A 46,XX,t(Cp+;Cq-) Translocation in a Girl with Multiple Congenital Anomalies and in Her Phenotypically Normal Father 46,XY,t(Cp+;Cq-)*

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It is clear that the detection of a chromosome aberration does not necessarily correlate with the presence of obvious physical or mental defects. For example, t(GqGq) or t(DqGq) balanced translocations may be found in phenotypically normal parents whose progeny have Down's syndrome. The present report described a balanced translocation involving the C group in father and daughter. The father is phenotypically normal, but the child has multiple anomalies.

Clinical Observations

The patient is the product of the first and only pregnancy for a 31-year-old mother and 41-year-old father. Despite no efforts at contraception the parents were married for about 12 years before the mother was able to conceive. She experienced no known previous spontaneous abortions. The mother's gestational period was full-term and was said to have been uncomplicated. The fetus was not exposed to any known drugs or radiation. Following an uneventful labour the infant was born at a local hospital by means of spontaneous vaginal delivery, the mother being under general anaesthesia. The Apgar score was recorded as 7. No resuscitation was necessary. The mother's post-partum period was unremarkable. The infant's birthweight was 2270 g., head circumference 43.1 cm., and total length 43.8 cm. She was kept in the nursery for 10 days because of poor feeding and intermittent episodes of

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FIG. 1a and 1b. The patient at age 3½ years.

FIG. 2. Mouth of the proposita showing the notched incisors.

cyanosis. The Guthrie test for phenylketonuria was negative.

She first sat alone at 2 years of age. At present she is able to maintain an erect position if supported. She is unable to pull herself up into a standing position and does not walk. The mother claims that the child is able to say 'mommy' and 'daddy', but the examiner has only observed babbling and 'blowing bubbles'.

Physical findings at the time of the child's initial examination were: weight 17 kg. (above the 75th percentile); length 94 cm. (above the 3rd percentile); head circumference 47.5 cm. (greater than 2 SD below the mean); blood pressure 95/80 mm. Hg (right arm supine); apical pulse 100 (regular); respiratory rate 22.

She appeared as a quiet, female infant with dull facies,

FIG. 3. Hand of patient showing mild flexion contractures of the 3rd, 4th, and 5th fingers.

sitting on the mother's lap playing with her fingers. Her play activity was characterized by seemingly purposeless movements of the upper extremities. Scalp hair was very fine. She had facial and truncal obesity. She was microcephalic, with occipital and facial flattening. The pinnae of both ears seemed disproportionately large. Facial features (Fig. 1a and 1b) revealed a small, 'up-turned' nose, prominent bilateral epicanthal folds, with narrow palpebral fissures (questionable bilateral ptosis), and slight hypertelorism. Coarse pendular nystagmus was evident bilaterally. The fundi were not abnormal. A red reflex was elicited bilaterally. The mandible was hypoplastic. She had a 'fish-shaped' mouth, with a coarse irregular tongue and a high-arched palate. There were 20 deciduous teeth, with greyish discoloured and notched upper central incisors (Fig. 2). There was no pterygium colli nor were there palpable masses in the neck which appeared shortened. Lymphoedema of the dorsal surfaces of both hands and feet was present. The fingers were short and fusiform in shape, with bilateral radial deviation of the 3rd, 4th, and 5th fingers. Mild flexion contractures of the 3rd, 4th, and 5th fingers were also noted bilaterally (Fig. 3). Suprascapular, deltoid, as well as thenar and hypothenar muscle atrophy was prominent bilaterally. A prominent crease was seen over the dorsal wrist. Satisfactory dermatoglyphs could not be obtained because of marked hypoplasia of the palmar dermal ridges and digital contractures. Neurological examination revealed an indifference to environmental events, no attempt to follow or reach for objects, and no social smile. The skeletal age was not retarded.

Except for moderate obesity, physical examination of the father was entirely within normal limits. No remarkable findings were detected on analysis of dermatoglyphic patterns from both parents.

A maternal aunt lost a child shortly after birth because 'he had a hole in the spine'. A paternal aunt has been married for 20 years and has never been pregnant.

Cytogenetic Studies

Chromosome preparations from cultures of whole peripheral blood were made, using a commercially prepared micromethod medium.* Thirty metaphases from the proposita all contained 46 chromosomes, and the karyotypes revealed a 46,XX,t(Cp+;Cq-) chromosome complement (Fig. 4). Both aberrant chromosomes in the complement are metacentric; one is the size of a No. 3 chromosome and the other appears to be just a little larger than a No. 16 chromosome.

The karyotype of the mother was normal, but that of the father was 46,XY,t(Cp+;Cq-) (Fig. 5). The parents of the father are dead, and his only sib, a sister with a fertility problem, has a 46,XX karyotype.

It has been established that structurally abnormal X chromosomes are the late replicating chromosomes in the complement (Muldal *et al.*, 1963; Lindsten, 1963; London *et al.*, 1964). Tritiated thymidine was added to another culture of the proposita's peripheral leuco-

* Grand Island Biological Co. Chromosome Medium 1A, Grand Island, N.Y., U.S.A.

FIG. 4. Karyotype of the probanda.

FIG. 5. Karyotype of the father.

cytes. This study showed that neither of the aberrant chromosomes was late labelling. An X chromosome does not appear to be involved in the translocation.

Discussion

Patau has suggested that trisomies of whole autosomes are restricted to the D, E, and G groups (Patau, 1964). However, chromosomes from groups other than D, E, and G can be trisomic in association with mosaicism or partial trisomies (Shaw, Cohen, and Hildebrandt, 1965; Bargman *et al.*, 1967). Patients have been described with various anomalies who showed partial trisomy of C group chromosomes, presumably resulting from a balanced translocation in one of the parents (Rhode and Catz, 1964; Lindsten *et al.*, 1965; Lejeune *et al.*, 1968).

In the present case both the father, who is normal, and the proposita, who is abnormal, appear to have a balanced translocation. However, it is suggested that undetectable amounts of genetic material may have been lost from the broken end of the smaller metacentric chromosome. This could account for the abnormalities seen in the proposita.

Summary

A 3½-year-old girl with multiple anomalies and a 46,XX,t(Cp+;Cq-) chromosome complement is presented. Her father, with a 46,XY,t(Cp+;Cq-) chromosome complement, is phenotypically normal.

Both patients appear to have balanced translocations.

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