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A trisomy for 10q24–qter from a familial translocation; t(4; 10) (q33; q24) in both grandparents

By

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A trisomy for 10q24—qter was found in a male infant. The clinical findings of the propositus were similar to those reported by other investigators. Both paternal grandparents are close relatives, and show the same balanced translocation, t(4; 10) (q33; q24). Their reproductive history reflected an extremely severe genetic imbalance. Four out of five children died in early infancy. The only living offspring is the father of the proband who has the balanced translocation.

Clinical Data and Findings

The propositus (Fig. 1) was born two years after a first pregnancy had ended in spontaneous abortion in the third month. At the proband's birth, the mother was 25 years, the father 34 years, of age. Both are normal clinically. The pregnancy was uneventful, delivery was at term and uncomplicated. Birth weight was 2700 g, length 53 cm, head circumference 34 cm.

At the age of 8 months, body weight was 8800 g, length 67 cm, head circumference 45 cm. Psychomotor development was retarded, the baby was unable to sit, contactless and dentition has not yet started.

The infant displayed a number of dysmorphic symptoms such as microcephaly, ptosis of eyelids, microphthal-

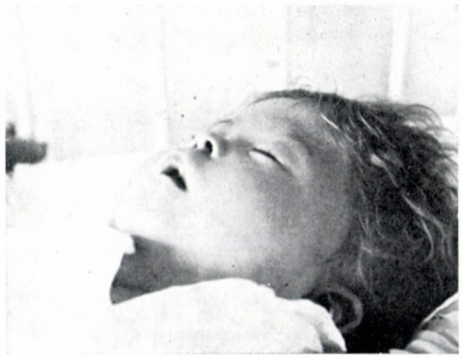

Fig. 1. The proband at 8 months of age

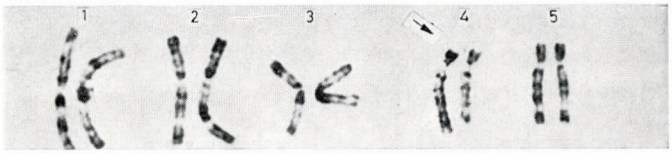

FIG. 2. The abnormal chromosome No. 4 found in the proband

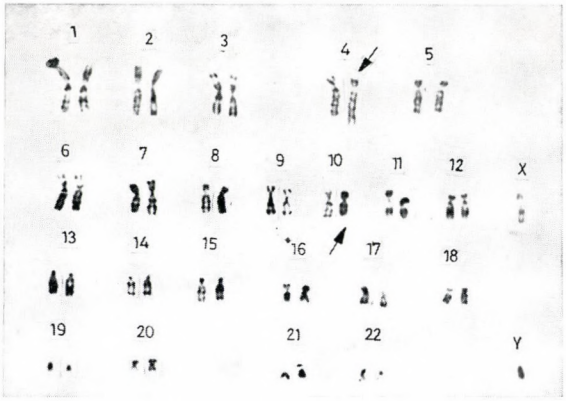

FIG. 3. The balanced translocation, t(4; 10) (q33; q24) in the karyotype of the father

mia with blepharophimosis and antimongoloid slants, small nose with depressed bridge, spacious forehead, micrognathia, malformed left ear, short neck, umbilical hernia, limitation of hip movements and hydrocele on the right side. The upper extremities showed hypertonicity and X-rays revealed a thoracolumbal kyphoscoliosis. Apart from an inspiratory stridor, other findings (cardiology, EEG, kidneys, etc.) were normal.

Chromosome Study

Chromosome studies of peripheral blood cultures revealed an abnormal chromosome No. 4 of the proband (Fig. 2). The abnormality proved to be a derivate chromosome from the balanced translocation of the father. The father has a translocation between the chromosomes No 4. and 10, (4; 10) (q33; q24) Fig. 3). On the basis of the identification of the paternal balanced translocation, the proband's karyotype is 46,XY,der(4),t(4; 10) (q33; q24) pat. Consequently, the malformed child shows a trisomy for the segment of 10q 24—qter of chromosome No. 10.

The same balanced translocation was present in both paternal grandparents.

Pedigree Analysis

As can be seen from the pedigree (Fig. 4), the paternal grandparents (I. 2 and I. 3) of the proband are second degree relatives and both have

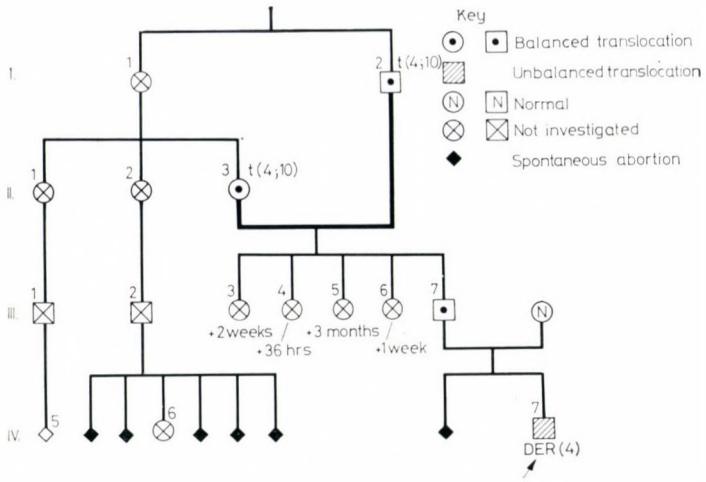

FIG. 4. The pedigree

the same balanced translocation. One may suppose that one of the parents of the grandfather and one of the grandparents of the grandmother must have had the same balanced anomaly and transmitted it to their offsprings. In this way, the chromosome anomaly must have passed through at least five generations.

Four out of five offsprings from the marriage of the grandparents (III. 3, III. 4, III. 5, III. 6) died in early infancy. They were all born at home and also died there. In this way no data could be obtained on their condition and the cause of death. It is, however, assumed that the bilateral heterozygosy had led to unbalanced chromosome abnormality in the offsprings and the cytogenetic anomaly manifested itself in fatal malformations.

The other relatives of the proband, the two sisters of the grandmother (II. 1 and II. 2) as well as their offsprings, could not be contacted.

DISCUSSION

Partial trisomy of chromosome 10 has been reported on several instances. In most of them trisomy for the distal part of the long arm was found in the karyotypes. Only one out of the reported 16 cases of 10q trisomy was described as a *de novo* chromosome mutation [10], the others originated from familial chromosome anomalies [1—9, 11—15]. In the reported families including our case, paternal transmission occurred seven times, maternal transmission in nine cases. The familial cytogenetic aberration was pericentric inversion in one case [1], the others were familial translocations that could mostly be followed through three or more generations.

TABLE I

The main clinical symptoms found in 11 patients with 10q trisomy

	Dutrillaux et al 1973	Forabosco et al 1975	Krøyer and Niebuhr 1975	Laurent et al 1973	Mulcahy et al 1974	Prieur et al 1975	Roux et al 1974	Tavlik et al 1973	Tsuchimoto and Bühler 1974	Yunis and Sanchez 1974	Present case
Age of proband	4.5m		18y	9m	17d	2.8m		11m	2d	6y	8m
Sex of proband	M	M	F	F	M	M	M	M	M	M	M
Trisomic segment	q24–qter	q24–qter	q25–qter	q22–qter	q24–qter	q24–qter	q24–qter	q24–qter	q22–qter	q34–qter	q24–qter
Balanced carrier	mother	father	father	mother	mother	father	mother	father	mother	father	father
Familial aberration	inv(10)	t(10; 18)	t(10; 18)	t(1; 10)	t(10; 13)	t(10; 17)	t(10; 22)	t(10; 14)	t(10; 15)	t(10; 15)	t(4; 10)
Hypotrophy	+	+	+	+	+	+	+	+	+	+	+
Mental retardation	+	+	+	+	+	+	+	+		+	+
Hypotonia	+	–	+		+	+	–	–		+	–
Hypertonia	–	–	–		–	–	–	+		–	+
Microcephaly	–	+	+			+	+	+	+	+	+
Characteristic face	+	+	+	+	+	+	+	+	+	+	+
Skeletal anomaly	+		+					+		+	–
Scoliosis		+	+	+		+		+		+	+
Visceral malformation	–	+	–		+			+			–

The banding technique allows to identify the size of the trisomic segment. In the reported cases it was the distal half of the long arm that occurred three times in the karyotypes of the patients. This means that it is possible for the zygote carrying the trisomy of this segment to avoid the effect of prenatal selection.

The characteristic clinical manifestations of 10q trisomy are as follows [11]. Growth retardation is the rule. The facial dysmorphy is characteristic, the patients resemble each other and are often referred to cytogenetic investigation with the suspicion of Down syndrome. The main clinical features of this chromosome syndrome are,

low birth weight;

somatic and severe mental retardation;

broad, round and flat face, high forehead, ptosis, narrow palpebral fissures with epicanthal folds, microphthalmia, small nose, prominent malar region, micrognathia, low set and poorly formed ears;

joint laxity, scoliosis, congenital heart defects and kidney malformations.

The main clinical findings of patients with trisomy of the long arm of chromosome 10 reported in the literature are summarized in Table I.

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