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Original Investigations

Partial Duplication of the Long Arm of Chromosome 5: A Case Due to Balanced Paternal Translocation and Review of the Literature

Larry A. Jones, Diane K. Jordan, Kutay Taysi*, Arnold W. Strauss, and Joseph K. Toth

The Edward Mallinckrodt Department of Pediatrics, Washington University School of Medicine, Divisions of Medical Genetics and Cardiology, St. Louis Children's Hospital, St. Louis, MO 63110, USA

Summary. A partial duplication of the distal segment of the long arm of chromosome 5 (q31→qter) was observed in an infant with congenital malformations and dysmorphic features. The phenotypically normal father had a balanced translocation between the long arm of chromosome 5 and the short arm of chromosome 9: 46,XY,t(5;9)(q31;p24).

The clinical and cytogenetic data obtained from six patients with partial duplications of two different long arm segments of chromosome 5 suggest that partial duplication of the distal long arm of chromosome 5 is associated with microcephaly, hypertelorism, epicanthus, strabismus, large upper lip, low-set, dysplastic ears, in addition to growth and psychomotor retardation. Partial duplication of the proximal part of the long arm of chromosome 5, on the other hand, is associated mainly with musculoskeletal abnormalities including muscle hypotrophy and hypotonia, scoliosis, lordosis, pectus carinatum, cubitus valgus, and genu valgum, in addition to psychomotor retardation. The dysmorphic features in this latter group include a bulging forehead, short nose, thick upper lip, low-set protruding ears and tapering, thin fingers.

Introduction

To our knowledge there have been only four previous reports of the partial duplication of long arm of chromosome 5 involving five patients. In four, the duplicated segment was limited to the distal part (Ferguson-Smith et al., 1973; Osztovics and Kiss, 1975; Zabel et al., 1978) and in one patient, to the proximal part of the long arm of chromosome 5 (Jalbert et al., 1975).

* To whom offprint requests should be sent

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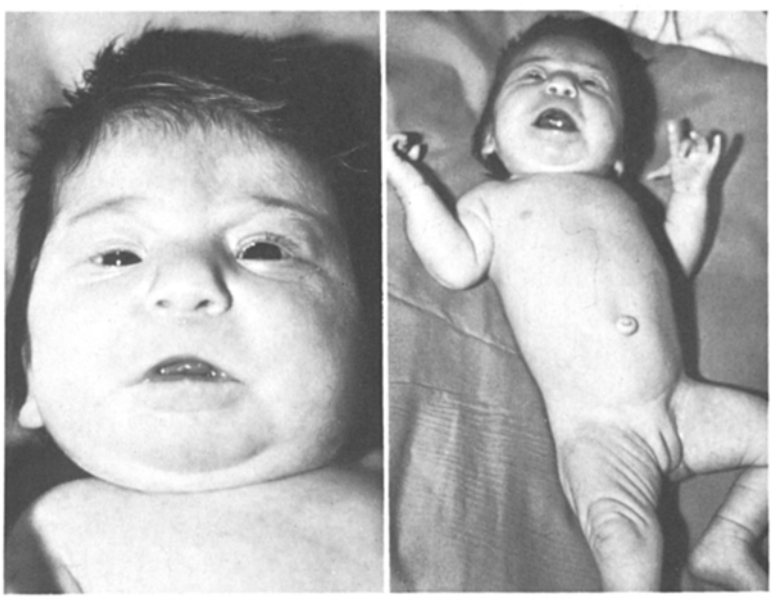
In this communication we report a further case of partial duplication of the distal segment of long arm of chromosome 5 and compare the clinical features of the patients with different duplicated segments of the long arm of chromosome 5.

Case Report

The patient, A.G., a 2-day-old white female, was the 2190 g product of a 36 week gestation, born to a 23-year-old primigravida. The pregnancy was complicated early in its course by an unspecific illness for which, after receiving a chest X-ray, the mother was treated with antibiotics. She also received another course of antibiotic treatment during the last trimester for cystitis. Decreased fetal heart rate was noted 10 min prior to the delivery, which was otherwise uncomplicated. The infant breathed spontaneously and the Apgar scores were 6 at 1 min and 8 at 5 min. The umbilical stump contained only one artery. The family history was negative for mental retardation and birth defects, and consanguinity was denied. The phenotypically normal father was 28 years old.

Physical examination revealed an active and hypotonic infant with dysmorphic features. The length was 43 cm (10th percentile), weight 2190 g (25th percentile) and head circumference 30 cm (less than 10th percentile). The head and face were remarkable for microbrachycephaly, a sloping forehead and a low frontal hairline. The palpebral fissures were short (1.2 cm bilaterally) and the nasal bridge was prominent. The inner canthal distance was 2 cm (50th percentile), the ears were low set and the mouth was carp-shaped. The upper lip was large, the philtrum was hypoplastic and the alveolar ridge was hypertrophic. Micrognathia and a short neck were also noted (Fig. 1A and B). Cardiovascular examination revealed a grade 2/6 systolic murmur at the left sternal border and an intermittent gallop rhythm. There was a periumbilical hernia. The external genitalia were normal. The left thumb was triphalangeal, hypoplastic and connected to the hand by a thin pedicle. Neurological examination showed hypotonia in the lower extremities, an incomplete Moro reflex and a poor suck. Dermatoglyphics revealed normal axial triradii, complex palmar creases and tibial arches on the hallucal areas. There were 8 whorls and 1 ulnar loop on the finger tips. The pattern on the left thumb was not discernible.



A B

Fig. 1A and B. The patient at age two months

Skeletal survey revealed only a triphalangeal thumb and the absence of the first metacarpal on the left hand.

The patient was seen again at the age of 2 months. Her weight was 2440 g (less than 3rd percentile), height 48.5 cm (less than 3rd percentile) and the head circumference 33 cm (less than 3rd percentile). She had feeding problems, and occasional cyanosis was observed when crying. The hypotonia noted initially had resolved. An alternating strabismus was noted. The liver was palpated 3 cm below the right costal margin. She had cardiomegaly with a right ventricular heave. There was a thrill and a grade 3/6 harsh pansystolic murmur at the left sternal border. The second heart sound was increased in intensity and single. ECG revealed bi-ventricular hypertrophy and right axis deviation. Chest roentgenograms demonstrated cardiomegaly with severe shunt vascularity and right atrial enlargement. Cardiac catheterization and angiocardiography revealed a large atrial septal defect, a large muscular ventricular septal defect and severe pulmonary hypertension. Pulmonary flow was five times systemic flow.

Cytogenetic Studies

Chromosome studies were performed on peripheral lymphocyte cultures of the patient and her parents. Slides were examined after G-banding using trypsin and R-banding with heat denaturation using acridine orange. The patient's modal chromosome number was 46 with extra chromosome material on the short arm of chromosome 9: karyotype 46,XX,9p+.

The karyotype of the father which revealed 46 chromosomes and a reciprocal translocation between the long arm of chromosome 5 and short arm of chromosome 9, was characterized as 46,XY,t(5;9)(5pter→5q31::9p24→9pter;9qter→9p24::5q31→5qter) (Fig. 2). The patient had inherited the derivative 9 chromosome from the father and one normal chromosome 5 from each parent, and she,

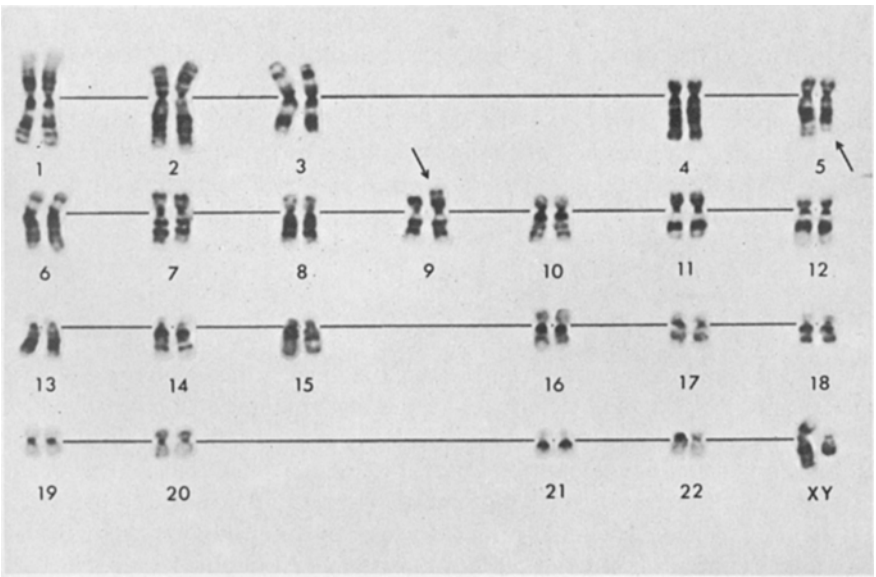


Fig. 2. Giemsa trypsin banded karyotype of the father showing the balanced translocation: 46,XY,t(5;9)(q31;p24)

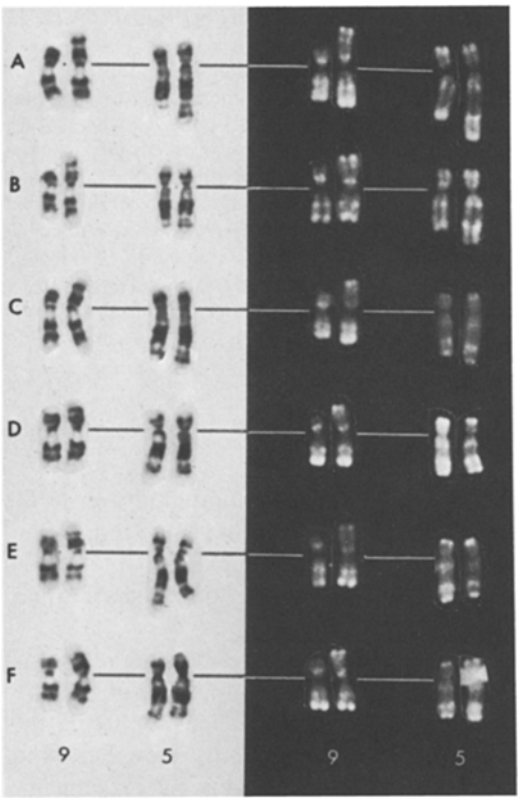


Fig. 3. G-banded (*left*) and R-banded (*right*) chromosomes 9 and 5 of the father (*A, B, C*) and of the patient (*D, E, F*) from six different cells

therefore, had duplication of the distal segment of the long arm of chromosome 5 (5q31→qter) (Fig. 3). We assumed that she must also be heterozygous for a deletion of 9p24→pter. Her karyotype can be formulated as: 46,XX,der(9),t(5;9)(q31;p24)pat, according to the Paris nomenclature. The karyotype of the mother was normal, and the other paternal family members who live in Mexico were not available for study.

Discussion

The clinical and cytogenetic findings of six patients identified as having partial duplication of 5q by banding techniques are summarized in Table 1. The subjects are divided into two groups according to their cytogenetic findings. In the first group of 5 patients, including the present patient, the duplicated segment involved the distal quarter of the long arm of chromosome 5 (distal to band q31 in four and q33 in one). The main clinical features in this group were growth and psychomotor retardation, microcephaly and certain dysmorphic features including hypertelorism, epicanthus, strabismus, large upper lip, low-set, dysplastic ears and dermatoglyphic abnormalities. The present patient had additional features

Table 1. Clinical and cytogenetic findings in six cases with partial duplication of the long arm of chromosome 5

	Ferguson-Smith et al.	Osztovics and Kiss		Zabel et al.	Present case	Jalbert et al.
		Case 1	Case 2			
Clinical features						
Age	4 yr.	8 mo.	10 mo.	8 mo.	2 days	$3^{7}/_{12}$ yr.
Sex	M	F	F	M	F	F
Maternal age (y)	26	24	29	33	23	24
Paternal age (y)	46	26	31	36	28	23
Gestation (weeks)		39	38	40	36	38–40
Birth weight (g)		2650	2700	2460	2190	2880
Birth length (cm)		42	49	46	43	
Growth/mental retardation	+/+	+/+	+/+	+/+	+/+	−/+
Craniofacial						
Microcephaly	+	+	+	+	+	−
Antimongoloid slant	+			+	−	−
Epicanthus			+		−	+
Strabismus		+	+		+	
Hypertelorism	+	+		+	−	
Prominent nasal bridge					+	+
Large upper lip		+		+	+	
Low-set/dysplastic ears	+	+	+	+	+	
Cardiac malformation			+		+	
Musculoskeletal abnormalities						
Muscle hypotrophy/ hypotonia						+/+
Scoliosis/lordosis						+/+
Spina bifida occulta						+
Pectus carinatum						+
Hip joint limitation		+		+		
Cubitus valgus/ genu valgum						+/+
Club feet				+		
Brachy/clinodactyly	+/+	+/−			+/−	
Cytogenetic findings						
Duplicated segment	5q31→qter	5q31→qter	5q31→qter	5q33→qter	5q31→qter	5q11→q22
	Distal duplication of 5q					Proximal duplication of 5q

including short palpebral fissures, hypoplastic philtrum and hypoplastic left thumb, which have not been reported previously. Some degree of clinical variability in the patients with identical duplicated segments is expected, since each patient may also have a monosomic segment for different chromosomes because of the reciprocal nature of the underlying translocations.

The clinical features of the single patient in the second group with the proximal duplicated segment of 5q (q11→q22) were different from those of the patients with partial duplication of the distal segment of chromosome 5. Although this patient had marked mental retardation, her height and head circumference were normal. The main clinical features were muscle hypotrophy and hypotonia and multiple skeletal abnormalities, which included spina bifida occulta, scoliosis, lordosis, pectus carinatum, cubitus valgus, genu valgum and pes planus. The dysmorphic features included a bulging forehead, short nose, thick upper lip, low-set, protruding ears and tapering, thin fingers.

The data presented in this paper suggest that the clinical features of duplication of the proximal and distal part of the long arm of chromosome 5 are different. Although both partial duplications are associated with psychomotor retardation, patients with distal duplication of 5q are characterized by microcephaly and certain dysmorphic features, whereas the main clinical features of duplication of proximal 5q are musculoskeletal abnormalities and different facial dysmorphism.

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References

Ferguson-Smith, M. A., Newman, B. F., Ellis, P. M., Thompson, D. M. G.: Assignment by deletion of human red cell acid phosphatase gene locus to the short arm of chromosome 2. Nature New Biol. **243**, 271—273 (1973)

Jalbert, P., Jalbert, H., Sele, B., Mouriquand, C., Malka, J., Boucharlat, J., Pison, H.: Partial trisomy for the long arm of chromosome No. 5 due to insertion and further "aneusomie de recombinaison'." J. Med. Genet. **12**, 418—423 (1975)

Osztovics, M., Kiss, P.: Familial translocation, t(2;5)(p23;q31). Clin. Genet. **8**, 112—116 (1975)

Zabel, B., Baumann, W., Gehler, J., Conrad, G.: Partial trisomy for short and long arm of chromosome No. 5. Two cases of two possible syndromes. J. Med. Genet. **15**, 143—147 (1978)

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