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Duplication 9p due to unequal sister chromatid exchange

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SUMMARY A case of trisomy 9p syndrome is reported. The karyotype showed a tandem duplication of the short arm and of the inverted heterochromatic block of chromosome 9. Unequal sister chromatid exchange seems to be the only possible cause of this finding.

Case report

The proband was referred for chromosome analysis when she was two years old because of multiple congenital malformations and psychomotor retardation. The parents were unrelated. The father was 37 and the mother 32 at the time of her birth. They had a normal 10 year old son. Two years before the birth of the proband a pregnancy ended in spontaneous abortion during the first trimester. The proband was born at 42 weeks' gestation by Caesarean section performed because of breech presentation.

Physical examination at two years showed an unusual facies with frontal bossing, deep set eyes, hypertelorism, bulbous nose, short philtrum, down turned mouth, large protruding ears, and short fifth fingers with clinodactyly. X ray examination showed delayed bone maturation and hypoplastic middle phalanges of the fifth fingers. Dermatoglyphic features included zygodactylous digital triradii *b* and *c*, bilateral simian creases, *t'* axial triradii on the left hand and *tt''* on the right hand. The patient was unable to walk, but could sit with support. Her mental development was subnormal. A clinical diagnosis of trisomy 9p syndrome was made.

CYTOGENETIC STUDIES

Chromosome analysis performed on cultured peripheral lymphocytes showed 46 chromosomes with an aberrant chromosome 9 in all 102 divisions analysed. The rearranged chromosome showed a pericentric inversion of chromosome 9 of the common type (p11q13) and the presence of extra chromosomal material attached to the short arm. G banding, R banding, C banding, and the Goyanes technique,¹ a procedure for specific staining of chromosome 9 paracentromeric heterochromatin, showed that both the short arm and the inverted heterochromatic block were duplicated.

The position of the centromeres was shown by comparative analysis using both C banding and the Goyanes technique. The centromeres and the paracentromeric heterochromatin are both darkly stained using the first method, while with the second, only the paracentromeric heterochromatin of chromosome 9 is darkly stained, as the centromeres do not band.

The father and brother of the proband had normal chromosome complements, while the maternal karyotype was 46,XX,inv(9)(p11q13) (figure). Therefore, a tandem duplication of maternal origin was proposed, the karyotype being: 46,XX,dup inv(9)(p11q13)mat, (pter→p12::q13→p11::p24→p12::q13→p11::q21→qter) (figure).

Discussion

Trisomy 9p is responsible for a well known clinical syndrome that has been described in about 100 cases.² It may be a cause of familial mental retardation as in most cases it results from adjacent segregation of a parental translocation.³

FIGURE Partial karyotype (a) from the patient and (b) from the mother. 1=G banding, 2=Goyanes banding. (c) The positions of the centromeres are shown (1) on G banding, (2) on C banding (darkly stained), (3) on Goyanes banding (unstained). (d), (e) Reconstruction of the duplication.

A 2:2 or, less frequently, 3:1 meiotic segregation of a familial balanced translocation are the most common causes of this chromosome imbalance. Free trisomy 9p and de novo non-reciprocal translocations have also been reported and are probably due to 2:2 or 3:1 segregation of a translocation arising de novo at gametogenesis. Only a minority of cases are due to duplication of the short arm and these usually result from a mirror duplication.⁴

Duplication of chromosome regions may be due to unequal meiotic crossing over, unequal exchange between homologous chromosomes before meiosis, or unequal sister chromatid exchange.⁵ In our case, the tandem duplication of a portion of the inverted chromosome 9 showed that the only reasonable explanation for the origin of the aberrant chromosome 9 was an unequal sister chromatid exchange

occurring in the maternal inverted chromosome before or at meiosis. Unequal meiotic crossing over or unequal exchange between homologous chromosomes before meiosis would have produced either derivative chromosome 9 with inverted extra material attached to a non-inverted chromosome or a non-inverted additional fragment attached to an inverted chromosome 9.

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A case of de novo interstitial deletion 3q

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SUMMARY A rare chromosome abnormality consisting of interstitial deletion 3q was found in a malformed girl. Chromosome analysis using G and Q banding showed deletion of bands 3q12→3q21: 46,XX,del(3)(pter→q12::q21→qter). The clinical features of the proband included severe psychomotor retardation, craniofacial asymmetry, hypertelorism, epicanthus, high arched palate, progressive scoliosis, multiple skin pigmentations, and renal abnormalities. The parents had normal karyotypes.

Case report

The proband, an eight year old girl, was the first child of unrelated, healthy parents, both of whom were 24 years of age at the time of her birth. She was born after an uncomplicated 40 week pregnancy and the delivery was normal. Her birth weight was 2600 g, length 47 cm, head circumference 30 cm, and chest circumference 30.5 cm. Mild asphyxia was present at birth. The umbilical cord was only 28 cm in length and weighed 400 g. Severe developmental retardation was present: she had head control at five months, sat alone at 20 months, and walked without support at seven years old. At the age of eight years she was unable to speak any meaningful words. Scoliosis was observed at the age of three months and developed into progressive, double structural scoliosis, despite conservative therapy (fig 1). It was convex to the left in the thoracic area and to the right in the lumbar area. She could maintain a standing position, but found it impossible to avoid bending forward. She had considerable growth

retardation. At eight years of age her height was 103.5 cm (−4.3 SD), weight 17.2 kg (−2.0 SD), head circumference 51.5 cm (−0.14 SD), and chest circumference 60.5 cm (−0.05 SD). The craniofacial appearance was abnormal (fig 2). Her head showed plagiocephaly with increased right frontal and left occipital diameter, but there was no palpable ridge along any cranial suture. Her face was asymmetrical and midfacial dysplasia was present. She had hypertelorism, epicanthic folds, a high arched palate, and a long pointed chin. Mild generalised hypotonia and joint contractures were observed. Freckle-like pigmentations were scattered on the face and forearms. Dermatoglyphs showed no specific abnormalities. Intravenous pyelography showed a renal anomaly involving incomplete duplication of the collecting system on the right side. There was no abnormality of the other internal organs including the cardiovascular system. A muscle biopsy from the quadriceps femoris revealed only type II fibre atrophy. Abnormal laboratory findings included anaemia with iron deficiency and excess of serum IgG. Functional tests of the kidney, liver, and thyroid were normal. Serum level of transferrin was not decreased.

CYTOGENETIC FINDINGS

Chromosome analysis of the proband from peripheral lymphocytes showed deletion of the long arm of chromosome 3 (fig 3). Using high resolution G and Q banding, the deleted portion of chromosome 3 was found to be q12→q21:46,XX,del(3)(pter→q12::q21→qter). The karyotypes of the parents were normal. The origin of the chromosome abnormality of the proband could not be established, because Q heteromorphism of chromosome 3 in the proband showed no difference in size or staining intensity.

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