Family implications of neonatal Gorlin's syndrome

D G R Evans, D G Sims, D Donnai

Abstract

Two very preterm infants (born at 29 and 25 weeks, respectively) were found to have abnormal ribs. Though this was thought unimportant at the time, it was subsequently shown to indicate that some members of their families had a dominantly inherited risk of developing skin cancer and other serious problems.

Case reports

CASE 1

A 22 year old mother with three sons was delivered by emergency caesarean section for breech presentation and placenta praevia. A boy weighing 1200 g was born at 29 weeks' gestation. Serious neonatal illnesses followed, and included idiopathic respiratory distress syndrome (treated with prolonged ventilatory support), tension pneumothorax, bronchopulmonary dysplasia, and episodes of acute circulatory collapse (needing full cardiopulmonary resuscitation). He also had convulsions with intraparenchymal haemorrhage, bleeding from puncture sites as a result of consumptive coagulopathy, acute renal failure (treated by peritoneal dialysis), ileal perforation (requiring laparotomy), and coagulase negative staphylococcal and candida septicaemias. Early routine chest radiographs showed incidentally that the right third and fifth, and the left fifth, ribs were bifid (fig 1). He had a large anterior fontanelle and open posterior fontanelle at 5 weeks of age. The opinion of a geneticist was sought.

The 25 year old father gave a history of dislocated shoulder from birth, examination of which showed Sprengel's deformity. He had pronounced frontal bossing with a head circumference of 62.8 cm (>5 SD above the normal mean). He had hypertelorism with an interpupillary distance of 6.8 cm (>2 SD above the normal mean) and downslanting palpebral fissures. Skull radiographs showed prominent

calcification of the falx cerebri and a pituitary fossa totally bridged by bone, and chest radiographs showed bilateral bifid ribs. The baby's elder brother aged 5 had had a skull radiograph done that showed calcification within the falx cerebri, but his other radiographs showed no abnormality. The 4 year old brother had been diagnosed as having arrested congenital hydrocephalus and chest radiograph confirmed the presence of two bifid ribs. The baby's 21 month old brother's head circumference was 52.8 cm (>2 SD above the normal mean), he had a bossed forehead, and hypertelorism with an interpupillary distance of 5.5 cms (>2 SD above the normal mean). Radiographs showed bifid anterior ends of his left third and fourth ribs, and minor scoliosis of his spine in the mid thoracic region. No members of the family had yet presented with basal cell carcinomata or jaw cysts.

CASE 2

Four and a half months after case 1 had presented, a 31 year old mother was transferred to this hospital with twins and polyhydramnios at 25 weeks' gestation. Fetal ultrasound studies suggested that the second twin had hydrocephalus. The first twin, a girl, was born by normal delivery at 25 weeks' gestation and weighed 825 g. Serious neonatal problems included idiopathic respiratory distress syndrome (treated with ventilator support), tension pneumothorax, and convulsions associated with intraparenchymal haemorrhage. A chest radiograph showed normal ribs. She died on the seventh day of life and postmortem examination was not performed.

The second twin (case 2), also a girl, was stillborn after breech delivery. Intensive resuscitation of the externally normal baby was successful. Idiopathic respiratory distress syndrome was treated with ventilator support but the baby died aged 29 hours. Chest radiographs showed that the right second, third, fourth, and fifth ribs were duplicated in the middle third, and that the left sixth rib was also bifid (fig 2). The scapulas were rotated medially and superiorly suggesting the possibility of Sprengel's deformity. Postmortem examination showed no other deformities and in particular, no evidence of internal hydrocephalus. In view of our recent experience with case 1 the parents were investigated further.

The baby's mother had had five jaw cysts removed since the age of 11 years. On examination she had a head circumference of 56.8 cm (>2 SD above the normal mean), pronounced frontal bossing, and pits in the palms of her hands and feet. She had multiple milia on her forehead, and hypertelorism, with an interpupillary distance of 6.5 cm (>2 SD above the

Figure 1 Radiograph of case 1 showing bifid ribs.

St Mary's Hospital,
Hathersage Road,
Manchester M13 0JH
Department of Medical
Genetics
D G R Evans
D Donnai

Department of
Paediatrics
D G Sims

Correspondence to:
Dr Evans.

Accepted 10 April 1991

Figure 2 Radiograph of case 2 showing the right second, third, fourth, and fifth ribs duplicated in the middle third, and bifid left sixth rib. Scapulas are rotated medially and superiorly suggesting Sprengel's deformity.

normal mean). There were no signs of basal cell carcinomata. Radiographs showed scoliosis of the spine, a calcified ovarian fibroma, calcification of the falx cerebri, and some minor rib anomalies on chest radiography.

Discussion

The appearance of early calcification of the falx, multiple rib anomalies, and hypertelorism in subjects with macrocephaly segregating in an autosomal dominant manner is highly suggestive of Gorlin's syndrome. Gorlin's syndrome is characterised by the association of

keratocysts of the jaw and multiple basal cell carcinomata.¹ Affected subjects have coarse facies, macrocephaly with frontal bossing, and hypertelorism. They may also have multiple milia on the face and pits in the palms and soles. Skeletal anomalies are usually present, including bifid ribs, vertebral anomalies, calcification of the falx, and bridging of the sella turcica—the last two of which are often present in early childhood. Sprengel's deformity and ovarian fibromata are other common features.

The main complications of asymptomatic basal cell carcinomata (third decade onward) and jaw cysts (second and third decade) necessitate regular (annual) screening with skin examination and orthopantomograms of the jaws. Major and disfiguring surgery is often required if these gene manifestations are not detected at an early stage.

Isolated bifid rib is present in 3–6/2/1000 live births,^{2,3} but in 60% of people with Gorlin's syndrome.¹ The finding of bifid ribs on chest radiographs of the two index cases was of no clinical importance at the time, but had major implications for other affected family members who have a high risk of developing jaw cysts (85%) and basal cell carcinomata (90%).

1 Gorlin RJ. Nevroid basal cell carcinoma syndrome. *Medicine* 1987;66:99–113.

2 Etter LE. Osseous abnormalities of thoracic cage seen in 40 000 consecutive chest roentograms. *AJR* 1944;51:259–63.

3 Ashbury HE, Wilding JG, Rogers FT. Roentgenological reports of chest examination made of registrants at US army induction station No 6, third corps area, Baltimore, Md, May 1, 1941 to March 31, 1942. *AJR* 1942;48:345–51.