Case reports

A malformed child with a recombinant chromosome 7, rec(7) dup p, derived from a maternal pericentric inversion inv(7)(p15q36)

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Abstract

We report a child with facial dysmorphic features, hypoplasia of the external genitalia, intestinal malrotation, congenital cardiac defect, and minor limb anomalies. Chromosome studies showed a recombinant chromosome 7, rec(7) dup p, resulting from a maternal pericentric inversion inv(7)(p15q36). Thus, this child had partial trisomy 7p in addition to a small distal monosomy 7. The clinical findings are compared with those found in previous reports of trisomy 7p. Finally, some general principles for genetic counselling are discussed.

Relatively few cases of pericentric inversion of chromosome 7 have been observed. No recombinants have been found in offspring of carriers of pericentric inversion of chromosome 7, except in the family published by Winsor *et al.*,¹ where two recombinants rec(7) dup q were observed.

In this report we describe a boy with a recombinant 7, rec(7) dup p, resulting from a maternal pericentric inversion.

Case report

The proband, a male, was the first child of young parents. Both were phenotypically normal and unrelated. Pregnancy and delivery were uneventful. Birth weight was 2850 g. Family history was unremarkable.

Clinical examination at birth showed multiple

anomalies. The head was macrocephalic with a wide anterior fontanelle, persistent metopic suture, and prominent forehead. He had a short nose with anteverted nostrils, depressed nasal bridge, long philtrum, macroglossia, and micrognathia. There were downward slanting palpebral fissures, epicanthic folds, and hypertelorism. The ears were low set and protruding. He also had sparse hair and arched eyebrows. He also had a short neck, widely spaced nipples, a small penis, and left cryptorchidism. Minor limb anomalies were noted including shortened upper extremities, small hands, short fingers, and broad thumbs. A systolic murmur was present and an initial cardiac examination suggested a ventricular septal defect. An echocardiogram showed a large verrucous excrescence in a dysplastic pulmonary valve.

At 4 days of life he was operated on for intestinal malrotation. Considerable dilatation of the sigmoid and left colon was observed. Clinical suspicion of Hirschsprung's disease was disproved by various

Figure 1 Patient aged 9 months.

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Figure 2 Partial karyotypes of the proband and his mother.

normal rectal biopsies. At the age of 14 months he was moderately retarded.

CYTOGENETIC STUDIES

Chromosomal analysis was done on peripheral blood lymphocyte culture using GTL banding. The proband showed a modal number of 46 chromosomes, including one long chromosome 7 with additional material on the distal end of the long arms. Chromosome study of the mother showed a pericentric inversion of chromosome 7. The inverted segment corresponded to more than two-thirds of the total chromosomal length. The breakpoints were localised at p15 and q36. Her karyotype was 46,XX,inv(7)(p15q36).

Based on the mother's karyotype we concluded that the abnormal chromosome 7 of the patient was a recombinant chromosome, which had originated as a result of one crossover within the inversion loop during maternal meiosis. This recombinant chromosome had a duplication 7p (p15→pter) and a small distal deletion 7q (q36→qter). The chromosomal constitution of this child can be described as 46,XX,rec(7) dup p, inv(7)(p15q36)mat.

Normal chromosomes were found in the father and the only maternal aunt. No other members of the family were available for cytogenetic investigation.

Discussion

About 20 cases of duplication 7p have been published.² Most of them were derived from familial reciprocal translocations involving different breakpoints in 7p and various other chromosomes. The presence of different trisomic portions of 7p, as well as the various associated monosomic regions, does not allow a phenotype/karyotype correlation to be established. Only three patients had 'complete' trisomy 7p.³⁻⁵

In a recent review, Milunsky *et al*² suggest that

duplication 7p is associated with a recognisable characteristic phenotype: dolichocephaly or microbrachycephaly, wide open fontanelles and wide sagittal and metopic sutures, hypertelorism, micrognathia, large and low set ears, choanal atresia/stenosis, joint contractures, and cardiac septal defects. Severe mental and physical retardation is the rule in patients surviving early infancy. Our patient had a dysplastic pulmonary valve, which was also present in the case of Odell *et al*.⁴ Partial monosomy of 7q appears to be a well defined syndrome.⁶ However, the facial appearance in our case is more similar to the patients with partial trisomy 7.

The risk of pericentric inversion carriers producing recombinants has been widely discussed. Sherman *et al*⁷ reviewed 216 pedigrees with balanced pericentric inversions and found an overall recombination risk of 3.4%. He also noted that female carriers had a greater risk of recombinant progeny (4.1%) than males (2.6%). Furthermore, carriers who were ascertained through an unbalanced proband in the family have a greater risk (6.9%) than those detected through a balanced inversion (1.2%).

The correlation between the size of the inverted segments and the occurrence of unbalanced offspring has been previously studied.^{1,8} All authors concluded that large inversions have a much worse genetic prognosis than small inversions. Crossing over within the inversion may be more likely and may lead to relatively small duplication/deletions and therefore embryos carrying them have a greater chance of viability. Conversely, smaller inversions resulting in recombinants with extensive imbalance are less compatible with life.

In conclusion, genetic advice to pericentric inversion carriers should be established for each family following the criteria mentioned above.

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