CYTOGENETIC STUDIES

Chromosome analysis of the patient was performed on peripheral blood lymphocytes. Using standard staining (G, C, and T banding methods) all cells showed only one normal homologue of chromosomes 1, 5, 10, and 12, together with four derived chromosomes (figure). The proband's karyotype was identified as a complex balanced translocation between chromosomes 1, 5, 10, and 12 which can be represented as: 46,XY,t(5;1;10;12)(5qter→5p13::12q24→12qter;1pter→1q42::5p13→5pter;10pter→10q24::1q42→1qter;12pter→12q24::10q24→10qter). The karyotype of both parents was normal.

Discussion

Complex balanced rearrangements in azoospermic males are rare events. Single balanced translocations have often been related to infertility in males. The infertility, in some cases, is due to spermatogenic arrest caused by the complexity of meiotic configurations.⁴

Unfortunately there is no information about the meiotic behaviour of complex chromosomal rearrangements. However, we can assume that, in the present case, the four derivative chromosomes

would have pairing difficulties leading to serious meiotic disturbances. Therefore one can speculate about the possibility that spermatogenic arrest and consequent azoospermia are directly attributable to the complex translocation detected in the patient and not to a chance association of both unrelated phenomena.

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A child with a recombinant of chromosome 8 inherited from her carrier mother

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SUMMARY A female child with mental retardation and dysmorphic features was found to have a duplication deficiency of chromosome 8: rec(8)dup q,inv(8)(p23q24), a recombinant product derived from a familial pericentric inversion, inv(8)(p23q24)mat. Clinical features of this previously undescribed inversion product are compared with other reported cases of partial trisomy for the distal long arm of chromosome 8, since this segment is thought to be primarily responsible for the phenotypic features of the trisomy 8 syndrome.

Since the introduction of banding techniques, pericentric inversions in human chromosomes have

been recognised with increasing frequency. Not all inversions give rise to unbalanced products and each must be assessed independently in order to calculate specific risk figures. In general, the risk of a recombinant chromosome being produced depends upon the size and position of the inversion and the particular segment involved.

There have been nine published cases of pericentric inversions of chromosome 8.¹⁻⁹ These fall into two main categories, distinguished by their arm ratios, risk of abnormal offspring, and coincidentally by their geographical distribution. The first group, which forms acrocentric type chromosomes inv(8)(p23q11),^{1,2} inv(8)(p23q12),³ and inv(8)(p11q24)⁴ found in the Scottish and Finnish populations, have no documented unbalanced progeny, while the second, which forms a metacentric type chromosome, inv(8)(p23q22),⁵⁻⁹ reported in several families of Mexican-American ancestry, has

so far resulted in 19 reported unbalanced recombinants.

The present case, in which an unbalanced recombinant was found, also forms a metacentric type chromosome, but differs from those previously reported by the position of the break in the long arms, resulting in trisomy for a small segment of 8q.

Case report

The proband (fig 1) is a 3 year old girl, the second child of a 24 year old, gravida 7 woman. The mother had a long history of neurosis and required psychiatric treatment. She maintained that five pregnancies had ended in miscarriage, although only two of these were clinically confirmed. During the present pregnancy she was treated with antibiotics at 16 weeks' gestation for urinary tract infection and was admitted to hospital at 38 weeks' gestation with premature onset of labour, which settled with rest and sedation.

Delivery, at term, was normal, birth weight 2730 g. Initial examination at 12 hours revealed a hypotonic baby without any significant physical abnormalities. Feeding was difficult during the first week and was complicated by vomiting and physiological jaundice.

Examination at 16 months of age revealed that general progress had been significantly delayed. Her length of 73.6 cm and weight of 8.03 kg were both around the 3rd centile. She was not yet walking unaided and sitting was unsteady. At 19 months, she had a febrile convulsion and has since had generalised seizures without any fever.

After referral for cytogenetic studies for developmental delay, a complete physical examination at the age of 20 months was carried out. This revealed an apparently healthy girl with a height of 75 cm (<3rd centile). The head was small and round

(circumference 46 cm, <3rd centile) with a broad forehead, flat occiput, and low posterior hairline. The face showed some dysmorphic features in the form of a wide depressed nasal bridge, telecanthus, wide palpebral fissures with slight antimongoloid slant, and mild synophrys. The nose was small with a downturned tip. The ears were also small with poorly formed lobules and were slightly low set. There was significant mid-face hypoplasia with a relatively wide mouth, prominent philtrum, downturned upper lip, and small, posteriorly directed chin. The hands were small with short fifth fingers and clinodactyly. No other skeletal abnormalities were observed. The cardiovascular system was normal. The central nervous system was also normal, except for mild hypotonia, probably of central origin. Developmentally, she was functioning around 1 year of age.

CYTOGENETIC STUDIES

G banding of methotrexate treated chromosomes from peripheral blood lymphocytes of the proband showed extra material on the short arm of chromosome 8 (fig 2c). Analysis of blood samples from the parents revealed that the mother had a pericentric inversion of a chromosome 8, inv(8)(p23q24) (fig 2a,b). The father's karyotype was normal. The proband's karyotype was, therefore, interpreted as having an unbalanced recombinant of chromosome 8, resulting in trisomy of the distal segment of the long arm and probable deficiency of a small portion of the distal short arm, rec(8),dup q,inv(8)(p23q24).

Further family studies showed that the inversion was also present in the mother's sister (fig 3), indicating that it had been inherited from one of their parents. It was not, however, possible to confirm this from chromosome analysis.

FIG 1 The proband aged 20 months.

FIG 2 Partial karyotype showing (a) diagram of chromosome 8, (b) inverted 8 in the mother, and (c) recombinant 8 in the proband.

FIG 3 Family pedigree.

Discussion

Reports of four distinct familial pericentric inversions of chromosome 8 have been published. All have involved large segments, yet only one inversion (p23q22) has resulted in unbalanced offspring. This has led to the suggestion^{6 7} that in inversions of chromosome 8, the influencing factor in the formation of unbalanced recombinants is the particular segment involved rather than the size of the inversion. The present report describes another familial inversion (p23q24) which has given rise to an unbalanced recombinant. While differing from the (p23q22) group in the position of the break in the long arm, it does include the same segment and forms a metacentric type chromosome. The group with no documented recombinants form acrocentric type chromosomes. It is possible, therefore, that the configuration of the homologues at meiosis is affected by the arm ratios, thus influencing the formation of recombinant chromosomes.

All recombinants, including the present one, have resulted in monosomy of a very small segment of the short arm, and trisomy of the distal segment of the long arm. Crossing over within the inverted segment at meiosis could result in a second recombinant with duplication of the short arm and deficiency of the long arm. This recombinant product has not yet been identified in the (p23q22) group and the incidence of miscarriage is not significantly raised,⁸ suggesting that the embryos are non-viable. It is possible that the bad obstetric history in II.2 is related to this second recombinant, since monosomy 8q24→qter may be less deleterious than monosomy 8q22→qter.

Comparison of clinical details of patients with dup 8qter, due either to a parental translocation or inversion, have resulted in a topological map of chromosome 8.¹⁰ Several authors have proposed that the major manifestations of complete trisomy 8 are due to the duplication of the distal segment of 8q.¹⁰⁻¹⁴ Evidence of this comes from cases with trisomy 8q22→qter, although two cases with trisomy 8q24, due to parental 8;22 translocation, also had many features of trisomy 8 syndrome, including the characteristic long, slender body, thick everted lower lip, and large dysplastic ears.

The present case does have some features in common with other cases of complete and partial trisomy 8, compared in the table, notably mental retardation, delayed development, hypertelorism, depressed nasal bridge, micrognathia, retrognathia, low hairline, short fifth fingers, and clinodactyly.

TABLE Comparison of clinical features most frequently observed in complete and partial trisomy 8.

	Trisomy 8	Trisomy 8q22→qter	Trisomy 8q24→qter	Present case: rec 8, dup q, inv 8(p23q24)
Normal birth weight	+	+	+	+
Delayed growth	+/-	+	+	+
Mental retardation	+	+	+	+
Congenital heart disease	+	+	-	-
Face shape	Long	Broad	Long	Broad
Depressed nasal bridge	+	+	+	+
Broad nose with upturned end	+	+	+	-
Antimongoloid slant of palpebral fissures	? Rare	+	+	-
Hypertelorism	+	+	+	+
Thick, everted lower lip	+	+/-	+	-
High arched palate	+	+	+	-
Retrognathia/micrognathia	+	+	+	+
Low set ears	+	+	+	+
Malformed ears	Large	Small	Large	Small
Low hairline	+	+	+	+
Narrow shoulders	+	+	+	?
Narrow pelvis	+	+	+	?
Extra vertebrae/ribs	+	-	-	-
Absent patellae	+	-	-	-
Short 5th fingers	+	+	+	+
Camptodactyly	+	+	+	-
Clinodactyly	+	+	+	+
Abnormal feet	+	+	+	-
Deep palmar/plantar furrows	+	+/-	+	-

However, many of the features evocative of the trisomy 8 syndrome, such as the long face with everted lower lip, large dysplastic ears, and abnormalities of the skeletal system, are absent.

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'Pure' partial trisomy 2q in a male owing to malsegregation of a maternal translocation t(X;2)(p22·3;q32·1)

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SUMMARY This report describes a male infant with partial trisomy 2q: 46,Y,der(X),t(X;2)(p22·3;q32·1)mat. The phenotype was compatible with partial trisomy 2q syndrome. Replication studies showed a random X inactivation in the mother. Soluble isocitrate dehydrogenase (IDH-1) dosage was within the expected range for a trisomic patient and favours the assignment of this locus to the region 2q32→qter.

Fifteen cases of distal trisomy 2q have been described so far.¹ We report here a new case owing to malsegregation of a maternal translocation t(X;2)(p22·1;q32·1) in a male child. This case is

similar to that described by Turleau *et al*² in a female and, although the two families live in neighbouring villages, they are believed to have no common ancestor.

Case report

The proband was born in 1980 after a normal pregnancy. Birth weight was 2300 g, length 45 cm, and head circumference 30·5 cm. Apgar score was 1 at 1 minute and 8 at 5 minutes. Dysmorphic features were present and a very wide fontanelle, reaching the bridge of the nose, was noticed. Examination at the age of 17 months showed persistent growth retardation (weight 8400 g, –2 SD; length 73 cm, –2 SD) and microcephaly (head circumference 42 cm). The craniofacial features (fig 1) were typical of distal 2q trisomy syndrome,¹ especially the downward slanting palpebral fissures, hypertelorism, flat