLHS in some cases.

Additional evidence for this hypothesis comes from the higher recurrence rate of the syndrome in subsequent pregnancies than in other forms of congenital heart disease, the high frequency of bicuspid aortic valves in first degree relatives, and the finding that some cases of HLHS occur in association with a number of syndromes including Turner's syndrome, Jacobsen syndrome, and trisomies 13 and 18.⁷

This case report illustrates how the findings from early fetal echocardiography with postmortem follow up can help to extend our understanding of the cause of HLHS. It is possible

that there are several candidate genes, which if affected lead to HLHS. They may lead to a primary defect of left heart development, as is likely in cases with mitral and aortic atresia, or result in reduced flow through the left heart, as in severe aortic stenosis with a patent mitral valve. Identification of the genes responsible for HLHS will require accurate knowledge of both the morphological and clinical phenotype of this condition from early fetal to neonatal life.

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