Pseudohermaphroditism with clinical features of trisomy 18 in an infant trisomic for parts of chromosomes 16 and 18: 47,XY,der(18),t(16;18)(p12;q11)mat

Summary. The case is presented of an infant who was diagnosed clinically as trisomy 18 with pseudohermaphroditism. Cytogenetic studies revealed an extra chromosome which represented a translocation chromosome derived from a balanced, reciprocal translocation between chromosomes 16 and 18: [der(18),t(16;18) (p12;q11)mat]. The infant’s mother and a number of her relatives were found to be translocation carriers: [46,XX,t (16;18)(p12;q11)].

The trisomy 18 syndrome has a number of typical clinical features. Many organs are affected with a varying degree of frequency; the abnormalities have however been fairly constant in large series of cases (Warkany et al, 1966). A number of genital abnormalities have been described, but to our knowledge no case of pseudohermaphroditism has been previously described, nor can we find any previous reports of the trisomic chromosome being a translocation chromosome involving chromosomes 16 and 18.

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Case reports

FIG. 1. (a) Detail of the infant's external genitalia, showing the hypertrophied clitoris and single perineal orifice (O); (b) Contrast injection demonstrating the urethra (U), bladder (B), and 'vagina' (V).

Fig. 2. Giemsa-banding of the E-group chromosomes and the extra small metacentric chromosome of the proband.

Fig. 3. Giemsa-banding of the E-group chromosomes of the mother showing the balanced reciprocal translocation.

Investigations

Complete blood count, microurine, urinary 17-ketosteroids, 17-hydroxycorticoids, 11-oxygenation index, and ECG were all normal. Dermatoglyphics showed five loops, three whorls, and two arches. EEG. showed a moderate degree of non-specific cerebral dysrythmia of a non-focal type. Radiological examination showed hypoplasia of the bodies of the third, fourth, and fifth cervical vertebrae with mild kyphosis. Both first ribs were short. Rhesus genotypes of the baby, its parents and maternal grandfather are shown in the Table.

Cytogenetic studies

Buccal smears, stained with cresyl violet acetate, were sex chromatin negative. Karyotypes were performed on the infant, the parents and the available maternal relatives. Blood cultures were performed on peripheral leucocytes using a modification of the method of Moorhead et al (1960). G-bands were produced using a trypsin technique modified from Seabright (1971).

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TABLE

Rhesus genotypes

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<tr>
<th>Subject</th>
<th>ABO</th>
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<th>P1</th>
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<table>
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<tr>
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<th>Duffy</th>
<th>Kidd</th>
<th>Wright</th>
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<td>K-, Kp(a−b+)</td>
<td>Lu(a−b+)</td>
<td>Fy(a+b+)</td>
<td>J(a−b+)</td>
<td>Wr−</td>
<td>A2, A12, 4A/A2, (W15), 4b</td>
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<td>Fy(a+b+)</td>
<td>J(a−b+)</td>
<td>Wr−</td>
<td>A2, (12), 4A/A2, (W15), 4b</td>
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</table>
identical metacentric chromosome replacing one of the number 18 chromosomes. One of the number 16 chromosomes was replaced by a chromosome resembling a C-group chromosome (Fig. 3). Centromere banding was performed on the mother to further delineate the break points of the translocation chromosomes. This showed the break points to be above the centromere of chromosome 16 and below the centromere of chromosome 18. The maternal relatives who had a similar karyotype are shown in the pedigree (Fig. 4). Amniocentesis was carried out on IV.9, at 16 weeks’ gestation; culture of the amniotic cells showed the fetus to be a female with the same karyotype as her mother.

Discussion

The clinical abnormalities in this infant are those usually found in trisomy 18 syndrome (Warkany et al., 1966) except for the fact that the dermatoglyphics are not the classical low arch dermal ridge pattern on six or more fingers as described by Uchida et al. (1961).

Genital abnormalities in trisomy 18 are much less common than other system anomalies. Warkany et al. (1966) in a review of 84 necropsies found a total of 18 genital abnormalities, compared with 58 reported urological abnormalities and an even higher number of cardiac malformations. Smith (1969) lists the genital abnormalities in trisomy 18, and describes most of them as only occasional features of the syndrome. Neither author mentions pseudohermaphroditism in his review.

The cytogenetic studies in this case show that the infant’s mother and some of her relatives have a balanced reciprocal translocation involving chromosomes 16 and 18. C- and G-banding shows the probable break points to be at 16p12 and 18q11 (Fig. 3) making her karyotype: 46,XX,t(16;18)(p12;q11). The small extra metacentric chromosome in the proband would then be: der(18), t(16;18)(p12;q11)mat.

It is interesting to speculate that the pseudohermaphroditism in our case could have been caused by an associated incomplete testicular feminizing syndrome which it closely resembles. In a review of hormonal and clinical aspects of hermaphroditism and the testicular feminizing syndrome, Polani (1970) attributes the cause to target-organ resistance with inability of the target organs to convert testosterone to dihydrotestosterone during fetal development. It does seem more likely however that the chromosomal anomaly in this case caused pseudohermaphroditism; this appears to be unique.

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REFERENCES


Pseudohermaphroditism with clinical features of trisomy 19 in an infant trisomic for parts of chromosomes 16 and 18: 47,XY,der(18),t(16;18)(p12;q11) mat.

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