Normal phenotype and partial trisomy for the G positive region of chromosome 21

SUMMARY A prenatally diagnosed male fetus and his mother, who was referred because of her advanced age, both carried an abnormal bisatellited chromosome 21 as an extra chromosome. The abnormal 21 was monocentric and the G negative band q22 and part of q21 had been deleted during formation. The phenotype of both the mother and child (at birth) was normal.

A number of published reports have supported the view that the phenotype of Down's syndrome can be present only with a trisomy of the long arm distal region of chromosome 21. These reports arise from essentially three groups of chromosome 21 abnormalities: discordant segregation of interstitially deleted chromosomes 21 (cases 1 and 2 of Aula *et al.*, 1973; Cervenka *et al.*, 1977); segregation of reciprocal translocations involving 21q (case 4 of Aula *et al.*, 1973; Williams *et al.*, 1975); and tandem translocations (Warkany and Soukup, 1963; Soudek *et al.*, 1966; Niebuhr, 1974; Hagemeijer and Smit, 1977).

The chromosome abnormality in the subjects of the present report is a corollary of the above statement, namely that there is an essentially normal phenotype expressed in probands with trisomy of the proximal part of the G positive band 21q21.

Materials and methods

G and C bands were prepared as described previously (Daniel and Lam-Po-Tang, 1976). N-banding was by the abbreviated method of 18 h incubation in 50% aqueous AgNO₃ at 50°C and counterstaining with 2% Giemsa.

Case report

The proband was a prenatally screened male fetus who, at birth, had a normal phenotype with none of the stigmata of Down's syndrome. The referral for prenatal diagnosis was made on the grounds of advanced maternal age (40 years). The mother had

no previous obstetric history as this was her first pregnancy. She was a trained nurse of normal intelligence and appearance, and she too had the

Fig. Bisatellited marker chromosome present as an extra chromosome in two normal individuals. Top 4 rows; marker and pairs 21 and 22. Top row, N bands showing N band positive long arm of marker; rows 2 and 3, G bands, long arm satellite visible; row 4, C bands showing marker with single C band block. Bottom row, satellite association of long arm of marker with a 21p (left) and short arm of marker with a 13p (right).

chromosome abnormality. It was concluded that the abnormality was compatible with a normal phenotype and the pregnancy was continued. A male sib of the mother had normal chromosomes, but the maternal grandparents were not available for study.

CHROMOSOME STUDIES

All clones detected prenatally in the proband had 47 chromosomes with an extra bisatellited chromosome smaller than a normal 21. A similar extra chromosome was detected in the mother. The marker had approximately 70% of the G positive band 21q21 present (Fig.) and this was clearly distinguishable from the proximal long arm region of any acrocentric other than 21. Furthermore, on C-banding, a single poorly defined C band region similar to that seen in a regular chromosome 21 was seen at the centromere. Immediately adjacent and distal to the G positive band was a second acrocentric constriction and satellite. On N-banding (top row, Fig.), the

terminal long arm satellited region was N positive in many cells. The G band morphology was asymmetrical, indicating that it was unlikely to be a tandem t(21;21), and was most probably the result of a reciprocal translocation between a 21, with a break within q21, and another acrocentric with proximal p12 breakpoint.

Discussion

This case is further confirmation for the hypotheses of Aula *et al.* (1973), Niebuhr (1974), and Williams *et al.* (1975) that a trisomy for the distal segment q22 of chromosome 21 is required for the expression of typical Down's syndrome. Other cases relevant to this argument are shown in the Table. The case of Hagemeijer and Smit (1977) is the most similar to the present case. That case and the patient (III.18) of Williams *et al.* (1975) with trisomy for most of q21 had few features of Down's syndrome but were mentally retarded. The present case with a trisomy for the proximal (?) half of 21q11 had a normal phenotype with no retardation and this contributes to the emerging pattern. There is a noticeable clinical similarity between the cases of Hagemeijer and Smit (1977) and Warkany and Soukup (1963) with only a few features of Down's syndrome, for example, mental but not physical retardation, large protruding tongue, flat nasal bridge, and little else. The patients in the present report represent a further stage of minimising the effect of extra chromosome 21 material on the phenotype. The larger issue of the probable paucity of structural genes within regions that are G positive must await documentation.

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Table Phenotype in partial trisomy 21.

Authors	Chromosomal imbalance	Phenotype
Warkany and Soukup (1963)	— G, + tan(G;G) Probably trisomy of q21 and part of q22	Few features of Down's syndrome, eg large protruding tongue, slight mongoloid slant, flat nasal bridge, hypertelorism. No dermatoglyphic features
Soudek <i>et al.</i> (1966)	— G, + tan(G;G)	Few features of Down's syndrome
Aula <i>et al.</i> (1973) Case 4	der15,t(15;21) Trisomy distal q21 and all of q22 + del(21) (q21) Trisomy of q22	Typical Down's syndrome
Cases 1 and 2		Many features of Down's syndrome
Williams <i>et al.</i> (1975) III.18	47, + der21,t(10;21) Trisomy proximal 21q21 and distal 10q26	Low posterior hair-line, fleshy external ears with attached lobules. Distal loops in each 3rd and 4th interdigital space. IQ61
III.5	46,der10,t(10;21) Breakpoints in 10q26 and 21q21 Trisomy 21q22 and part of 21q21 and monosomy distal 10q26	Typical Down's syndrome
Hagemeijer and Smit (1977)	— 21 + tan(21;21) Trisomy for all of 21q21	Moderate mental retardation, epicanthic folds, flat nasal bridge, open mouth, and short, broad hands
Present case bJE 815/77	+ der21,t(21;?) (q21;p12) (identity of second acrocentric unknown) Trisomy of 70% 21q21	Mother and male child of normal intelligence and appearance

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Trisomy 20p from maternal t(3;20) translocation¹

SUMMARY A case of trisomy 20p resulting from a maternal translocation t(3;20) is described. QM and BUdR banding techniques were used for its identification. A round face with oblique palpebral fissures, strabismus, cardiac and vertebral abnormalities, mild psychomotor retardation, together with poor co-ordination and speech impediment, are the most typical features of the proband.

Few cases of trisomy 20p are to be found in published reports. Recently, Centerwall and Francke (1977)

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documented 3 new cases in the same family and reviewed the other 10 reported cases belonging to 5 families. In all cases the trisomy was the result of anomalous segregation of balanced parental translocation.

In this paper we report a case of trisomy 20p resulting from a balanced maternal translocation t(3;20) segregating in a large family.

Case report

The subject is a female, born 1.1.74, at 38 weeks' gestation, to a gravida 1 mother, after a gravidic toxemia which complicated the end of the pregnancy. The mother and father were 23 and 31 years old, respectively, at the time of her birth. Though the child was born after a normal delivery, she had mild fetoneonatal distress. Birthweight was 2750 g. Haemodynamic studies showed Fallot's tetralogy.

On physical examination after surgery at 4 years of age she had: normal weight and height, microcephaly (<3rd centile), round face, short upward slanting palpebral fissures with downward displacement of the medial corner, moderate hypertelorism, short nose with large nares, and bilateral convergent strabismus (Fig. 1).

According to the Terman-Merrill scale, there was psychomotor retardation of 1 year compared to a normal subject which, 5 months later, appeared greatly improved (retardation of 6 months). The

Fig. 1 The proband at the age of 4½ years.