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Partial trisomy 16 as a result of familial 16;20 translocation

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SUMMARY Although trisomy 16 is well recognised in spontaneous abortuses,[1] it is infrequent in livebirths and there is little information about the clinical effects.[2 3] We report two sibs with partial trisomy 16q resulting in infant death. Both children were severely growth retarded with small elfin faces, prominent foreheads, low set ears, abnormal external genitalia, and intractable diarrhoea.

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Case reports

The first child of healthy unrelated young parents was born after an uncomplicated pregnancy by normal delivery at term. The child weighed 2125 g at birth and her head circumference was 31·5 cm. She had distinctive facies, with a prominent forehead, small chin, and low set ears. She had bilateral fusion of the middle and fourth toes and very prominent labia majora. On the third day she developed watery diarrhoea which necessitated intravenous fluid therapy. Her condition improved briefly although

the undiagnosed diarrhoea persisted until the fifth week of life when she suddenly deteriorated and died. Necropsy showed a small VSD but no other macroscopic congenital anomalies and no histology was done.

The second pregnancy resulted in a premature small for dates but healthy female. The third pregnancy resulted in a 10 week miscarriage about which there is no information. A fourth uncomplicated pregnancy resulted in a normal delivery at 36 weeks' gestation of a male infant. He weighed 1875 g at birth, length 46 cm, and head circumference 31·7 cm. Gestational assessment confirmed his maturity. External congenital anomalies included a small elfin face with a prominent forehead and low set ears, giving him an almost identical appearance to the child who had died 8 years earlier (fig 1). He had severe hypospadias with a bifid scrotum, dystrophic nails on all digits, and rockerbottom feet. A soft systolic murmur compatible with a VSD was audible after the third day of life. At 48 hours he became pale and hypotonic and developed frequent watery motions but no vomiting. He was never hypoglycaemic and there was no evidence of infection. Faecal fluid contained 2% reducing substances which persisted despite giving only dextrose feeds. Serum electrolytes were normal although initially the urea was raised (11·3 mmol/l) and he had a moderate metabolic acidosis. He was parenterally fed but the diarrhoea persisted despite subsequent trials of various infant formulae and loperamide. Serum electrolytes remained normal with the exception of moderate hypokalaemia which was easily corrected. No bacteria or viruses were isolated from stool specimens. A barium follow through showed a normal bowel and a chest *x*-ray showed a normal heart with slight prominence of the lung vessels. The skull *x*-ray showed defective ossification of the parietal and frontal bones. Analyses of blood and urine showed no evidence of a metabolic disorder. Diarrhoea persisted until he died at 18 days. Permission for necropsy was refused.

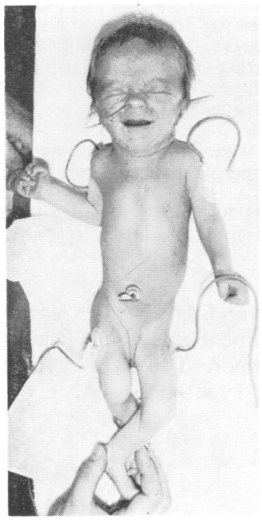

FIG 1 *Physical appearance of second abnormal child.*

CYTOGENETIC FINDINGS

The karyotypes of both abnormal infants were 46,XX or XY,−20,+der(20),t(16;20)(q13;p13)pat. The breakpoint of the long arm of chromosome 16 appeared to be at band q13 just below the heterochromatic region and on chromosome 20 at band p13 (fig 2).

FAMILY STUDIES

Cytogenetic analysis performed in 1976 after the birth of the first infant identified the translocation. The parents at that time were both 16 years of age, the implications of this translocation were not clearly understood, family studies were not attempted, and subsequent pregnancies were not monitored by amniocentesis. After the birth of the second child with the unbalanced translocation, both parents had matured considerably and further family studies were

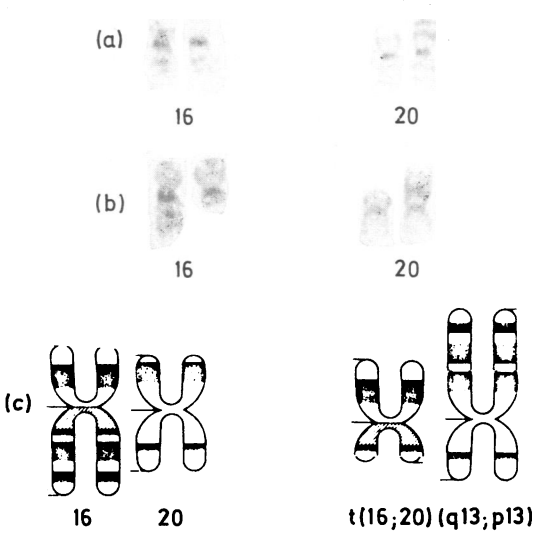

FIG 2 *Partial karyotypes of (a) the probands, and (b) the father. (c) Diagrammatic representation of breakpoints.*

initiated. The translocation was found in other members of the family, although in no other part of the family was there any history of obstetric failure or abnormal livebirths. All the relevant members of the family have now received genetic counselling. The original family have recently completed a further pregnancy which was monitored by amniocentesis, and the infant is a carrier of the balanced form of the translocation.

Discussion

Yunis *et al*[2] reported the first case of a liveborn infant with a partial trisomy 16q–. This trisomy is almost identical to ours although the case report of Yunis *et al*[2] does not state at what age the infant died. Since then, data have been accumulating on the effect of partial monosomy and partial trisomy of chromosome 16.

Most of the chromosomal anomalies are the result of a balanced translocation of parental derivation, which also involves either monosomy or trisomy of other chromosomes in the karyotype. Although early reports of full trisomy 16 do exist[4–6] they predated banding techniques and cannot be included in an attempt to define a syndrome. Full trisomy 16 is well reported in spontaneous abortion and generally results in disorganised embryos with very little evidence of development. Limited postnatal survival is possible with both partial trisomy 16p and 16q.[3 7]

Roberts and Duckett[3] reviewed published reports and included three cases of partial trisomy 16p, three cases of partial trisomy 16q, and one case with partial trisomy 16p and 16q. The most common features described in both of these trisomies were digital deformities, low birth weight, small malformed facies, which included low set abnormal ears, small palpebral fissures, and hypoplastic mandible. These anomalies are also consistent with anomalies found in many other chromosomal aberrations. Ridler and McKeown[7] reported trisomy 16q arising from a maternal 15p;16q translocation. The breakpoint on the 16 was at q11 and the involvement of chromosomal material was similar to that in the two cases reported here. The anomalies found included a small and emaciated infant with a small elongated head, a narrow face, and a very low hair line; the child was described as having leprechaun-like facies. The skin was wrinkled, the limbs were abnormally flexed, and the hands showed a transverse palmar crease on the right and clinodactyly of both fifth digits. The infant died after 12 days.

The two cases presented here suggest an association between the intractable diarrhoea, which was the apparent cause of death in both, and partial trisomy 16. There is no report of this in any of the other cases.

Although there are perhaps still insufficient data to attempt to define a syndrome for partial or full trisomy 16, the most notable characteristics are intrauterine growth retardation, particular abnormalities of the face with downward slanting palpebral fissures, abnormal nose and ears, micrognathia, flexion deformities of the limbs and digits, and heart defects. Although many of these anomalies are found in association with other chromosome aberrations it is the particular facial appearance which suggests the trisomy for this chromosome.

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