Ring (13),t(2;6) associated with familial fragile (16)

Fragile sites consist of isochromatid chromosome breaks which take place at specific sites along a chromosome and segregate as simple Mendelian traits.^{1,2} While the Xq28 fragile site is regarded as a marker for X linked mental retardation, the fragile sites on autosomes are regarded as normal uncommon variants. The present case supports the idea that the presence of fragile sites may constitute a risk factor which should be taken into account in clinical diagnosis. In addition, a fragile site may indicate some chromosomal instability.

The patient described here is the third child of a young non-consanguineous couple with no known exposure to mutagenic or teratogenic agents. The other two children are healthy. A previous pregnancy ended in spontaneous abortion at 12 weeks. At the age of 2 months the proband was noted to be microcephalic (34 cm) with a large anterior fontanelle. The facies was peculiar with a prominent nasal bridge, hypertelorism, elongated prominent philtrum, short upper lip, small and slender chin, and low set folded ears. Other features included congenital leukoma, short neck, absence of nipples, cutis marmorata, and anterior anal dislocation without atresia. Skeletal x-ray examination was unremarkable. Cytogenetic studies were carried out on peripheral blood in Difco TC 199 medium. In all cells 46 chromosomes were found with a ring 13 and a 2q6p translocation. In addition, gaps, breaks, or deletions at band 16q21 were present in 15 of 100 cells examined. The extra acentric fragment corresponding to the chromosomal segment distal to band 16q21 was CBC and N negative. About the same percentage of cells (13%) expressing the fragility at band 16q21, with the same characteristics, was observed in the mother's karyotype. The karyotype of the proband

was therefore, 46,XX,r(13),t(2;6)(q24;p22),fra(16q21)mat (figure).

Structural or numerical chromosomal anomalies, increased abortion rate, and malformation syndromes without karyotype anomalies may be associated with fragile sites more often than suspected.³ Previous observations and this case must lead us to regard the chromosome 16 fragile site as a risk factor for de novo chromosomal abnormalities. The presence of a fragile site might be the result of the expression of a gene responsible for increased chromosomal instability and therefore a tendency to produce breaks. In our case at least four independent breakages might be suspected. The history of a previous abortion is also noteworthy.

It may be prudent to carry out fetal karyotype analysis whenever one of the parents is a known carrier of a fragile site. Moreover, fragile sites should be tested for in all de novo chromosomal abnormalities and particularly in those with more complex rearrangements.

VALERIO VENTRUTO, ANGELO RINALDI,
SILVIO RENDA, MARIANO STABILE,
MARIA MICHELA RINALDI, MARIA LUIGIA CAVALIERE,
NICOLA CONTE, AND VINCENZO AVETA
*Servizio di Genetica Medica, Ospedale A Cardarelli,
Napoli, Italy.*

References

- 1 Sutherland GR. Heritable fragile sites on human chromosomes. I. Factors affecting expression in lymphocyte culture. *Am J Hum Genet* 1979;31:125-35.
- 2 Sutherland GR. Heritable fragile sites on human chromosomes. II. Distribution, phenotypic effects, and cytogenetics. *Am J Hum Genet* 1979;31:136-48.
- 3 Côté GB, Katsantoni A. The fragile site on the long arm of chromosome 16. *Ann Genet (Paris)* 1980;23:214-3.

Correspondence and requests for reprints to Professor V Ventruto, Servizio di Genetica Medica, Ospedale A Cardarelli, 80131 Napoli, Italy.

FIGURE Patient's karyotype (R banding) showing the 2q:6p translocation, the ring 13, and the fragile site at 16q21.

Received for publication 15 September 1983.

Accepted for publication 21 October 1983.