Case reports

Journal of Medical Genetics 1989, **26**, 577–589

Duplication of distal 17q from a maternal translocation: an additional case with some unique features

A CAINE*, D M KNAPTON*, R F MUELLER†, P J CONGDON‡, AND D HAIGH§

*Regional Cytogenetics Unit, St James's University Hospital, Leeds; †Department of Genetic Counselling, and ‡Department of Paediatrics, Leeds General Infirmary; and §Department of Paediatrics, Bradford Royal Infirmary.

SUMMARY A female with multiple dysmorphic features was found to have an unbalanced karyotype with duplication of the distal long arm of chromosome 17 and deletion of the terminal region of the short arm of chromosome 12. This was derived from a reciprocal translocation in the mother, 46,XX,t(12;17)(p13.3;q23). Clinical findings are presented and comparison with other reported cases of distal 17q duplication shows several unique features in our case.

Duplication of 17q is very rare with only a dozen reports published.^{1,2} Many of the dysmorphic features in the cases reported are similar and it is now becoming a recognisable syndrome. One de novo case has been interpreted as a tandem duplication of 17q25→qter based on the previously reported features of such duplications.³ Most cases, however, are inherited and are the result of segregation from a balanced translocation in one of the parents. The deletion of material from the other chromosome involved in the translocation appears to have a minimal clinical effect.

Case report

The proband was the first child of unrelated parents, the mother being 25 years of age. The pregnancy was normal apart from the mother taking lorazepam and diethylpropion hydrochloride throughout the pregnancy. Ultrasound scans carried out at 17, 21, and 25 weeks by dates indicated gestational ages of 12, 17, and 21 weeks, respectively. Dating at the last scan was assessed by femur length and abdominal

circumference since biparietal diameter measurements were not possible owing to the fetal position. The mother was induced at 38 weeks because of high blood pressure and a large increase in weight. She was given a trial of labour because of her short stature, but fetal distress ensued resulting in an emergency caesarian section.

After a difficult delivery by cephalic presentation, a markedly hydropic female baby was born, birth weight 3900 g. There was no respiratory effort and intubation was difficult owing to massive oedema (fig 1). Bilateral thoracentesis was performed and the infant was transferred to a ventilator and an exchange transfusion was performed. An intra-

FIG 1 X ray of chest and abdomen showing massive oedema of subcutaneous tissues (↔) and calcification in the gall bladder (→).

FIG 2 Partial karyotypes showing $t(12;17)(p13.3;q23)$. (a) Chromosomes 12 and 17 from the proband showing $der(12)$, $t(12;17)(p13.3;q23)$. (b) Chromosomes 12 and 17 from the mother showing balanced translocation, $t(12;17)(p13.3;q23)$. In (a) and (b) the normal chromosome is on the left and the translocated chromosome is on the right of each pair with breakpoints indicated by arrows. (c) Idiogram of normal chromosomes 12 and 17 with breakpoints indicated by arrows.

abdominal catheter was placed to drain ascitic fluid and repeated transfusions of albumin and blood were given for hypoalbuminaemia and anaemia. Dysmorphic features included low set ears, hypertelorism, widely spaced nipples, shield chest, and short neck. In addition, a heart murmur was noted which echocardiography showed to be the result of a patent ductus arteriosus. X rays showed increased bone density with calcified deposits in the sternum and gall bladder, the latter probably resulting from gall stones (fig 1). Abdominal ultrasound showed a bright echogenic pattern in the kidneys.

Chromosome analysis was requested shortly after birth owing to the grossly hydropic appearance and the dysmorphic features indicated.

The oedema lessened concurrent with a reduction in the infant's weight to 1.9 kg. There was a gradual improvement but survival was not possible without continued ventilatory support and she died aged two weeks. Permission for a necropsy was declined.

Haemoglobin electrophoresis was normal, no blood group incompatibility was detected, and both TORCH titres and viral cultures were negative.

CYTOGENETIC FINDINGS

Peripheral blood lymphocytes were cultured from the proband for chromosome analysis using GTL banding. The analysis showed an unbalanced karyotype with additional material on the short arm of chromosome 12. Only the mother was available for follow up studies and she was shown to have a balanced reciprocal translocation between chromosomes 12 and 17, 46,XX, $t(12;17)(p13.3;q23)$. The proband's karyotype was therefore 46,XX,-12,+ $der(12)$, $t(12;17)mat$ with a duplication of 17q23→qter and a terminal deletion of 12p13.3→pter (fig 2).

Discussion

Abnormalities of chromosome 17 appear to be fairly uncommon, with duplication of 17q being extremely rare. Most of the published reports of distal 17q duplication are the result of segregation from a parental balanced reciprocal translocation, but a few occur as de novo events. A distinct clinical picture is beginning to emerge which can include mental retardation, severe growth retardation, psychomo-

tor delay, frontal bossing and temporal 'retraction', microcephaly, a large mouth with thin lips and downturned corners, a cleft or high arched palate, micrognathia, low set malformed ears, a short and/or webbed neck, a widow's peak, a low posterior hairline, widely spaced nipples, congenital heart defects, renal anomalies, rhizomelia, polydactyly, and hyperlaxity of limb joints. Several of these features were present in our case although her early death and lack of necropsy prevented further, more detailed examination being carried out. Interesting clinical findings in our case were the massive oedema, anaemia, and calcified gallstones. These features have not been described in any of the previous reports. It is possible that they may be the result of the deletion of the terminal region of 12p. However, there have been very few published reports of 12p deletions and clinical manifestations have been non-specific with phenotypic variation probably resulting from differences in the size of the deleted segment. The unique features described in our case have not been recorded in any of the cases of 12p deletion.⁴

Recognition of syndromes, whether chromosomal, single gene, or those of unknown aetiology,

is important for early diagnosis and initiation of cytogenetic analysis, when appropriate, because of the important implications for genetic counselling, for family studies to detect others at risk, and for prenatal diagnosis. New cases with additional or unusual features are important both for the further delineation of the syndrome and to describe features which may be useful in diagnosis, whether prenatally or in the newborn period. Further follow up was not possible in our case because the parents returned abroad to their country of origin.

References

- 1 Bridge J, Sanger W, Mosher G, *et al.* Partial duplication of distal 17q. *Am J Med Genet* 1985;22:229-35.
- 2 Serotkin A, Stamberg J, Waber L. Duplication 17q mosaicism: an infant with features of Ellis-van Creveld syndrome. *J Med Genet* 1988;25:258-60.
- 3 Orye E, Van Bever H. De novo distal trisomy 17q. *Ann Genet (Paris)* 1985;28:61-2.
- 4 Kivlin JD, Fineman RM, Williams MS. Phenotypic variation in the del(12p) syndrome. *Am J Med Genet* 1985;22:769-79.

Correspondence to Dr A Caine, Regional Cytogenetics Unit, St James's University Hospital, Beckett Street, Leeds LS9 7TF.

Moebius' syndrome with unilateral cerebellar hypoplasia

M G HARBORD, J P FINN, M A HALL-CRAGGS, E M BRETT, AND M BARAITSER

The Hospitals for Sick Children, Great Ormond Street, London WC1N 3JH.

SUMMARY A case is reported of a child with Moebius' syndrome who also has unilateral cerebellar hypoplasia. We suggest that this combination of abnormalities could result from a vascular disruption occurring in the basilar artery early in its development.

Moebius' syndrome consists of congenital unilateral or bilateral facial weakness and loss of abduction of the eye, which are interpreted clinically as defects of the seventh and sixth cranial nerves.¹ The involvement of other cranial nerves or abnormalities of the extremities, such as syndactyly, agenesis of digits, or defective branchial musculature, are common, but it is unusual to find gross structural brain abnormalities.^{1,2}

We report a patient with Moebius' syndrome who also has unilateral cerebellar hypoplasia.

Case report

A male infant was born at term by a normal vaginal delivery and his birth weight was 3250 g. An amniocentesis had been performed during the pregnancy owing to advanced maternal age, but the pregnancy was otherwise uneventful. In the neonatal period he was noticed to have a right convergent squint and right sided facial weakness, although he breast fed without difficulty.

He smiled at 10 weeks and from five months he was able to roll over from the prone to the supine position. He could pass objects from one hand to the other by six months, although his mother noticed that left hand preference had already become established and there were occasional jerky movements of his right arm.

When reviewed at seven months there had been no change in his condition. His head circumference (44.3 cm), weight (7.8 kg), and length (69 cm) were