Triploidy arising from a first meiotic non-disjunction in a mother carrying a reciprocal translocation

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Abstract

We report on a 22 year old mother, a carrier of a 6;14 balanced reciprocal translocation, who aborted a triploid conceptus carrying a similar translocation. We showed the maternal origin of this triploidy, after non-disjunction at meiosis I. The phenotypic expression as a non-molar pregnancy, the contribution of the maternal translocation, and possible aetiological factors of triploidy are discussed.

The presence of an additional haploid set of chromosomes (triploidy) is a condition occurring in about 1% of clinically recognisable pregnancies. The great majority of triploid conceptuses abort spontaneously. Only a very small number survives to term, presenting as abnormal infants who usually die in the immediate postnatal period.¹

Triploidy may arise from various mechanisms including mitotic irregularities in germ cell precursors, lack of normal division in either the first or second meiotic division of either parent, or dispermy. In the series of Jacobs *et al*,¹ 78 triploids were informative as to their mechanism of origin: 57 (73%) had two paternal complements and 21 (27%) were maternally derived. Of the 21 digynic triploids, eight resulted from an error at meiosis I and 13 from an error at meiosis II.

Triploidy is not maternal age dependent but has been postulated to be associated with maternal coffee consumption at the time of conception.² More recently an association with maternal preconception irradiation has also been suggested³; the study of Alberman *et al*⁴ found triploid abortuses in the group of mothers having received the highest dose of irradiation.

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We report here an unusual case of triploidy associated with a reciprocal translocation of chromosomes 6 and 14 where both the extra haploid set of chromosomes and the translocation were maternal in origin.

Case report

A 22 year old G5 P0 A4 woman was admitted at 8 weeks of gestation for threatened abortion. Her past medical history included irradiation for an unspecified blood disease and four previous abortions between seven and 12 weeks of gestation. After her third abortion, she was referred for genetic counselling and was found to be a carrier of a balanced reciprocal translocation with a 46,XX,t(6;14)(p23;q24) chromosomal complement.

The product of conception received in the pathology department was not hydropic on macroscopic examination. One representative section submitted showed decidua and one cluster of non-hydropic villi.

Fibroblasts grown for cytogenetic studies showed a triploid conceptus with a 69,XXY,t(6;14)(p23;q24) karyotype (fig 1). Comparison of the heteromorphic chromosomes 14 of both parents and the fetus showed that the extra haploid set of chromosomes resulted from a non-disjunction at meiosis I in the mother (fig 2). Studies of additional heteromorphic chromosomes indicated that chromosomes 13 and 21 also supported a maternal meiosis I origin.

Discussion

Triploidy accounts for 16 to 17% of chromosomally abnormal conceptuses.^{3,5} Most cases are paternally derived and dispermy has been found to be the most common mechanism involved.⁵ Digynic triploids (two sets of chromosomes contributed by the mother) account for 24 to 36% of the cases.^{1,3,6} In addition, two large series showed that in digynic triploids, errors in the second meiotic division are relatively more frequent than in the first one.^{1,3} Our patient is unusual not only in that the extra haploid set is maternally derived but also in showing a meiosis I non-disjunction in a mother carrying a reciprocal translocation.

The presence of a balanced rearrangement in a

Figure 1 Triploid conceptus with a 69,XXY,t(6;14)(p23;q24) karyotype.

Figure 2 Heteromorphic chromosomes 14 of both parents and the conceptus indicating maternal origin resulting from a non-disjunction at meiosis I.

parent has often been suggested to be associated with an increased risk of aneuploidy. The abnormal pairing configurations produced by such a rearrangement at meiosis have been proposed to interfere with normal meiotic segregation and this has been shown to occur in some organisms such as *Drosophila*.⁷ Support for

this idea in human material has been mainly from anecdotal reports of families in which trisomy or monosomy X has been found in the offspring of parents with a balanced rearrangement.⁸ Since the parental chromosomal studies have usually been done only because of the aneuploidy in the children, these reports cannot be used to prove the validity of the hypothesis.

Lundsteen *et al*,⁹ however, indicated that they could find no evidence of an interchromosomal effect and suggested that studies of parental origin of the extra chromosome might help to solve the problem. For example, Gustavson and Wahlstrom¹⁰ provided proof that aneuploidy was independent of a reciprocal translocation carried by the mother when she gave birth to a child with 47,XXY. Similar findings were reported by Uchida and Freeman.¹¹ Warburton¹² reported lack of evidence for increased risk of incidental trisomy among the progeny of balanced translocation carriers in the European collaborative study and the New York State chromosome registry. The role of parental structural chromosomal abnormalities in the development of partial moles has been examined. In a study of 125 partial moles,¹³ 125 mothers and 106 spouses were karyotyped and a balanced Robertsonian translocation was found in one father. Thus, the incidence of structural chromosomal abnormalities in parents with partial moles was not higher than that of the general population. Further

studies are necessary to see whether the same conclusion could be drawn for at least some cases of triploidy, for example, those not owing to dispermy.

The pathological correlation of triploidy with partial hydatidiform mole is well established.¹⁴ Cytogenetic studies have shown that in triploid partial moles, the extra haploid set is almost always of paternal origin, and that in non-molar triploids the extra set is of maternal origin.¹ In addition, two tetraploid partial hydatidiform moles have been reported which could have resulted from trispermy or from fertilisation by one diploid and one haploid spermatozoa.¹⁵ Since these tetraploid cases also provide unequivocal morphological examples of partial moles, the genetic element which is causally related to a molar, complete or partial, phenotype is the excess of the paternal over the maternal haploid contributions.¹⁵ This relates to the proposed hypothesis of genomic imprinting, where the maternal and paternal genomic contributions are not equivalent functionally. Experiments in which activated murine eggs were variously reconstituted with exogenous male and female pronuclei pointed to some dependence of the extraembryonic tissues, notably trophoblast, on the paternal genome, while maternal genes are apparently necessary for the development of the embryo proper.¹⁶

Our case was macroscopically non-hydropic and microscopic examination showed mostly decidua with a cluster of non-hydropic villi. This was expected, as the maternal chromosomal contribution exceeded the paternal one.^{1 17}

Triploidy has been suggested to be associated with maternal irradiation and coffee consumption.² Alberman *et al*⁴ studied the role of maternal pre-conception irradiation in spontaneous abortions and selected a subset of 103 abortuses with abnormal chromosomal constitutions; of these, 18 were triploids. Triploidy was found in the group of mothers who received the highest dose of irradiation. Uchida and Freeman³ interviewed 94 mothers with triploid conceptuses and found that 46% of them had a history of pre-conception abdominal x ray examination compared to 22% in age matched controls. It is not clear, however, how this association might be causal as most triploid conceptuses result from dispermy or events occurring at the time of conception. In our patient, however, irradiation may have played a role as the triploidy was maternal in origin. In the light of

this, assertions about the statistical significance of this association must await further studies where the origin of triploidy should be examined in relationship to the time of maternal exposure. Similar studies would be useful in examining the association between triploidy and maternal coffee consumption at the time of conception.

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- 1 Jacobs PA, Szulman AE, Funkhouser J, Matsuura JS, Wilson CC. Human triploidy: relationship between parental origin of the additional haploid complement and development of partial hydatidiform mole. *Ann Hum Genet* 1982;46:223-31.
- 2 Kline J, Stein Z, Sussa M, Warburton D. Socioeconomic differences in spontaneous abortions. *Am J Epidemiol* 1980; 112:439.
- 3 Uchida IA, Freeman VCP. Triploidy and chromosomes. *Am J Obstet Gynecol* 1985;151:65-9.
- 4 Alberman E, Polani PE, Fraser Roberts JA, *et al*. Parental X-irradiation and chromosome constitution in their spontaneously aborted foetuses. *Ann Hum Genet* 1972;36:185-93.
- 5 Procter SE, Gray ES, Watt JL. Triploidy, partial mole and dispermy. An investigation of 12 cases. *Clin Genet* 1984;26: 46-51.
- 6 Lawler SD, Fisher RA, Pickthall VJ, Povey S, Evans MW. Genetic studies on hydatidiform moles. I. The origin of partial moles. *Cancer Genet Cytogenet* 1982;5:309-20.
- 7 Grell RF. A new hypothesis on the nature and sequence of meiotic events in the female of *Drosophila melanogaster*. *Proc Natl Acad Sci USA* 1962;48:165-72.
- 8 Lejeune J. Autosomal disorders. *Pediatrics* 1963;32:326-37.
- 9 Lundsteen C, Zestewark S, Philip J. A familial balanced 2/5 translocation associated with trisomy 21 in one individual. *Hum Hered* 1974;24:88-99.
- 10 Gustavson KH, Wahlstrom J. Trisomy 9p and XYY syndrome in siblings. *Clin Genet* 1977;11:67-72.
- 11 Uchida IA, Freeman VCP. Trisomy 21 Down syndrome. II. Structural chromosome rearrangements in parents. *Hum Genet* 1986;72:118-22.
- 12 Warburton D. Genetic factors influence aneuploidy frequency. In: Dellarco V, Voytek PE, Hollaender A, eds. *Aneuploidy: etiology and mechanisms*. New York: Plenum Press, 1985: 133-48.
- 13 Vejerslev LO, Fisher RA, Surti U, Wake N. Hydatidiform mole: parental chromosome aberrations in partial and complete moles. *J Med Genet* 1987;24:613-5.
- 14 Szulman AE, Philippe E, Boué JG, Boué A. Human triploidy: association with partial hydatidiform moles and nonmolar conceptuses. *Hum Pathol* 1981;12:1016-21.
- 15 Surti U, Szulman AE, Wagner K, Leppert M, O'Brien SJ. Tetraploid partial hydatidiform moles: two cases with a triple paternal contribution and a 92,XXXXY karyotype. *Hum Genet* 1986;72:15-21.
- 16 Barton SC, Surani MAH, Norris ML. Role of paternal and maternal genomes in mouse development. *Nature* 1984;311: 374-6.
- 17 Vejerslev LO, Fisher RA, Surti U, Wake N. Hydatidiform mole: cytogenetically unusual cases and their implications for the present classification. *Am J Obstet Gynecol* 1987;157:180-4.