Familial dicentric translocation t(13;18)(p13;p11.2) ascertained by recurrent miscarriages

SUMMARY A dicentric translocation is described involving chromosomes 13 and 18 in which the centromere of chromosome 13 was suppressed. The translocation was ascertained by repeated miscarriages and was found in three generations of phenotypically normal carriers.

Familial dicentric translocations have not been reported in man other than in Robertsonian fusions (Daniel and Lam-Po-Tang, 1976). Other dicentric translocations have been described involving at least one non-acrocentric chromosome. The latter,

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Fig. 1 Pedigree.

Fig. 2 Translocation dic(13;18). Upper row: G bands of 13,t,18(3 cells); lower row: C bands of 18,t,13(2 cells). c, centromere; sat, satellites; sc, suppressed centromere.
in reports so far (Šubrt et al., 1971; Niebuhr, 1972; Warburton et al., 1973; Pallister et al., 1974; Nakagome et al., 1976; Roberts et al., 1977), have been accompanied by sufficiently large euchromatic deletions to have rendered their carriers incapable of transmission. In this report a new dicentric is described, involving an acrocentric and sub-metacentric chromosome, which was ascertained by repeated miscarriages and found in three generations of normal carriers.

Case report

The pedigree is shown in Fig. 1. The proposita (II.2) presented at 30 years of age with a history of seven pregnancies and one living child. There were five miscarriages occurring at 12/40, 10/40, three at 8/40, and a macerated stillborn male delivered at 32/40 with multiple abnormalities including hydrocephalus and spina bifida. A further conceptus (III.6) was prenatally diagnosed as a chromosomally normal male and was confirmed as such at birth. The sibs of the proposita, a sister of 32 years with 3 normal children and a brother of 26 years with one child, had no (nuclear) family history of miscarriages. The mother (I.1) of the proposita had four miscarriages, two at 8/40 and two at 10/40 weeks’ gestation. The maternal grandmother also had three children at intervals of 6 and 7 years, but there is no reliable record of whether or not miscarriages occurred.

Fig. 3 Translocation dic(13;18). N-banded metaphase showing N band block and absent remnant Cd band in translocation chromosome (large arrow). Cd, remnant Cd bands. Chromosomes 1 and 16 and some G and D chromosomes labelled.
Case reports

Chromosome studies

G- and C-banding were performed as described previously (Daniel and Lam-Po-Tang, 1976). N-banding was by the simple method (Bloom and Goodpasture, 1976) of 18 hours incubation in 50% aqueous AgNO₃ at 50°C and counterstaining with Giemsa. A fusion translocation between the short arms of chromosomes 13 and 18 was found in the proposita, her sibs, mother, and nephew (III.7). The G positive band 18p11.2 was reinforced in the translocation chromosome by the satellites of chromosome 13 (Fig. 2). The satellites could be clearly seen in the C-banded translocation chromosome (Fig. 2), and the satellite stalks were also present on N-banding (Fig. 3). Therefore, the centromere of chromosome 13 was present though a centric constriction was never observed at that site. There was a net deletion of the G negative terminal band 18p11.3 and the 13p telomeric region.

Discussion

In contrast to the previous reports of dicentric translocations involving one submeta/metacentric chromosome, this translocation is familial. The phenotype of the carriers is normal notwithstanding the small deletion of a G negative region. This deletion must be small compared with those occurring in the other cases who, apart from one relatively normal girl (Warburton et al., 1973), range to the severely retarded (Nakagome et al., 1976). The fact that this translocation has been transmitted through three generations, and possibly a fourth considering the interval between the offspring of the maternal grandmother, indicates its stability. The suppression of one (usually the acrocentric) centromere in these dicentrics is likely to be the mechanism of this stability. At this stage of our understanding of centromeric suppression, it is important to document the karyotypes at meiotic metaphase II and of the products of miscarriages in these carriers as further cases are described.

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References


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The 9p— syndrome

SUMMARY A 13-year-old boy with 9p—(p22→pter) is reported. He had many features in common with previous 9p—cases, as well as several distinctive features including polydactyly and precocious puberty. Cytogenetic studies revealed a de novo deletion distal to band 9p22, which was the reported site of chromosome break in 9 of the 10 previous 9p—cases. Evaluation of the human GALT enzyme suggests that its locus is not on the deleted segment.

Ten patients have previously been described with deletion of a distal portion of the short arm of chromosome 9 (Orye et al., 1975; Alfi et al., 1976; Servile et al., 1976; Kuroki et al., 1977; Nielsen et al., 1977). The patients had several features in common which suggest a recognisable syndrome: mental retardation, trigonoccephaly or prominent forehead, flat occiput, flat nasal bridge, antverted nostrils, long philtrum, micrognathia or retrognathia with wide gonial angle, abnormal auricles, short
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