SHORT REPORTS

Parental origin of extra chromosomes in persons with X chromosome tetrasomy

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48,XXXX and 49,XXXXY chromosome constitutions are rare and while several such polysomies have been described in the past, the parental origin of the supernumerary chromosomes has only been described in a few cases.^{1,2} More recently, difficulties owing to the reduced informativeness of the Xg antigen marker have been overcome by the use of X linked restriction fragment length polymorphisms (RFLPs) and, particularly, of multiallelic RFLPs. Using X linked DNA markers, we have analysed a group of four families with X chromosome tetrasomy, one with 48,XXXX and three with 49,XXXXY.

The four probands had developmental retardation with at least some of the common dysmorphic features described in X chromosome tetrasomy,³ namely, upward slanting palpebral fissures, broad nasal bridge, epicanthus, and hypogenitalism. The chromosomal constitution and ages of the probands and their parents, as well as the results of the RFLP studies in the four families with X chromosome tetrasomy, are shown in the table. In all the 49,XXXXY subjects, the intensity and pattern of the bands observed indicates maternal origin of the X chromosomes. The family of proband 3 was only informative for the *BglII* polymorphism at locus *DXS15*. Our findings in the 49,XXXXY subjects agree with the pattern of inheritance of the extra X chromosomes

reported in similar patients.^{1,2} The proposed mechanism of non-disjunction occurring in both meiosis I and II is also supported by our results, suggesting a common cause in the mothers of all the patients.

The pattern of inheritance of the X chromosomes in the 48,XXXX patient, that is, one paternal allele together with both maternal alleles, one of them in double dose (figure), differs from the two other cases reported so far with this karyotype,^{1,2} in whom no paternal X linked alleles were found. Among the various possible hypotheses for the mechanism of formation of X tetrasomies, the one proposed by Race and Sanger,¹ based on the assumption that an unstable pentasomic X egg was formed followed by postzygotic anaphase lag of an X chromosome, could explain the origin of these three cases. It is also more likely than the coincidental occurrence of meiotic non-disjunction errors in both parents, which would otherwise be needed to explain the formation of the previously reported X tetrasomies.^{1,2} An alternative mechanism, which applies exclusively to our 48,XXXX patient, could be non-disjunction between homologous X chromosomes at first meiosis and sister chromatids in one of the X chromosomes at second meiosis.

The mean maternal age in our 49,XXXXY patients was increased (34.4 years). However, when data on mean maternal age from 25 families with 49,XXXXY, including the pre-

Summary of the results of the cytogenetic and DNA polymorphism studies in X chromosome tetrasomies.

Family	Chromosome constitution	Age* (y)	X chromosome RFLPs used			
			Locus <i>F8C</i> , <i>IVS18</i> <i>BclI</i> alleles	Locus <i>DXS2</i> <i>BclI</i> alleles	Locus <i>DXS25</i> <i>EcoRI</i> alleles (kb)	Locus <i>DXS15</i> <i>BglII</i> alleles
1						
Proband	49,XXXXY	7	2,2,2,2	5,5,8,8	6-1,6-1,6-3,6-3	ND
Father		37	2	6	5-9	ND
Mother		33	2,2	5,8	6-1,6-3	ND
2						
Proband	49,XXXXY	9	1,1,2,2	6,6,7,7	5-5,5-5,5-9,5-9	ND
Father		40	—	—	—	ND
Mother		35	1,2	6,7	5-5,5-9	ND
3						
Proband	49,XXXXY	4	2,2,2,2	6,6,8,8	3-8,3-8,4-2,4-2	2,2,2,2
Father		37	2	6	3-8	1
Mother		35	2,2	6,8	3-8,4-2	2,2
4						
Proband	48,XXXX	21	1,2,2,2	5,8,4,4	4-3,5-9,5-9,6-5	ND
Father		34	1	5	4-3	ND
Mother		30	2,2	4,8	5-9,6-5	ND

*Parent's age at birth of child.
ND = not determined.

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sent ones, are compared with average maternal age at parturition, no maternal age effect can be seen (28.8 *v* 28.2 years).

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- 1 Race RR, Sanger R. Xg and sex-chromosome abnormalities. *Br Med Bull* 1969;25:99-103.
- 2 Hassold T, Pettay D, May K, Robinson A. Analysis of non-disjunction in sex chromosome tetrasomy and pentasomy. *Hum Genet* 1990;85:648-50.
- 3 Zaleski WA, Houston CS, Pozsonyi J, Yink KL. The XXXXY chromosome anomaly: report of three new cases and review of 30 cases from the literature. *Can Med Assoc J* 1966;94:1143-54.

RFLP analysis. (A,B) *BclI* polymorphism at locus DXS52; (C,D) *EcoRI* polymorphism at locus DXS255. Lanes 1, 2, 3 family 4 (lane 1 mother, lane 2 proband, lane 3 father); lanes 4, 5 family 2 (lane 4 mother, lane 5 proband); lanes 6, 7, 8 family 3 (lane 6 mother, lane 7 father, lane 8 proband).