euchromatin in bands 9q11, 13, and 21. This hypothesis finds support in cases of trisomy 9p where additional long arm material was also present. These cases have recently been reviewed by Sutherland *et al.* (1976). Though mild urogenital abnormalities were present in addition to 9p+ symptoms in some patients trisomic for 9pter→9q11 or 12, the accumulation of additional malformations was striking in those individuals trisomic for additional material distal to 9q13. Micrognathia, urogenital anomalies, cranial suture abnormalities, and early death were noted in patients trisomic for 9pter→9q2. It is possible that the most significant lesion in our case was loss of part of band 9q21.

Deletion mapping studies indicated no segregational abnormalities for the red cell or serum markers tested. Since both parents had normal karyotypes, the rearrangement originated *de novo*, probably in gametogenesis. C banding was performed on both parents in the hope of determining the origin of the rearrangement via No. 9 secondary constriction polymorphisms. The secondary constrictions of both parents were normal in size and uninformative. A normal male child has since been born to the couple.

The multiple anomalies of our patient do not fall into the pattern of any recognised chromosomal syndrome. With the exception of ring chromosomes, only two other cases of long arm deletion have been reported. The patient of Smith *et al.* (1973) had unusual facies, lumbosacral myelomeningocele, dilatation of the ventricles, upward slanting of the palpebral fissures, a heart murmur, bilateral talipes equinovarus, partial malrotation of the bowel, and urogenital abnormalities. A very confusing cytological picture emerged for this patient, a deletion of two-thirds of the long arm and the presence of one or two presumably related fragments. An exact description of the deleted material was not reported. The second case, that of Newton *et al.* (1972), was found to have a 9q- chromosome similar in appearance to a No. 16, as in our patient. Here, fluorescent staining revealed a *de novo* deletion of the secondary constriction; no loss of adjacent euchromatin was reported. Clinically, a comparison of these two patients does not suggest a syndrome. The case of Newton *et al.* (1972), a 22-year-old institutionalised man, was found to have epilepsy, hypertelorism, contracture of the left elbow, hyperextensibility of the metacarpophalangeal joints, and an IQ judged to be untestable. The only points of similarity with our case are hypertelorism and, possibly, mental retardation.

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Partial trisomy 20 (20q13) and partial trisomy 21 (21pter→21q21.3)¹

SUMMARY A patient with a double partial trisomy 20 and 21 with mild mental retardation and multiple congenital anomalies is presented. Despite trisomy for a substantial portion of chromosome 21, the patient showed only minor stigmata compatible with Down syndrome.

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In this report, a family is presented in which a child with multiple congenital anomalies has a double partial trisomy 20 (q13) and 21 (pter→q21.3) resulting from a balanced translocation carried in her family for at least three generations. In spite of being trisomic for the short arm, centromere, and proximal half of the long arm of chromosome 21, the patient displayed only a few of the phenotypic features commonly observed in Down syndrome. This adds evidence to the suggestion that the pathogenic segment of chromosome 21 rests primarily but not exclusively on the distal light band of the long arm of such chromosome (q22).

Case report

A white girl, the product of an uncomplicated full-term pregnancy and delivery, birthweight 3.3 kg, and with no medical neonatal complications was admitted at 10 days of age for hyperbilirubinaemia of unknown aetiology which required one exchange transfusion. She was readmitted at 6 months because of poor muscle tone and several minor congenital anomalies. Physical examination revealed the following: round face, prominent and somewhat confluent eyebrows, long curly eyelashes, epicanthal folds, bilateral esotropia, depressed nasal bridge, and open mouth (Fig. 1). Teeth and tongue were normal. The dorsal aspect of both feet and hands were prominent but without oedema and had a square appearance. In general, fingers and toes appeared short.

Fig. 1. The patient.

The neck was short but without skin folds. The cardiovascular system showed no abnormalities. Trunk and extremities appeared normal. There was a generalised increase in subcutaneous fat all over the body. Pelvis and skull x-ray films were normal, with no findings suggestive of mongolism. Fingerprints showed 9 ulnar loops and a whorl on the right 5th digit; no simian crease was present; and the *atd* angle was normal. Developmental milestones have been mildly delayed in that she did not walk alone until age 16 months, and now at age 25 months, she has only a 7-word vocabulary. The Cattell Infant Intelligence Scale gave a mental age of 17 months. The Vineland Social Maturity Scale was at 21 months, and her social development at the level of 18 to 21 months. At the present time, she has a normal head circumference (47 cm) with a small anterior fontanelle, a weight of 9.9 kg (3rd centile), and a height of 81 cm (3rd centile). One 3-year-old female sib has normal mental and physical development and no physical abnormalities. There is no family history of psychomotor retardation or congenital anomalies.

CYTOGENETIC STUDIES

Chromosomal studies were done according to the technique described by Yunis and Sanchez (1975). The proband's karyotype showed 47 chromosomes with a normal sex complement. The extra chromosome was smaller than those of the G group (21-22) and its banding pattern characteristics resembled a partially deleted chromosome 21. In an attempt to establish the identity of the abnormal chromosome both parents were studied. The father's karyotype was normal. The mother's karyotype showed two abnormal chromosomes identified as Nos. 20 and 21. One of the chromosomes 20 had an enlarged long arm with two extra bands present in the distal portion; a No. 21 chromosome was lacking approximately the distal half of the long arm (Fig. 2). A careful analysis of elongated early metaphase chromosomes suggested that these abnormal chromosomes were the result of a balanced translocation 20/21 with break points located at bands 20q13 and 21q21.4, respectively (Fig. 3A and 3B). According to the Paris Conference nomenclature (1971), the mother's karyotype can be described as 45,XX,t(20;21)(q13;q21.4). The proband's maternal grandfather proved to have the same chromosomal rearrangement. Other members of the family showed normal chromosomes. It should be pointed out that the use of elongated chromosomes of early metaphase has allowed the visualisation of some sub-bands not described by the Paris Conference. The schematic representation of chromosomes 20 and 21 (Fig. 3A and 3B) clearly indicates the bands present in both chromosomes. It is also important to note that in this

Fig. 2 Karyotype of the patient's mother. Note abnormal chromosomes 20 and 21.

Fig. 3 (A) Schematic representation of normal (left) and derivative (right) chromosomes 20 and 21. Arrows indicate break points. (B) Giemsa banded chromosomes 20 and 21 from the patient's mother. Note in second row the differences in the pericentromeric heterochromatin of chromosomes 20. (C) Patient's partial karyotype: chromosomes 20 and 21 are normal; the extra chromosome is identical to the derivative chromosome 21 of the mother.

family one of the chromosomes 20 shows a pericentric inversion of the pericentromeric region (Fig. 3B and 3C). As far as the authors are aware, this is the first instance of such variation or polymorphism reported for this chromosome.

A detailed analysis of the proband's chromosomes showed that the abnormal extra chromosome was identical to the derivative chromosome 21 present in the mother and that, consequently, the patient is trisomic for the small distal light band of the long arm of chromosome 20 (band 20q13) and for the short arm, centromere, and proximal half of the long arm of chromosome 21 (bands 21pter→21q21.3). Her karyotype is described as 47,XX,+der(21)t(20;21)(q13;q21.4)mat.

Discussion

The patient presented here has a double partial trisomy (20q13;21pter→21q21.3). Given the large segment of chromosome 21 present in excess, it was not surprising to note clinical manifestations compatible with Down syndrome. These included epicanthic folds, bilateral esotropia, depressed nasal bridge, open mouth, short neck, square hands and feet, increased number of ulnar loops, and poor muscle tone. In spite of these phenotypic characteristics, however, it was not possible to diagnose the patient as having Down syndrome since she lacked some of the most discriminating findings in this condition (mid-facial hypoplasia, flattening of occiput, large fontanelles, mongoloid slant of palpebral fissures, speckled iris, lens opacity, protruding tongue, ears with angular overlapping helix, prominent antihelix, and small ear lobes, reduced iliac and acetabular angles, and absence of frontal and sphenoidal sinuses) (Gorlin, 1974). Williams *et al.* (1975) have recently observed that the segment of chromosome 21 largely responsible for the pathogenesis of Down syndrome is localised in the distal light band of the long arm of chromosome 21 (q22.1→21qter). The present report does not contradict these findings but suggests that the segment 21pter→21q21.3 may not be completely devoid of phenotypic effects when present in the trisomic state.

Partial trisomy for the long arm of chromosome 20 has been briefly cited only once (Fawcett *et al.*, 1975). The patient described was trisomic for the same chromosome segment as ours (20q13) but, in addition, showed a sizeable partial trisomy 14 (14pter→14q22) that was considered to be largely responsible for the phenotypic manifestations found. Though some of the phenotypic characteristics of the patient reported here (round face, prominent eyebrows, long curly eyelashes, increased subcutaneous fat) could be

attributed to a partial trisomy for the telomeric band of the long arm of chromosome 20 (20q13), such suggestion must be made with caution until new cases are described and the clinical findings compared.

The patient represents a typical example of a 3:1 segregation at meiosis in which a balanced maternal reciprocal translocation involving an acrocentric chromosome results in a relatively high frequency of unbalanced products. This phenomenon has been repeatedly observed in man (Hamerton, 1971; Sanchez *et al.*, 1974; Lewandowski *et al.*, 1976).

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