Familial translocation 15/22. A possible cause for abortions in female carriers

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Summary. A familial Robertsonian translocation 15/22 was ascertained through a female carrier whose four pregnancies ended in missed abortions. Eleven 15/22 translocation carriers were detected in three generations among 23 family members investigated. The four proven female carriers, apart from the probanda, have miscarried seven out of 14 pregnancies. The kindred suggests that the 15/22 translocation in female carriers may cause an increased risk for miscarriage.

In a study of 5049 consecutive newborn children, Friedrich and Nielsen (1973) found one boy who had a translocation 45,XY,t(15q22q), which was inherited from the mother. He was physically normally developed; his family has been described by Friedrich, Nielsen, and Sehested (1972). To the best of our knowledge this was the only reported family with a D/G translocation positively identified as a 15/22 translocation by the banding technique.

Methods

Chromosome preparations were made from cultures of peripheral blood by the method of Moorhead *et al* (1960). Colchicine was added to the cultures 2 hours before harvesting. The hypotonic solution used was 0.075 M KCl for 10 minutes. The fixative, methanol:acetic

acid (3:1), was added and slides were prepared by the air dry technique. The ASG (acetic/saline/Giemsa) technique was used for banding chromosomes. The slides were incubated for 1 hour at 60° C in 2 × SSC (0.3 M sodium chloride plus 0.03 M tri-sodium citrate) after which they were rinsed briefly with de-ionized water and stained in Giemsa for 30 minutes (Gurr's Giemsa R.66, 2 ml to 50 ml of buffer at pH 6.8 made with Gurr's buffer tablets). Finally they were rinsed again briefly in de-ionized water and dried by blotting.

Family report

The family was ascertained because the probanda had four pregnancies all of which ended in missed abortions. The probanda (III.15, Fig. 1) was found to be a translocation carrier 45,XX,t(15q22q), her husband had a normal karyotype. She must have inherited the translocation from her deceased father (II.9, who died at the age of 40 from malignant melanoma) as

FIG. 1. Family pedigree.

FIG. 2. Karyotype of IV.2, one of the 15/22 Robertsonian translocation carriers. (ASG staining.)

some of his sibs were found to be carriers of the same translocation. The grandparents (I.1 and I.2) were both deceased. The grandfather and grandmother died at the age of 80 and 73, respectively. All the available and cooperative sibs of translocation carriers and their offspring were karyotyped (Figs. 1 and 2). There were 11 karyotyped translocation carriers in the kindred; five of them were males. All the translocation carriers were physically and mentally normal, some being university graduates. Relatives with normal karyotypes were also normal except IV.26, a nephew of the proposita who was severely mentally retarded with some areas of depigmentation of the skin. All individuals who

were karyotyped were interviewed and complete conceptual histories were obtained before karyotyping. Apart from the proposita, the four other proven adult female carriers (II.7, II.8, III.1, and III.14) have miscarried seven out of 14 pregnancies. The majority of miscarriages were in the first trimester but some were in the second and one early in the third trimester. The wives of the four married proven male translocation carriers (II.1, III.3, III.10, and III.12) had 16 pregnancies, five of which ended in spontaneous abortions. One of their offspring (III.2) died as a newborn because of a spinal defect. I.2 is reported to have had six spontaneous abortions and three children who died (the order of the pregnancies

of I.2 is not known). Either I.2 or I.1 is presumed to have been a translocation carrier as they had several translocation carrier children.

Discussion

The family studied by Friedrich *et al* (1972) did not show any abortions in female 15/22 translocation carriers, but the family was very small and the translocation carriers had only very few pregnancies. Infertility has been recorded in balanced t(DqDq) heterozygotes (Walker and Harris, 1962/1963; Kjessler, 1964; Yunis *et al*, 1964; Wilson, 1971). Sparkes and de Chieri (1970) suggested that the carrier of a chromosome translocation might be at increased risk for having recurrent abortions. At least one female 14/21 translocation carrier was ascertained because of multiple abortions (Cohen, 1971).

The finding of seven miscarriages among 14 pregnancies of four 15/22 translocation heterozygotes suggests a causal effect. The proposita, who was ascertained because of four missed abortions, was excluded from the calculation, but this may be an overcorrection for ascertainment bias.

The finding of five miscarriages among 16 pregnancies of the wives of four male 15/22 translocation heterozygotes may also be indicative of a trend but the data from this family are too few to reach any conclusions about fetal wastage of male translocation carriers or segregation ratios. Reports of more families with this type of translocation may provide such data. It seems that karyotyping the abortions

of the translocation carriers may provide important information about the cause of the abortions.

Addendum

Two further balanced carriers of t(15q22q) were reported by Jacobs *et al* (1974). One of them, who was ascertained through a survey of prisoners, has inherited the translocation from his mother. The other, ascertained through a survey of patients in a mental subnormality hospital, was a new mutant.

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