Meiosis in two human reciprocal translocations

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SUMMARY Analysis of meiotic chromosomes from two human male translocation heterozygotes is reported. One had total sterility after maturation arrest and chain configurations at meiosis, and the second had abnormal children who were presumed to be genetically unbalanced.

The meiotic behaviour of human reciprocal translocations has recently been reviewed by Chandley *et al.* (1976), who found among their cases a male heterozygous for a balanced reciprocal 9;22 translocation (Chandley *et al.*, 1972), who was studied for infertility after 14 years of childless marriage. This man showed maturation arrest and chain configurations at meiosis, the first report of such an association in man, though such cases of male sterility had been reported by Lyon and Meredith (1966) and Cacheiro *et al.* (1974) in mice carrying reciprocal autosomal translocations.

This paper presents the meiotic findings of two human reciprocal translocations. One of them is the second known case in man, showing chain configurations at meiosis and associated total male sterility.

Material and methods

The two cases came from the Infertility Clinic of the Fundación Jiménez Díaz. They were studied after all other urological causes of infertility had been ruled out.

After preparing cultures of peripheral blood lymphocytes (Arakaki and Sparkes, 1963), the chromosomes were analysed by G-banding (Seabright, 1971) and Q-banding (Caspersson *et al.*, 1970). Testicular biopsies were removed under local anaesthesia and meiotic preparations were made by a modified version of the technique of Evans *et al.* (1964). The preparations were stained by Giemsa and the C-banding method of Chandley and Fletcher (1973).

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Results

CASE 1. 46,XY,t(9;11) (q34;q13)

This case (FJD Registry No. 2522/74), aged 33, was childless after 6 years of investigations for infertility. In the lymphocyte cultures, a clear translocation between two C-group chromosomes was found. With G and Q-banding, a reciprocal translocation between the long arms of chromosomes 9 and 11, 46,XY,t(9;11)(q34;q13) was found. The skin biopsy showed the same abnormality. A family study revealed normal karyotypes in three brothers of the proband. The father was dead and the mother could not be studied. It seems that the translocation was *de novo* since the other sibs studied presented no abnormalities.

The spermiogram showed severe oligospermia (1300/ml) with a high percentage of abnormal forms and practically non-existent motility. Unfortunately the spermiogram did not give figures. Histological analysis revealed hypospermatogenesis with remarkable absence of mature forms (Fig. 1). At meiosis all the stages of the cycle were found. The Table shows the marked reduction in the number of cells in the second meiotic metaphase. The analysis correlated well with the findings of the spermiogram and the testicular biopsy. An analysis of cells in diakinesis gave a mean chiasma frequency of 48 per cell. All the quadrivalents found (Table) had the form of an open chain resulting from probable failure of chiasma formation in one arm of the translocation cross at meiotic prophase (Fig. 2).

CASE 2. 46,XY,t(2;11) (p21;q25)

This case (FJD Registry No. 3152/75), aged 40, presented at our Genetic Counselling Section because over the past two years his wife had had two

Fig. 1 Case 1. Histology of testicular tissue.

Fig. 2 Case 1. Configuration of somatic chromosomes: probable chiasma position: chain IV at diakinesis.

Table Distribution of analysed cells

Case	Karyotype	Spermato- gonial metaphase	First meiotic metaphase	Second meiotic metaphase	Total
1	46,XY,t(9;11) (q34;q13)	5 (6.6%)	68 (86.0%)	6 (7.4%)	79
2	46,XY,t(2;11) (p21;q25)	8 (6.0%)	64 (48.4%)	60 (45.6%)	132

pregnancies resulting in the birth of a boy and a girl with similar severe malformations. These consisted of polydactyly, hand contracture, cleft palate, cardiopathy, and unspecified renal malformations. They died 19 and 32 days after birth, respectively. An 8-year-old son was phenotypically normal.

The cytogenetic studies showed that he had a balanced translocation between chromosomes 2 and 11, 46,XY,t(2;11) (p21;q25). The surviving son had a normal male karyotype. We were unable to examine any other member of the family. Unfortunately, no spermiogram or testicular histological analysis were obtained. The meiotic studies showed all the stages of spermatogenesis. The Table shows the percentage of cells in each phase. The mean chiasma count for

diakinesis was rather low at 35.0. The normal mean number of chiasmata per cell is 50.61 ± 3.87 (Paris Conference, 1971). The quadrivalent was always in the form of a ring (Fig. 3).

Discussion

Though we report these two cases together, there are some important differences between them. Case 1 seems to be, as far as we know, only the second case of a human translocation to show chain configurations at meiosis and associated total male sterility. Such translocations have also been reported in mice (Lyon and Meredith, 1966). These authors, and Chandley *et al.* (1972, 1976), who described the first case in humans, believe that the maturation breakdown followed by total sterility is the consequence of the telomeric and centromeric break points leading to the formation of chain quadrivalents at meiotic metaphase, conditions which are present in our case. The few cells which are able to complete spermatogenesis and produce gametes are clearly not present in sufficient numbers to achieve fertilisation.

Fig. 3 Case 2. Meiotic karyotype.

This type of translocation, causing total sterility in mice and men, is also characterised by the presence of a very small marker chromosome in the blood. This is the small (t^2) product of the translocation which may be passed on to the F_1 progeny by 3:1 disjunction at anaphase I in female heterozygotes, leading to the production of tertiary trisomic offspring.

The second case had a history of subfertility and different findings in meiotic studies. He had ring configurations at diakinesis and no apparent spermatogenic failure, in spite of the low mean chiasma count with a normal distribution of cells through spermatogenesis. It is concluded that alternate segregation led to the production of the normal son, and adjacent I or II to the two malformed children. However, karyotypes were not done for these two children to elucidate the exact mechanism of production.

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References

- Arakaki, D. T., and Sparkes, R. S. (1963). Microtechnique for culturing leucocytes from whole blood. *Cytogenetics*, **2**, 57–60.
- Cacheiro, N. L. A., Russell, L. B., and Swartout, M. S. (1974). Translocations, the predominant cause of total sterility in sons of mice treated with mutagens. *Genetics*, **76**, 73–91.
- Caspersson, T., Zech, L., Johansson, C., and Modest, E. J. (1970). Identification of human chromosomes by DNA-binding fluorescent agents. *Chromosoma*, **30**, 215–217.
- Chandley, A. C., Christie, S., Fletcher, J., Frackiewicz, A., and Jacobs, P. A. (1972). Translocation heterozygosity and associated subfertility in man. *Cytogenetics*, **11**, 516–563.
- Chandley, A. C., and Fletcher, J. (1973). Centromere staining at meiosis in man. *Humangenetik*, **18**, 247–252.
- Chandley, A. C., Seunanez, H., and Fletcher, J. (1976). Meiotic behaviour of five human reciprocal translocations. *Cytogenetics and Cell Genetics*, **17**, 98–111.
- Evans, E. P., Breckon, G., and Ford, C. E. (1964). An air-drying method for meiotic preparations from mammalian testes. *Cytogenetics*, **3**, 289–294.
- Lyon, M. F., and Meredith, R. (1966). Autosomal translocation causing male sterility and viable aneuploidy in the mouse. *Cytogenetics*, **5**, 335–354.
- Paris Conference (1971). Standardization in human cytogenetics. *Birth Defects: Original Article Series*, **8**, No. 7, 1972. The National Foundation—March of Dimes, New York.
- Seabright, M. (1971). A rapid banding technique for human chromosomes. *Lancet*, **2**, 971–972.
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