population doublings. However, this in vitro test may or may not duplicate in vivo conditions producing loss of the Yq−. The degree of deletion may also be a factor in its instability.

When the fetus has a Y chromosome without the fluorescent segment, since the phenotype is unknown, it is important to quantify the size of the fetal and paternal Y chromosomes and compare them to standards for variation in the size of normal Y chromosomes. The availability of testing for HLA and H−Y associated antigen on amniotic fluid cell cultures would have helped to establish paternity and the presence of the Y chromosome, respectively, in the case of the de novo Yq− reported here. However, the possibility of a small translocation or mosaicism for 45,X would have remained. Existing methods do not rule out this possibility. The cultures are derived from a very small number of cells which proliferate in vitro. Mosaicism can be missed because these few cells may not be representative of the fetus. Furthermore, evidence indicates that the major cell type in second trimester amniotic fluid cell cultures is derived from trophoblastic tissue and, as such, represents fetal membranes but not the fetus proper.8

Since they lacked complete knowledge of the consequences of the Yq− chromosome, the parents' decisions in this case were influenced in a major way by their fear of aborting a child that could be normal, their concern that another pregnancy would not have possible clinical abnormalities.

We would like to acknowledge the help of Holly Downey, Virginia Dunbar, Rusha Jordan, Linda Shulin, and Suzanne Trusler.

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References

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13q−/r(13) mosaicism

SUMMARY A 2-month-old female infant with typical features of the 13q− syndrome was found to be a hitherto unreported mosaicism consisting of 46,XX,del(13)(q22)/46,XX,r(13)(p13q22). Both ends of the 13q− and r(13) chromosomes were AgN banding positive. Therefore, it was assumed that they had retained the satellite stalks. Two possible mechanisms were proposed for the genesis of the mosaicism. Firstly, the patient started with the 13q− chromosome, which then underwent breakage and reunion at both ends to form the r(13) chromosome. Secondly, the patient started with the r(13) chromosome, which reopened at or close to the joining point to form the 13q− chromosome.

More than 70 cases of 13q− syndrome have been reported. They include both those with a chromosome 13 with a partial deletion of the long arm (13q−), and those with a ring chromosome 13[r(13)]12. However, there has been no instance
reported of 13q−/r(13) mosaicism. This paper describes such mosaicism in a 2-month-old female infant. Possible mechanisms for the occurrence of the mosaicism will be discussed.

Case report

The patient, a girl, was born to a 27-year-old mother and a 34-year-old father. The delivery at 40 weeks' gestation was uneventful. At her birth, she weighed 1500 g, measured 38.5 cm, and her head circumference was 27.7 cm. When examined at 2 months of age, the patient had several malformations, including a narrow forehead, lateral displacement of the inner canthi leading to short palpebral fissures, epicanthic folds, a broad nasal bridge, protruding upper central incisors, a high-arched palate, low set ears, and micrognathia.

The neck was short and webbed. The thumbs were small and proximally located. There was a simian line on the right palm. The feet were small and the fourth toes overlaid the third. The pelvis was narrow and the hip joints were contracted. The anus was imperforate. Computerised axial tomography of the skull showed the presence of holoprosencephaly. Ophthalmological examination showed abnormal blood vessels in the ocular fundi. Examination of serum electrolytes showed hypernatraemia (150 to 175 mmol/l) and hyperchloraemia (120 to 130 mmol/l), which persisted from the second day of life. Serum immunoglobulin levels and the ratio of T and B lymphocytes were within normal limits. There was no increase of haemoglobin A2. X-rays showed spina bifida occulta in a sacral vertebra.

CYTOGENETIC STUDIES

Chromosome preparations were made from repeated cultures of peripheral blood lymphocytes. A total of 283 metaphases was counted and analysed visually, and of these, 30 were analysed photographically (table). The modal chromosome number was 46. There were three distinct cell lines: 231 cells contained a Dq− chromosome, 40 cells had a r(D) chromosome, and the other 12 cells had a C (half moon) shaped chromosome, which may be interpreted as a reopened r(D) chromosome.

It is remarkable that no cell with a missing chromosome 13 was encountered. Trypsin G and Q banding showed the abnormal D chromosome to be derived from a No 13 with deletion of bands distal to 13q22 (fig 1a−d, 2). Ag N banding showed a cluster of silver dots at band p12 of both the 13q− and r(13) chromosomes (fig 1e, f). This would indicate that satellite stalks were retained in both of the abnormal chromosomes. Therefore, the proband's karyotype was interpreted as 46,XX,del (13)(q22)/46,XX,r(13)(p13q22). A total of 500 interphase nuclei was screened, but neither micro-nuclei nor internuclear bridges were detected. The karyotypes of the parents were normal.

<table>
<thead>
<tr>
<th>TABLE</th>
<th>Frequency of abnormal D chromosomes in cultured lymphocytes</th>
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<tr>
<td></td>
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<tr>
<td></td>
<td>45</td>
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FIG 1 Abnormal chromosome 13. a−c; GTG banded chromosome 13. Left column shows deleted chromosome 13 and right column shows ring chromosome 13. d; Q banding showed a bright spot at the pericentromeric region of a ring chromosome (white arrow). e; black arrow shows a silver dot at p12 of the ring. f; A C (half moon) shaped 13q− chromosome.
FIG 2  Breakpoints on abnormal chromosome. Upper row shows del(13)(q22) and lower row shows r(13)(p13q22).

Discussion

Our patient had multiple malformations usually found in 13q− syndrome with deletion of bands distal to q22. They included microcephaly with narrow forehead, holoprosencephaly, laterally displaced inner canthi with small palpebral fissures, broad nasal bridge, high arched palate, low set ears, micrognathia, webbed short neck, a simian line, small and proximally located thumbs, narrow pelvis, imperforate anus, and small feet with overriding fourth toes. Both of the 13q− and r(13) chromosomes in her mosaic karyotype had deletion of bands distal to q22. Therefore, the clinical findings support the results of the cytogenetic analysis. Neither a rise in haemoglobin A2 concentration, as is the case with deletion of bands 13q21−q31,4 nor bilateral retinoblastoma, as is associated with deletion of sub-band 13q14.2,5 was observed in our patient. However, since the retinoblastoma resulting from 13q− does not usually become manifest until the second year of life, it may be too early to confirm its absence in our infant.

Two alternative mechanisms are conceivable for the genesis of the mosaicism in our case. (1) She may have started with a 46,XX,13q− cell line, later breakage and reunion at both ends of the 13q− chromosome resulting in the second cell line with a r(13) chromosome. (2) Alternatively, she may have started with a r(13) chromosome, and the reopening of the ring at or close to the rejoining point produced a 13q− chromosome.

The fact that both of the 13q− and r(13) chromosomes were N banding positive indicated that they retained the satellite stalks and possibly a part of the satellite. According to the dogma of integrity of the telomere,8 the broken end of a chromosome is unstable, but satellites and satellite stalks may be an exception to the rule. Several instances have been reported of a stable acrocentric chromosome whose satellites or satellite stalks were deleted.7,8

The 13q− chromosome in the present case had satellites on conventional staining and stalks proved on N banding. Therefore, if mechanism (2) were the case, the breakpoint in the ring chromosome must have been within the satellites, and consequently a part of the satellites must have been left attached to the distal end of the long arm of the 13q− chromosome. It is difficult to visualise this, because there is no method available for staining the satellites specifically. It should be noted, however, that the distal ends of the long arms of 13q− were never involved in satellite association, while its short arms, with satellites and satellite stalks, were frequently in association.

References

45,X/46,XY/47,XY,+21 mosaicism in a hypogonadal phenotypic male

SUMMARY A phenotypically normal male was found to have a chromosomal complement of 45,X/46,XY/47,XY,+21. This mosaic pattern has been reported only twice before. Although the patient had apparently fathered two children, he now has progressive impotence, absence of sperm in the seminal fluid, atrophic testes, almost complete absence of germ cells in testicular biopsies, high plasma LH and FSH, and a low normal testosterone. There were no physical characteristics of Turner's or Down's syndromes except for dermatoglyphic features commonly associated with the latter. These observations in this patient emphasise the value of chromosomal studies in multiple tissues in cases of mosaicism with atypical clinical features.

Sex chromosomal mosaicism is known to be associated with various abnormalities of sexual differentiation.1 It has been observed in sterile or fertile phenotypic males and females, in subjects with ambiguous genitalia, and in true hermaphrodites. In normal sexual organogenesis, the presence of a normal Y chromosome and its associated H-Y antigen has been regarded as the determinant for the differentiation of the ambisexual fetal gonads into testes.2 Further differentiation in the male depends on the testes-derived Müllerian inhibiting factor and testosterone.

Trisomy 21 has been observed in association with sex chromosomal anomalies such as in Klinefelter's syndrome, XYY syndrome, triple X syndrome, Turner's syndrome, and mosaic 45,X/47,XY,+21.

Received for publication 22 October 1979.

This paper reports a phenotypic male with 45,X/46,XY/47,XY,+21 mosaicism, which has been reported only twice previously but without any clinical details.3,4

Case report

The proband, a 48-year-old black male, was admitted to the Hines Veterans Administration Hospital in 1977 for evaluation of recurrent chest pain since 1973. Previous stress electrocardiogram, coronary angiography, and right and left heart catheterisation had been normal. Testicular atrophy was discovered by routine physical examination and led to cytogenetic studies.

The patient had been aware of his small testes since adolescence, but virilisation was normal. He married, considered himself to have normal libido and sexual activity, and believed that he fathered two normal male children. A transurethral resection was performed in 1975 for benign prostatic hypertrophy. The patient complained of progressive impotence over the past year. He was the third child of four sibs (two males and two females). There was no history of infants with congenital malformations or spontaneous abortions in his wife or his mother.

Physical examination showed a muscular, non-eunuchoidal, well virilised male with normal external genitalia (fig 1). The testes were 2.5 cm long

FIG 1 The proband, a normal phenotypic male.