

A case of deletion 2q35→qter and a peculiar phenotype

JOSÉ MARIA SÁNCHEZ AND ANA MARIA PANTANO

Fundación de Genética Humana, Salta 661, 1074 Buenos Aires, Argentina.

SUMMARY A girl with a high and micro-brachycephalic cranium (but without craniosynostosis), antimongoloid palpebral fissures, external strabismus, microsomy, a peculiarly shaped nose, soft tissue syndactyly in the right hand and both feet, and psychomotor retardation was found to have a deletion of chromosome 2 (q35→qter) and a Robertsonian translocation 13;14 inherited from her healthy father. The girl's phenotype is compared with the only other case reported involving a similar deletion.

slight external strabismus, short, thin nose with hypoplasia of the nasal alae and downward pointing tip, long philtrum, macrostomia, thin lips, high palate, micrognathia, and triangular and prognathic chin. The ears were low set and posteriorly rotated with maldeveloped antihelices, particularly on the

Few deletions of chromosome 2 have been reported, perhaps because of their low frequency or their high lethality, or both.

The list of syndromes including acrocephaly and syndactyly is increasing and persons with two or more forms of acrocephalosyndactyly have been found in the same family.¹ All the acrocephalosyndactyly syndromes described up to now have a Mendelian pattern of inheritance.²

We report here a patient in whom several features of an acrocephalosyndactyly syndrome were present, probably the result of a deletion of chromosome 2 from q35→qter. A diagnosis of acrocephaly could not be made in the strict sense because there was no craniosynostosis.

Case report

The patient, a female, was born to a non-consanguineous mother and father aged 28 and 25 years respectively, whose only previous pregnancy resulted in a normal boy. The pregnancy was normal and delivery was spontaneous. Birth weight was 2100 g. Some days later the infant presented with fever and anorexia owing to a urinary infection which was successfully treated with antibiotics.

The baby was referred for genetic evaluation at 21 days. Physical examination showed (figs 1 and 2): weight 2300 g, height 43 cm, and head circumference 31 cm; these values are below the 5th centile. Her cranium was high and short, with an anterior fontanelle of 2 × 2 cm and open sutures. There was an antimongoloid slant to the palpebral fissures,

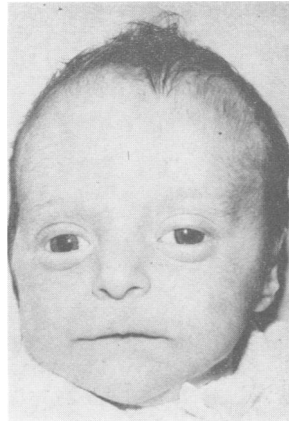


FIG 1 Patient's front view showing high forehead, slight external strabismus, hypoplastic nasal alae, macrostomia, and triangular chin.

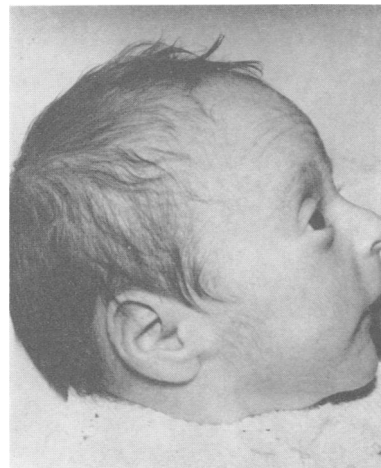


FIG 2 Lateral view of patient showing acrocephalic cranium, low set ears, peculiar nose, and micrognathia.

left. The neck was short with redundant nuchal skin. Both hands showed simian creases and ulnar deviation of the 3rd, 4th, and 5th fingers. The distal phalanges of the fingers were cone shaped. In the right hand there was soft tissue syndactyly between the 3rd and 4th fingers. In both feet (fig 3) there was complete soft tissue syndactyly of the 3rd to 5th toes and partial soft tissue syndactyly of the 2nd and 3rd. The baby had slight hypotonia but her reflexes were normal.

A further physical examination at 9 months of age showed marked developmental and psychomotor delay. She could not sit and had only two hypoplastic central incisors with enamel dysplasia.



FIG 3 Bilateral syndactyly of the 2nd to 5th toes.

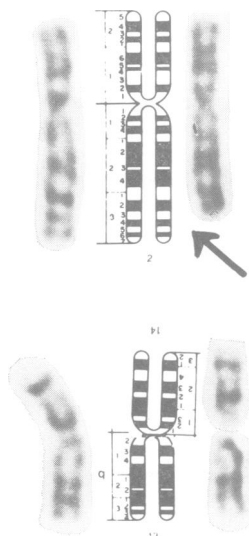


FIG 4 Chromosome abnormalities found in the proband: (above) deletion $2q35 \rightarrow qter$; (below) Robertsonian translocation 13;14 (G banding).

X-ray examination revealed open cranial sutures, a small anterior fontanelle, ovoid shaped orbits with mongoloid orientation, two carpal ossification centres, hypoplasia of the second phalanx of the 2nd, 4th, and 5th fingers on the right hand and the 2nd to 5th on the left, and marked hypoplasia of the first phalanx of the big toes. There was no osseous syndactyly between the toes. An excretory urogram was normal.

CYTOGENETIC STUDIES

Chromosome preparations were obtained from peripheral blood lymphocytes and G banded.³ A Robertsonian translocation 13;14 and a deletion of chromosome 2 ($q35 \rightarrow qter$) (fig 4) were present in the patient; therefore her karyotype was $45,XX,rob(13;14),del(2)(q35 \rightarrow qter)$. The mother's karyotype was normal and the paternal one was $45,XY,rob(13;14)$.

Discussion

The patient's phenotype strongly suggested an acrocephalosyndactyly syndrome based on the cranial shape, downward slanting palpebral fissures, external strabismus, and syndactyly in the right hand and both feet. However, the lack of craniosynostosis, some of the facial features including the nose, and the microsomy, suggest a different aetiology.

Very few cases of chromosome 2 long arm deletions have been reported.⁴⁻⁷ None of them was a true terminal deletion and all but one were interstitial deletions involving more proximal segments than ours. The report of Warter *et al*⁸ was of a 7 year old girl with a deletion $2q34 \rightarrow q36$ arising from a non-reciprocal translocation (2;6). Their patient shares some craniofacial features with ours, including microcephaly with a similarly shaped cranium, macrostomia, maldeveloped antihelices, small nasal alae, and downward pointing tip of the nose. She also had a simian crease (although unilateral), but lacked the syndactyly that is present in our patient. However, it has to be considered that the patient described here has a true deletion, while in Warter's case a portion of the chromosome 6 ($q21 \rightarrow qter$) was translocated to the band 2q34, and therefore a position effect cannot be excluded. Our patient also has a Robertsonian translocation 13;14 inherited from her normal father.

Robertsonian translocations have been thought to play a role in non-disjunction of other chromosomes and particularly in trisomy 21 through an inter-chromosomal effect. Nevertheless, we think that in our patient the coexistence of the translocation 13;14 and the deletion of chromosome 2 is coincidental.

References

- ¹ Jackson CE, Weiss L, Reynolds WA, Forman TR, Peterson JA. Craniosynostosis, midfacial hypoplasia and foot abnormalities: an autosomal dominant phenotype in a large Amish kindred. *J Pediatr* 1976;**88**:963-8.
- ² McKusick V. *Mendelian inheritance in man*. 6th ed. Baltimore: Johns Hopkins University Press, 1982.
- ³ Seabright M. A rapid banding technique for human chromosomes. *Lancet* 1971;ii:971-2.
- ⁴ Jones LA, Taysi K, Dengler DR, Heersma JR. Interstitial deletion of long arm of chromosome No 2 in a girl with phenotype resembling the Seckel syndrome. *Am J Hum Genet* 1980;**32**:74A.
- ⁵ McConnell TS, Kornfeld M, McClellan G, Aase J. Partial deletion of chromosome 2 mimicking a phenotype of trisomy 13: case report with autopsy. *Hum Pathol* 1980;**11**:202-5.
- ⁶ Antich J, Carbonell X, Clusellas N. De novo interstitial deletion of the long arm of chromosome 2 in a malformed newborn karyotype 46,XY,del(2)(q12q14). *Clin Genet* 1981;**19**:439.
- ⁷ Shabtai F, Klar D, Halbrecht I. Partial monosomy of chromosome 2. Delineable syndrome of deletion 2(q23-q31). *Ann Genet (Paris)* 1982;**25**:156-8.
- ⁸ Warter S, Lausecker CH, Pennerath A. Etude chromosomique et clinique d'une fillette porteuse d'une deletion (2)(q34 q36). *Hum Genet* 1976;**32**:225-7.

Correspondence and requests for reprints to Dr J M Sánchez, Fundación de Genética Humana, Salta 661, 1074 Buenos Aires, Argentina.

Familial pericentric inversion (13) detected by antenatal diagnosis

EDNA L MALTBY

Centre for Human Genetics, 117 Manchester Road, Sheffield S10 5DN.

SUMMARY A recombinant rec (13), dup q chromosome was diagnosed in a 17-week fetus following amniocentesis. Subsequently, a familial pericentric inversion of chromosome 13 was seen to be segregating in the family and the same recombinant 13 was present in a mentally retarded aunt of the fetus. The clinical features of the carriers of the inversion product are discussed with reference to previous cases.

Most cases of familial pericentric inversions are detected following the birth of an abnormal child, owing to an unbalanced recombinant chromosome forming after crossing over in a meiotic inversion loop. A family is presented in which an inverted 13 had been segregating for at least three generations before a routine amniocentesis carried out for an unrelated problem showed an abnormal fetal chromosome complement.

Case report

Amniocentesis was performed upon a 24 year old primigravida at 16½ weeks' gestation as she had spina bifida occulta and was anxious. The fetal chromosome complement was 46,XX,13p+. Chromosome analysis of the parents' blood revealed the mother to be carrying a pericentric inversion of chromosome 13, inv(13)(p13q22) and the father's

karyotype to be normal. The fetal karyotype was interpreted as 46,XX,rec(13),dup q,inv(13)(p13q22) and the pregnancy was terminated at 22 weeks. At necropsy, the fetus was shown to have hexadactyly on all four limbs, bilateral clefts in the upper lip and palate, eyes of normal size, a fusion of the antero-inferior aspects of the cerebral hemisphere, absence of olfactory bulbs and nerves, and a Meckel diverticulum in the gastrointestinal tract.

When the parents were seen for genetic counselling, it was discovered that there was a family history of miscarriage and children with polydactyly (fig 1). The mother's 18 year old sister (III.7) was mentally retarded and had phenotypic abnormalities. Trigonocephaly, combined with mild micrognathia, microphthalmia, epicanthic folds, a long philtrum, poor teeth, heavy eyebrows, and long thick eyelashes led to a distinct facial appearance (fig 2). There were accessory auricles on the right ear, capillary haemangiomas on the back of the neck, and a highly arched palate. She displayed delayed physical and mental development and was said to be irritable. Hexadactyly on all four limbs had been repaired while she was a child. Gene marker studies on esterase D (EsD), an enzyme marker associated with the region 13q14, showed normal levels and served only to confirm that the breakpoint of the inversion was distal to 13q14, or that EsD is proximal to 13q22.

Chromosome preparations from lymphocyte cultures were G banded and silver stained to identify NOR regions. These techniques confirmed the