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11q— syndrome

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A female patient with deletion of the long arm of chromosome 11 is reported. Signs of cranio-facial dysmorphism were a slightly protuberant occiput, dolichocephaly, narrow forehead, antimongoloid slanting of palpebral fissures, carp shaped mouth, mild retrognathia, low hair line, clenched hand with overlapping fingers. The patient died at 3 months of age. Obduction showed a ventricular septal defect and gallstones.

Since the first description of 11q monosomy by Jacobsen et al. (7), 22 further cases have been reported. A delineation of the 11q— syndrome can be based on this material as the reported cases are mostly of de novo type and with few exceptions, the breakage occurred at the same site of the long arm. The present report gives a detailed description of an additional case of 11q deletion and outlines the characteristic features of the syndrome.

Case Report

A. N., a female child, was born from the third pregnancy of her mother. Both parents were healthy and were unrelated. At the birth of the probanda, the mother was 30 and the father 36 years old. The patient had a normal, healthy brother 8 years her senior, born from the first pregnancy. The second pregnancy was aborted in the 10th week of gestation; detailed information concerning this miscarriage was not available. The family history was unremarkable regarding congenital malformations and repeated fetal losses.

The probanda (Fig. 1) was born at the 40th week of gestation. Birth weight was 3350 g, body length, 55 cm, and head circumference, 36 cm. The baby had respiratory difficulties during the first week of life, then she had repeatedly upper respiratory tract infections. She developed normally until the age of 3 months when she suddenly died of pneumonia.

Clinical and cytogenetic examinations were done at 3 weeks of age. Slightly protuberant occiput, dolichocephaly, narrow forehead, clenched hands with overlapping fingers raised a suspicion of 18-trisomy, although prenatal development was not retarded.

Signs of cranio-facial dysmorphism included a slightly protruding forehead with narrow temples, antimongoloid slanting of palpebral fissures, hypertelorism, small upturned nose, down-turned carp shaped mouth, mild retrognathia, high arched palate, low-set ears. The small tongue was

located posteriorly. The posterior hair line was low. The hands were permanently clenched with overlapping of the second and third fingers over the thumb. A slight systolic murmur could be heard.

Radiographs were normal. Red and white blood count, platelet count, serum electrolytes and hepatic enzymes were normal. Autopsy revealed ventricular septal defect of small size and two gallstones.

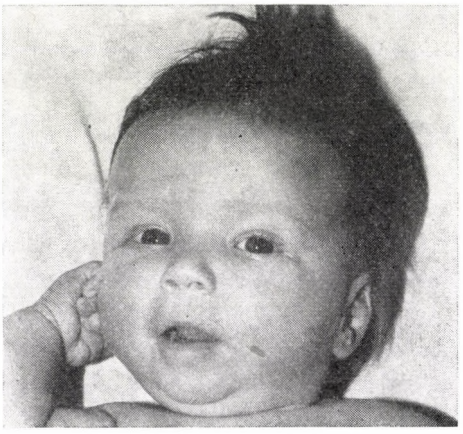

FIG. 1. The patient at 2 months of age

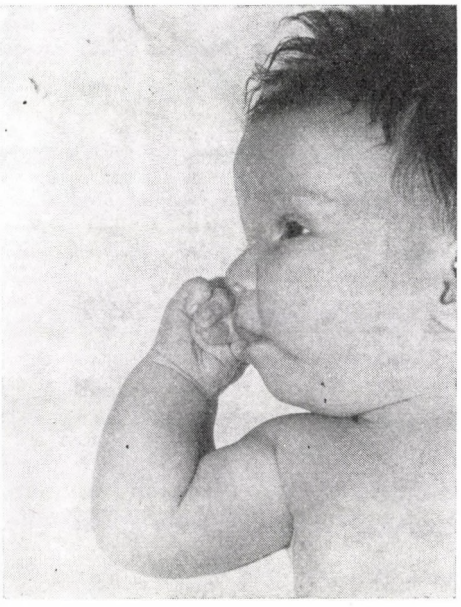

FIG. 2. The clenched hand and overlapping fingers

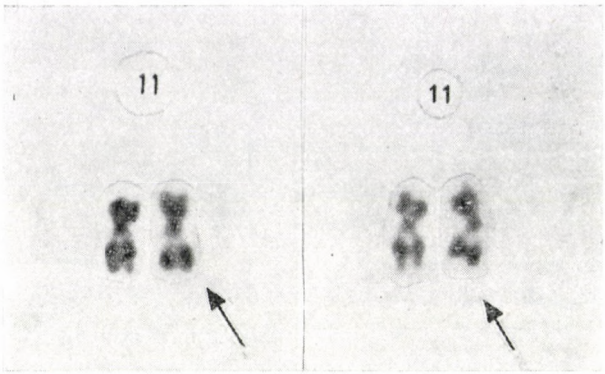

FIG. 3. Chromosome pairs 11 from the patient's karyotype

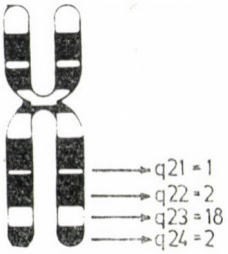

FIG. 4. Distribution of breakpoints in 23 cases of 11q— syndrome

Cytogenetic findings

Slides from routinely cultivated lymphocytes were stained by GAG technique for differential analysis. In all investigated metaphases a deletion of the distal segment of the long arm of chromosome 11, namely q23-qter was observed (Fig. 3).

The karyotype of the patient was thus 46, XX, del(11) (q23). Banded karyotypes of the parents were normal.

DISCUSSION

Up to now, we know of 23 cases of 11q monosomy. 18 originated de novo, 2 were products of a paternal translocation and the type of origin could not be defined in 3 cases (Table I). It is remarkable that the syndrome occurred mostly in females; there were only 3 males among the 23 patients. The average maternal age proved to be 26.7 ± 3.50, the paternal age was 28.9 ± 6.2.

The breakpoints were determined as q23 in most of the cases (18/23). In 4 patients, breakpoints were defined at the adjacent bands q22 and q24 and in one case the deleted chromosome segment was about the half of the long arm (Fig. 4). Fraccaro et al. (5) studied 42 cases with 11q; 22q translocation and breakpoint analyses showed that q23 was a site with high preferential predisposition to breakage.

In the light of the breakpoint analyses it seems probable that a large deficiency, a deletion longer than half of the long arm of chromosome 11 would not be viable. Although nearly half of the patients (11/23) were more than one year old, lethality was considerable in the first year of life. Out of 12 patients under one year of age at the time of the observation, 8 died in infancy (Table I). The postnatal survival rate in cases with small deficiency must also be low, probably not higher than that of patients with other partial monosomy, i.e. 4p–, 5p–, etc.

Severe major malformations are rare in this syndrome. Therefore, the factors leading to early death cannot be general. Severe, multiple major malformations were reported only in a single case (10). It is rather the immaturity (1, 11, 7) and re-

TABLE I

Cytogenetic data, age, sex and parental age in cases with 11q–

		Origin of 11q–	Deleted segment	Age	Sex	Parental age	
						mother	father
Bresson & Noir 1977		de novo	q23–qter	+ 7 d	F	25	21
Cassidy et al 1977		,,	q23–qter	9 m	F	31	35
Engel et al 1976		,,	q23–qter	4.5 y	F	21	20
Faust et al 1974		,,	q21–qter	9 y	F	30	30
Felding & Mittelman 1979		,,	q22–qter	+ 6.5 m		30	30
Frank & Riccardi 1977		,,	q23–qter	7 m	F	33	36
Kaffee et al 1977		,,	q23–qter	+ 22 d	F	23	25
Laurent et al 1979	1		q24–qter	4.5 y	F	26	27
	2	,,	q24–qter	3 m	F	31	31
Lee & Sciorra 1979		,,	q23–qter	+ 23 d	F	24	27
Linarelli et al 1975		,,	q22–qter	12 y	M	32	33
Lippe et al 1980		,,	q23–qter	26 m	F	22	26
Mulcahy & Jenkyn 1977		,,	q23–qter	18 m	F	26	31
Schinzel et al 1977	1	,,	q23–qter	2.5 y	M	24	25
	2	,,	q23–qter	17 m	F	30	31
Turleau et al 1975		,,	q232–qter	14 m	M	24	22
Zabel et al 1977		,,	q23–qter	9 m	F	21	23
Present case		,,	q23–qter	+ 3 m	F	30	36
Larson et al 1976	1	?	q23–qter	23 m	F	34	39
	2	?	q23–qter	15 y	F	15	19
Leonard et al 1979		?	q23–qter	+ 25 d	F	35	43
Jacobsen et al 1973	1	(11 ; 21) pat.	q23–qter	+ 19 m	F	24	25
	2	,,	q23–qter	+ 28 d	F	23	29

TABLE II

Clinical data of patients with 11q—

Investigators	Birth weight	Perinatal problems	Growth retardation	Psychomotor retardation	Recurrent infection	Trigonocephaly	Ptosis of eyelids	Globular nose	Carp mouth	Micro-retrognathia	Clenched hands
Bresson & Noir 1977	2700	+	•	•	•	+	−	+	+	+	−
Cassidy et al 1977	3090	−	−	+	−	+	+	+	+	+	−
Engel et al 1976	2175		+	m	+	+	−	+	−	+	−
Faust et al 1974	2000	−	+	+	+	−	−		−	+	−
Felding & Mittelman 1979	1580	+	+	+	+	+	+	+	+	+	+
Frank & Riccardi 1977	3250	+	−	+	−	+	+		−	+	−
Kaffee et al 1977	3500	+	•	•	+	−	−		−	+	−
Laurent et al 1979 1	2500	−	+	+	−	+	+	+	−	+	−
2	2450	−	−	•	−	−	+	+	−	+	−
Lee & Sciorra 1981	2450	+	•	•	+	+	−	+	+	+	+
Linarelli et al 1975	2350	+	+	+	+	+	+	+	−	+	−
Lippe et al 1980	3400		+	+		−	−	+	+	+	−
Mulcahy & Jenkyn 1977	2600	+	+	+	+	−	−	+	+	+	−
Schinzel et al 1977 1	3090	+	−	+	−	+	+	+	+	+	+
2	3310	−	−	+	+	+	+	+	+	+	−
Turleau et al 1975	2300	−	+	+	−	+	+	+	+	+	−
Zabel et al 1977	2750		+	+	−	+	−	+	−	+	−
Present case	3350	+	+	+	+	−	−	+	+	+	+
Larson et al 1976 1	3480	−	+	+	+	−	+		−	−	−
2	1380	+	+	+	+	−	−		−	−	−
Leonard et al 1979	2350	−	•	•	•	+	−	+	+	+	−
Jacobsen et al 1973 1	2000	+	+	+	−	+	−			+	−
2	1700	+	•	•	•	+	•			+	−

current infections (4, 8 and the present case) which are responsible for death. Perinatal problems, such as respiratory distress, prolonged jaundice, thrombocytopenia, hypoglycaemia were observed in half of the cases with low and normal birth weight alike (1, 4, 6, 7, 8, 9, 10, 12, 14, 15 and the present case). Recurrent infections were mentioned in nearly half of the patients (3, 4, 8, 9, 12, 14, 15 and in the present case).

In the survivors, psychomotor retardation seems to be obligatory although in different degrees, as in some cases mental retardation was slight (3, 17). Growth retardation probably becomes evident only after one year of age (3, 7, 9, 12, 13, 14, 16).

A clinical suspicion of 11q— syndrome can be based on the combination of the following, mainly characteristic, signs of cranio-facial dysmorphism (Table II): the skull is dolichocephalic with keel-shaped protuberant forehead, flattened occiput and narrow temples. This configuration may be very pronounced; out of 23 cases, in 15 cases trigonocephaly was stated radiographically. Nearly constant symptoms are the globular, upturned nose with aplastic ridge, the small, carp shaped mouth, the slightly receding chin and ptosis of the upper eyelids. All these features result in a strikingly characteristic look of the patients, although in several cases it is only the chromosome analysis that reveals the syndrome.

The protuberant occiput, absence of trigonocephaly as well as the clenched hands with overlapping fingers were misleading in the clinical diagnosis of our case. Clenched hands were observed in 3 further patients. Schinzel et al. (15) described in one of their two patients clenched hands with ulnar deviation of the index fingers which overcrossed the thumb and middle fingers. Lee et al. (10) observed clenched hands with bilateral fifth finger camptodactyly accompanied by multiple malformations as an unusual finding in 11q— syndrome. These observes have pointed to the similarity between the clinical picture of 11q- and 18-trisomy. Felding and Mittelman (4) reported clenched hands with supernumerary digits on both sides and the baby was small for dates. This is an association characteristic more of 18-trisomy than of the 11q- syndrome. In view of these observations in 4 patients with 11q— syndrome, the statement of Lee et al. (10) can be supported that 11q monosomy must be considered in the differential diagnostics of 18-trisomy.

Besides the afore-mentioned dysmorphic signs which give the characteristically, funny appearance of patients with 11q— aberration, there are other minor symptoms not consistently observed. The palpebral fissures are variably oriented, epicanthus, hyper- or hypotelorism, long philtrum, coloboma, low set ears have been mentioned in several cases. Out of the major malformations, congenital heart defects occur.

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