Familial chromosome translocation t(3;18)(p21;p11)

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SUMMARY A familial translocation t(3;18)(p21;p11) was observed in a newborn male. He had multiple malformations resulting from partial trisomy 3 and partial monosomy 18. The mother, maternal uncle, and maternal grandmother were found to be balanced translocation carriers. A daughter of the maternal uncle with similar malformations probably had the same unbalanced karyotype as the proband.

Numerous cases of unbalanced chromosomal rearrangements, especially unbalanced translocations with multiple anomalies, have been described in published reports. However, there are only a few cases in which malformations are the result of partial trisomy for the short arm of chromosome 3. Therefore, we present a family with a balanced translocation t(3;18)(p21;p11) in two successive generations and two malformed children probably with the same unbalanced form of the translocation, partial trisomy for the short arm of chromosome 3.

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Case reports

CASE 1

The proband (III-8) was the first child of a 24-year-old mother and a 24-year-old father. The pregnancy was complicated by hyperemesis. The boy was born spontaneously 23 days post-term, birthweight 3040 g, length 51 cm, and head circumference 30 cm.

The microcephalic baby had a bilateral cleft lip and palate (fig 1), causing a broad, blown-up lower face, and a flat and retracted nose. The eyes had an antimongoloid slant, wide interorbital distance, bilateral epicanthus of the lower lids, and small palpebral fissures. The ears were low set, but of normal shape. There was bilateral pterygium colli and short neck, a loud holosystolic murmur, and bilateral cryptorchidism (fig 2).

X-ray of the skull showed a turriccephalic configuration and premature closure of all cranial sutures

FIG 1 *Facies of proband.*

FIG 2 *Genital region of proband.*

FIG 3 Pedigree of family.

except the sagittal suture and the anterior fontanelle. There were no renal or urinary tract anomalies on venous pyelogram. The child was continuously hypothermic (33.5°C) in spite of recurrent infections of the upper respiratory tract. Generalised seizures were observed from the second week of life. Finally, bronchiolitis and pneumonia led to death at the age of 10 months.

At necropsy, the following were seen: ventricular and atrial septal defects, ectasia of the pulmonary arteries, bronchiolitis and purulent pneumonia, and Meckel diverticulum of 3 cm length.

FIG 4 Karyotype of proband.

CASE 2

This was a first cousin (III·4) of the proband. The female baby was the first child of a 24-year-old mother and a 28-year-old father. The pregnancy was uncomplicated and the birth was at term by breech presentation. Birthweight was 1950 g and length 46 cm. There was a cleft palate and cleft lip on the right side, oblique palpebral fissures, low set ears, bilateral simian creases, and slight camptodactyly. Death occurred after 24 hours from profuse bleeding.

The family pedigree is shown in fig 3.

CYTOGENETIC FINDINGS

Chromosome analysis of case 1 was performed on a whole blood culture in Chromosome Medium IA

(Gibco) and stained with 2% Giemsa solution (fig 4). One chromosome 18 was missing and in its place there was an abnormal metacentric chromosome, one arm of which resembled 18q. The other arm contained a Giemsa dark band in the distal third of the chromatids. Identification of the additional material was not possible.

Chromosome analyses were performed on lymphocytes of the parents (II·7, II·8) of the proband, the maternal grandparents (I·3, I·4), a maternal aunt (II·6), and the maternal uncle (II·5).

Giemsa banded metaphases of the mother (Fig 5), the grandmother, and the maternal uncle of the proband showed a translocation between chromosomes 3 and 18. The breakpoint of chromosome 3 probably lies

FIG 5 Karyotype of proband's mother.

TABLE Clinical symptoms of partial trisomy 3 syndrome (enlarged table of Ballesta and Vehi¹)

Sign	Rethoré <i>et al</i> ²			Ballesta and Vehi ¹	Sachdeva <i>et al</i> ⁴		Surana <i>et al</i> ³	Our cases	
Chromosome aberration	Ins(7;3)			t(3;4)	t(3;12)		t(3;22)	t(3;18)	
Trisomic segment	3(p21→p26)			3(p23→pter)	3(p21→pter)?		3(p2→pter)	3(p21→pter)	
Case	1	2	3		1	2		1	2
Birthweight (g)	3700	3830	2190	2360	1520	1700	3030	3040	1950
Length (cm)	47	49	47	47	?	?	53	51	46
Head circumference (cm)	35	36	33	30	?	?	34.5	30	2
Sex	M	M	M	M	F	M	M	M	F
Gestation	40	40	38	?	?	37	38	>40	40
Death	4 mth	—	3 d	—	36 h	6 mth	5 d	10 mth	24h
Microbrachycephaly	+	—	+	+	+	Unusual facial appearance	—	+	Various facial anomalies
High arched forehead	+	+	+	+	?		?	—	
Temporal retraction	?	+	+	+	?		?	—	
Square face	+	+	+	+	?		?	+	
Prominent cheeks	+	+	+	+	?		?	+	
Hypertelorism	+	+	+	+	?		?	(+)	
Epicanthus	+	+	+	+	?		?	+	
Big mouth with drooping corners	+	+	+	+	?		?	+	
Cleft palate and/or cleft lip	—	—	+	—	—		+	+	
Retrognathia	+	—	—	+	+		?	—	
Short neck	+	+	+	+	?	?	?	+	?
Digestive tract malformations	+	—	—	+	+	—	+	+	—
Limb malformations	+	—	—	+	+	—	—	—	+
Abnormal digital pattern	+	+	+	+	?	?	?	?	?
Vitium cordis	+	—	—	+	—	+	+	+	+
Abnormalities of genitalia	+	+	—	—	—	+	+	+	—
Abnormalities of kidneys	—	+	—	—	—	+	—	—	+

between the centromere and band p21; the break-point of chromosome 18 seems to be in p11. Since the translocation carriers are healthy, it can be assumed that the translocation is reciprocal. Alternatively, the loss of the 18 material has no effect at all. The familial translocation could be described as follows: t(3;18)(3qter→3p21::18p11→18pter;18qter→18p11::3p21→3pter).

The karyotype of the proband, trisomic for the short arm of chromosome 3, could be described as follows: 46,XY,der(18)t(3;18)(p21;p11).

The mother has a marker chromosome 1qh+, which was also detected in her brother and her mother.

Chromosome analysis of case 2 was not performed.

Discussion

The family history, the chromosome findings in the parents, and the similarity of the clinical symptoms make it most probable that the same chromosome rearrangement caused the malformations in the proband and his first cousin. Unfortunately, no photographs and no chromosome analysis are available for the latter. Both children must be considered to be partially trisomic for 3p21→3pter and monosomic for a very small part of the short arm of chromosome 18 (p11→pter). Ballesta and Vehi¹

reviewed four cases of partial trisomy 3, three of which were brothers and sisters first described by Rethoré *et al*.² The clinical symptoms are less well reported by Surana *et al*.³ in a case of a partial trisomy 3. The cases of Sachdeva *et al*,⁴ which were also described briefly showed a different phenotype with micrognathia, incompletely closed peritoneum, and uterus bicornis. Partial trisomy 3 with the symptoms of Cornelia-de Lange syndrome⁵ might be the result of a trisomic part of the long arm of chromosome 3, since banding techniques were not used in 1966. The symptoms of the cases are compared in the table.

The prominent features in our cases are microcephaly, cleft lip or palate or both, and malformed mouth. Temporal retraction as described by Ballesta and Vehi is in our case the consequence of the microcephaly and the blown-up cheeks. However, since the same symptoms are repeatedly seen in malformation syndromes resulting from different chromosome abnormalities, the clinical pictures of these children do not seem to form a specific pattern in the sense of a 3p trisomy syndrome. Since the trisomic parts of 3p are of different size in each case, characteristic symptoms can hardly be expected.

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