A Child with Multiple Congenital Malformations and a 46,XX,t(Bq+;Dq−)/45,XX, -B, -D, +der(B), t(Bq+;Dq−)

Karyotype

Summary. A case of a female infant with malformations of extremities and mental and growth retardation is reported. The karyotype showed a 46,XX, t(Bq+;Dq−)/45,XX, -B, -D, +der(B), t(Bq+;Dq−) mosaicism. The clinical findings in relation to the long arm deletion of a B-group chromosome are discussed.

A case is presented of a child with malformations whose karyotype demonstrates a translocation between the long arm of a B and the long arm of a D chromosome.

Case Report

The proposita, born 3 March 1971, was the second child of a 24-year-old mother and a 34-year-old father. She was born after 42 weeks' gestation; labour being induced. Pelvic radiology was performed in the mother on the 10th day of pregnancy. The patient was referred to the genetic clinic because of multiple congenital malformations. Deformities of the arms had been noted at birth and the patient had looked ill.

On physical examination (6 August 1971), weight was 3540 g, height 60 cm, and head circumference 38 cm. The head was dolichocephalic. The ears were flared and large. Hypertelorism, blue sclerae, and highly arched palate with cleft soft palate were present. A bluish colour was noted in the circumoral region (Fig. 1).

Examination of the neck, heart, lungs, and genitalia showed them to be normal. The examination of the abdomen showed the liver 3-5 cm below the right costal margin and the spleen 1-5 cm below the left costal border.

The left arm was shorter than the right with absence of the ulna and fourth and fifth fingers. The right hand showed syndactyly of third and fourth fingers, with proximal implantation of the fifth (Fig. 2). The lower limbs were thin, the third toe of the left foot was proximally implanted and hidden underneath the other (Fig. 3).

The patient did not hold up her head nor sit. Muscle tone and tendinous reflexes were normal. Dermal ridges of the left hand were hypoplastic. In the right hand there were both proximal and distal axial triradii, a whorl in the interdigital area III and a vestigial pattern in the thenar eminence, an ulnar loop on the first finger, whorls on the second, third and fourth fingers, and no recognizable pattern on the fifth.

Haematological tests showed anaemia. Urine analysis, hepatic function tests, glucose, urea, creatinine, and uric acid investigation all yielded normal results.

An electrocardiogram showed a right ventricular enlargement with left ventricular strain, although a congenital heart defect could not be confirmed. Radiological studies showed absence of left ulna and fourth

Fig. 1. The proposita aged 5 months.

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Fig. 2. The right hand of the proposita; note syndactyly of third and fourth fingers and proximal implantation of the fifth.

Fig. 3. The proposita's feet; note overlapping of second and fourth toes over the third.

Fig. 4. Partial karyotypes of the population of two cells.
and fifth metacarpals. The right hand showed cutaneous syndactyly without osseous involvement.

A gastroduodenal x-ray suggested an obstruction at the second or third duodenal portion. An intravenous urogram evidenced duplication of the pelvis of the left kidney.

She was subsequently admitted to the hospital on three occasions and treated for bronchopneumonia and urinary tract infection. She died during her last admission at the age of 11 months with serious mental and growth retardation. No necropsy was performed.

**Cytogenetic Study**

Peripheral lymphocytes were cultured for chromosome study; 50 cells were analysed, in 43 of them (86%) the chromosome number was 45, a D-group chromosome was missing, and a B-group chromosome had an increase in length of the long arm. In seven cells (14%) the chromosome number was 46, with only five elements of the D group, the same abnormal B chromosome, and an extra G-group element. The karyotype of both parents was normal.

The cytogenetic findings in the patient was interpreted as a translocation between the long arms of a B and the long arms of a D chromosome. The product of the translocation containing the centromeric portion of the D and the distal portion of the long arm of the B chromosomes was lost in the majority of the cells, resulting in mosaicism (Fig. 4).

Various attempts were made to identify the chromosomes involved in the translocation, however autoradiographic study failed to give consistent patterns.

**Discussion**

Since neither parent carried a translocation, the chromosomal rearrangements must have arisen in the germ cells of one or other parent or during a very early cleavage division of the egg. One product of the translocation was lost at a subsequent cell division giving rise to two cell populations. The cells with 46 chromosomes (14%) appear balanced and the rest (86%) are monosomic for the centromeric portion of a D and the telomeric region of the long arm of a B chromosome.

A search of the literature has revealed 10 patients with abnormalities involving a possible deficiency of the long arm of a B(4-5) chromosome. Six of these had ring formation and three had simple deletions of the long arm of a B-group chromosome. Table I shows the clinical features in these cases.

The present patient had mental and growth retardation, a peculiar face, malformed upper extremities with absence of ulna and postaxial adactyly in the left arm, and syndactyly with proximal implantation of fifth finger in the right hand.

Although it is difficult to make a genotype-phenotype correlation with such a small number of cases, the presence of upper limbs abnormalities in cases with a long arm deletion of a B-group chromosome seems constant.

### Table I

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An Inherited Small Extra Chromosome:
A Mother with 46,XX,t(17;22) (p13;q1) and a Son with 47,XY, + der(22) mat

Summary. A boy with multiple congenital anomalies was found to have a small extra chromosome. This small chromosome was interpreted as a der(22) mat because his mother was a balanced carrier with 46,XX,t(17;22) (p13;q1) chromosomes. It is hoped that with the use of the banding techniques many karyotypes will be revaluated and reinterpreted. The mother's karyotype was erroneously interpreted earlier as a 21/22 translocation.

A small extra chromosome has been linked to two specific syndromes. Schachenmann et al (1965), Weber, Dooley, and Sparkes (1970), and Gerald et al (1968) described anal atresia, vertical colobomata of the iris, bilateral preauricular fistulas, and other congenital defects in a condition called 'the cat eye syndrome'. Abbo and Zellweger (1967) proposed a syndrome under the noncommittal name 'the syndrome of the (supernumerary) metacentric chromosome' with characteristics including severe mental retardation, irritability and even destructiveness, muscular hypotonia, retinal coloboma, and other constitutional stigmata. We reported (Borgaonkar, Schimke, and Thomas, 1971b) on five unrelated patients with a small metacentric extra chromosome and pointed out that it is difficult to assess the clinical significance of a karyotype containing a small extra chromosome. In two of these patients no serious clinical problems were noted whereas in the remaining three the multiple congenital abnormalities were neither striking nor fitting the descriptions of the above two syndromes. Since there are several possible mechanisms by which the extra chromosome material can arise it is possible that the extra chromosome has a different origin in each case.

In the present report the source of the small extra chromosome is known since the mother carried both products of a 17/22 translocation. It is rare that an inherited small chromosome product of a translocation can be documented.

Case Report
C. C. (JHH 131 89 28), a white male, born on 27 May 1967, was the product of an uneventful second pregnancy. Development was rather unremarkable; he had walked at 16 months, his teeth were normal, and he spoke a few words. Genitalia were normal and no abnormalities...