A mentally retarded child with a translocation involving chromosomes 12 and 19

Summary. This report concerns a \textit{de novo} reciprocal translocation between the long arms of the chromosomes 12 and 19 in a mentally retarded child with bilateral radioulnar synostosis, agenesis of the corpus callosum, and several minor congenital malformations.

Many instances of autosomal translocations in man have been reported. Since the introduction of the banding techniques it is possible to identify the chromosomes involved in the rearrangements. This report concerns a female child with severe psychomotor retardation, bilateral radioulnar synostosis, and agenesis of the corpus callosum. On cytogenetic study, she appeared to have a reciprocal translocation between the long arms of chromosomes 12 and 19.

Case report

The patient, a girl, is the third child in a sibship of six. Her parents and sibs are phenotypically normal. Her unrelated father and mother were 25 and 23 years old, respectively at the time of her birth. Hereditary abnormalities are unknown among the relatives. Pregnancy was uncomplicated and delivery spontaneous and at term with a birth weight of 3000 g. The neonatal period was uneventful. Psychomotor development was slow during infancy. She did not walk before the age of 2 years.

At examination at 61 years, length was 110 cm and head circumference 52 cm. She showed slight hypertelorism and synophrys. Her ears were low-set and slightly dysmorphic (Fig. 1). Two extra nipples were present on the thorax. Her fingers showed arachnodactyly and there was syndactyly between the second and third toes. A bilateral restriction of pronation-supination movement was noticed. The flexion creases of the hands and feet were normal.

Neurological examination revealed only a subnormal motor development.
Ophthalmological examination showed strabismus divergens alternans and pallor of the optic discs was found.

On psychological examination the patient showed poor mental development since intellectual assessment on the Wechsler pre-school and primary scale of intelligence gave scores of 50 (verbal IQ) and 45 (performance IQ). Her behaviour was rather negativistic, probably as a reaction to her intellectual subnormality. She was very distractable, agitated, and hyperactive. She showed perseverations, echolalia, and other primitive reactions.

Radiological examinations revealed a normal osseous maturation and no abnormalities of the skull, the spine, nor the thorax. Just below the elbows radioulnar synostoses were observed. No abnormalities were seen in the intravenous pyelogram. The electroencephalogram showed only minor alterations with some excess of irregular slow components for the child's age. The pneumencephalogram gave a picture of total corpus callosum agenesis.

Routine blood, urine, and cerebrospinal fluid examinations revealed no abnormalities. Endocrinological tests showed no abnormalities (PB; HI; T3; T4; Ca; P; cortisol rhythm; GTT; growth hormone). The 24-h excretion values of VMA, HVA, and 5-HIAA were normal. The data were also normal for SGOT, SGPT, LDH, LDH-isoenzymes, CPK, acid phosphatase, alkaline phosphatase, transketolase, and uric acid.

The dermatoglyphic data of the hands of the patient and her parents are summarized in Tables I and II. Both hallucal areas of the patient's feet showed loops which opened distally. The blood group and serum factor phenotypes of the proposita and her parents show no deviation from the expected inheritance pattern (Table III).

**TABLE I**

<p>| Palmar Formulae and (a-b) Angles of the Patient and Her Parents |
|-----------------------------|-----------------------------|</p>
<table>
<thead>
<tr>
<th>Palmar Formulae</th>
<th>(a-b) Angles</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient</strong></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>9-7.7.5.3-(a-b)-A.O.O.O.L/d</td>
</tr>
<tr>
<td>Right</td>
<td>11-7.7.3-(a-b)-A.O.O.O.L/d</td>
</tr>
<tr>
<td><strong>Mother</strong></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>7.9.5.1-(a-b)-A.V.O.L.L</td>
</tr>
<tr>
<td>Right</td>
<td>7.9.7.4-(a-b)-A.V.O.L.L</td>
</tr>
<tr>
<td><strong>Father</strong></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>9-7.7.5.1-(a-b)-L/A(a-b)-O.O.O.O.1/d</td>
</tr>
<tr>
<td>Right</td>
<td>11.9.7.3-(a-b)-A.O.M.L.O</td>
</tr>
</tbody>
</table>

**TABLE II**

<table>
<thead>
<tr>
<th>Finger Ridge Count</th>
<th>(a-b) Ridge Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Finger Ridge Count</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Left</strong></td>
</tr>
<tr>
<td><strong>I</strong></td>
<td><strong>II</strong></td>
</tr>
<tr>
<td>Patient</td>
<td>19/0</td>
</tr>
<tr>
<td>Mother</td>
<td>20/0</td>
</tr>
<tr>
<td>Father</td>
<td>21/21</td>
</tr>
</tbody>
</table>

Cytogenetic studies

Chromosome examinations of the patient and her parents were carried out on lymphocyte cultures using a modification of the method described by Moorhead et al (1960). Preparations of these cultures were stained with a modification (Scheres, 1972) of Seabright's method (1972).
The modal number of chromosomes of both the patient and her parents was 46. Examination of the karyotypes revealed two abnormal chromosomes in the patient’s cells and none in those of the parents. Careful analysis of a number of metaphases of the patient showed that the abnormal chromosomes resulted from a reciprocal translocation between the long arms of the chromosomes 12 and 19 (Fig. 2).

We consider the chromosomal constitution of the proposita to be: 46,XX,t(12:19)(12pter→12q15::19q13→19qter;19pter→19q13::12q15→12qter) according to the Paris Conference nomenclature (1971). It was not possible to establish or to exclude whether chromosomal material was deleted from one or both the chromosomes involved.

**Discussion**

The chromosomal aberration in the proposita was interpreted as a reciprocal translocation between the long arms of chromosomes 12 and 19. In the absence of evidence of mosaicism in the proposita or in one of her parents it is most likely that the translocation arose de novo during meiosis.

The patient displayed a number of phenotypic and developmental abnormalities. It is not possible to say if these are the result of the chromosomal aberration or purely coincidental. According to the banding patterns of the two abnormal chromosomes the translocation appears to be balanced. However, the possibility must be taken into account that the clinical anomalies are caused by a small deletion in one or both chromosomes involved. In addition, a gene position effect should be considered as a possible explanation for the patient’s symptomatology.

The occurrence of a radioulnar synostosis in the mentally retarded patient led us to carry out a chromosomal examination as this combination has been described in patients with a chromosome constitution of 48,XXXX (Peña et al, 1974) or 49,XXXXX (Berger et al, 1973). The autosomal dominant acrocephalosyndactyly syndromes (Holmes et al, 1972) in which radioulnar synostosis may also occur, could be excluded on the basis of the patient’s symptomatology.

The agenesis of the corpus callosum is probably only one aspect of a dysgenesis of the central nervous system and occurs in various syndromes with or without chromosomal aberrations (Warkany, 1971).

The use of 12/19 translocation cells in hybridization experiments may contribute to gene assignments in one or both of these chromosomes. This type of research is however not carried out in our laboratory.

### Table III

<table>
<thead>
<tr>
<th>Patient</th>
<th>MMS</th>
<th>P&lt;sub&gt;1&lt;/sub&gt;</th>
<th>Lu(a&lt;sup&gt;-&lt;/sup&gt;)</th>
<th>CcDEe</th>
<th>K&lt;sup&gt;-&lt;/sup&gt;</th>
<th>Fy(a&lt;sup&gt;-&lt;/sup&gt;)</th>
<th>Gc</th>
<th>H&lt;sub&gt;p&lt;/sub&gt;</th>
<th>Gm</th>
<th>Am</th>
<th>Inv</th>
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<tbody>
<tr>
<td>A&lt;sub&gt;αβ&lt;/sub&gt;</td>
<td>MMS&lt;sup&gt;-&lt;/sup&gt;</td>
<td>P&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Lu(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>CcDEe</td>
<td>K&lt;sup&gt;-&lt;/sup&gt;</td>
<td>Fy(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>Gc</td>
<td>H&lt;sub&gt;p&lt;/sub&gt;</td>
<td>Gm</td>
<td>Am</td>
<td>Inv</td>
</tr>
<tr>
<td>Mother</td>
<td>MNS</td>
<td>P&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Lu(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>CcDEe</td>
<td>K&lt;sup&gt;-&lt;/sup&gt;</td>
<td>Fy(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>Gc</td>
<td>H&lt;sub&gt;p&lt;/sub&gt;</td>
<td>Gm</td>
<td>Am</td>
<td>Inv</td>
</tr>
<tr>
<td>Father</td>
<td>MMS&lt;sup&gt;-&lt;/sup&gt;</td>
<td>P&lt;sub&gt;1&lt;/sub&gt;</td>
<td>Lu(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>CcDEe</td>
<td>K&lt;sup&gt;-&lt;/sup&gt;</td>
<td>Fy(a&lt;sup&gt;-&lt;/sup&gt;)</td>
<td>Gc</td>
<td>H&lt;sub&gt;p&lt;/sub&gt;</td>
<td>Gm</td>
<td>Am</td>
<td>Inv</td>
</tr>
</tbody>
</table>

**Fig. 2.** Partial karyotype of the patient showing the normal chromosomes 12 and 19 and the two translocation elements.

2a: Comparison of the lower parts of the translocation elements with the corresponding parts of the chromosomes 12 and 19.

2b: Comparison of the upper parts of the translocation elements with the corresponding parts of the chromosomes 12 and 19.
The authors are indebted to Professor Dr J. E. A. van de Heuvel for the ophthalmological investigations; Dr H. O. M. Thijsen for the radiological examinations; Dr J. C. N. Kok for the biochemical investigations; Dr L. E. Nijenhuis of the Central Laboratory of the Netherlands Red Cross Blood Transfusion Service for carrying out the blood group and serum factor examinations. They are grateful for the technical assistance of Mrs I., van der Mee-Wienen, Miss I. Eder, Miss J. Caris, and Mr A. Smits.

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Dicentric Y chromosome in mixed gonadal dysgenesis

Summary. A 15-year-old girl was investigated because of ambiguous genitalia. Her chromosome studies showed a 45,X/45,Xdic(Yq) mosaicism. The identity of the dicentric Y chromosome was demonstrated by its typical fluorescent banding patterns. Histological evidence of mixed gonadal dysgenesis with intragonadal tumour was observed, confirming the occurrence of gonadoblastoma associated with mosaicism in which at least one cell line bears a Y chromosome.

A recent review by Davidoff and Federman (1973) has put into clear perspective the findings of abnormal sex development in individuals with a differentiated gonad on one side, alone or associated with a streak gonad on the other. While mixed gonadal dysgenesis has been reported fewer than 70 times in the literature, the association of this syndrome to dicentric Y chromosomes appears to be documented in only six patients (Cohen et al., 1973).

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Case report

The patient, a 15-year-old girl, was admitted to the Pediatric Service for evaluation of ambiguous genitalia. She was born in the Colombian countryside and although abnormal genitalia were noted at birth, she was not seen by a physician until the age of 9. No investigation or treatment of her disorder was undertaken. Details of the pregnancy, delivery, and early development are not available. The patient has three sisters and three brothers, apparently healthy. She was reared as a female but shortly before her 15th birthday, because of repeated comments by her sisters concerning her unusual genitalia, she asked for medical advice in Bogota.

Physical examination revealed a small, talkative, apparent female with a height of 134 cm and a weight of 47 kg. There was discrete temporal recession of the hairline but facial hair was absent. The palate was high arched. There was no evidence of breast development and the nipples were asymmetric. She had a mild pectus excavatum. No murmurs were heard on auscultation of the heart and the peripheral pulses were full and equal. The neck was not webbed and the thyroid was not enlarged. The upper extremities showed no cubitus valgus. The genitalia exhibited scant pubic hair and a phallus measuring 5 cm partially covered by a foreskin and with a blind urinary meatus (Fig. 1). A small introitus and vagina were easily seen. Through an infantile speculum a cervix was visualized. The remainder of the examination was unremarkable.

The X chromatin on a buccal smear was negative. On a 24-hour urine collection the 17 ketosteroids measured 4.1 mg/24h (14.2 μmol/24h); the 17 hydroxysteroids 3.5

REFERENCES


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