Case reports

has been observed in humans,¹¹⁻¹³ and this topic has been considered theoretically with particular regard to mouse chromosomes.¹⁴ A similar scheme of dissociation and isochromosome formation was proposed by Vianna-Morgante and Nunesmaia¹⁵ to explain the production of a subject with iso-21q trisomy 21 from a 15q21q balanced translocation, and by Fryns *et al*¹⁶ to explain a case of trisomy 13 mosaicism from a de novo 13q13q translocation. Atkins and Bartsocas¹⁷ also possibly observed such an event, although the trisomic cell line in their case was the major line. It thus seems that dissociation of some centric fusion translocations may be expected to give rise to chromosomally unbalanced subjects in a small number of instances.

The reason for this occasional appearance of an unstable dicentric is of obvious interest. Daniel and Lam-Po-Tang¹⁸ and Hsu *et al*¹⁹ have reviewed Robertsonian translocations in man and concluded that most, if not all, of these are actually dicentric and, as with dicentrics in general, the reason for their stability is the suppression of the activity of one of the two centromeres. It is also possible that this stability is not absolute and that, if carefully searched for, a small percentage of cells in many Robertsonian translocation heterozygotes will show evidence of dissociation. These dissociated chromosomes, which may appear as two acrocentrics in satellite association, may still be connected by interchromosomal strands.²⁰

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Monosomy 22 with mosaicism

SUMMARY A 2-year-old male child with mosaicism for monosomy of chromosome 22 is described. He had moderate psychomotor retardation, generalised hypotonia, large ears, epicanthus, synophrys, and cutaneous syndactyly between all the fingers.

Before the availability of chromosome banding techniques, attempts to delineate syndromes resulting from monosomy of G group chromosomes were

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FIG 1 General appearance of the patient.

complicated by the inability to distinguish between chromosomes 21 and 22.^{1,2} With the advent of banding techniques, chromosome 21 could easily be differentiated from chromosome 22.³ Only one patient with monosomy for chromosome 22 has been reported so far.⁴ Ours is the first case of mosaicism for monosomy 22.

Case report

The proband, a 2-year-old male child, was born at term after an uncomplicated pregnancy and normal delivery to a 30-year-old mother and 33-year-old

father. The two older sisters of the index patient were normal, but both of his elder brothers had died in infancy from unknown causes. There was no consanguinity.

His early motor and mental milestones were greatly delayed: he smiled at 9 months, held his head up at 1 year, and rolled over at 1½ years.

On examination, he was 65 cm in length, weighed 5 kg, and had an occipitofrontal circumference of 35 cm, all below the 3rd centile. He had flat facies, narrow hairy forehead with synophrys, mild epicanthus, upward slanting palpebral fissures, prominent nasal bridge, thin lips with a marked overbite,

(b)

(a)

FIG 2 (a) Partial karyotype showing monosomy 22; (b) a metaphase.

Case reports

and large, low set ears with a well formed helix. The lenses and fundi were normal. Systemic examination showed marked failure to thrive, hypotonia, mental retardation, unilateral undescended testis, and small penis (fig 1). Both arms were normal in length. There was loose skin over the dorsal aspect of the metacarpophalangeal joints and an increase in fine palmar creases.

Dermatoglyphic examination showed bilateral simian creases, two arches, one radial loop, and two ulnar loops on each hand. His palms appeared to be longer than usual because of syndactyly of the skin between all fingers. All joints were hyperextensible. His mental age was around 9 months.

LABORATORY STUDIES

Routine haematological, biochemical, and urinary studies were normal. His bone age was within normal limits.

Fifty metaphases, obtained by standard leucocyte culture techniques and stained with Giemsa, were analysed. Twelve of the metaphases had 45 chromosomes. Each of these cells lacked one chromosome 22: 45,XY,-22 (fig 2). In 38 other metaphases the chromosomal complement showed a normal 46,XY pattern. The chromosomal pattern of the mother was normal.

Discussion

Despite the fact that banding techniques have been in use for almost a decade now, only one case of monosomy 22 without mosaicism has been described.⁴ Our patient is the first case of mosaicism for monosomy 22, the majority of cells (38 of 50; 76%) having a normal 46,XY karyotype.

Patients with partial deletion of G group chromosomes have two different clinical syndromes: G_1 (antimongolism) and G_2 (involving chromosome 22). The patient of DeCicco *et al*⁴ with monosomy 22 did not correspond to either of these. In patients with ring chromosome 22, as reported by Hunter *et al*,⁵ mental retardation, microcephaly, growth failure, and hypotonia were found, as in other deletion 22 syndromes. In our patient, minor anomalies such as flat occiput, epicanthus, full eyebrows, dental malocclusion, and cutaneous syndactyly were also present, as in r(22) patients. More cases will have to be documented in detail, however, before a specific monosomy 22 syndrome can be delineated.

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Variable expression in Pfeiffer syndrome

SUMMARY A female infant with Pfeiffer syndrome (acrocephalosyndactyly V) is presented. Her mother has no limb malformations, but has craniofacial features which strongly suggest that she is also affected, although more mildly.

This family indicates that wide intrafamilial variation of Pfeiffer syndrome is possible and suggests that without detailed investigation mildly affected subjects can remain undiagnosed, which may lead to erroneous genetic counselling.

In 1964, Pfeiffer¹ described a family in which eight subjects in three generations had a syndrome consisting of craniosynostosis, broad thumbs and big toes, and partial soft tissue syndactyly of the hands and feet. Vertical transmission of the trait, and the fact that males and females were equally affected, supported an autosomal dominant mode of inheritance. Because of the close phenotypic similarity to the Apert syndrome, Pfeiffer reported this family as having a mild form of that syndrome. However, in pedigree studies, no transition from one type to the other was observed. The syndromes are recognised by most investigators as separate entities,² although recent reports^{3 4} have cast doubt on this conclusion.

We report a girl with typical Pfeiffer syndrome whose mother has abnormalities limited to the cranium and face, suggesting she is mildly affected.

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