Y autosome translocation and complex chromosome rearrangement in cri du chat syndrome

SUMMARY An unbalanced Y autosome translocation t(5;Y) and an apparently balanced translocation t(2;13) are identified with the Q and R banding in a 7-year-old boy with severe encephalopathy and a multiple malformation syndrome. At birth, the clinical diagnosis of 'cri du chat' syndrome based on the characteristic crying was not confirmed after karyotyping, using conventional staining techniques.

References

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In the 'cri du chat' syndrome, the deletion of the chromosome 5 short arms may sometimes go unnoticed when a more complex chromosome rearrangement is associated. We present one such case wherein the deletion is only identifiable using chromosome banding techniques.

Case report
This male infant was the first child born to a healthy 25-year-old mother and 27-year-old father. A 2-year-old brother is normal. The family history is negative with the exception of a first pregnancy terminating in spontaneous abortion at 2 months. After an uneventful full-term pregnancy, birthweight was 2250 g. On the third postnatal day, considerable hypotrophy necessitated his admission to hospital.

Physical examination yielded the characteristic anomalies of hypertelorism, epicantic folds, downward-slanting palpebral fissures, moon-shaped facies, and an underscended left testis. In addition, a peculiar high-pitched cry was noted, evoking the diagnosis of a 'cri du chat' syndrome. Using conventional staining techniques, the karyotype in 1968 showed that the two no. 5 chromosomes were morphologically normal but there was a translocation between a no. 2 and a group D chromosome. Parental karyotypes were normal.

Complete re-examination was performed at age 7 years and showed hypotrophy (weight, 17 kg; height, 115 cm; span, 119 cm; lower segment, 54 cm) with considerable microcephaly (head circumference, 48 cm; thoracic circumference, 55 cm). The cranial and facial malformations (Fig. 1a and 1b) consisted of the previously noted signs in addition to a poorly outlined philtrum, absence of the lateral inferior incisors with poor dental articulation, and large external ears with a highly pronounced auricular helices. Thoracic asymmetry was evident with flattening of the left hemithorax; hypotonic abdominal musculature and umbilical hernia were present. Anomalous dermatoglyphic patterns were found with bilateral simian creases and diminished total ridge count (Table).

Psychomotor retardation was severe, with an intelli-
Table Dermatoglyphs of the propositus

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<th>Palm</th>
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Fig. 2 Karyotype of the propositus (R banding): t(2;13) showing abnormal staining of the chromosome no. 5 short arms.
gence quotient of 30. Language was rudimentary and often replaced by mimicry and gesticulation; walking movements were faltering; elementary autonomy was acquired. Considerable lability of character was also observed.

Ophthalmological testing indicated no abnormalities; both the electroencephalogram and electrocardiogram were normal. Intravenous pyelography disclosed horseshoe kidney. Skeletal radiography was normal except for upper thoracic scoliosis; bone age was 7 years. Laboratory evaluation was normal (especially endocrine and enzyme blood values).

Chromosome studies were performed on cultured lymphocytes. After heat-controlled denaturation, all mitoses examined by R-banding showed an apparently balanced translocation between a no. 2 and a no. 13 chromosome: t(2;13) (p32;q13). In addition, labelling of the short arms of one no. 5 chromosome was usually abnormal though the centromeric index remained intact (Fig. 2). Quinacrine mustard staining, followed by Q-banding, showed intense fluorescence of the short arms of the involved no. 5 chromosome, thus allowing the conclusion of an unbalanced translocation between the no. 5 and Y chromo-

somes: t(5;Y) (p13;q11) (Fig. 3). Consequently, deletion of the no. 5 chromosome short arms is indeed present associated with a partial Y disomy and is responsible for the ‘cri du chat’ syndrome. Different staining techniques yielded a normal maternal karyotype, whereas in the father fragility of the no. 13 chromosome at the q22 band was observed in 7% of the mitoses. The Q band polymorphism in the parents did not disclose any particularly fluorescent regions.

Discussion

Concerning presumptive Y autosome translocations, there is no doubt that implication or enlargement of brilliantly fluorescent satellites may appear very similar to cases of long arm Y-translocation. In the present case the possibility that the strongly fluorescent material, which is observed on the short arm of one chromosome no. 5, is satellite material is ruled out by both the unnoticeable Q band polymorphism in the parents and the lack of satellite association involving the rearranged chromosome no. 5. Few cases of Y-autosome translocation have been reported but the technique of quinacrine mustard staining followed by fluorescence study now permits identification which was formerly impossible. According to Nielsen and Rasmussen (1976) the frequency of such a rearrangement in the general population appears to be approximately 1 in 2000. The most common type is clearly an unbalanced t(Y/15). Most of the reported cases with presumptive translocation have been discovered because of some phenotype abnormalities. When a second sex chromosome is present and the translocated portion of the Y chromosome is supernumerary, sex differentiation is generally normal and the morphological abnormalities are attributable to quantitative modification of the autosomal material.

To our knowledge the present case is the first one in which an unbalanced translocation between the no. 5 and the Y chromosome is responsible for a ‘cri du chat’ syndrome.

Concerning the t(2;13) translocation, Genest et al. (1971) documented 30 cases of rearrangements of the no. 2 chromosome of which 5 involved group D chromosomes. In fact, using the banding techniques, it appears that the t(2;13) is frequently observed, either in a balanced form or at the origin of partial 2q or 13 trisomy (Giraud et al., 1977). It is probable that the double accident should originate in the same paternal germ cell because the Y chromosome is involved.

Moreover, though the fragility of the paternal chromosome no. 13 is localised at a point uninvolved in the translocation, the question of its possible role in the occurrence of the anomalies by the so-called inter-chromosomal effect may be raised.

These two associated rearrangements, which can
only be accurately described using R and Q banding, imply that 4 chromosome breaks occurred: this raises the problem of such complex anomalies frequently reported in association with the ‘cri du chat’ syndrome (Catti and Schmid, 1971; Taillemite et al., 1973; Berger et al., 1974).

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References


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Erythropoietic protoporphyria, heterozygous cystinuria, and reduced peptidase A activity in a patient with 46,XX/46,XX,18q—mosaicism

SUMMARY An interesting patient with a deletion of the long arm of chromosome 18 is presented. Her symptoms are severe in comparison with some other 18q—patients, yet she was found to have a mosaicism with a normal 46,XX karyotype in about 20% of her cultured lymphocytes. In addition, she had erythropoietic protoporphyria, was heterozygous for type II or III cystinuria, and had reduced levels of peptidase A activity. Detailed studies on the patient, her family, and two additional 18q—patients suggest that the association with erythropoietic protoporphyria is coincidental and that the cystinuria gene was inherited from the patient’s father. The reduced peptidase A activity, however, supports earlier observations that the peptidase A locus maps in the q22 to terminus region of chromosome 18.

A recognisable syndrome has emerged in association with a deficiency of part of the long arm of chromosome 18 which has been referred to by some as the ‘carp-mouth’ syndrome (Lejeune et al., 1966). Cytogenetically, the deletion usually involves one-quarter to one-third of the terminal portion of the long arm. Most reported cases have been spontaneous. A few, however, have occurred in families where a balanced translocation involving chromosome 18 is segregating. At least 6 cases have been reported with mosaicism (46,XX/46,XX,18q—). In addition to the more common 18q—syndrome, several cases have been reported with deletions of the short arm of 18 and a few with ring 18 chromosomes.

The following report presents an interesting patient with the ‘carp-mouth’ syndrome.

Case report

This white female patient (K.B.) was born in 1967 after an uneventful pregnancy and delivery. She was the fifth of six children born to healthy, unrelated parents. The family history was negative, except for a maternal aunt with severe mental retardation of unknown aetiology. Our patient weighed 2.3 kg at birth, and presented a serious feeding problem from the third day of life. In 1966, she was evaluated for developmental retardation. A diagnosis of diffuse brain damage with mental retardation, ocular difficulties, severe hyptonia, and bilateral equinus deformity of the feet was made. Casts were applied to correct a left calcaneous valgus and right tibial torsion and forefoot varus. Her head size was 40 cm (5 cm below expectations). The fundi revealed greyish discs, but there was no hyperplasia of the iris and no Brushfield spots. The lower limbs were held in a frog-leg attitude. The deep tendon reflexes in the lower limbs were absent. There was no Babinski and no Moro reflex. Urine studies were negative for sugar, protein, acetone, and reducing substances. A ferric chloride test was negative. X-ray studies of the skull

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