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Progression of fetal heart disease and rationale for fetal intracardiac interventions

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Pulmonary atresia;
Hypoplastic left heart syndrome

Summary The outcome of cardiac disease diagnosed before birth is paradoxically worse than that diagnosed postnatally. In part, this is because fetal screening detects cases that are already showing failure of cardiac growth which are usually progressive with secondary damage to the myocardium, lungs and brain. Fetal valvuloplasty has been proposed for cases of critical aortic and pulmonary stenosis or atresia, and atrial septostomy for a restrictive oval foramen associated with aortic stenosis, hypoplastic left heart syndrome and transposition of the great arteries. The rationale for fetal therapy is to restore forward flow and reduce intraventricular pressure, thus improving coronary perfusion and minimizing ischaemic damage. Successful valvuloplasty has reduced systemic venous pressures and reversed fetal hydrops, thus prolonging pregnancy. It has resulted in improved ventricular growth in some cases and spontaneous opening of a closed oval foramen with normalization of pulmonary venous waveforms. These signs suggest better fetal cardiopulmonary development and improved surgical outcomes.

Introduction

By 50 embryonic days, the fetal heart has developed from a cardiac crescent to assume its final morphological form. Left and right sidedness of fetal organs, including the heart, have been determined and defects in signalling, responsible for structural malformations, have left their mark; apart from small septal defects, these are usually irreversible.[1,2] We are unable to image the heart diagnostically until about 12–14 weeks of gestation using modern ultrasound techniques, but we can already appreciate the effect that abnormal fetal flow patterns have begun to play in further remodelling valves, their supporting ventricles and great arteries.[3] Significant progression may be defined as secondary damage to the heart and lungs, resulting from abnormalities of growth and flow, so that a biventricular repair is no longer possible after delivery. Disease progression occurs in

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most conditions, except minor septal defects, but the most aggressive progression of disease is seen in congenital heart defects (CHDs) with aortic or pulmonary stenosis, and often results in hypoplasia of the supporting ventricle, thus precluding its use in the postnatal circulation.

Progression of a cardiac lesion may be monitored most easily using a combination of morphological and physiological parameters. There are a few studies that document the natural history of cardiac growth for specific fetal malformations.[4] These provide helpful information on growth of valves and ventricles throughout gestation. Cardiac malformations in the fetus are associated with abnormalities of flow through the atrioventricular valves (usually regurgitation), increased velocities through the semilunar valves, reversal of flow in the arterial and venous ducts and aortic isthmus, and abnormalities of pulmonary venous Doppler. Reversal of flow with atrial contraction in venous duct waveforms is seen in very early gestation as part of normal development. It may be seen later as a result of increased right atrial pressure when atrioventricular regurgitation is severe or the oval foramen is restrictive, but is not usually a sign of fetal hypoxaemia in this setting.[5] Serial studies of pulmonary venous Doppler are useful to assess left atrial pressure where there is left heart obstruction. Abnormal waveform patterns, characterized by reversal of flow in late diastole, may be seen in association with hypoplastic left heart syndrome and biphasic reversal with severe mitral regurgitation due to critical aortic stenosis (Fig. 1a).[6] Although simple transposition of the great arteries is not usually considered to be a malformation that 'progresses', serial evaluation of pulmonary venous and oval foramen flows may detect those who do badly because they develop early pulmonary venous congestion and haemorrhage.[7]

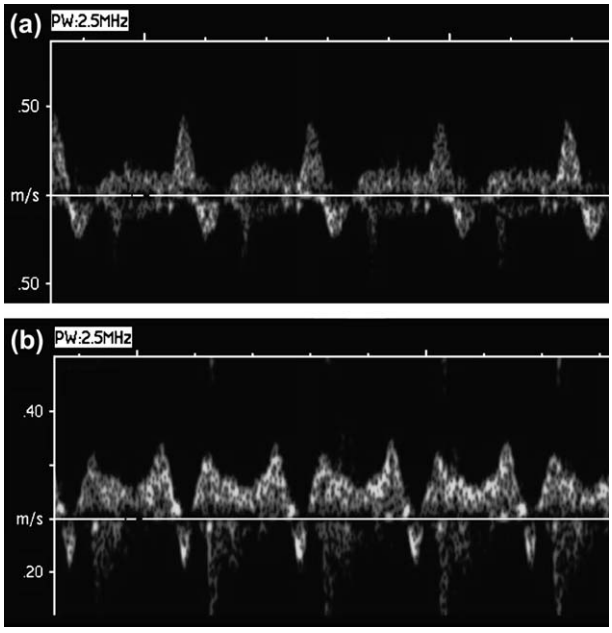

Figure 1 (a) Reversal of flow with atrial contraction in a fetus with critical aortic stenosis due to raised left atrial pressure secondary to closure of the oval foramen. (b) Normalization of pulmonary venous return following successful aortic valvuloplasty, resulting in spontaneous opening of the oval foramen.

Associated malformations and counselling

Extracardiac abnormalities and/or aneuploidy are associated with one-third of cases of major congenital heart disease. Patient management should be shared with a fetal medicine specialist, and karyotyping should be offered where appropriate.[8] Counselling may be difficult, particularly when the scan is performed in early gestation or there is suboptimal imaging. Some major defects may only become apparent later in gestation, such as diaphragmatic hernia, or may be missed altogether. These may have a major impact on perinatal management plans and result in significant comorbidity. Syndromes such as Noonan syndrome may show subtle or no cardiac pathology early in pregnancy, but progress rapidly later in gestation or postnatally.

The evidence base used to counsel parents for surgery is usually from large postnatal surgical series where the majority have not had a fetal diagnosis. It is more realistic to counsel parents based on the relatively few unselected series that document the outcome of all, including those diagnosed prenatally, many of whom will not reach the surgeon. These reports are often much less optimistic.[9,10] There are several reasons for this, including the presence of associated malformations and aneuploidy. However, the degree of secondary myocardial damage is also likely to play an important role. Fetuses with a subtle response to early aortic stenosis are not likely to be detected in a screening programme where colour flow mapping and Doppler do not form part of the protocol. Therefore, those that are detected have either more advanced stenosis and/or an exaggerated myocardial response to it, resulting in a dilated or hypertrophied myocardium with ischaemia and resultant fibrosis. This may damage the papillary muscles and result in a dilated left atrium secondary to severe mitral regurgitation. Fetal wellbeing may be further compromised by this atrial distension, leading to arrhythmia and/or fetal hydrops.