Partial trisomy for short and long arm of chromosome no. 5

Two cases of two possible syndromes

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SUMMARY We report 2 patients from different families with malformation-retardation syndromes caused by a partial trisomy of the long and of the short arm of chromosome 5, respectively (case 1: 46,XX,der(3),t(3;5)(p27;p13)mat; case 2: 46,XY,der(22),t(5;22)(q33;q13)pat). Several members of these families were balanced translocation carriers. Our cases are compared with those cited in the literature. The possibility of delineating a 5p- and a 5q-partial-trisomy syndrome is discussed.

Aberrations of chromosome No. 5 almost always lead to the phenotype of a 'cri-du-chat' syndrome. Partial trisomies of chromosome No. 5 are rarely found and usually involve the short arm (Lejeune *et al.*, 1964; Laurent and Robert, 1966; de Capoa *et al.*, 1967; Noel *et al.*, 1968; Warter *et al.*, 1973; Opitz and Patau, 1975; Monteleone *et al.*, 1976). Three cases with partial trisomy for the long arm of chromosome No. 5 have been described in the literature: one concerning the proximal part of the long arm (Jalbert *et al.*, 1975), and two cases concerning the distal part of the long arm (Ferguson-Smith *et al.*, 1973; Osztovcics and Kiss, 1975). We report a case of partial trisomy 5 p (case 1) and a case of partial trisomy 5q (for the distal part) (case 2).

pupil but normal pupillary reflexes. There was a pointing lower lip, small upper lip, high arched palate, and moderate macroglossia. The patient had small narrow hands with long well-formed fingers. The toes showed a clinodactyly and zygodactyly II and III. Dermatoglyphs showed no abnormalities. The statomotor and psychomotor development were retarded during the first year of life. At the age of 12 months the hypotonic patient was unable to control

Case reports

CASE 1

This female child (Fig. 1) was born at term after an uneventful pregnancy, birth weight was 3050 g, length 51 cm, head circumference 38 cm. She was the second child of nonconsanguineous parents, a 24-year-old mother and 32-year-old father. Both parents and their first child, a 3-year-old girl, were phenotypically unremarkable, and the family had a normal medical history.

Clinical examination showed a hypotonic female newborn with scaphocephaly, flat face, depressed nasal bridge, mongoloid slanting of the palpebral fissures, a discrete pupillary dilatation of the right

Fig. 1. Case 1 at the age of 12 months.

her head movements, and the child could sit only with support as there was severe kyphosis. At the age of 9 months infantile spasms with hypsarrhythmia in the electroencephalogram were observed. X-ray examinations at the age of 3 months showed joint limitation of the hips. Electrocardiogram and computer tomography of the head showed no abnormalities.

CASE 2

This boy (Fig. 2) born at term after an uneventful pregnancy, birthweight 2460 g, birth length 46 cm, was the third child of healthy and nonconsanguineous parents. The mother and the father were 33 and 36 years old, respectively. A 7-year-old sister and a 6-year-old brother of the patient were phenotypically normal. The family medical history was unremarkable. At birth the patient showed microcephaly (32.2 cm, <3%), joint limitation of the hips, clubfeet, and an inguinal hernia.

We saw the child for the first time at the age of 8 months. The most obvious clinical features were dystrophy and growth retardation (weight 3900 g, <3%, length 61 cm, <3%) and microcephaly (head circumference 39.5 cm, <3%). The face was abnormal because of hypertelorism, broad nasal bridge, anti-mongoloid slanting of palpebral fissures, large upper lip, small mouth, and large, low-placed, and dysplastic ears. Clinical investigation disclosed respiratory stridor, a diastasis of the musculus rectus, joint limitation of the hips, and a severe statomotor and psychomotor retardation. A right bundle-branch block and a sinus tachycardia were observed in the electrocardiogram.

Fig. 2. Case 2 at the age of 9 months.

Electroencephalogram indicated an inconstant side difference. Further development was impaired by repeated attacks of tachycardia, accompanied by hypoxaemia. The child died at the age of 10 months from acute heart failure. Necropsy showed no abnormalities of the central nervous system nor of the thoracic or abdominal organs.

Cytogenetic studies

Chromosomal studies were carried out using orcein staining and G-banding techniques (Wang and Fedoroff, 1972). The investigations yielded the following results:

Fig. 3. Case 1, chromosomes 3 and 5 (G-banding): (a) mother, (b) sister of the propositus, (c) case 1.

Fig. 4. Case 2, chromosomes 5 and 22 (G-banding): (a) father, (b) sister of the propositus, (c) case 2.

CASE 1

Propositus: 46,XX,der(3),t(3;5)(p27;p13)mat (Fig. 3c); partial trisomy for 5p13 → pter resulting from the balanced translocation of the mother. Mother: 46,XX,t(3;5)(p27;p13) (Fig. 3a); carrier of a balanced 3/5 translocation. Father: 46,XY. Sister of the propositus: 46,XX,t(3;5)(p27;p13) (Fig. 3b); carrier of the balanced translocation. Grandparents: 46,XX; 46,XY.

CASE 2

Propositus: 46,XY,der(22),t(5;22)(q33;q13)pat (Fig. 4c); partial trisomy for 5q33 → qter resulting from the balanced translocation of the father. Father: 46,XY,t(5;22)(q33;q13) (Fig. 4a); carrier of a balanced 5/22 translocation. Mother: 46,XX. Sister of the propositus: 46,XX,t(5;22)(q33;q13) (Fig. 4b); carrier of the balanced translocation. Brother: 46,XY. Grandfather: 46,XY.

Discussion

PARTIAL TRISOMY 5P

Schinzel (1976) in his synopsis of 7 published cases from 5 different families described a trisomy 5p syndrome with severe mental retardation but without specific physical abnormalities or malformations. Opitz and Patau (1975) believed that the symptoms of the earlier published cases were too unspecific to be characterised by a specific syndrome. On the other hand, they described a child with malformations and partial trisomy from a family with carriers of a balanced 5/12 translocation. From the symptoms shown by this child, and 5 dead children with similar clinical features (but cytogenetically not investigated) from the same family, they attempted to define a trisomy 5p syndrome, features of which were normal intrauterine development, growth failure, mental retardation, hypotonia, recurrent respiratory infections, and malformations of the skull, the central nervous system, the lungs, and the kidneys. Table 1 lists the symptoms of the published cases and those of our own. Unfortunately from several patients the clinical data are scarce, but the variability of the symptoms of cases with trisomy 5p is obvious. There are, on the one hand, the patients with mental retardation only and, on the other hand, patients, who show in addition multiple malformations, as described by Opitz and Patau (1975) and Monteleone *et al.* (1976). Our first case seems to be intermediate between these extremes. A relation can be postulated between the clinical aspects and the extent of the trisomic chromosomal segment. This segment is usually region 5p14-15; in our case it was band 5p13, and in the case of Opitz and Patau (1975) and Monteleone *et al.* (1976) almost the complete short arm of chromosome No. 5 (5p12-15 and 5p11-15, respectively). The interpretation is difficult because there is no localisation of break-points in the cases investigated without banding methods. The extent of a reciprocal translocation in the balanced translocation carriers, therefore, remains uncertain, and the effect of the possible partial monosomy for the end of that chromosome, on which the 5p material is translocated is difficult to verify. Nevertheless we can state that with the increasing amount of the chromosomal segment present in a trisomic state, a defined trisomy 5p syndrome becomes more obvious, the major symptoms being normal birthweight and length, macrocephaly, psychomotor and statomotor retardation, hypotonia, facial dysmorphism involving slight mongoloid slanting of the eyes, epicanthus, depressed nasal bridge, and possibly seizures. Further delineation of the syndrome will be possible when additional information on trisomy 5p cases is available. The majority of the trisomy 5p cases including our own patient are female. Almost all cases of partial trisomy 5p have been

Table 1 Clinical findings in patients with partial trisomy 5p

Partial trisomy for 5p (trisomic segment)	Lejeune <i>et al.</i> (1964)	Laurent and Robert (1966)	de Capoa <i>et al.</i> (1967)	Noel <i>et al.</i> (1968)	Warter <i>et al.</i> (1973)	Opitz and Patau (1975)	Monte- leone <i>et al.</i> (1976)	Case 1
	p (14)15	p (14)15	~1/2p	~1/2p	~1/3p	p 14,15	p 12-15	p 11-15
Sex	♀	♀	♂	♀	♀	♀	♀	♀
Age (y)	17	11/12	1 5/12	20	8	7	4 4/12	Newborn
Gestation (w)	40	40	37			40	40-43	40
Birth weight (g)	2500	3000	3120			3500	4020	3050
Birth length (cm)							57	51
Growth failure/dystrophy	+					(+)		
Statomotor retardation			+			(+)		+
Mental retardation	+	+	+	+	+	+	+	+
Seizures			(+)	(+)	+	+	+	+
Hypotonia						+	+	+
Macro-/dolicho-/scaphocephaly		+	+			+	+	+
Facial dysmorphism:								
Mongoloid slant			+			(+)		+
Epicanthus						(+)	+	(+)
Pupillary anomalies						+	+	+
Hypertelorism	+		(+)				+	+
Depressed nasal bridge			+			+	+	+
Macroglossia			+				+	+
Dysplastic ears					(+)	+	+	(+)
Hand and foot anomalies (mainly clinodactyly)	(+)		(+)		(+)	(+)	+	(+)
Dermatoglyphs (increased ulnar loops)	(+)		(+)	(+)	(+)		(+)	(+)

diagnosed because there were sibs with 'cri-du-chat' syndrome. In the observations of Opitz and Patau (1975), Monteleone *et al.* (1976), and in our case, however, the clinical features of the child with partial trisomy were the only reason for performing a cytogenetic investigation. Children with 'cri-du-chat' syndrome were absent in these families. Comparing the symptoms of both, it seems unjustifiable to establish the trisomy 5p syndrome as a 'countertype' of the 'cri-du-chat' syndrome.

PARTIAL TRISOMY 5Q

Our second case is comparable with those reported by Ferguson-Smith *et al.* (1973) and Osztovcics and Kiss (1975). Ferguson-Smith *et al.* (1973) gave only a brief clinical description of a child with partial trisomy 5q31 → qter (and partial monosomy 2p23 → pter). Osztovcics and Kiss (1975) reported on a family with 2/5 translocation, and two children with a diagnosed partial trisomy 5q31 → qter. The clinical findings of the cases are summarized in Table 2. All patients have

Table 2 Clinical findings in patients with partial trisomy 5q

Partial trisomy for 5q (trisomic segment)	Ferguson-Smith <i>et al.</i> (1973)	Osztovcics and Kiss (1975)	Case 2
	q 31-35	q 31-35	q 33-35
Sex	♂	♀	♂
Age (y)	4	8	10/12
Gestation (w)		39	40
Birth weight (g)		2650	2460
Birth length (cm)		42	46
Growth failure/dystrophy	+	+	+
Statomotor retardation	+	+	+
Mental retardation	+	+	+
Microcephaly	+	+	+
Facial dysmorphism:			
Antimongoloid slant	+		+
Epicanthus			(+)
Strabismus		+	
Hypertelorism	+	+	+
Depressed nasal bridge			(+)
Large upper lip		(+)	+
Dysplastic ears	+	+	+
Short fingers/clinodactyly	+	+	+
Clubfeet			+
Joint limitation of hips		+	+
Hernia			+
Cardiac malformation			+

the following features in common: inborn dystrophy, growth failure, psychomotor and statomotor retardation, microcephaly, facial dysmorphism, hypertelorism, antimongoloid slanting of the eyes, slight epicanthus, strabism, large upper lip, large and dysmorphic ears, cardiac malformation, and joint limitation of the hips. Those symptoms found in patients with partial trisomy for the distal part of 5q may suggest a new clinically distinguishable syndrome, but future observations of similar cases are necessary for the exact delineation of this chromosomal aberration.

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