Case reports

long arm have presented with secondary amenorrhoea only.^{16 17}

Phenotypically normal persons with partial duplication of the X chromosome have shown preferential inactivation of the abnormal X,^{4 5} but this is also true of the large isodicentric chromosomes. In circumstances in which excess X chromosome material does not appear to be inactivated various congenital abnormalities are present.⁴⁻⁶ We have looked at the X inactivation pattern in our patient. Five hours after the introduction of BrdU about 25% of the mitoses showed no BrdU incorporation on either X chromosome, 64% showed symmetrical incorporation on both parts of the abnormal chromosome, and the remaining 11% showed incorporation on only one half of the abnormal X chromosome. However, unlike the cases reported by Sarto and Therman⁹ and Maraschio *et al*⁷ with p arm fusion, and a case of q arm fusion,⁸ the later replicating portion of the chromosome would appear to be unrelated to the position of the functioning centromere. It seems improbable that these findings indicate that half the chromosome remains active, but reflects more the time of exposure to BrdU; X chromatin in the interphase cells was uniformly large and often bipartite. It does suggest that the onset of replication is separately determined in the two parts of the abnormal chromosome.

The explanation of the clinical effect of this chromosomal abnormality thus remains obscure. One possibility is that the large dicentric chromosome presents pairing problems at meiosis which leads to failure of the female gonad.

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Recurrent spontaneous abortions due to a homologous Robertsonian translocation (14q14q)

SUMMARY A female with a history of recurrent spontaneous abortions was shown to carry a balanced Robertsonian translocation involving the No 14 homologues. One abortus had trisomy 14 with a 46,XX, -14, +t(14q14q)mat karyotype.

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Fecundity in carriers of homologous Robertsonian translocations is discussed.

Balanced homologous Robertsonian translocations, despite being rare, have been reported as a cause of recurrent spontaneous abortions in all the acrocentric autosomes.¹⁻⁵ Only one such case involving the No 14 homologues has been described (subject ÅS in Hultén and Lindsten⁶ and Caspersson *et al.*¹). We report here a second case involving chromosome 14 and discuss fecundity in homologous Robertsonian translocation carriers.

Case report

The proband, a 22-year-old phenotypically normal woman, was referred for cytogenetic investigation because of a history of spontaneous abortions. Her menarche occurred at the age of 13 and her menstrual cycle has been slightly irregular. At the age of 18 she had an appendectomy when a small right ovarian cyst was punctured. An x-ray investigation of the abdomen, urine electrolyte levels, and a blood count were normal. Subsequent gynaecological examinations have revealed no abnormality. During 4 years of marriage she has had five spontaneous abortions, the last of which occurred after the ascertainment of her cytogenetic abnormality. In each case the clinical symptoms were similar with bleeding through the vagina at a gestation of about 12 weeks. Evacuation of the uterus produced only placental tissue on each occasion except the last when the products of conception included a 5 × 2 cm congested gestation sac containing a 5 mm long embryo, from which fibroblast cultures were established for cytogenetic

investigation. Following the fifth abortion the proband has elected for sterilisation and is considering the adoption of a child.

CYTOGENETIC STUDIES

Chromosome preparations were made and banded using standard techniques. Each metaphase from lymphocyte cultures of the proband showed a count of 45 which resulted from a balanced Robertsonian translocation involving the No 14 homologues; her karyotype was thus 45,XX,t(14q14q) (figure a). The fifth abortus had a karyotype of 46,XX,-14,+t(14q14q)mat (figure b) and was therefore trisomic for chromosome 14. Lymphocyte cultures of the husband, parents, and four sibs of the proband showed normal karyotypes.

Discussion

Balanced Robertsonian translocations are relatively common in man, occurring at a frequency of 1 in 1100 in newborn infants.⁷ The proportion of these translocations that involve homologous chromosomes appears to be extremely small, as indicated by the paucity of such published reports.

In general, carriers of homologous Robertsonian translocations are phenotypically normal. However, some carriers of t(15q15q) have been reported with Prader-Willi syndrome, putatively as the result of breakage in the region of band 15q11⁸ or loss of the segment 15q11→q13.⁹

Theoretically, carriers of homologous Robertsonian translocations are unable to produce normal children since all the gametes should be either nullisomic or disomic for the chromosome involved in the translocation. In cases of t(13q13q) and t(21q21q) the trisomic zygotes occasionally survive to term and such carriers may therefore be ascertained both through their abnormal children^{10,11} and multiple abortions.^{2,3} However, liveborn cases of trisomy 14,^{12,13} and 22 (for example Shokeir¹⁴) are extremely rare although these trisomies are relatively frequent in surveys of spontaneous abortions,¹⁵ trisomy 14 occasionally resulting from an unbalanced homologous Robertsonian translocation.¹⁶ Thus, phenotypically normal carriers of t(14q14q) (Caspersson *et al.*¹ present case), t(15q15q) (for example Žižka *et al.*⁵), and t(22q22q) (reviewed by Kirkels *et al.*¹⁷) have apparently only been ascertained through multiple spontaneous abortions, the zygotes presumably being trisomic (as in one abortus of the present case) rather than monosomic, since monosomy for chromosomes 14, 15, or 22 has not been reported in spontaneous abortion surveys.¹⁵ Consequently, in contrast to balanced non-homologous

FIGURE Partial GTG banded karyotypes of (a) proband and (b) fifth abortus.

Robertsonian translocations which are generally inherited,⁷ balanced homologous Robertsonian translocations are considered to originate de novo immediately after fertilisation or in early embryogenesis.^{18,19} However, in two cases transmission of a balanced homologous t(22q22q) from a mother to a phenotypically normal daughter has been established.^{17,19} This anomalous inheritance could be explained either by fertilisation of an ovum carrying the translocation by a sperm nullisomic for chromosome 22 or by early post-zygotic loss of a chromosome 22 from a trisomic zygote.^{17,19}

These latter reports therefore complicate the issue of genetic counselling in couples where one partner has a homologous Robertsonian translocation. Previously it was assumed that phenotypically normal offspring were not possible and sterilisation has been advocated.³ However, carriers might now be counselled that, although the chance of having a normal child is probably very small, it remains an unquantifiable possibility and that, if couples elect for a pregnancy, fetal karyotyping could be undertaken should the gestation reach 16 weeks.

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Pregnancy in a patient with 47,XX,i(Xq) karyotype

SUMMARY A phenotypically normal woman with a 47,XX,i(Xq) karyotype is reported. She has had two successful pregnancies monitored by prenatal diagnosis with the delivery of normal offspring. The presence of a structurally abnormal third X chromosome has not demonstrably affected this patient or her reproduction.

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