Trisomy 3p23→pter and monosomy 11q23→qter in an infant with two translocation carrier parents

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SUMMARY A newborn male infant with multiple congenital abnormalities was found to be trisomic for 3p23→pter and monosomic for 11q23→qter. His parents were both carriers of a balanced reciprocal translocation. Considerable overlap in phenotype-karyotype correlations was found between the two chromosomal syndromes in the patient.

Hook and Hamerton¹ reported that 0.09% of newborns have an insertional or balanced, not

Received for publication 26 September 1987.
Accepted for publication 2 October 1987.

including Robertsonian, translocation. The chance mating of two such carriers would be about 1 in 1 234 568. Not surprisingly then, there are few cases reported where both members of a couple are translocation carriers.²⁻⁴ This report presents an infant with congenital malformations resulting from a chromosomal imbalance inherited from his translocation carrier father and a balanced translocation inherited from his mother.

Case report

A newborn Hispanic male infant was evaluated for multiple congenital anomalies. He was the product

FIG 1 Chromosome pairs involved in translocations from the proband, mother, and father. Arrows indicate translocated segments.

of a 23 year old G5 P3012 mother and a 26 year old father. Spontaneous vertex delivery occurred at 37 weeks' gestation. The birth weight was 1870 g (10th centile), length 43 cm (10th centile), and head circumference 31.2 cm (10th centile). Facial anomalies included microphthalmia, short palpebral fissures (each 1.25 cm) with antimongoloid slant, hypertelorism, bilateral cataracts, anomalous, low set, posteriorly rotated ears, and a narrow palate. The infant also had a short, webbed neck and a shield chest with widely spaced nipples (8.5 cm, 55th centile). Grade 1 hypospadias and bilateral cryptorchidism were present. The hands had bilateral simian creases. There was overlapping of the second finger over the third and the fifth finger over the fourth. The fingers of the left hand had an ulnar drift. The dermatoglyphics showed seven whorls, two ulnar loops, one arch, and the axial triradius in the τ position. In the feet, the second toe overlapped the third. An echocardiogram showed a large VSD, PDA, and an overriding aorta with minimal evidence of pulmonary stenosis. Cranial sonogram revealed a small midline structure in the area of the quadrigeminal plate believed to represent a plate cyst or a cavum vergae. The infant died on the 36th day of life from congestive heart failure and *Staphylococcal aureus* sepsis. Permission for necropsy was refused.

CYTOGENETIC STUDIES

The patient had a 46,XY,t(3;6)(p21;q11),11q+ chromosome complement in a GTG banded study from peripheral blood cultures. Examination of the parental karyotypes showed that the mother is a balanced t(3;6) (p21;p11) carrier, and that the father is a balanced t(3;11)(p23;q23) carrier (figs 1 and 2). Thus, the patient is trisomic for 3p23→3pter and monosomic for 11q23→11qter. The patient's brother has a 46,XY karyotype and his sister a 46,XX,t(3;11)(p23;q23)pat karyotype. Both sibs are phenotypically normal and the parents are not consanguineous. No other family members were available for study.

Discussion

Theoretically, there are 16 possible zygotic combinations from the balanced reciprocal translocation parents. Twelve would be unbalanced and four would be balanced. The parents in this case have had five pregnancies and have two living children. The first pregnancy resulted in a liveborn male with ambiguous genitalia and low set ears who died eight hours after birth. The second and third pregnancies resulted in two phenotypically normal children, a 46,XY male and a 46,XX,t(3p;11q)pat

female. The fourth pregnancy resulted in a miscarriage at four months and the fifth pregnancy is the proband. No cytogenetic studies or necropsies were performed on the products of the first and fourth conceptions, but unbalanced chromosome

FIG 2 Diagrammatic representation of chromosomes from the mother and father showing the breakpoints involved in the translocations.

Case reports

TABLE A comparison of clinical features found in trisomy 3p2, monosomy 11q2, and our proband.

Clinical findings	Ref 5 6	Ref 5 7	This report
	3p+	11q-	
High forehead, frontal and parietal bossing	+	-	-
Trigonocephaly, scaphocephaly	-	+	-
Square face, heavy cheeks	+	+	+
Scant medial eyebrows	+	-	-
Short palpebral fissures with downward slant	-	-	+
Hypertelorism	+	+	+
Broad, flat nasal bridge	+	+	+
Short nose with large nasal tip	+	-	-
Bulbous nose, wide aplastic bridge	?	+	-
Short, prominent philtrum	+	?	-
Poorly defined philtrum	?	+	-
Harelip/cleft palate	+	+	-
Narrow palate	-	+	+
Large mouth, downturned corners	+	+	+
Thin lips	?	+	-
Micrognathia	+	+	+
Low set, poorly folded ears	+	-	-
Low set, prominent antihelix, underdeveloped ear lobe	-	+	+
Short neck	+	+	+
Redundant skin on nape	+	-	+
Heart disease: PDA, VSD	+	+	+
Short, chubby hands and fingers	+	+	-
Widely spaced nipples	+	-	+
Cutaneous syndactyly	+	+	+
Dermatoglyphics: excess of whorls	+	-	+
Deep crease between 1st and 2nd toes	+	-	-
Hypospadias, testicular ectopy	+	+	+
Growth retardation	+	+	+

complements are considered to be the most likely cause of the two losses.

The proband has a trisomy 3p23→pter and a monosomy 11q23→qter. To the best of our knowledge, all reported trisomy 3p2 cases have resulted from a parental rearrangement, while most cases of 11q2 monosomy occur de novo.⁵ The associated monosomies in the trisomy 3p2 cases did not appear to have a significant effect on the phenotype, and the reported cases were similar in appearance.

It is difficult to determine the effect of the monosomy on the phenotype of the proband because trisomy 3p2→pter and monosomy 11q2→qter have many features in common (table). They include hypertelorism, a large mouth with downturned corners, micrognathia, short neck, hypospadias, testicular ectopy, short chubby hands

and fingers, cutaneous syndactyly, heart disease (PDA, VSD), and growth retardation. Some of the more striking features associated with the two chromosome abnormalities, such as the frontal bossing and temporal indentation in trisomy 3p2 and the trigonocephaly in monosomy 11q2, were not present in our patient.

A certain amount of phenotypic variability is expected in the various chromosomal syndromes, and this probably depends on a variety of factors including the location of breakpoints and the compensatory effects of the remainder of the genome. For these reasons, and the considerable phenotypic overlap of such cases, it may be difficult to assess and correlate the contribution of various deletions and duplications to the specific clinical findings.

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