Chapter 6

Increased nuchal translucency and fetal aortic incompetence due to a dysplastic bicuspid valve

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Research Letter

A 39-year-old pregnant woman was referred for prenatal diagnosis due to an increased risk of aneuploidies due to her age and a nuchal translucency (NT) of 9.7 mm measured at 13+3 weeks’ gestation. Ductus venosus Doppler investigation showed a reversed flow during the ’a’ wave and a pulsatility index for the veins of 2. No specialised fetal echocardiography was performed at this time and no obvious structural fetal anomalies were noted. Amniocentesis was performed, (due to the unfavourable position of the placenta for chronionic villus sampling), revealing a normal female karyotype, (no 22q11 deletion).

A detailed ultrasound examination performed at 20 and 21 weeks’ gestation showed no obvious structural anomalies, except for mild nuchal edema and suspicion of cardiac pathology. A fetal echocardiogram showed a situs solitus levocardia with atrio-ventricular and ventriculo-arterial concordance. The atria were normal and the foramen ovale was non restrictive with normal right to left shunting over it. The atrioventricular valves were normal without any regurgitation. There were two normally sized ventricles. The pulmonary valve was normal. The aortic valve annulus measured 1.5mm and was smaller than the pulmonary valve annulus (3.8mm). The aortic valve appeared thickened and bicuspid. A flow velocity of 1.2 m/s was measured over it. The aortic root was dilated. A high-velocity jet of aortic regurgitation extending at least 2/3 of the depth of the left ventricle was seen on Colour Doppler. The ductal and aortic arches were normal. The systemic and pulmonary venous drainage was normal. There was no pericardial effusion or ascites.

The couple was counselled by a paediatric cardiologist, a gynaecologist and a geneticist. In view of the poor prognosis of prenatally detected aortic regurgitation, the parents chose for termination of pregnancy. This was performed by chemical induction. Psychological support was provided by a social worker. A 585g premature fetus was born by vaginal delivery at 22 weeks’ gestation. The post mortem examination revealed a mildly dysmorphic fetus with hypertelorism, facial asymmetry, a cleft in the soft palate, a webbed neck, low set ears, clinodactyly, clubbed feet and abnormal, irregularly positioned toes. Examination of the fetal heart showed an abnormal aortic valve with a missing valve leaflet and the remaining leaflets composed of thickened myxomatous tissue (Figure 1). The mitral valve was also dysplastic and of similar myxomatous tissue. The left ventricle showed some hypertrophy (left ventricular wall of 4.5mm as opposed to the right ventricular wall thickness of 2.5mm). There was no evidence for an aortico-left ventricular tunnel. The foramen ovale was unusually large. The tricuspid and pulmonary valves were normal.

A case of aortic regurgitation due to a missing aortic valve leaflet detected in a 21 week fetus by fetal echocardiography has been described. Usually the detection of aortic regurgitation in a neonate or fetus suggests the diagnosis of an aortico-left ventricular tunnel comprising of an abnormal channel originating in the ascending aorta, bypassing the aortic valve and terminating in the left ventricle (Paladini et al., 1998). Other causes of aortic regurgitation, such as a complete absence of the aortic
valve or with a monocuspid aortic valve, are very rarely seen on prenatal echocardiograms (Toews et al., 1975; Marek et al., 1996; Paladini et al., 1998; Eronen et al., 2003).

Aortic regurgitation is a rare but serious cardiac lesion in the fetus as it produces a chronic volume overload of the left ventricle and leads to the development of fetal hydrops (Marek et al., 1996; Paladini et al., 1998; Eronen and Heikkila, 2003). Aortic regurgitation and the sometimes associated aortic stenosis can lead to severe left ventricular hypertrophy, ventricular dilation and myocardial fibrosis. Postnatally the systemic vascular resistance increases, aggravating the aortic insufficiency with detrimental effects. Eronen and Heikkila (2003) described a case with a dysplastic pulmonary valve and absent aortic valve cusps. Despite performing an emergency caesarean section at 31 weeks, their patient died postnatally due to an exacerbation of the aortic insufficiency causing coronary steal.

In our case, at the time of the echocardiography, there was not yet direct evidence for cardiac dysfunction, however, left ventricular volume overload can be assumed on the basis of the documented left ventricular hypertrophy. The aortic valve was small, being about half the size of the pulmonary valve, adding an additional pressure overload to the left ventricle. Both features were likely to become more pronounced with advancing gestation and, as aortic regurgitation is a progressive disease, cardiac failure was likely to have developed in the course of the pregnancy.

Figure 1. Cross section through the great vessels above the semilunar valves, the abnormal, bicuspid aortic valve (arrow) is seen on the right.
In chromosomally normal fetuses an increased NT is associated with a broad spectrum of developmental disorders including a variety of rare genetic syndromes and cardiac defects (Makrydimas et al., 2003; Atzei et al., 2005). The risk of major cardiac anomalies increases with increasing NT thickness (Atzei et al., 2005). In our case the NT measurement was significantly increased at 9.7mm. A variety of cardiac anomalies, involving both the right and the left heart, have been described in association with an enlarged NT (Atzei et al., 2005). However, the association between this rare cardiac abnormality and an enlarged nuchal translucency is novel.

In our case the persistence of nuchal edema in the second trimester was an additional factor prompting pregnancy termination due to the increased risk of a genetic syndrome with impaired neuro-development. The post mortem examination revealed mild dysmorphic features and structural anomalies. It is thus not clear if the increased NT was associated with the cardiac defect or if it was an indicator of an as yet unspecified genetic syndrome or both. The list of genetic syndromes associated with increased nuchal fluid is constantly increasing. Cardiac anomalies occur commonly in these syndromes. Noonan syndrome is a good example often presenting with an increased NT, pulmonary stenosis and hypertrophic cardiomyopathy (Bekker et al., 2007).

The neck and heart both originate from ectomesenchymal tissue. Normal cardiac chamber development depends on a normal flow pattern and sequence of expression of growth factors (Stekelenburg-de Vos et al., 2003). Neural crest ablation results in flow disturbances followed by the development of heart defects, suggesting that altered flow, and not the lack of migration, links the neck edema and the cardiac defects.

Cardiac dysfunction in our fetus may partially explain the excessive and persistent nuchal fluid accumulation, however recent data, where cardiac function was measured at 11-14 weeks’ gestation, does not support the notion of cardiac failure as the cause of the increased nuchal translucency (Huggon et al., 2004). The abnormal ductus venosus flow pattern seen in this fetus supports a haemodynamic disturbance (Bilardo et al., 2001). Other possibilities include abnormal lymphatic and vascular development and alterations in the dermal cellular matrix. The definitive answer remains uncertain.
References


