Mosaicism presumably related to a Y/6 translocation in a boy with multiple congenital abnormalities

**Summary** A 3½-year-old boy was referred for chromosomal evaluation because of mental and developmental retardation, peculiar facies, and abnormalities of the extremities.

Karyotype analysis disclosed the presence of 46 and 47 chromosome cell lines. The 46 chromo-

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some line contained 4 normal G group chromosomes and an abnormally small Y identified by G banding. Further investigation with Q and C band techniques revealed that the missing segment of the Y, the distal long arm, had been translo-
cated to the end of the long arm of a number 6 chromosome. This de novo rearrangement appeared to be balanced and was found in all cells examined. The 47 chromosome line, which had a frequency of 10% in the patient’s leucocytes, was identical to the 46 line except for the presence of an additional copy of the small chromosome.

The morphology and banding patterns of the two small acrocentrics in the aneuploid line were found to correspond to those of the der (derivative) Y in the euploid line.

The cytogenetic findings suggest that the translocation was followed by non-disjunction of one of its products resulting in mosaicism. Possible causes for the clinical and karyotypic abnormalities are discussed.

Fluorescent banding has greatly facilitated the study of structural changes involving the Y chromosome.

Translocation of the distal segment of Yq is easily determined by this technique, and a number of such exchanges have been reported. Some of these translocations (Noel et al., 1971; Friedrich and Nielsen, 1972; Frund et al., 1972) have had no apparent phenotypic effects on the individuals carrying them. In other cases (Develing et al., 1973; Gilgenkrantz et al., 1973; Pfeiffer et al., 1973) Y autosomal changes have occurred in association with deleterious phenotypic abnormalities. We wish to report a case of a de novo translocation in which the entire distal fluorescent segment of the Y has become attached to the tip of 6q. Though no loss of chromosomal material is detectable, the propositus is moderately retarded and has multiple congenital abnormalities. His cytological picture is complicated by the presence of an aneuploid cell line containing the translocation and what appears to be two copies of the derivative (der) Y. This cell line occurs with a frequency of 10% in the patient’s leucocytes.

**Case report**

The propositus is a 3½-year-old caucasian boy with developmental and mental retardation, peculiar facies, and abnormalities of the extremities. The mother was 42 and the father 51 at the time of birth. The mother, who was unaware of the pregnancy, underwent cholecystectomy preceded by a series of X-rays about the time of conception. She had also...
taken antibiotics (oxytetracycline dihydrate Urythos) plus mild tranquillisers during this period. No other accidents, trauma, or exposure to hazardous agents were reported for the rest of the pregnancy. Delivery by caesarean section occurred at 34 weeks' gestation. Birthweight was 3032 g (6 lb 11 oz) and length was 49·5 cm. The infant was given an Apgar score of 9 at 1 minute.

During his first 3 months, the propositus was described as irritable and required medication to sleep. A fall from a dressing table onto a carpeted floor at age 2 months resulted in no apparent injury. The parents became concerned with the boy's slow rate of development. He sat at 19 months, walked at 23 months, began speaking single words at 35 months, and is presently not toilet trained.

Physical examination at 41 months revealed a head circumference of 48 cm (less than 3rd centile), weight of 13·6 kg (10th centile), and a height of 92 cm (less than 3rd centile). Examination of the head revealed a slight flattening of the occiput and frontal bossing. The ears were low set and prominent. An antimongoloid slant and hypertelorism were present. The nasal bridge was prominent and the nose small and bulbous. Micrognathia, a wide cupid bow mouth with downward turning angles of the lips, short frenulum, and a shallow wide-arched palate were also observed. Abnormalities of the extremities included hyperextensibility of carpometacarpalphalangeal joints bilaterally, bilateral clinodactyly, and bilateral dorsiflexion of the first toe. Muscle tone was somewhat diminished. External genitalia were that of a normal prepubertal male, and both testes were descended. Other systems appeared normal. CBC's and urinalysis were normal. Dermatoglyphic findings (Table) show anomalies of the distal triradii of both hands. Triradii are displaced bilaterally, and there is an additional triradius on the right palm.

Psychological evaluation done at age 40 months revealed a moderately retarded child with an IQ of 51 on the Stanford–Binet scale, and a social quotient of 72 on the Vineland Social Maturity scale.

The family history is unremarkable. The propositus has 4 older normal sibs.

### Cytogenetics

Conventional karyotype analysis with regular Giemsa staining revealed the presence of two cell lines. An abnormally small acrocentric chromosome was seen in the patient's 46 line. In the second cell line, this same chromosome appeared to be present in duplicate, resulting in a 47 count. A total of 200 leucocyte metaphases were studied. Two counts of 100 cells were performed at an interval of 5 months. Eleven per cent of the first 100 cells, and 9% of the second contained the two small acrocentrics. A 45 chromosome line was not encountered in either analysis. Fibroblasts were unavailable.

The small acrocentric in the euploid line was confirmed by G banding as a deleted Y. Additional studies using C and Q banding techniques clearly showed that the missing portion of Yq had been translocated to the terminal end of one No. 6 chromosome. Neither a reciprocal exchange nor loss of any chromosomal material could be shown. The translocation products were found in all cells examined.

The two small acrocentrics in the aneuploid line were found to be identical to the der Y of the 46 line in both morphology and banding (Fig. 1). The patient's karyotype is, therefore, 46,X,t(Y;6) (q12;q27)/47, X,t(Y;6) (q12;q27) + der Y (Fig. 2).

The parents' karyotypes were normal. The father's Y was normal in both size and banding characteristics. No trace of a small acrocentric nor of a brightly fluorescing segment on a No. 6 was detected.

### Discussion

The presence of multiple congenital abnormalities and an abnormal karyotype in the same individual suggest a disease of chromosomal origin. The cytogenetic findings in our case are compatible with the following aetiological considerations: (A) The patient's phenotype may reflect a submicroscopical deletion of either or both chromosomes involved in the exchange. (B) An undetected reciprocal exchange occurring between the 6 and Y would result in partial trisomy for a small amount of 6q in the aneuploid line. Hence the phenotype could be a consequence of additional autosomal material. An extra dose of active

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**Table: Summary of dermatoglyphic findings**

<table>
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<th>Right</th>
<th>Left</th>
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<tbody>
<tr>
<td><strong>Fingers</strong></td>
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<tr>
<td>Patterns</td>
<td>W R W U U</td>
<td>W R U U U</td>
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<tr>
<td>Ridge count</td>
<td>16 8 17 19 13</td>
<td>17 4 7 8 10—119</td>
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<tr>
<td><strong>Palms</strong></td>
<td></td>
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<tr>
<td>Creases</td>
<td>Normal</td>
<td>Normal</td>
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<tr>
<td><em>std angles</em></td>
<td>41°</td>
<td>43°</td>
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<tr>
<td>Patterns</td>
<td>3rd &amp; 4th interdigital</td>
<td>4th interdigital</td>
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<tr>
<td>Triradii</td>
<td>C—displaced radially between middle and ring finger; D—replaced by two triradii which are radially displaced between ring and little fingers and which have small whorl formed between them</td>
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<tr>
<td></td>
<td>Two triradii seen between ring and little fingers; however, no triradii seen between middle and ring fingers</td>
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<td><strong>Soles</strong></td>
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<td>Hallucal</td>
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W, whorl; R, radial loop; U, ulnar loop.
Fig. 1  Partial karyotype of the propositus showing Y/6 translocation and mosaicism. On the left are G, Q, and Giemsa stained No. 6's 21's, 22's, and Y from the 46 line. To the right are the 2 der Y's found in cells with a 47 count. The Q-banded 21 with bright satellites was also present in the father.

Fig. 2  Full Q banded karyotype from a 46 count cell. The karyotype of the aneuploid line is the same except for the presence of an additional copy of the der Y.
Y material in a small percentage of cells is insufficient to explain the clinical defect. (C) It is possible that position effect may have produced the abnormal phenotype by inducing hemizygosity for a distal portion of 6q. In Drosophila (Baker, 1968) position effect variegation is caused by breakage in both heterochromatic and euchromatic segments followed by an exchange which places the euchromatic segment adjacent to the broken heterochromatin. A similar effect has not been shown in man, though our case may fit the cytological criteria. (D) The cytogenetic findings indicate that both small acrocentrics are der Y's; however, an alternative source for the extra chromosome cannot be completely disregarded. (E) Neither pregnancy nor delivery was uneventful, and the translocation and mosaicism may be benign karyotypic abnormalities coincidental or secondary to prenatal trauma. Because of these confounding factors, a diagnosis of chromosomal disease remains unclear.

The origin of the karyotype can be traced initially to the translocation which must have occurred before first cleavage, since no normal cell line has been found in the patient. Non-disjunction giving rise to the 47 line must have occurred after the exchange, since the additional chromosome appears identical to the translocation product. Two explanations can be offered regarding the proximity of the cytological events. If both exchange and non-disjunction occurred in gametogenesis, a zygote with 47 chromosomes would have resulted. Subsequent loss of one der Y would have had to occur to produce the 46 chromosome line. Alternatively, exchange before first cleavage, mitotic non-disjunction of the der Y, and selective loss of the resulting X line might have occurred. Non-disjunction might have been the result of structural damage caused by the antecedent translocation, perhaps through a bridge-breakage-fusion event followed by stabilisation of the Y chromosomes. There is no cytological evidence for present instability of the der Y in our patient. Both der Y's appear to have the same structure and length, and in no cells was a dicentric found.

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References

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A dicentric no. 15 chromosome with two satellite regions

SUMMARY A case of an inherited chromosome no. 15 with two centromeres and two satellite regions is described and its origin postulated. The chromosome appears to have no clinical significance.

Stable dicentric chromosomes have been reported for X and Y isochromosomes (Cohen et al., 1973; de la Chapelle and Stenstrand, 1974; Howell et al., 1976) and for some Robertsonian translocations (Niebuhr, 1972a; Daniel and Lam-po-tang, 1976). Less common are those formed by translocations between acrocentrics and other autosomes (Niebuhr, 1972b; Warburton et al., 1973).

A case of a no. 15 chromosome with two centromeric regions and two regions of satellite material is presented which was first encountered during routine analysis of an amniotic fluid.

Case report

Two samples of amniotic fluid from a 35-year-old woman at 22 weeks' gestation were sent to the authors from outside this region. The indication for amniocentesis was advanced maternal age. Preliminary ultrasound examination had revealed a twin pregnancy and an attempt was made to obtain fluid from each sac.