In conclusion, it should be remembered that the diagnosis of this syndrome can only be suspected on clinical grounds alone and requires cytogenetic confirmation.

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References


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Triple mosaicism 45,XY,−18/46,XY/47,XY,+18

Summary A patient with symptoms clinically resembling Edwards's syndrome is presented. Cranial asymmetry, thoracic and lumbar hemivertebrae, and an additional rib were the unusual features. The cytogenetic studies revealed the coexistence of three separate cell lines with 45,XY,−18/46,XY/47,XY,+18 complement.

Group E triple mosaicism has been reported twice in published medical reports (Backus and Darien, 1968; Bricarelli et al., 1971). These two cases presented with congenital asymmetry, scoliosis, and, in addition, Sprengel's deformity and vertebral and rib anomalies were noted in one patient (Backus and Darien, 1968). We wish to present a further case, the first to be confirmed by chromosome banding, which showed the aberration to be associated with chromosome 18.

Case report

A 17-day-old male baby was referred from the nursery because of a strangulated inguinal hernia. The baby was the second child of normal, unrelated, healthy, Jewish parents of Yemenite origin. The family history was uninformative. The mother was treated with progestational agents from the 12th to the 20th week of pregnancy because of threatened abortion. The infant was born by caesarean section at 32 weeks because of an accidental maternal antepartum haemorrhage. The birthweight was 1370 g.

Physical examination on admission revealed an acutely ill premature baby, weighing 1400 g. Marked asymmetry of the skull as a result of prominence of the right parietal and occipital bones was evident. Mild retrogrenathia was noted. The left ear was smaller, lacking a lobulus. The index and middle fingers were flexed and overlapping and rocker-bottom feet were prominent. There was lateral displacement of the nipples and the sternum was short. Marked scoliosis of the spine with convexity to the right was present. A grade 3 systolic heart murmur was found, shown later by cardiac catheterisation to be because of a large ventricular septal defect and a persistent ductus arteriosus. The abdomen was distended, and an irreducible right inguinoscrotal hernia was present. The rest of the physical examination was normal.

Complete blood count, biochemical analysis, and serological tests for syphils, cytomegalic inclusion virus, rubella, and toxoplasmosis were negative.

Under local anaesthesia, resection of a necrotic ileal loop was performed. There was initial improvement, but he developed congestive cardiac failure. At the age of 67 days he died of extensive bilateral pneumonia.

Additional findings at necropsy were an enlarged right cerebral hemisphere, corresponding to the asymmetry observed, absence of the left kidney, and enlargement of the right one with a double ureter. Also present was a right hemivertebra at T10 with a complete additional rib, and the first lumbar vertebra was 'Y'-shaped.

Cytogenetic studies

Cytogenetic studies, using peripheral blood lymphocytes of the child and both his parents, were performed according to the method described by Moorhead et al. (1960). G-banding was performed by the method of Seabright (1971), modified by
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Fig. Group E chromosomes of trypsin banded aneuploid metaphases, the upper 3 with an extra chromosome 18, the lower 2 from the monosomic line.

using 0.06% trypsin in calcium and magnesium-free Hank's solution. C-banding was performed according to the method of Arrighi and Hsu (1971).

Fifty metaphase figures of the baby's peripheral blood lymphocytes, cultured in three different flasks simultaneously, were studied. Three separate cell lines were identified, 45,XY,−18/46,XY/47,XY, +18, in relative proportions of 1:8:1 (Fig.). One hundred metaphase figures were examined in each of the parents. Both had a normal karyotype.

Discussion

The coexistence of three separate cell lines could be the result of a postzygotic non-disjunction, as postulated by Backus and Darien (1968) in a similar case. The relative distribution of the cells with 45/46/47 chromosomes, in proportions of 1:8:1, respectively, suggests that the error occurred in the third cleavage.

The most prominent clinical feature was marked asymmetry. Several authors have described asymmetry as a leading sign in trisomy 18 mosaicism, sometimes clinically resembling the Russel-Silver syndrome (Chauvel et al., 1975). Hook and Yunis (1965) suggested that at a critical period during embryogenesis, trisomy 18 cells predominated on one side of the body, while cells with a normal karyotype predominated on the other. Similar mechanisms may be involved in the asymmetry observed in mosaics for trisomy 8, trisomy 22 (Purvis-Smith et al., 1976), short arm deletion of chromosome 4 (Lewandowski and Yunis, 1975), and diploid triploid mosaicism (Böök and Santesson, 1960; Ferrier et al., 1964). The scoliosis found in our case was caused by two extra hemisegments on the right side, with an additional complete rib. Robinson et al. (1971) drew attention to vertebral anomalies in trisomy 18 mosaicism. They presented a case with 14 thoracic segments with complete ribs and multiple coronal cleft vertebrae. Rib and vertebral anomalies have similarly been reported in 13q deletion syndrome (Chenke et al., 1978), 4p trisomy, 7q trisomy, 8 trisomy, and other chromosomal aberrations (Lewandowski and Yunis, 1975).

It may be surmised that an abnormal chromosomal composition could lead to abnormal segmentation during early embryogenesis.

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References


The Prader-Willi syndrome with a 15/3 translocation

SUMMARY A de novo translocation of 15q to 3p with complete monosomy of 15p and partial monosomy of 15q was detected by trypsin banding on peripheral lymphocytes of a 5-year-old boy with Prader-Willi syndrome (severe mental retardation, dyslalia, cryptorchidism, and muscular hypotonia). The pathogenic role of chromosome 15 abnormalities in the aetiology of this syndrome is discussed.

About 10% of patients with Prader-Willi syndrome show cytogenetically detectable abnormalities of a D chromosome, usually the translocation of one of the D chromosomes to another chromosome. Hawkley and Smithies (1976) suggest that it is chromosome 15 which is involved in the pathogenesis of this syndrome.

Using the trypsin banding method (Burkholder and Comings, 1972), we have detected a de novo unbalanced translocation of the distal part of the long arms of chromosome 15 to the short arms of chromosome 3 in a patient with Prader-Willi syndrome.

Case report

The boy was the first child of healthy young parents; his birthweight was 2750 g, length 50 cm. Psychomotor retardation was obvious from the first months of his life. He started to walk at the age of 20 months and to speak at 3 years. Now, at 5 years old, his mental ability corresponds to debilitas gravis. Other clinical symptoms are obesity (+4.5 sigma), muscular hypotonia, genu valga, cryptorchidism, and dyslalia (Fig. 1).

His parents and younger brother are healthy with a normal karyotype.

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There was complete monosomy of the short arms and partial monosomy of the long arms of chromosome 15, and probably also monosomy of a small part of the short arms of chromosome 3 (Fig. 2).

The karyotype was 45,XY,−3,−15, +t(3;15) (p25;q15) or 45,XY,−3,−15, +t(3;15) (3qter→3p25::15q15→15qter).

Discussion
The unbalanced chromosomal translocation described is quite rare; we have failed to find a similarly abnormal karyotype in published reports. The clinical signs of our patient support the hypothesis of Hawkley and Smithies (1976) about the role of the short arms of chromosome 15 in the Prader-Willi syndrome. Some of the other karyotypes of reported patients are also in agreement with this hypothesis.