Partial trisomy 7p associated with familial 7p;22q translocation

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SUMMARY A newly described partial trisomy of the short arm of chromosome number 7 is reported in a familial translocation between 7 and 22. The unbalanced translocation was found in one family member, the proband, and the balanced form in 5 other members. The possibility of this translocation being a rare telomeric attachment previously undescribed in humans is discussed. Prominent clinical features include general mental and motor retardation, microbrachycephaly, and cardiac and oral abnormalities.

The advent of various banding techniques, particularly G banding, has enabled the accurate identification of several minute structural alterations in the last few years. Described here is one such case in which a small portion of the short arm of number 7 was translocated to the long arm of chromosome number 22. This is one of the first reported cases involving partial trisomy of the short arm of chromosome 7. Familial studies of this condition have shown 5 balanced carriers and 1 affected individual in 3 generations. The proband was a 15-month-old boy with general mental and motor retardation. Physical abnormalities included high palate, split uvula, microbrachycephaly, and increased transillumination of the frontal area of the skull.

Case reports

CASE IV.1

The proband (Fig. 1) was the product of the first pregnancy of an 18-year-old mother and a 22-year-old father who were not related. At birth he weighed 2951 g and was 47 cm in length.

At 2 months of age a grade 2 systolic murmur was heard at the apex of the heart and it was noted that he had low set ears and a small mandible. At 15 months of age he was referred for chromosomal analysis because of his very retarded mental and motor development and congenital heart abnormalities.

At this time physical examination showed weight and height in the third centile and head circumference in less than the third centile. Appetite and weight

were poor from birth and he tired easily. His diet had been mostly milk and few solids. There was increased perspiration around the head and neck. He did not smile, roll over, sit up, pull up, or stand but was able to move his hand to his mouth. Other abnormalities included high broad palate, split uvula, microbrachycephaly, and increased transillumination of the frontal area of the skull. Heart abnormalities at this time revealed a normal first sound and a second sound that was split, with accentuation of the pulmonary closure. There was a grade 3/6 ejection murmur along the upper left sternal border transmitted into the lungs and a third heart sound along the left sternal border followed by a grade 3 diastolic murmur.

Electrocardiogram and echocardiogram revealed complete form of atrioventricular canal and evidence of right ventricular hypertrophy without left ventricular hypertrophy. Radiographs showed an enlarged thymus and heart. An EMI scan showed hypoplasia or atrophy of the brain with a dilated ventricular system and enlarged subarachnoid spaces.

Results of laboratory tests for sweat chloride, total thyroxine, and serum calcium were normal. Examination of urine was negative. Haemoglobin was 10 g/dl and cellular morphology of peripheral blood showed hypochromia and microcytosis, suggestive of chronic iron deficiency anaemia.

CASE III.3

The father of the proband was phenotypically normal and in general good health. He was a high school graduate and self-employed farmer.

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Fig. 1 Family pedigree of the propositus with 46,7p partial trisomy.

CASE III.6

This was a phenotypically normal aunt of age 18. She had 1 child who was phenotypically normal and was expecting a second child.

CASES III.8 AND III.10

Two uncles of the propositus, ages 17 and 9 respectively, were phenotypically normal and healthy.

CASE II.2

The paternal grandfather of the propositus was phenotypically normal. He had two brothers who were mentally retarded (II.3 and II.4).

Cytogenetic studies

Leucocyte culture from whole blood was used for standard karyotype preparation according to the procedure outlined by Hungerford (1965). The trypsin procedure of Seabright (1971) was slightly modified for the G banding using 0.0025% trypsin in Earle's solution for 10 to 12 minutes. Chromosomes were

stained with the conventional Giemsa method of Sumner *et al.* (1971).

Thirty cells of the propositus were counted to establish the modal number and 4 G-band karyotypes were prepared to confirm the 7p partial trisomy. For all other individuals at least 10 cells were counted and a minimum of 3 G-band karyotypes analysed for the balanced translocation.

The modal count in all 12 cases was 46. Karyotypes of the propositus showed an extra band on the long arm of a number 22 chromosome (Fig. 2). The same band was present in the father (III.3) (Fig. 3), an aunt (III.6), two uncles (III.8 and III.10), and the grandfather (II.2). These people also had a band missing on the short arm of a number 7 chromosome (Fig. 2). The break point in the number 7 chromosome appears to be in the 7p21 band.

Six members of the family had normal chromosomes. The individuals II.3, II.4, and III.1 are deceased or otherwise unavailable for study but were mentally retarded and thus are believed to have been affected with the partial trisomy also.

Fig 2 Partial karyotypes of the propositus and carrier relatives showing normal chromosomes 7 and 22 and the abnormal derivatives. (a) IV.1, the propositus; (b) III.3, the father; (c) III.6, aunt. Karyotypes of all carrier relatives were similar to b and c.

Discussion

This is a report on a 15-month-old boy with partial trisomy of the short arm of the number 7 chromosome. To our knowledge no published report involving partial trisomy of the short arm of number 7 exists, though a few cases have been catalogued by Borgaonkar and Bolling (1976). Single band translocation between the long arm number 7 and number 21 resulting in partial trisomy has been beautifully shown by G banding (Bass *et al.*, 1973). Long arm anomalies of chromosome 7 have been reported much more frequently than the short arm as the review by Lewandowski and Yunis (1975) illustrates.

Breakage and rejoining between chromosomes 7 and 22 may be explained in one of two ways. This may represent a reciprocal translocation between the two chromosomes involved, in which case the break point in the number 22 chromosome would be in the q13 band or an undefinable sub-band thereof.

Designation by the short system would be 46,XX or XY,t(7;22)(p21;q13) for the balanced type and 46,XY,der22,t(7;22)(p21;q13)pat for the unbalanced propositus. By the detailed system the balanced form would be 46,XX or XY,t(7;22)(7qter→7p21::22p1→22qter;22pter→22q13::7p21→7pter).

Fig. 3 Karyotype of the father of the propositus. The arrows indicate the abnormal number 7 and 22 chromosomes. Similar karyotypes were obtained for all balanced carriers.

A second possibility is that there was a break in the number 7 chromosome at band p21 and the translocation of the deleted portion to the telomere of 22. Designation for this would be 46,XX or XY,t(7;22)(p21;qter) by the short system and 46,XX or XY,t(7;22)(7qter → 7p21;22pter → 22qter::7p21 → 7pter) by the detailed system for the balanced form. The karyotype of the propositus if this were the case would be 46,XX,der22,t(7;22)(p21;qter)pat. We tend to believe from the G band analysis that the latter may well be the case.

The possibility, then, exists that this represents a rare type of simple translocation in which the deleted end of number 7 is attached to the telomere of 22. Stock and Hsu (1973) have described examples of centromere to centromere, centromere to telomere, and telomere to telomere attachments in mammalian chromosomes of several species. This arrangement has not been described in humans, but, nevertheless, we wish to introduce the possibility. Studies of meiotic behaviour of the chromosomes would also be of help in establishing whether this is a one or two break arrangement, particularly if either G banding of prematurely condensed chromosomes (PCC) (Unakul *et al.*, 1973) or the prophase-synchronisation (Yunis, 1976) method is used. Co-operation from the family for these studies is unlikely, however.

The establishment of defined clinical characteristics for the 7p partial trisomy syndrome has to await further reports of this condition. However, prominent physical abnormalities include cardiac, cerebral, and oral abnormalities as well as mental and motor retardation.

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