Suspected fetal anomalies

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Abstract

Assessment of the unborn patient following the initial detection of a fetal structural anomaly involves further detailed ultrasound scanning, usually followed by other investigations to ascertain the extent of the abnormality, and to attempt to identify an underlying cause. Although many congenital fetal anomalies are sporadic, some are associated with maternal infections or medical disorders, such as diabetes, and others are caused by underlying pathological genetic variants. As the understanding of the human genome advances, the proportion of 'idiopathic' congenital anomalies will decline. The new molecular technologies of array hybridization and non-invasive prenatal diagnosis will move the specialty of prenatal diagnosis into a new era in the very near future. However, there will always be a place for careful history taking, as one of the cases below illustrates.

Diagnosis of maternal disease following clinical assessment of fetal anomalies allows maternal treatment in order to prevent progression of disease, prevent further fetal consequences and may even have implications for the family and other siblings. Similarly, the diagnosis of genetic disorders allows for focused earlier testing in future pregnancies, and may also have wider implications for the family.

This journal has published a number of articles previously which use case histories to illustrate the principles of prenatal diagnosis and management. This article adds three further cases. The details of the anomalies are less important than the processes by which the final diagnoses were reached.

Keywords bladder exstrophy; fetal limb abnormalities; free fetal DNA; maternal diabetes; Okihiro syndrome; sacral agenesis

Introduction

Once a fetal structural abnormality is detected antenatally, detailed assessment is undertaken by fetal medicine specialists to confirm the diagnosis, determine its extent, identify the presence of other structural abnormalities and counsel regarding the implications for the fetus, the pregnancy and the neonate. Antenatal diagnosis enables the couple to exercise informed choice. Some abnormalities may be serious and the couple may be offered the option of termination of pregnancy. Whereas some abnormalities may benefit from antenatal treatment, others may require early intervention following delivery.

The outcome and prognosis for the fetus or the neonate depends on the presence of other associated structural abnormalities, underlying chromosomal or genetic abnormalities, the interventions and treatment options available for the structural abnormality and the short and long-term handicap incurred to the child as a result of the abnormality. The presence of underlying chromosomal or genetic abnormalities is associated with an increased incidence of learning difficulties and multiple structural abnormalities, which may or may not be detected before the birth and may confer significant disability and a limited life expectancy. Isolated structural abnormalities usually have a better prognosis.

The assessment of fetal structural abnormalities should also include a detailed maternal medical history, including enquiry about drug use during the pregnancy, both prescribed and illicit, and family history. Medical conditions such as diabetes and medications such as anti-epileptics are associated with an increased incidence of structural malformations. If an underlying maternal medical condition such as poorly controlled diabetes is revealed for the first time during assessment of fetal structural abnormalities, then it becomes important to manage the maternal medical condition to prevent any other adverse outcome for the mother as well as the fetus. Detailed family history can sometimes point towards a genetic aetiology, which may have implications for the mother, the unborn child, and other family members.

In addition to detailed history, further investigations may be needed to give more information regarding the extent and prognosis of the condition. These investigations may be in the form of other imaging modalities e.g. magnetic resonance imaging (MRI) scan in case of fetal brain abnormalities, or may involve inquisition of the fetal genotype, either invasively using CVS or amniocentesis, or non-invasively using free fetal DNA studies of maternal blood.

Case 1: Diagnosis of maternal type 1 diabetes following diagnosis of fetal structural abnormality at 26 weeks gestation

An 18-year-old woman in her first pregnancy, thought to be fit and well, was referred to a fetal medicine unit for further assessment at 26 weeks gestation following detection of fetal talipes on her detailed scan a number of weeks earlier. She had previously declined Down syndrome screening. A scan by the fetal medicine team showed that both femurs were below the 3rd centile with normal abdominal and head circumference measurements, and normal amniotic fluid index. Additional structural abnormalities were identified on the scan including the failure of ossification in the lower spine, consistent with sacral agenesis (see Figures 1 and 2), persistent dorsiflexion and abnormal appearance of the left foot (Figure 3), a ventricular septal defect (VSD) with possible overriding of aorta, and a single umbilical artery.

A fetal MRI was performed to assess the fetal spine and spinal cord and this confirmed sacral agenesis with the spinal cord ending at a higher level than normal with a blunted appearance. Normal intracranial anatomy was noted (Figure 4). Fetal echocardiography by a paediatric cardiologist confirmed the presence

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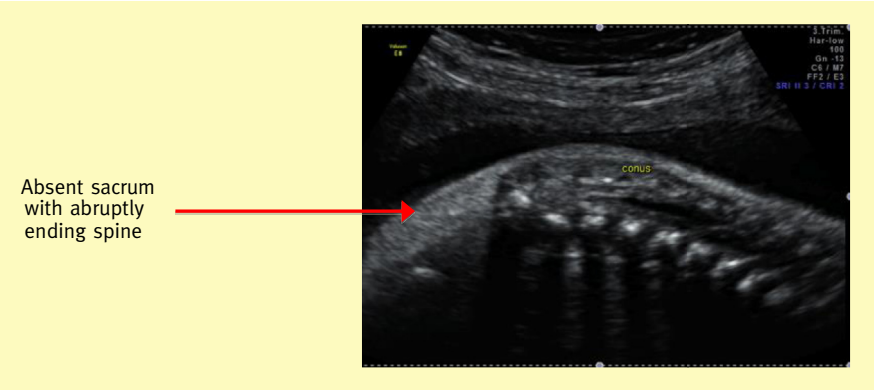

Figure 1 Ultrasound image of fetal spine in sacral agenesis.

of a ventricular septal defect with an over-riding narrowed aorta, and the possibility of sub-aortic stenosis.

She was counselled regarding the potential implications of these abnormalities for the baby and possible causes for the multiple structural abnormalities were discussed, including diabetes and chromosomal abnormalities.

The finding of sacral agenesis prompted an oral glucose tolerance test (GTT) and an HbA1c level. The HbA1c was 85 mmol/mol (normal range: 30–59) and the capillary blood glucose was 14.2 mmol/litre, with a markedly abnormal oral glucose tolerance test. Detailed history at this stage also revealed frequent episodes of glycosuria earlier in the pregnancy and a family history of diabetes. Her father was diagnosed with type 1 diabetes at the age of 13 years and apparently died at the age of 27 secondary to renal failure. Her paternal grandmother had type 2 diabetes and her cousin's sister from her father's side had diabetes in pregnancy and was subsequently diagnosed with type 1 diabetes.

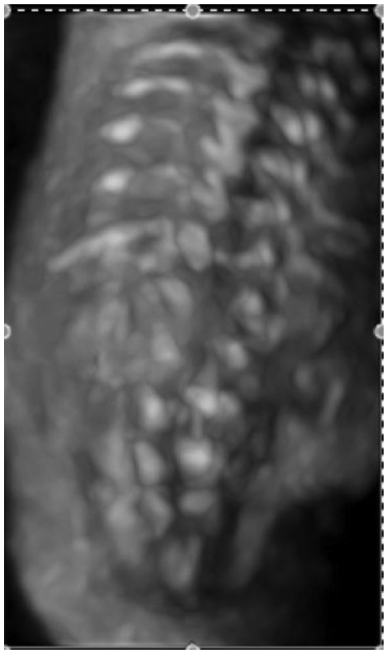

Figure 2 Three-dimensional image of spine showing small sacral stump.

Although maternal diabetes was considered to be the most likely cause, the possible implications of an underlying chromosomal abnormality in the fetus were also discussed, including the high chance of significant learning difficulties. Amniocentesis was offered but declined at that stage because of fears of preterm labour. A late amniocentesis at 34–36 weeks was suggested. She received specialized counselling from a paediatric surgeon and cardiologist. The option of termination of pregnancy was discussed in the event of an underlying chromosomal disorder.

The implications of caudal regression syndrome for the child, including the possibility of problems with gait and walking, and bladder, bowel and sexual dysfunction were described. The child would be expected to be of normal intelligence if the chromosome analysis was normal. She was made aware that it is very difficult to predict the exact extent of problems until further assessment of the lower limb and bladder function by orthopaedic surgeons and urologists after the birth of the child.

She was started on long and short-acting insulin, and was taught home blood glucose monitoring. She was monitored on a regular basis by the fetal medicine team for fetal growth and wellbeing and by the diabetes team with regards to her glucose control.

An ultrasound scan at 30 weeks gestation revealed polyhydramnios and a macrosomic fetus with short long bones. She was a poor attender of hospital appointments and she did not attend any further appointments after 33 weeks. She delivered a baby boy weighing 3080 g by ventouse delivery following

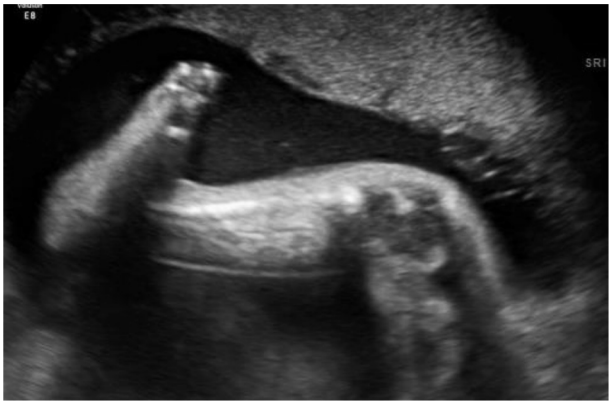

Figure 3 Persistent dorsiflexion and abnormal position of the left foot.