Antenatal screening and fetal intervention

Brian W Davies

Abstract

Congenital malformations are a common cause of reduced life expectancy and disability and can affect all body systems. Therefore, they are relevant to all surgeons. One in fifty children will have a major or significant congenital anomaly at birth. Since the advent of antenatal ultrasound (US) there has been the potential to diagnose many congenital anomalies before birth. This can forewarn parents and clinicians, so that treatment can be started promptly following birth rather than waiting for the baby to become symptomatic. It has also raised the possibility of treatment in-utero with the goal of stopping or reversing the pathological effects of the anomaly on the developing tissues, which will, hopefully, reduce morbidity and mortality once the baby is born and thus improve outcomes. This article focuses on congenital anomalies relevant to surgeons, initially looking at screening and diagnosis and how this may affect treatment and surgery following delivery. The second part will look at some of the interventions that have been attempted to treat 'surgical' congenital anomalies in-utero.

Keywords Antenatal screening; antenatal ultrasound; congenital diaphragmatic hernia; lower urinary tract obstruction; spina bifida

Screening

In the UK, antenatal screening is offered to all pregnant women. This involves:

1. Blood tests to look for red cell anomalies (sickle cell, thalassaemia), blood-borne infections (syphilis, hepatitis B, HIV), red cell antibodies and rhesus status in the mother, and, in combination with an early pregnancy ultrasound, the potential risk that the baby has a trisomy chromosomal anomaly.
2. Ultrasound (US) scanning. All are offered an early ultrasound scan at 11–14 weeks gestation, and a detailed structural scan to look for congenital anomalies at 18–21 weeks.

It is vital for both clinicians and parents to appreciate that these tests:

1. Will not detect all anomalies and that a number of serious life-limiting conditions cannot be detected until after birth. This is also true for the infant with multiple congenital anomalies, where one or two anomalies can be seen, but the tests may not be able to detect the other anomalies, thus the parents and clinician may not have the full picture of the child's diagnosis or prognosis until after birth. For example, in the VACTERL association (Vertebral, Ano-rectal, Cardiac, Trachea-oEsophageal, Renal and Limb), the cardiac, vertebral, limb and some of the renal anomalies can often be seen on the 20 week scan. However, the oesophageal atresia and ano-rectal anomaly probably will not be able to be seen.
2. That not all anomalies seen will have an impact on the child, and the scan may find some incidental conditions that will resolve spontaneously or will not require any treatment nor limit life in any respect.
3. Have varying degrees of accuracy (i.e. sensitivity and specificity). Some conditions can be detected with high precision, for example, gastroschisis where the intestines are seen within the amniotic fluid. However, for other conditions, US may be suggestive rather than conclusive. For example, the combination of polyhydramnios and minimal or no fluid seen within the fetal stomach may be indicative of oesophageal atresia; however, this will need post-natal tests to confirm or refute. This is more likely to be seen later in pregnancy, rather than on an 18–21 week scan. Often the scan shows 'markers' that can in some cases indicate pathology. For example, when 'echogenic' bowel is seen (when the intestines look brighter than usual), in approximately 50% of cased this indicates intestinal pathology of a variety of causes, including meconium ileus due to cystic fibrosis. However, in the other 50%, the babies have normal intestinal function and growth.

Further antenatal tests are used selectively, depending upon the results of the above, or if the parents' family history indicates that other tests are required. These can involve testing the parents (for example, if the scan shows features that may be consistent with cystic fibrosis [CF], both parents can be tested to see if they are carriers of the common mutations of the CF gene), or testing the baby. The baby's chromosomes can be checked by invasive tests including chorionic villus biopsy or amniocentesis. Both these have a quoted 1% risk of inducing a miscarriage, thus cannot be taken lightly. More recently, testing for cell-free fetal DNA (cffDNA) within a blood sample taken from the mother is possible for some conditions. This looks for fragments of DNA that have come from the placenta. It can be done relatively early in the pregnancy (from approximately 10 weeks). As this has no risk of miscarriage, it is highly likely that this technology will develop rapidly in the next few years. There is currently research into whether or not to adopt cffDNA screening for common aneuploidies (trisomy 13, 18, 21 and Turner's syndrome (XO)) into the UK screening programme. Direct fetal blood sampling is possible in later pregnancy and can be done at the same time giving intravenous treatment to the baby. Most commonly this would be for in-utero blood transfusions in cases of fetal anaemia. Fetal magnetic resonant imaging MRI scans are possible and can add detail to the findings of antenatal US. This is most commonly performed when there are concerns about brain development. Table 1 lists the potential complications of screening.

Antenatal counselling

When an antenatal anomaly has been detected, it will need to be confirmed and explained to the parents. Initially this will be done by the local obstetrician or screening midwife. Following this, a prompt referral to a regional fetal medicine department is usually made, where the parents can meet with a feto-

Brian W Davies *MB ChB FRCS (Paed Surg) is a Consultant Paediatric Surgeon at Nottingham Children's Hospital, Queen's Medical Centre, Nottingham, UK. Conflicts of interest: none declared.*

Complications of antenatal screening

Complication	Causes	Significance
Miscarriage	Chorionic villus biopsy Amniocentesis	Death of fetus
Unnecessary parental distress	False positives; lack of precision/specificity of 'markers' of anomalies	Psychological distress and sometimes clinical depression
Unnecessary invasive tests	False positives; lack of precision/specificity of 'markers' of anomalies	Potential for miscarriage
Missed diagnoses[a]	False negatives	Baby presents with symptoms and suffers complications that might have been avoided if treatment had commenced earlier
Reduction in society's value of people with disabilities	Emphasis on in-utero diagnosis with potential termination of pregnancy for serious disabilities	Parents who chose to continue with pregnancy feel under pressure to undergo a termination Patients may not feel valued
Termination of pregnancy based on gender alone	Society/family preference (Parents learn the likely sex of baby from a sonographer and seek a termination from another provider)	Large number (millions) of 'missing' girls in some societies Beware this occurs in most countries

[a] Conditions that can sometimes be diagnosed on routine US scanning, thus excludes those conditions that cannot be seen at 18—21 weeks.

Table 1

maternal obstetrician and ideally a clinician who has experience of looking after children born with that condition. This gives the opportunity for them to meet one of the team who will continue to be involved in the care of their child following birth, and also for balanced counselling to be given. Following this, plans for the ongoing care of both mother and baby, including timing, method, and place of delivery can be made (see Table 2).

Antenatal counselling aims to inform the mother/parents of the condition, outline the treatment required, and explain the impact on the child (and family) both initially and lifelong. Any uncertainty in either the diagnosis or the possible associated other anomalies also need to be discussed. A balanced presentation of the potential risks of mortality and morbidity, as well the potential for a good outcome, needs to be given. It is important to remember that once the parents are given the diagnosis of a congenital abnormality, they will usually go through a bereavement-like process as their previous dreams of having a 'perfect' baby will have been broken. Therefore, as is the case after any serious diagnosis has been given, they may well only remember very little of what is said at this initial appointment. As such, carefully written information and arrangements for follow-up multiple appointments are essential. Similarly, experience shows that this group of patients have nearly always explored their baby's condition further 'on-line' before subsequent appointments.

My practise has been to see ladies/couples on their second visit to the feto-maternal clinic. I find it helpful to watch the relevant part of the US, as for many conditions this helps me to know what end of the spectrum of complexity of the condition this infant is likely to have. For example a small exomphalos would usually be repaired with a single operation, whereas a large one may need staged management and both can be associated with serious associated abnormalities, and thus by observing the scan myself, it is more likely that I can estimate which method is more likely to be suitable for a medium-sized exomphalos. During counselling, I would, of course, mention the full range of potential surgical options.

The counselling begins by asking how much the parents understand about the condition. This can be really helpful, so that any misunderstandings can be clarified and expectations understood from the start. For some conditions, photographs of previous babies are very useful, for example gastroschisis, where the intestines are eviscerated through a small defect in the abdominal wall adjacent to the umbilical cord. However, it is always important to judge this carefully as not all parents will want to see these. Parents will be keen to know the practicalities, including confirmation of the diagnosis, timing of surgery, likely length of stay in hospital, and the follow-up schedule. Similarly, the surgeon can reinforce the importance of breast milk feeding and how this can still make a real difference to the baby especially if they have a gastrointestinal anomaly. By mentioning the importance of postoperative pain relief, you will demonstrate that you are concerned about the things that they are worried about and this will help reduce their fears. Parents will often have a lot of questions, and therefore, it is important to make sufficient time for the counselling process and not to appear rushed. It is really helpful to then summarize the consultation in a letter to the lady/couple.

Fetal intervention

In-utero treatment has been attempted for a range of congenital anomalies. The following three conditions illustrate well the rationale for and the challenges of fetal intervention.

Congenital diaphragmatic hernia (CDH)

This is a severe malformation with up to 40% mortality. This significant mortality is due to poor development of the lungs that,