Stable dicentric autosome, tdic (8:22)(p23:p13), in a mentally retarded girl

SUMMARY A dicentric autosome, tdic(8:22)(p23:p13), was found in all metaphase cells examined from the peripheral blood of a mentally retarded girl. It is suggested that the centromere of chromosome 22 was inactive, allowing the dicentric to behave as a monocentric element. The involvement of acrocentric chromosomes in the stable dicentric autosomes of man is discussed.

Stable dicentric autosomes in man have only rarely been described. We report here a new case involving chromosomes 8 and 22.

Case report

S.R. was a female born after an unremarkable 41-week pregnancy and a slightly prolonged, but otherwise normal, delivery. There was no neonatal anxiety but she was late in her milestones. At 12 years she was a friendly co-operative girl, light in weight, and with head circumference on the 50th centile. She was slightly prognathous, with a narrow high arched palate. Her eyebrows were prominent. She had long arms and fingers, and bilateral simian creases. Her IQ on the Wechsler Scale was 60. Full clinical, radiological, and biochemical investigations failed to show any further abnormalities. Her 41-year-old parents and her 14-year-old brother were phenotypically normal. There was no other relevant family history.

Cytogenetic studies

Chromosome preparations were made from peripheral blood in the usual manner. Analysis of the orcein-stained material gave a consistent count of 45 in each complete metaphase. There were three chromosomes in the G group, 15 in the C group, and an extra metacentric chromosome resembling a No. 3, which had an achromatic gap and, frequently, a secondary constriction.

Giemsa-trypsin-banding (Seabright, 1971) showed the presence of only one chromosome 8 and one No. 22. The additional metacentric chromosome was found to be a dicentric involving the other chromosomes 8 and 22 (Fig. 1). Satellite material of chromosome 22 was still present in the dicentric chromosome, appearing as a discrete band and frequently associating with the satellites of the remaining acrocentrics (Fig. 2). In orcein-stained material the absence of staining in the satellite

![Fig. 1 G-banded karyotype of the proposita. The dicentric chromosome is arrowed.](http://jmg.bmj.com/ on April 20, 2017 - Published by group.bmj.com)
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stalks often gave them the appearance of an isochromatid break or gap, but in banded cells the outlines of the swollen stalks were usually visible. There appeared to be a small deletion of material from the short arm of the No. 8 involved in the dicentric, but this was difficult to ascertain because no complete band was missing. The translocation chromosome was thus interpreted as dic(8:22)(p23:p13) (Fig. 2).

The centromere of the No. 8 involved in the dicentric appeared normal in all the metaphase cells examined. With orcein-staining the centromere of the No. 22, however, was not always recognizable, because it appeared to separate prematurely, especially in the more condensed chromosomes. G-banding showed the centromere of the No. 22 as a single band even where no constriction was detectable, while C-banding (Sumner et al., 1971) frequently showed a separate block of heterochromatin on each chromatid at the level of the centromere of the No. 22 (Fig. 3).

No abnormality was detected in the chromosomes of the parents and brother of the proposita.

Discussion

According to classical cytogenetics, dicentric chromosomes are unstable because there is a tendency for anaphase-bridge formation, resulting in breakage or non-disjunction. However, a small number of stable dicentric chromosomes have been reported. The first of these was in wheat, Triticum aestivum, where Sears and Cámara (1952) suggested that stability could be attributed to the presence of a normal 'primary' centromere and a weaker 'secondary' centromere. A similar situation may exist in the stable dicentric chromosomes that have been found in man. In several cases of dicentric X (Distèche et al., 1972; de la Chapelle and Stenstrand, 1974; Therman et al., 1974; Yanagisawa and Yokoyama, 1975; Howell et al., 1976, and in the human dicentric autosomes described by Niebuhr (1972a, b) and Warburton et al. (1973), generally only one centromere was morphologically evident, even though two centromeres were indicated by banding techniques. The majority of such dicentric chromosomes were not entirely stable. In the case reported by Niebuhr (1972a), dissociation of the dicentric was observed in 4% of the metaphase cells, and mosaicism of human sex chromosome dicentrics was found in the majority of the cases described (inter alia Cohen et al., 1973; R. T. Howell, S. H. Roberts, and R. J. Beard, unpublished).

In the present report the premature separation of the centromere of the No. 22 might indicate that this centromere was inactive and, therefore, unable to

![Fig. 2](http://jmg.bmj.com/)
**Fig. 2** The dicentric chromosome in association with chromosome 8. Bands 22p13 (satellites) and 8p23 of the dicentric are indicated.

![Fig. 3](http://jmg.bmj.com/)
**Fig. 3** The appearance of the dicentric chromosome: (a) with orcein staining, (b) with G-banding, and (c) with C-banding. Note the variation of the centromere of chromosome 22.
attach itself to the spindle. Thus it would allow the dicentric to behave as a monocentric element dominated by the centromere of the No. 8. There was no evidence of mosaicism or breakage, but these events could not be ruled out as they might be lethal or sublethal and consequently not seen in the cultured cells. Such instability of the dicentric at critical stages of embryonic development might have contributed to the abnormalities of the proposita. However, it is likely that the formation of the dicentric was preceded by the deletion of the tips of both chromosomes, and it is probable that any loss of material from the No. 8 would have contributed to the abnormal phenotype.

It is of interest that, in the stable dicentric autosomes so far reported in man (present case; Niebuhr, 1972a, b; Warburton et al., 1973; Šubrt et al., 1971), acrocentric short arm material was translocated into an intercentric position, where, in at least two cases (present case; Warburton et al., 1973), it retained its function of nucleolar organizer, as indicated by its association with acrocentric chromosomes. It is possible that satellites are particularly susceptible to participation in chromosomal rearrangements. This, and the compatibility of loss of acrocentric short arm material with normal development (Nielsen et al., 1974) might, in part, explain the involvement of acrocentrics in the dicentric chromosomes referred to above. However, in the present case and those reported by Niebuhr (1972a, b) and Warburton et al. (1973), the centromere of the acrocentric chromosome (or one acrocentric in dicentric Robertsonian translocation chromosomes) usually appeared to be partially or completely non-functional. It is, therefore, suggested that there may be a tendency for the centromeres of acrocentrics in dicentric chromosomes to become inactivated, making it possible for stability to be achieved. This may be an important factor in the involvement of acrocentrics in the stable dicentric autosomes of man.

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Mental retardation with 45 chromosomes 45,XX, -5, -14, +der(5) t(5,14)(p15;q13) mat due to familial balanced reciprocal translocation

SUMMARY

A girl with severe mental retardation and odd facies and some features of the cri-du-chat syndrome was found to have only 45 chromosomes. Her karyotype was 45,XX, -5, -14, +der(5) t(5,14)(p15;q13) mat. Her mother and her two sisters were found to be balanced reciprocal translocation carriers having 46 chromosomes, one of which was a very small (14pter→14q13::5p15→5pter) that was missing in the proposita.

The very few cases of 3:1 meiotic disjunction resulting in 45 chromosome offspring have been recently reviewed in this journal by Lindenbaum and Bobrow (1975). To the best of our knowledge the present report is the first of a family with a balanced reciprocal translocation involving chromosomes 5 and 14 detected because the proposita was a mentally retarded unbalanced 45 chromosome offspring. A
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