Neural tube defects — prenatal diagnosis and management

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SUMMARY

Neural tube defects rank second to congenital heart disease as a major cause of congenital malformation. Recent developments in ultrasound have improved prenatal diagnosis. Due to anomaly scans at 18 weeks gestation and the availability of a genetic clinic, prenatal diagnosis of neural tube defects at the Royal Maternity Hospital was 91.2% during 1987–1989. However, only 50% of parents accept termination of pregnancy and it is questionable if prenatal diagnosis is of benefit to those who wish to continue with the pregnancy. Parents may accept the situation better at birth, having had time to come to terms with it, helped with support from the obstetrician, clinical geneticist, paediatrician, genetic nurse and social worker. For some affected fetuses who have better muscle function and leg movement at term it appears from the literature that the outcome may be improved by caesarean section delivery. In Ireland fetuses with neural tube defects will continue to be delivered, as termination is unacceptable to many, but despite this there may be a positive benefit from prenatal diagnosis of neural tube defects. Prospective randomised controlled trials are needed to confirm benefit from delivery by caesarean section for fetuses with a good prognosis. As a result of prenatal diagnosis of a neural tube lesion the fetus should enjoy benefit in terms of physical morbidity, and the parents should benefit in terms of psychological morbidity.

INTRODUCTION

Neural tube defects are a heterogeneous group of malformations resulting from failure of neural tube closure up to the fourth week after conception. They have a multifactorial origin and range widely in severity from anencephaly to surgically correctable meningocele. They may be accompanied by neurologic, musculoskeletal, urologic and developmental abnormalities. They rank second to cardiac
abnormalities as a cause of major congenital malformation, with a wide variation in prevalence worldwide and a well recognised increased prevalence in Northern Ireland of 3.3 per 1000 deliveries. Hydrocephalus is present in 80% of cases with spina bifida.

Recent ultrasound developments have resulted in better detection of these conditions prenatally. Anencephaly was the first fetal malformation detected by ultrasound and in 1986 Nicolaides described ultrasonic markers of neural tube defects, scalloping of the frontal bones called 'the lemon sign' and anterior curvature of the cerebellar hemispheres called 'the banana sign'. An alternative to ultrasound is biochemical screening by measurement of maternal serum alpha-fetoprotein. At present there is no alpha-fetoprotein screening in Ireland and its use in Great Britain is controversial.

Prenatal diagnosis of a major malformation allows the parents the option of termination of pregnancy, but it is questionable if it is of any benefit to them if termination is unacceptable. The aim of this paper is to report our experience with the diagnosis and management of pregnancies complicated by neural tube defects.

METHODS

Since 1987 in the Royal Maternity Hospital, all women who book early are offered an ultrasound scan performed at 18 weeks' gestation by ultrasonographers. A scan carried out at booking allows gestation to be confirmed thus ensuring accurate timing of this anomaly screening scan. Very few women refuse to have this anomaly scan booked. Any woman at risk of a child being affected with a neural tube defect either due to a past obstetric or family history, is offered referral to the genetic clinic. Recently maternal alpha-fetoprotein screening has been introduced for a trial period. These latter procedures are offered as an 'opt-in' service. If an abnormality is detected by an ultrasonographer at 18 weeks' gestation, an obstetrician is immediately informed. The obstetrician then informs the parents of the findings and an appointment is made for the next genetic clinic. At the genetic clinic the parents are seen by a clinical geneticist, prior to a further ultrasound scan and confirmatory tests performed by an obstetrician trained in perinatal medicine. Management is individualised after careful discussion involving the parents, obstetrician and clinical geneticist regarding the severity of the lesion and prognosis for the child.

If the parents decide that the pregnancy should be terminated, this is performed using gemeprost pessaries. Should termination be unacceptable, the parents receive full support throughout the remainder of the pregnancy. Recently, delivery by elective caesarean section at 37 weeks’ gestation is offered to parents, where it is felt that there is a good prognosis for the child. Based on postnatal criteria established by Lorber in 1971 a good functional prognosis is predicted if the lesion is below the first lumbar vertebra, and is not associated with severe kyphoscoliosis, severe hydrocephalus or other gross congenital defects.

Pregnancies complicated by neural tube defects which were managed in the Royal Maternity Hospital during the three year period 1987–1989 are reviewed. The figures were obtained from delivery record books, genetic clinic records and the Infant Surgical Unit in the Royal Belfast Hospital for Sick Children.

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RESULTS
During the three year period there were 34 pregnancies complicated by neural tube defects among 10,042 deliveries, a prevalence of 3.4 per 1000 deliveries. Of the 34 cases, 13 were anencephalics and 18 were spina bifida with or without hydrocephalus. Three cases were isolated hydrocephalus. Seventeen were female fetuses, 13 male and four unknown.

Over 90% of the cases were diagnosed prenatally (Table I). The three undiagnosed were a closed myelomeningocele, an occipital meningocele and a case with hydranencephaly. These cases were 'missed' diagnoses rather than 18 week anomaly scans not done, or refused. Of the three cases diagnosed in the third trimester one was booked at 33 weeks' gestation. 76.5% of the cases were diagnosed in the second trimester and an abnormality was missed initially in 14 women who had scans prior to 14 weeks' gestation. 41% of the abnormalities were diagnosed at the routine antenatal clinic by ultrasound scan. These were mostly anencephalic fetuses diagnosed at the booking visit, or fetuses with hydrocephalus noted later in the pregnancy. 35%, mainly spina bifida, were identified at the 18 week scan by the ultrasonographers and 15% were diagnosed at the genetic clinic in women who were high risk and had accepted genetic counselling.

| Table I | Prenatal diagnosis of neural tube defects |
|---------|-----------------------------------------|
| **Time of diagnosis** | **No of cases (%)** |
| 1st trimester | 2 (5·9) |
| 2nd trimester | 26 (76·5) |
| 3rd trimester | 3 (8·8) |
| Undiagnosed | 3 (8·8) |

Sixteen women decided to have the pregnancy terminated after prenatal diagnosis. Of 13 women with anencephalic fetuses nine (69%) opted for termination and of 18 women with spina bifida fetuses seven (39%) opted for termination. The severity of the lesion did not always appear to influence the decision, as four women with anencephalic fetuses continued with the pregnancy (Table II). Marital status also appeared unimportant, as four of the women were unmarried at the time of diagnosis; one was late booked, one decided to terminate the pregnancy and two married after the diagnosis was made and before the delivery.

| Table II | Action taken after prenatal diagnosis of neural tube defect |
|----------|----------------------------------------------------------|
| **Action** | **No of cases** |
| Termination of pregnancy | 16 (9 anencephaly 7 spina bifida) |
| Continuation of pregnancy | 15 (4 anencephaly 11 spina bifida) |
| Undiagnosed | 3 |

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Two fetuses diagnosed ultrasonically as having encephaloceles had large cystic hygromas at delivery. Of the 18 patients who continued with the pregnancy, eight had delivery by caesarean section, five electively at 37 weeks' gestation and three as emergency procedures. Ten women had vaginal delivery, four with associated destructive procedures. The perinatal outcome is shown in Table III. All the babies delivered by caesarean section had five-minute Apgar scores greater than seven. The follow up of the nine babies who survived the neonatal period is shown in Table IV.

**Table III**

**Perinatal outcome of pregnancies after prenatal diagnosis of neural tube defects**

| Mode of delivery | No of cases | Outcome          |
|------------------|-------------|------------------|
| Vaginal delivery with or without destructive procedure | 10 | 8 stillbirths 1 early neonatal death 1 livebirth |
| Caesarean section | 8 | 8 livebirths |

**Table IV**

**Follow up of neonates after prenatal diagnosis of neural tube defects**

| Mode of delivery | Follow up                        |
|------------------|----------------------------------|
| Normal vaginal delivery | Alive and well                   |
| Elective caesarean section | 4 early closure with or without shunt Alive and well 1 unsuitable for closure Alive |
| Emergency caesarean section | 2 alive and well 1 died at 15 months |

**DISCUSSION**

The incidence of neural tube defects during 1987–1989 in the Royal Maternity Hospital is similar to the higher than normal prevalence recognised throughout Northern Ireland. Compared with other studies which report equal distribution of anencephaly and spina bifida, we found 52% spina bifida compared with 38% anencephaly.4 We found a preponderance of abnormality among female fetuses. Despite achieving a diagnosis in 90% of cases, it was initially missed in fourteen women who had a scan prior to 14 weeks' gestation, due to difficulty in clear visualization of the spine and cerebellum before 18 weeks. No case of open neural tube lesion was missed in those women booked for confinement in the Royal Maternity Hospital who had a routine ultrasound scan at 18 weeks' gestation (approximately 10,000 during the three year period).

Regarding prenatal diagnosis, efficacy is described as detection and termination of those cases within a given population who are known to be affected in utero.
A discrepancy between diagnosis and efficacy exists due to several factors. Firstly, women not being screened either because they book late or decline screening, secondly, inaccuracy of the test itself and lastly, failure to terminate the pregnancy. In the present study efficacy was 47% which is comparable with other studies, but in studies from England only 10% of women diagnosed as carrying a fetus with neural tube defects declined termination compared with 50% in our population. In our clinic the parents are fully supported in whatever decision they make regarding the pregnancy, and it is therefore difficult to question why some decide not to have an affected pregnancy terminated, but it is felt that in most cases it is on religious or conscience grounds.

The recent introduction of gemeprost pessaries has improved the termination procedure and has almost eliminated the need for extra-amniotic prostaglandin. It is important that a fetus delivered after an induced abortion for an abnormality is sent for examination by a paediatric pathologist and by a clinical geneticist experienced in dysmorphology, as this may influence subsequent genetic counselling.

This point is highlighted in a report from the Manchester Regional Centre where of 71 cases aborted for neural tube defects, 56 were confirmed, two also had cleft palates, five had multiple abnormalities, three had autosomal recessive malformations, and one had a cystic hygroma; all of these may lead to an increased risk in subsequent pregnancies. In the majority of our cases although the fetus was examined by a clinical geneticist, postmortem examination was refused by the parents. The importance of this procedure should be explained to the parents.

In our study some of the parents of an anencephalic fetus, who had declined termination, requested early delivery in the third trimester. At this stage these parents accept 'early delivery' as opposed to 'termination', and we regard this as supporting the parents in their choice rather than failure of the support system offered to them. Chervenak et al in 1984 feel that termination at this stage is both moral and legal if the fetus is affected with a condition incompatible with postnatal survival by more than a few weeks, characterised by total or virtual loss of cognitive function, and where highly reliable diagnostic procedures are available. Anencephaly fulfils these criteria, with a study of 102 cases reporting no false positives or false negatives in prenatal diagnosis. The results of our study were similar.

Major chromosomal aberrations may be associated with neural tube defects as may other anatomical abnormalities and these should be excluded by a detailed ultrasound scan by an experienced sonographer and by other appropriate investigations e.g. amniocentesis or cordocentesis. The team involved in counselling should include the obstetrician, clinical geneticist, neonatologist, paediatric surgeon, genetic nurse and social worker. Where the parents elect to continue with the pregnancy or when the diagnosis is made late, they should receive full support throughout the antenatal period.

One advantage of prenatal diagnosis is that it allows choice of timing and mode of delivery to provide optimal outcome. For those who opt to continue with a pregnancy after anencephaly has been diagnosed, vaginal delivery should obviously be aimed for. However, parents should not be told that the child will die immediately, as some survive for short periods. A retrospective study of 130 cases
with meningomyelocele by Stark and Drummond in 1970,12 reported 14% showing signs of cerebral birth injury. The authors considered that for many neonates the neurologic deficit increased during vaginal delivery. There is evidence from Luthy et al13 that if a fetus with spina bifida has good muscle function and leg movement by the time the lungs are mature, paralysis is minimised by an elective caesarean section at 37 weeks’ gestation prior to the onset of labour. This study is the only prospective one; though it was not randomised. It compares 47 children delivered by elective caesarean section with 113 delivered vaginally or by caesarean section after the onset of labour. Of those born by pre-labour caesarean section subsequent motor function was better, but neonatal complications and subsequent intellectual performance showed no difference between the two groups. The authors claim better outcome was due partly to a less-impaired series of cases, partly because of selection of only the least-impaired for caesarean section and less damage to the infants as a result of the method of delivery. A group from North Carolina reviewed 32 affected children delivered by caesarean section compared with 40 delivered vaginally who were followed up for one year. They showed no significant difference in mortality, hospital stay, neurologic or developmental status.14

Of the group delivered vaginally, three developed meningitis compared with only one in the section group but a larger study would be needed to show any significance in this finding. Our findings, although not randomised or comparable, show a poor outcome associated with vaginal delivery, only one of ten surviving.

For the family the quality of life is important. Of the nine survivors in our study one died at the age of 15 months, one required no treatment after delivery, one had a lesion too extensive for closure and the remaining six required closure of the defect. It is impossible to compare the two groups as the cases with better prognosis were chosen for operative delivery and therefore introduce bias in favour of better outcome.

What is the future regarding prenatal diagnosis of neural tube defects? It is generally anticipated that a decreasing number of children will be born with these conditions as primary prevention and prenatal diagnosis advance further. However, in Ireland, whether the defect is diagnosed by ultrasound, serum alpha-fetoprotein or amniocentesis, we will continue to deliver affected babies as termination is unacceptable to many parents. It is possible that prenatal diagnosis may not only contribute to decreasing the number of affected children but may also decrease the associated morbidity and mortality for those who wish to continue with the pregnancy. Regarding the mode of delivery, each case needs to be assessed individually. Only a prospective randomised controlled trial involving a group of centres will prove any potential benefit from elective caesarean section.

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