Case reports

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Partial proximal trisomy of the long arm of chromosome 5 (q13→q22) resulting from maternal insertion der ins(10;5)

SUMMARY Five members of our study family were carriers of a balanced insertion (10;5) (q22;q13q22). One of the children had psychomotor retardation and malformations resulting from a partial trisomy of the proximal long arm of chromosome 5, having received the maternal der(10). Amniocentesis identified another case of partial proximal trisomy in a fetus of a subsequent pregnancy. This clinical and family study is compared with two other published cases of proximal trisomy 5q.

A fairly large number of cases of partial trisomy 5p have been published and the corresponding clinical syndrome described. Cases of trisomy 5q are rare and usually involve the terminal region. Only two cases of proximal trisomy 5q have been published,[1 2] one being the result of maternal insertion,[1] as in our case.

In this report, we will present our clinical findings and the family history and correlate our study with other published case studies of partial trisomy 5q.

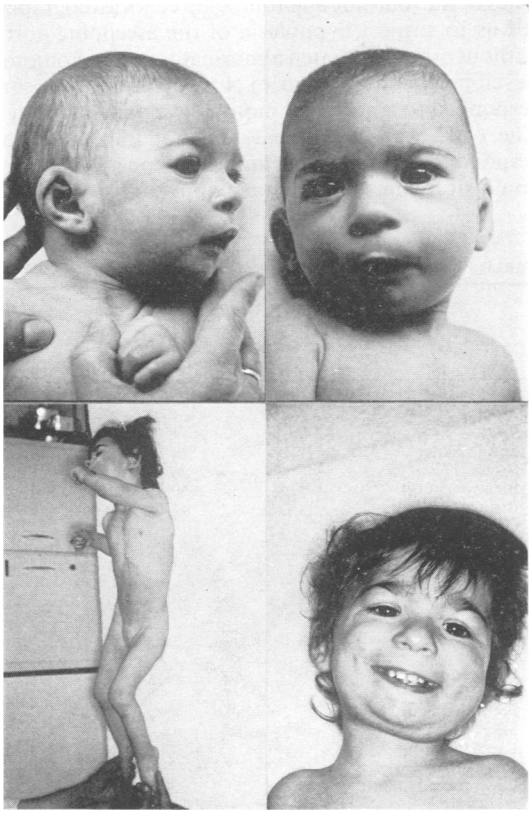

FIG 1 *Proband (III·1) at the ages of 5 months (above) and 4 years (below).*

Case report

CLINICAL DESCRIPTION

The proband (III·1) was born at term on 26 January 1976 to unrelated parents. The mother was 22 years old and the father was 25. During pregnancy we noted retardation of fetal development, the uterine length being 30 cm at term. At birth, the baby weighed 2300 g and examination of the placenta showed discrete villous hypotrophy. Apgar score was 4 at 1 minute and 9 at 5 minutes.

From the beginning, we noted a dysmorphic syndrome. Head circumference was 33 cm with a thoracic circumference of 28·5 cm and a height of 46 cm. The microcephaly was accompanied by facial dysmorphia with protrusion of the middle level of the face, protruding upper dental arch, vaulted palate, retracted chin, and discrete epicanthus, mostly inferiorly (fig 1). A coccygeal pit was also present. The clinical examination revealed hypertonia of the lower extremities and a systolic mesocardial murmur. Subsequently, the psychomotor and growth retardation became more pronounced. The microcephaly corresponded to approximately −4 SD.

We saw the patient again at the age of 4. The child's weight was 9·1 kg (−4 SD), height 89 cm (−3·5 SD), and head circumference 42 cm (−5 SD). Besides the upper maxillary protrusion, the vaulted palate, and the epicanthus, the facial dysmorphism included an antimongoloid slant, 'comma' eyebrows with a thickened base and narrowed extremity, and asymmetrical ears with a thickened helix on the right ear and a poorly differentiated helix on the left ear.

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The neurological examination revealed hypotonia of the trunk in contrast to hypertonia of the lower extremities and considerable generalised amyotrophy. Cardiovascular examination revealed a 2/6 systolic murmur over the aortic area. The characteristics of the murmur and follow-up echocardiography led us to suspect hypoplasia of the ascending aorta without other associated abnormalities. Psychomotor development at the age of 4 years 2 months corresponded to a normal 9 month developmental level. The child was incontinent, did not talk, walk, or respond to her name. She ambulated on all fours and could sit by herself. She was happy and smiling and played with toys. Radiological examination revealed no abnormalities other than scoliosis. The bone age was between 5 years 9 months and 6 years 10 months (ulnar epiphyseal point).

Dermatoglyphs showed five arches on the fingertips and bilateral *t'* axial triradii.

CYTOGENETIC STUDY

From lymphocyte culture, it was determined that the karyotype was 46,XX,10q+.The QFQ, GTG, and RBA techniques did not permit identification of the nature of the genetic material (fig 2). The same abnormality was found in fibroblast cultures. A

TABLE *Clinical and cytogenetic findings in 15 cases of distal trisomy 5q and 4 cases of proximal trisomy 5q*

	Ferguson-Smith et al[3]	*Osztovics and Kiss*[4]		*Bartsch-Sandhoff and Liersch*[5]		*Watanabe et al*[6]	*Zabel et al*[7]	*Jones et al*[8]
		Case 1	*Case 2*	*Case 1*	*Case 2*			
Clinical features								
Age	4 yr	8 mth	1 yr 4 mth	4 mth	7 yr	5 mth	8 mth	2 mth
Sex	M	F	F	F	F	F	M	F
Maternal age	26	24	29	28	22	28	33	23
Paternal age	46	26	31	30	24	34	36	28
Birthweight (g)		2650	2700	2400	3250	2740	2450	2190
Birth length (cm)		42	49	47	51	47	46	43
Growth retardation (size/weight)	+	+/+	+/+	+/+	+/+		+/+	+/+
Psychomotor retardation	+	+/+	+/+		+/+		+/+	
Microcephaly	+	+	+	+	+	+	+	+
Antimongoloid slant	+				+		+	−
Epicanthus		+	+			+		−
Hypertelorism	+	+					+	−
Strabismus		+	+	+	+			
Prominent nasal bridge							+	+
Micrognathism							+	+
Large upper lip		+					+	+
Low-set/large ears	+/+	+/+	+/+	+/			+/+	
Downturned mouth				+	+			
High palate								
Umbilical hernia				+				+
Inguinal hernia				+				
Cardiac malformation			+	+	+	+	+	+
Hypotonia				Hypertonia			+	+ Sucking failure
Muscle hypotrophy								
Scoliosis/lordosis							Kyphosis, sacrococcygeal pit	
Joint limitation		Hip					Hip	
Sternal malformation								
Spinal malformation							Rectum diastasis	
Feet							Club feet	
Brachy/clinodactyly	+	+					+	Dysplastic thumb
Other malformations								
Cytogenetic findings								
Duplicated segment	q31→qter	q31→qter		q33→qter		q31→qter	q33→qter	q31→qter
Parental karyotype	t(2;5)	t(2;5)		t(5q;8p)pat		t(5;13)mat	t(5;22)pat	t(5;9)pat

cytogenetic study was done on the parents, but there was no evidence of any abnormality.

FAMILY HISTORY

In 1974 the first pregnancy ended after 4 weeks. In 1976 a second spontaneous abortion took place in the 5th week of pregnancy. No study was undertaken on the abortus. In 1977 an amniocentesis was done during the fourth pregnancy, because of the family history, despite apparently normal parental karyotypes. A 46,XX,10q+ karyotype, identical to that of the proband, was discovered (fig 3). Abortion was undertaken. The fetus of female sex was 31 cm long and weighed 700 g. There was craniofacial dysmorphism with hypertrophy of the upper dental arch, microretrognathism, and an antimongoloid slant. We noted hyperlaxity of the ligaments of the 5th left toe and an internal deviation with overlapping on the 4th left toe. Anatomical studies revealed a cardiac malformation of large vessel transposition and interventricular septal defect associated with pulmonary atresia and isthmic stenosis.

The parental karyotypes were then carefully restudied. In the mother we discovered a direct balanced insertion of the long arms of chromosome

Rodewald et al[9]		*Curry et al*[10]				*Lazjuk and Lurie (1980, personal communication)*	*Jalbert et al*[1]	*Kessel and Pfeiffer*[2]	*Personal observations*	
Case 1	*Case 2*	*Case 1*	*Case 2*	*Case 3*	*Case 4*					*Fetus abortion*
3 yr 2 mth	6 mth	22 yr	21 yr	21 yr	16 yr	Newborn	4 yr	6 yr	4 yr	
F	F	F	F	M	M	F	F	F	F	F
25	30	28	29	19			24	33	22	26
30	35						23	33	25	29
1700	2700	2940	2760	2760	2724	2545	2880	2800	2300	700
32	47					48		48	46	31
+/+	+/+	+/+	+/+	+/+	+/+		−/+	+/+	+/+	
+/+	+/+	+/±	+/±	+/+	±/−		±/−	+/+	+/+	
+	+	+	+			Trigonocephaly, arhinencephaly	High forehead + −	High forehead	High forehead	
+	−						−	+	+	+
−	+	+	+				+ −	+	−	
+						+	+		−	
+		+		+	+				−	
Broad		+	+				+ Bulbous	Bulbous	Bulbous	
+	+							+	+	+
−	−						+		+	+
+	+	/+	/+	/+	/+	+/	+/+		+/+	+/
+										
						+		+	+	
			+	+	+					
CIA			−				+	−	+	+
							Williams-Beuren syndrome?		Williams-Beuren syndrome?	
							Asthenia	+	Axial hypotonia	
							+		+	
							+/+	+/+	+	
				+					Coxa valga	
							Pectus carinatus	Funnel chest	−	
							Spina bifida occulta		Coccygeal pit	
		Short toes				4th/5th toes				5th/4th toes
Double thumb		+				+	Thin fingers			
						Genital malformation, two supernumerary spleens				
q31→qter	q31→qter	q34→qter				q31→qter	5q11→q22 insertion	q13→q22 tandem duplication	q13→q22 insertion	q13→q22 insertion
t(5;11)mat	t(5;11)pat	t(5;16)mat				t(5;10)mat	t(1;5)mat	Normal	ins(5;10)mat	ins(5;10)mat

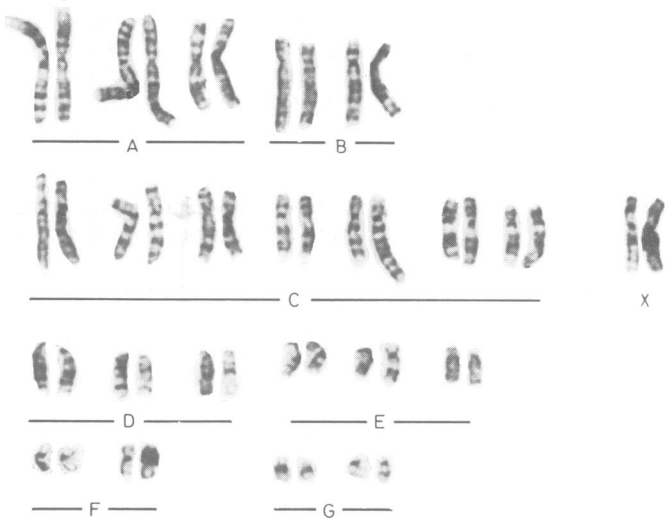

FIG 2 *Karyotype of proband (III·1) (GTG banding).*

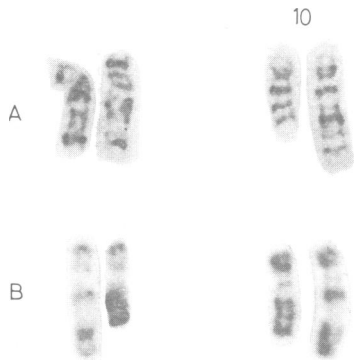

FIG 3 *A, fetus (III·2): chromosomes 5 and 10 (GTG banding); B, mother (II·1): chromosomes 5 and 10 (RHG banding).*

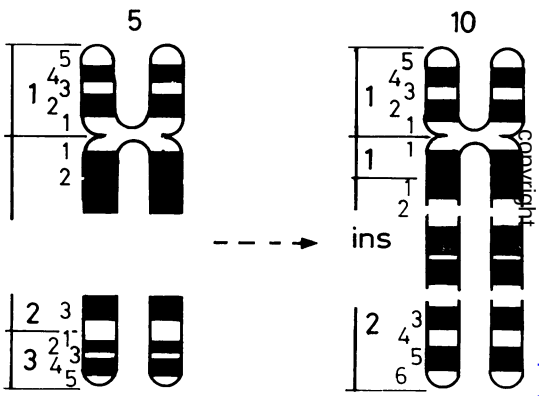

FIG 4 *Diagram of G banding of mother (II·1) with ins(10;5)(10pter→10q22::5q13→10qter;5pter→5q13::5q23→5qter).*

5 into the long arms of chromosome 10 (fig 3). After QFQ, GTG, RHG, and RBG studies, we concluded that the karyotype was 46,XX, dir ins(10;5)(q22;q13 q22) (fig 4). The proband and the fetus were 46,XX,−10,+der(10) ins(10pter→10p22::5p135q22 ::10q23→10qter)mat. Hence they were trisomic for 5q from 5q13 to 5q22. The family pedigree showed that the balanced insertion was present in the grandmother (I·1) of the proband, in her uncle (II·3), and in her aunt (II·6) (fig 5).

Lastly, in 1979, amniocentesis showed that the karyotype of the current pregnancy was a normal 46,XY. On 11 December 1979 a normal boy weighing 4200 g and 54 cm in length was born and his subsequent development was perfectly satisfactory.

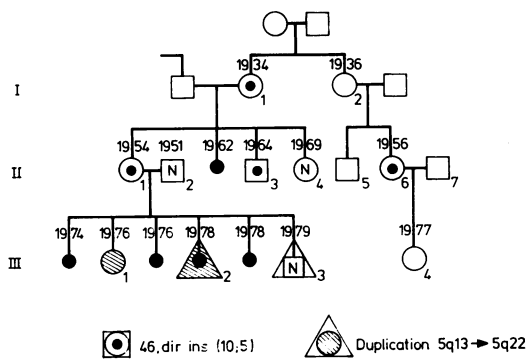

FIG 5 *Family pedigree.*

Discussion

We have accumulated 19 cases of partial trisomy 5q (table) including 15 girls and four boys.

In 15 cases, the trisomy was distal and resulted from a balanced parental translocation between a chromosome 5 and the following chromosomes: 2 (twice), 8, 9, 10, 11, 16, 19, and 27. Rodewald *et al*[9] subdivided the distal trisomies 5q into two groups according to clinical and cytogenetic findings. One group was that in which the duplicated segment was from 5q31 to 5qter (6 cases) (Lazjuk and Lurie, 1980, personal communication)[ε 4 6 8 9] and from 5q33 to 5qter (3 cases).[5 7] They have in common the following clinical symptoms: low birthweight, psychomotor retardation, brady- and clinodactyly, as well as facial dysmorphism, strabismus, epicanthus, a protruding nose base and prolongation of the forehead, oversized top lip, and large protruding ears. Only one child (Lazjuk and Lurie, 1980, personal communication), who died 2 hours after birth, had genital and severe nervous system malformations.

A second group was that in which the duplicated segment included only the bands from 5q34 to 5qter[10] and in which the clinical symptomatology was less severe, including only hypotrophy and strabismus.

Proximal trisomy 5q was demonstrated in four cases if the fetus is included. The duplicated segment ranged from 5q11[4] or 5q13 to 5q22 (our observation).[8]

Two families exhibited insertion, while one other family exhibited tandem duplication. These two types of abnormalities are relatively rare.

The three girls had (besides psychomotor retardation) comparable facial dysmorphism including high forehead with median vaulting, bulbous nose with nostrils oriented downwards, externally flattened supraorbital margin and falling eyebrows, short philtrum and protruding upper lip without Cupid's arch, malpositioned teeth, small chin, and large protruding ears. They also presented skeletal abnormalities (sternum, spine) and muscular hypotrophy.

Dermatoglyphic patterns have in common arches on the fingertips and bilateral *t'* axial triradii in two cases. No simian crease was observed.

In two cases, the cardiopathy associated with the facial dysmorphism was similar to Williams-Beuren syndrome. The pulmonary atresia with an open ventricular septum observed in the fetus can be considered an extreme form of malformation of the ejection channels of the heart.

In conclusion, apart from already described distal 5q trisomies,[9] it seems at last possible to describe a syndrome corresponding to duplication of a proximal segment 5q13 to 5q22. Further investigations are necessary to describe this syndrome more precisely.

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