Familial pericentric inversion (10) and its effect on two offspring

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SUMMARY A pericentric inversion (10)(p15q24) was observed in three generations of a family. One daughter of the inversion carrier was found to have the inv(10) and trisomy 18. The other offspring had a recombinant (10) chromosome.

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Case report

A pericentric inv(10)(p15q24) was observed in three generations of a family. The family came to our attention when the proband (III.5, fig 1) was born, showing clinical features of Edwards' syndrome. She was born at 40 weeks' gestation after a normal pregnancy. Birth weight was 1780 g. She died at 10

FIG 1 Family pedigree.

FIG 2 GTG banded metaphase from the proband (III.5) showing the inverted and normal chromosomes 10 (long arrows) and the trisomy 18 (short arrows).

days. She was the second child of unrelated parents; the mother was 35 and the father 48 years old.

Another malformed child was born to the same couple one year later. This second child (III.6) was a boy also born at term after an uneventful pregnancy.

The amniotic fluid was meconium stained. Apgar score was 9 at 1 minute. At birth he weighed 2000 g, length was 51 cm, and head circumference 26 cm. Dysmorphic features included dolichocephaly, high and large forehead, arched eyebrows, microphthalmia, hypertelorism (interpupillary distance 3.5 cm), epicanthus, antimongoloid slants, narrow palpebral fissures, flat and broad nose bridge, high arched palate, prominent upper lip, microretrognathia, low set ears, long thin fingers, ulnar hand deviation, clinodactyly, and a gap between the first

and second toes. Examination of the chest and heart was normal. At 2½ months of age, he weighed 4180 g and his head circumference was 39.5 cm.

CYTOGENETIC STUDIES

Chromosome analyses of cultured lymphocytes by Q, G, and T banding were performed. The proband's karyotype was 47,XX,inv(10)(p15q24), +18 (fig 2). The inv(10) was also present in her mother. The father's chromosomes were normal. The same inversion was found in four other members of the family (I.2, II.7, III.4, and III.8).

The second child (III.6) carried a recombinant abnormal chromosome 10: 46,XY,rec(10)dup q, inv(10)(p15q24)mat (fig 3). Therefore the boy had a duplication of 10q24→qter and a deletion of distal p15.

FIG 3 GTG and QFQ banding of (a) normal chromosome 10, (b) inv(10)(p15q24), and (c) recombinant (10), dup q, inv(10)(p15q24).

Discussion

Segregation analysis of the inversion through three generations showed a carrier to non-carrier ratio of 4:3.

As a direct result of the meiotic behaviour of the inversion, a recombinant chromosome 10, similar to that described by Dutrillaux *et al.*¹ was found in III.6, who showed the clinical features of the partial trisomy 10q syndrome.²

In addition to the risk related to the segregation of the inverted chromosome itself, an interchromosomal effect may also exist which could influence non-disjunction involving another chromosomal pair.

The existence of this chromosomal interference in animals has been demonstrated, particularly in *Drosophila*.³ In man, this effect has been observed mainly in balanced translocations⁴ and in only a few instances of pericentric inversions (excluding those affecting chromosome 9).⁵⁻⁹

In the present family, the occurrence of trisomy 18 in the offspring of an inversion carrier adds to the evidence supporting this type of chromosomal effect. However, the age of the parents (35 and 48) may also have contributed to the aneuploidy.

Nevertheless with regard to genetic counselling, in addition to the risk directly attributed to the balanced rearrangement, the influence of an interchromosomal effect should also be considered.

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