Short reports

Parental origin of the X chromosome in a patient with a Robertsonian translocation and Turner's syndrome

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Abstract
We report on a proband with both a Robertsonian translocation and Turner's syndrome. Study of the parental origin of the X chromosome performed by microsatellite analysis indicates paternal origin of the X chromosome (Xpat). The occurrence of chromosome aberrations as a consequence of interchromosomal interactions is discussed.

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The occurrence of X chromosome monosomy and a Robertsonian translocation in the same person is rare. To our knowledge, there have been only two previous cases published.^{1,2} In both the Robertsonian translocation was familial and of 13;14 type.

The present report deals with a new case of monosomy X combined with t(13;14). As the translocation was paternally inherited, we wanted to evaluate if the second aberration (XO) had the same origin.

Simple dinucleotide sequence repeats have been shown to be highly polymorphic and useful in genetic analysis since they are readily assayed by PCR.³ Therefore, we based our analysis on the microsatellite marker located at the extreme terminus of the dystrophin gene.⁴

The proband, a 16 year old girl, was admitted to hospital because of short stature and primary amenorrhoea. Physical examination showed phenotypic characteristics of Turner's syndrome: small mandible, epicanthic folds, hypertelorism, low set ears, short neck with pterigium and low W shaped posterior hair

line, shield chest, undeveloped breasts with widely spaced hypoplastic nipples, cubitus valgus, short fourth and fifth metacarpals, short fifth finger with clinodactyly, and gonadal dysgenesis. Her intelligence was normal. At the time of birth her mother was 22 and her father was 23 years old. Her parents had a second daughter, six years younger and phenotypically normal. The mother had no history of spontaneous abortion and the father is a phenotypically normal male.

Chromosome analysis was performed on trypsin G banded chromosome preparations from peripheral lymphocyte cultures; 50 metaphases were scored.

Polymerase chain reaction was carried out on DNA extracted from blood samples. The oligonucleotides⁴ allowed the amplification of markers DYS1 and DYS111, with a size range of 177 to 185 bp and 219 to 225 bp, respectively. Reactions and conditions of the amplification were as described by Feener *et al*⁴ and the PCR products were electrophoresed on a 5% non-denaturing polyacrylamide gel (figure A). The alleles of the marker were separated on a 10% non-denaturing polyacrylamide gel and visualised by ethidium bromide staining (figure B).

In the proband's lymphocytes, besides monosomy X, cytogenetic analysis showed the presence of a Robertsonian translocation: 44,X,t(13q;14q) (data not shown). The translocation chromosome was inherited from her father, whose karyotype was 45,XY,t(13q;14q). The karyotypes of her mother and sister were normal.

Amplification of the DYS1 marker was not informative in our family (data not shown).

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Detection of the DYS111 marker by gel electrophoresis after PCR. Amplified DNA of the father (F), mother (M), and child (C) is indicated. Lane M/C has mixed PCR products of the mother's and child's DNA. Lane W is a DNA molecular weight marker VIII (Boehringer) with relevant fragments given in bp.

However, PCR products of DYS11 clearly showed that the proband had inherited the paternal X chromosome, as they are both hemizygous for the same allele, while the mother is homozygous for the different marker allele (figure B).

The occurrence of two or more chromosome aberrations in the same person is presumed to be the result of an interchromosomal effect. There are reports of synaptic anomalies of other bivalents in the presence of a Robertsonian translocation, and also of associations between translocation trivalent and sex vesicle in the pachytene of Robertsonian translocation carriers.⁵ In the report of Salamanca *et al*² the translocation 13q;14q of the patient was maternally inherited and the parental origin of the X chromosome could not be traced. Laszlo *et al*¹ concluded that there was no convincing evidence of an interchromosomal effect in the case of their patient.

The discovery of highly polymorphic PCR markers³ using specific X linked oligonucleotides has made possible a new approach in the molecular diagnosis of Turner's syndrome, as well as the assignment of parental origin of the single X chromosome in affected subjects. Analysis of the parental origin of the retained X chromosome in our proband showed the presence of the paternal X (Xpat), indicating that the Robertsonian translocation has not influenced paternal gametogenesis. However, a Robertsonian translocation could influence non-disjunction in early embryogenesis.

Recent data⁶ support the hypothesis of Hook and Warburton⁷ that some degree of mosaicism is necessary for survival in early pregnancy. Even if a second cell line is not

detected, its existence can not be excluded.⁶ We did not find any mosaicism in lymphocytes analysed both with cytogenetic and molecular techniques, and other tissues were not available for further investigation. The phenotype of our patient is typical of Turner's syndrome. However, because Xpat is inherited in 21% of 45,XO conceptuses,⁸ as well as the finding that only about 20% of cases of Turner's syndrome are apparently non-mosaic,^{6,8} the loss of the Xmat chromosome during embryonic development seems to be more likely than non-disjunction in maternal meiosis.

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