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FIG 3 Proposed recombination event giving rise to recombinant chromosome.

of chromosomal material most likely occurred during recombination through transfer to the reciprocal product. However, the consequences of their loss may not be recognised at the clinical level.

de la Chapelle *et al*³ described two inversions involving small segments of chromosome 10. One type, *inv*(10)(p11q21), produced a more metacentric chromosome and was observed in two probands and nine of their relatives. The second inversion, *inv*(10)(p11q11), appeared in a less metacentric chromosome 10 with minimal alteration in banding pattern and occurred in one proband and seven relatives. Presence of the inversion chromosome in the clinically abnormal probands may have been coincidental, since all sixteen relatives who were also heterozygous for the inversion appeared clinically normal. No chromosomally unbalanced offspring were observed in the three families included in this series. A patient described by Dutrillaux *et al*² possessed a duplication/deficient recombinant chromosome 10 that was apparently derived from an inversion chromosome 10 (*inv*(10)(p15q24)) carried by his mother. Lack of consent from the maternal grandparents of our case precluded testing of other family members for carrier status for the inversion chromosome.

We believe this is the first published report of a pericentric inversion of chromosome 10 contributing to the production of an acrocentric derivative. Although Ferguson-Smith⁵ tentatively described such an event, the chromosome involved was later identified as chromosome 8 by banding procedures.⁶

The karyotype of our patient was independently

confirmed by the Cytogenetics Laboratory, Children's Memorial Hospital, Chicago, Illinois.

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A 13-year-old girl with karyotype 47,XX,+i(22)(qll)

SUMMARY A 13-year-old girl presented because of abnormal pubertal development. She was found to have an isochromosome of 22 in addition to a normal female chromosome complement. Investigation also showed moderate mental retardation.

Excluding minute fragments, the incidence of supernumerary small marker chromosomes is low. In the series of Freidrich and Nielson,¹ three were found among 5029 consecutive live born children in Denmark, and Gerald and Walzer² found an incidence of 0.8 per 1000 among 3543 newborns. In

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the latest data, the incidence was 2 in 13 939 newborn infants.³ These markers are found more frequently in surveys of mentally retarded subjects, 3 in 504,⁴ and three were found in 1255 severely retarded patients.⁵

This report documents a patient with unusual presentation, who was found to have a supernumerary marker chromosome.

Case report

The patient presented at the age of 13 years with asymmetrical pubertal breast development (which later equalised). She was the third child born to healthy non-consanguineous parents when the mother was 28 and the father 31 years of age. There were three healthy sibs and one male stillbirth in the sibship. Both parents came from very large families and there were no significant genetic anomalies present on either side. Her birthweight was 3.3 kg at 40 weeks' gestation with no neonatal complications. She lived at home and attended a special school class for slow learners. Menstruation had not yet occurred. There was no history of any fits.

On examination, her height was 152 cm (25th centile), weight was 29.1 kg (below the 3rd centile), and head circumference was 55 cm (75th centile) with a prominent occiput. She had an odd thin face, with microphthalmia, shallow orbits, underdeveloped supraorbital ridges, hypoplastic maxillae, marked micrognathia, and a high palate. She had long thin hands and tapering fingers and the feet showed pes cavus bilaterally. There was moderate thoracic scoliosis and considerable kyphosis. Pubic hair was present and the left breast was more developed than the right. Clitoromegaly and labial hypertrophy were noted. There was no hirsutism.

Investigations included hormone assays which showed serum 17-hydroxy progesterone, dehydroepiandrosterone sulphate, and testosterone to be normal. This excluded adrenal hyperplasia.

Serum levels of follicle stimulating hormone and luteinising hormone were within normal limits. Laparoscopy showed a small 2 cm uterus. Both ovaries were smooth and white with a suggestion of thickened capsule and the right one was enlarged and polycystic. IQ assessments, using the revised WISC, showed a verbal scale IQ 72, performance scale IQ 49, full scale IQ 58. An electroencephalogram was abnormal.

Cytogenetic investigations were performed on peripheral blood using standard techniques⁶ and gave a modal chromosome count of 47 in all 55 cells examined. An extra small marker chromosome was present, shown in the figure. G banding⁷ showed that the chromosome was bisatellited and dicentric, and a G positive band was present at each end below the

centromere. The bisatellited nature of the marker was seen only in cells with elongated chromosomes (for example, the top row of G banded chromosomes and the second and third row of C banded chromosomes in the figure). R banding⁸ showed a central

FIGURE Partial karyotypes from the proband showing the G group chromosomes with the extra marker chromosome arrowed. c=conventional staining. G, R, C, and N show the chromosomes from banded cells.

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dark band and C banding⁹ showed two areas of heterochromatin at the centromeres at each end of the marker. NOR banding¹⁰ showed four areas of darkly staining NOR material at each end of the extra chromosome, although not in every cell studied. By each technique the rest of the chromosome complement was normal. There was no evidence of mosaicism. The abnormal chromosome associated with other acrocentrics with the same frequency that we usually record and both ends were involved with equal frequencies. A buccal smear was positive in the normal female range.

We considered that the most likely interpretation of this extra marker was that it was an isochromosome derivative of a chromosome 22 with the breakpoint at q11. An alternative possibility was translocation between two acrocentrics, which could also produce a bisatellited dicentric chromosome. The distance of the central R band from the centromere and the amount of R banded material present, combined with the symmetrical pattern of G and C banding in cells with elongated chromosomes, were the factors against such a translocation. The break at 22q11 was followed by reunion of the sister chromatids at this point and loss of the terminal fragment of the 22q. The karyotype is 47,XX,+i (22)(q11). Although dicentric in structure, most cells showed functional suppression of one centromere.

Chromosome analysis with G and C banding of both parents was normal.

Dermatoglyphic study of the patient showed the finger patterns to consist of nine ulnar loops, one double loop whorl, and the total finger ridge count was 172 (normal range 127 ± 50). On the palms, total *ab* ridge count was 64 (normal range 80 ± 10). There were narrow *atd* angles, bilateral ulnar displacement of *t*, and on the left there was an accessory *d* triradius.

Discussion

The abnormal chromosome described in this case is a dicentric bisatellited chromosome 22, which could be evaluated only with the use of multiple banding techniques. Other cases of extra markers have been reported, some being described before banding was available,^{11 12} and in other reports the origin of the extra chromosome was not identifiable, either because of its small size¹³ or indefinite banding patterns.¹⁴ Gutierrez *et al*¹⁴ reported an extra small chromosome which was seen to be dicentric and bisatellited and the karyotype of their patient was very similar to the case reported here, but the abnormal chromosome in their case was considered to have resulted from Robertsonian translocation of two acrocentrics.

Phenotype-karyotype correlation in patients with supernumerary small chromosomes is difficult, because although many of these chromosomes may be similar, no two appear to be exactly alike. In the case of Gutierrez *et al*¹⁴ the proband had the anomalies of the Sturge-Weber syndrome but the same extra chromosome was present in six relatives in three generations, all of whom were phenotypically normal. In our patient the abnormality had arisen *de novo*. She also had various dysmorphic features which did not fit well with a known syndrome, and her gynaecological presentation was unusual. As she was partially tetrasomic for long arm 22 material (pter→q11) some similarity to trisomy 22 could have been expected and in fact a few features were present. Trisomy 22 has recently been described,^{15 16} and of the features frequently encountered our patient had mental retardation with marked growth retardation, micrognathia, skeletal abnormalities, and abnormal external genitalia, for which no gynaecological or endocrinological cause was demonstrated. She did not have congenital heart disease, cleft palate, preauricular tags, sloping palpebral fissures, or microcephaly.

It has been pointed out that there are very mild cases of trisomy 22 on record¹⁷ who may show almost normal intelligence and only one or two of the common symptoms. The phenotypic features may depend on which segment of the chromosome is in excess. This has been exemplified by the case report of a 16-year-old girl with partial trisomy 22 (bands pter→q12) who also had some features of the syndrome but not all.¹⁸ The present case suggests that the presence of segment pter→q11 of chromosome 22 in quadruple does not have an additive effect on the phenotype.

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Duplication-deletion with partial trisomy 1q and partial monosomy 3p resulting from a maternal reciprocal translocation rcp(1;3)(q32;p25)

SUMMARY A mother with a translocation rcp(1;3)(q32;p25) gave birth to a son with duplication of 1q32→qter and deletion of 3p25→pter.

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At 17½ years of age, the proband was severely mentally retarded and presented a pattern of multiple minor dysmorphic stigmata and anomalies, including hypertrichosis, synophrys, ocular hypertelorism, ptosis, convergent squint, cleft uvula and narrow palate, poorly modelled auricles, funnel chest, kyphoscoliosis, umbilical and inguinal hernias, and cubitus valgus. He had normal stature and did not have any apparent malformations.

Before chromosome banding techniques, duplication-deletions could usually only be assumed from the clinical picture when the deletion of a particular chromosome segment was known to cause specific clinical features. Banding techniques allowed the determination of a variety of duplication-deletions. The present report adds a further example to this list, a case of monosomy 3p25→pter and trisomy 1q32→qter following a maternal reciprocal translocation.

Case report

The proband, a male, was the youngest of three children. The birthweights of his maternal half-brother and his sister were 3750 g and 4120 g, respectively. His father and mother were 35 and 36 years old at his birth. After an uneventful pregnancy, vertex delivery took place at 38 6/7 weeks of gestation. He had neither asphyxia nor cyanosis. Weight at birth was 2910 g (10th to 50th centile), length was 46 cm (15th centile), and head circumference was 33 cm (10th to 50th centile). The placenta weighed 620 g and was normal on inspection, the umbilical cord containing three vessels. His mother remembered him as "hairy, like a little animal," but no other abnormalities were noticed at birth. He fed poorly and regurgitated frequently during and after feeding. At the age of 4 months he was referred for paediatric evaluation because of suspicion of delayed motor development. Weight (6.15 kg) and head circumference (41 cm) were at the 25th centile while length (59 cm) was about the 3rd centile. He did not smile, or fix on objects with his eyes and only rarely followed objects, or lift his head from a prone position. Spontaneous movements were poor, and muscle tone was suspected to be increased. A pattern of minor dysmorphic stigmata was observed (fig 1a, b), notably synophrys and bushy eyebrows, intermittent convergent squint, recessed mandible, short neck with limited excursion, bilateral inguinal hernias and a small umbilical hernia, and short hands, feet, fingers, and toes. Inspiratory stridor and