Case reports

A complex rearrangement involving three autosomes in a phenotypically normal male presenting with sterility

SUMMARY This paper reports a rearrangement involving three autosomes: 11, 12, and 21. The translocation carrier, a 31-year-old azoospermic male, is phenotypically normal.

Three-chromosome rearrangements associated with sterility in man are uncommon. With the exception of reports in chronic myeloid leukaemia, there have been 16 instances involving three chromosomes in published reports. This patient represents the seventeenth such case. In only three of the 16 previous reports had the rearrangements arisen de novo. In the remaining 13 cases, the subjects carrying the translocations were phenotypically normal females who were detected through a partially monosomic or trisomic child. This is apparently the first case of a phenotypically normal male presenting with azoospermia.

Case report

The proband was a 31-year-old male who presented with an 8-year history of sterility (fig 1). Physical examination showed a phenotypically normal male, 151 cm tall. Secondary sexual characteristics were normal and the testes and spermatic cord appeared normal.

The patient was the eldest of five sibs born to non-consanguineous parents. The mother was 18 years old and the father 23 years old at the time of his conception. The mother had no history of abortion either before or after his birth. Three younger sibs were female and all of them are married, two of them with children. The youngest sib was a male who was not married at the time of this report. No family history of sterility could be elicited.

LABORATORY FINDINGS

The semen analyses showed azoospermia and a testicular biopsy showed diminished spermatogenesis (fig 2).

CYTOGENETIC STUDIES

Standard leucocyte microculture using peripheral blood was done and the chromosome preparations were G banded, C banded (Scheres modified in this laboratory), and silver stained for nucleolar organiser regions (Bloom and Goodpasture, modified by G R Sutherland, personal communication to D S Krishnamurthy, 1980). Seventy-five metaphases were examined and all cells showed a partial deletion of the long arm of chromosome 11 and derivative chromosomes 12 and 21 (fig 3). No mosaicism for this rearrangement was observed. G banding showed...
FIG 3  G banded partial karyotype showing deleted chromosome 11 and derivative chromosomes 12 and 21 and their diagrammatic representations.

that the proband's karyotype could be represented as: 46,XY,t(11;12;21)(11pter→11q22::12pter→12q13::11q22→11qter;21qter→21pter::12pter·12q13→12qter.) Silver staining was negative in the derivative chromosome 21 and at the point of deletion on the long arm of chromosome 11. The absence of acrocentric associations with the deleted 11 confirmed that the satellite region from the derivative chromosome 21 had not been translocated to the deleted 11. Chromosomal analysis could not be done on the rest of the family members as they were uncooperative.

Discussion

To the best of our knowledge, sterility in males with chromosome rearrangements involving three or more chromosomes has not been reported previously. A review of reports on similar translocations in females has, however, shown reduced reproductive fitness but never sterility.8-18

The NORs from the derivative 12;21 chromosome did not stain with Ag nor were they found translocated onto another chromosome. It would, therefore, seem valid to assume that a portion of the short arm of chromosome 21 along with its nucleolar organiser region has been lost as anacentric fragment. This rearrangement would then be an unbalanced one and consequently this man would be monosomic for this particular region of chromosome 21.

Apart from carrying the genes coding for ribosomal RNA, the short arm of chromosome 21 does not have any other functional genes attributed to it. It seems unlikely, therefore, that specific genes influencing the production and viability of sperm are lost through the monosomy and that this is the cause of sterility in this man. However, loss of chromatin material from this region of the chromosome would affect meiotic pairing. This would serve to form a chain rather than a ring configuration during zygote. Such chain formation has been known to be responsible for male sterility in mice.19-21

The basis of sterility in the patient is essentially defective spermatogenesis leading to azoospermia. The complex structural rearrangement in the genome may impair zygote and later stages of spermatogenesis because the derivative chromosomes fail to pair characteristically. It is, however, not clear why such complex rearrangements do not appear to cause sterility in females.

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References

Yq— in a child with livedo reticularis, snub nose, microcephaly, and profound mental retardation*

**SUMMARY** A child with terminal deletion of the long arm of the Y chromosome (Yq—) presented with marked livedo reticularis, snub nose, microcephaly, short stature, and other dysmorphic features. He was profoundly mentally retarded. Most of the patients with Yq— have been reported as having varying dysmorphic features, mental retardation, and short stature. This child, in addition to the above, has livedo reticularis and microcephaly. He was of normal birthweight and, therefore, does not come into the syndrome of microcephaly, snub nose, livedo reticularis, and low birthweight dwarfism. Further information on Yq— should be obtained to ascertain if consistent patterns of abnormalities exist.

Cases with terminal deletion of the long arm of the Y chromosome (Yq—) have presented with a range of findings, from normal intelligence and normal male development, normal fertility, aspermia, varying dysmorphic features (major and minor), mental retardation, and short stature (table). In only one of these was the Yq— familial.

The case described here, in addition to short stature, congenital abnormalities, and mental retardation, had marked livedo reticularis and microcephaly.

**Case report**

The proband (fig 1), born on 18.7.71 and at 5 years 7 months of age and at 8 years 7 months of age, was the youngest and third-born child. At the time of his birth, his father and mother were 26 and 27 years of age, respectively. The pregnancy and delivery were uncomplicated and the birthweight was 3200 g. Mild respiratory distress developed 24 hours after birth. His head circumference at birth was reported to be 35 cm. His head circumference at 10 months of age was 43 cm, and at 23 months of age...