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Chromosome 6q deletion: Report of a new case and review of the literature

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ABSTRACT

The authors report an additional case of partial monosomy of the long arm of chromosome 6 [46,XY,del (6)(q22 → qter)]. Our patient has a large segment beyond 6q25 deleted, then severe psychomotor retardation is expected to occur.

INTRODUCTION

Deletions of the long arm of chromosome 6 are rare. To date, only 41 patients have been reported (Mikkelsen and Dyggve, 1973; Narahara *et al*., 1991; Meng *et al*., 1992; Valtat *et al*., 1992). The reported cases have involved different chromosomal regions of 6q, and the patients showed variable, multiple congenital anomalies. Twenty-two of these patients had terminal deletions of varying lengths, while the remaining ones had interstitial deletions of 6q. We report one additional case of terminal deletion of 6q and compare the clinical and cytogenetical data with the previously reported cases.

CLINICAL REPORT

The patient, a white boy, was the result of the first pregnancy of a 19-year-old mother with an unrelated 26-year-old father. He was born at term, and at the time of examination he

was 1 year and 7 months old. The family history was unremarkable. Pregnancy was uncomplicated, and labor was rapid. Birth weight was 2,850 g (3rd percentile), and length was 51 cm (5th percentile). He was born cyanotic, and Fallots tetralogy was diagnosed by echocardiography during the neonatal period.

The first genetic consultation was at the age of 3 months for congenital heart disease and facial dysmorphic features characterized by round face and large ears.

At 1 year and 7 months, his occipito-frontal head circumference was 40 cm (< -2DS), length 78 cm (< 5th percentile) and weight 8,560 g (< 5th percentile). Facial dysmorphies included round face, brachycephaly, upslanting palpebral fissures, strabismus, broad nasal bridge, large ears with simplified helix, and micrognathia (Figure 1). The palate was high and intact. The neck was short and the thorax long and narrow. A cardiac systolic murmur was heard. Genitalia were normal. There was clubbing of fingers and toes, and the distal third of the right, fifth finger was very hypoplastic. Sindactily between third and fourth toes was also observed (Figure 2). Skin showed a marked multiplication of creases in the hands and feet with generalized redundant skin. Psychomotor development was extremely delayed.

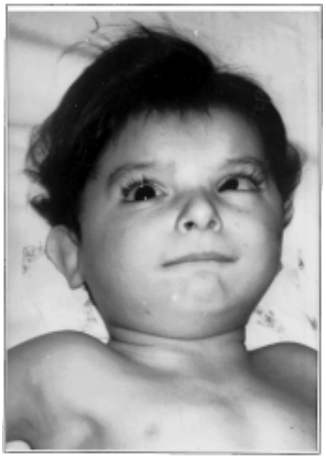

Figure 1 - The propositus at one year and 7 months.

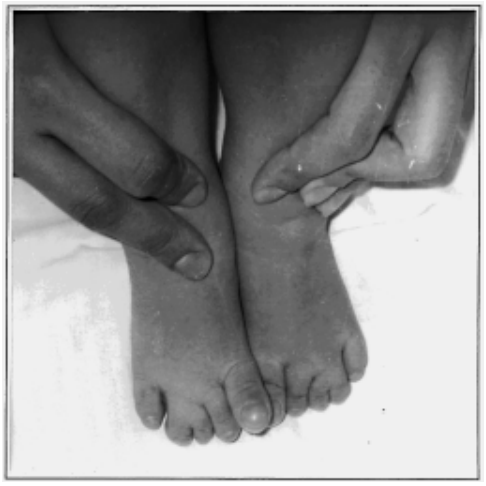

Figure 2 - Sindactily between third and fourth toes.

Ophthalmologic consultation disclosed no retinal pigmentary abnormality. A skeletal survey showed eleven pairs of ribs, scoliosis, and hypoplastic distal and media phalanges in digits 2 through 5 (Figure 3a and b). Abdominal ultrasonography and tomography disclosed no abdominal malformation.

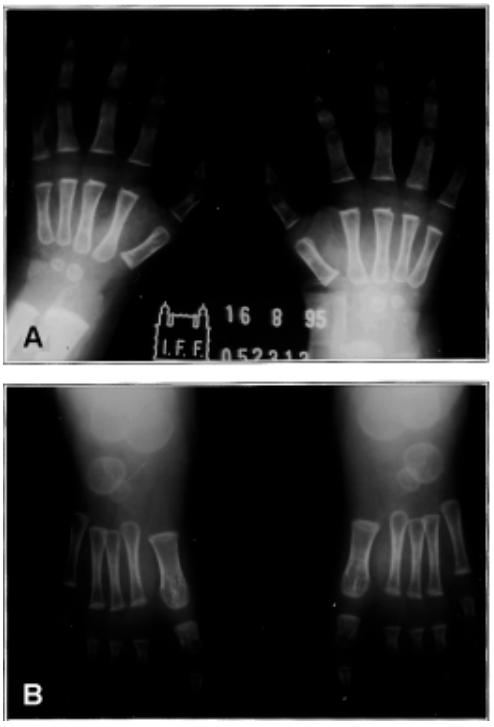

Figure 3 - a,b: Radiographs showing hypoplastic terminal phalanges of hands and feet, particularly the fifth finger and toe.

CYTOGENETIC FINDINGS

Metaphases from the proband and both parents were obtained by standard peripheral blood lymphocyte culture technique (Moorhead *et al*., 1960). For chromosome analysis, slides were stained by the trypsin-Giemsa method (Seabright, 1971). Thirty cells from each individual were examined. Proband chromosome analysis showed that each cell had part of the long arm of chromosome 6 deleted. The break occurred at 6q22 resulting in a 46,XY,del(6)(q22 → qter) karyotype (Figure 4). No chromosome abnormalities were found in the parents.

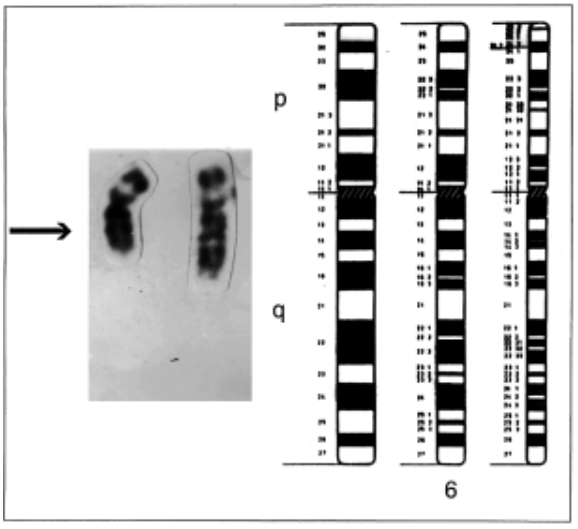

Figure 4 - Chromosome 6 showing terminal deletion of (6)(q22 → qter).

DISCUSSION

Deletions of chromosome 6q are rare. Forty-two cases with various types of 6q deletions

have been reported so far. Twenty-two patients with terminal deletions of 6q have been published (Mikkelsen and Dyggve, 1973; Milosevic and Kalicanin, 1975; Kueppers *et al*., 1977; Hagemeijer *et al*., 1977; Bartoshesky *et al*., 1978; Liberfarb *et al*., 1978; Golberg *et al*., 1980; Fryns *et al*., 1986; Rivas *et al*., 1986; Stevens *et al*., 1988; Ito *et al*., 1989; Shen-Schwarz *et al*., 1989; McLeod *et al*., 1990; Oliveira-Duarte *et al*., 1990; Krassikoff and Sekhon 1990; Narahara *et al*., 1991; Meng *et al*., 1992; Valtat *et al*., 1992), and twenty patients with interstitial deletions have also been reported (McNeal *et al*., 1977; Nakamore *et al*., *1980; Cote et al*., 1981; Schinzel, 1984; Schwartz *et al*., 1984; Young *et al*., 1985; Yamamoto *et al*., 1986; Matkins, *et al*., 1987; Slater *et al*., 1988; Glover *et al*., 1988; Lonardo *et al*., 1988; Park *et al*., 1988; Turleau *et al*., 1988; Chery *et al*., 1989; Bzduch and Lukacova, 1989; McLeod *et al*., 1990; Narahara *et al*., 1991; Valtat *et al*., 1992).

Table I summarizes the clinical and cytogenetical findings in 23 cases of terminal 6q deletion, including the present case. They have in common mental retardation, microcephaly, typical dysmorphic facial features and congenital heart defects. These clinical findings suggest the occurrence of a clinical syndrome associated with terminal 6q deletions (Young *et al*., 1985; Narahara *et al*., 1991). Some patients, like ours, had a round face and short neck (Fryns *et al*., 1986; Rivas *et al*., 1986; Narahara *et al*., 1991; Meng *et al*., 1992), and most had malformed ears (Milosevic and Kalicanin, 1975; Kueppers *et al*. 1977; Bartoshesky *et al*., 1978; Liberfarb *et al*. 1978; Steven *et al*., 1988; Ito *et al*., 1989; Shen-Schwartz *et al*., 1989; Oliveira-Duarte *et al*., 1990; Krassikoff and Sekhon, 1990; Valtat *et al*., 1992).

Table I - Clinical findings of patients with terminal 6q deletions.

Deletion	q21 → qter	q22 → qter	q23 → qter				q24 → qter	q25 → qter												q26 → qter		
Reference	a	b	c	d	e	f	g	h	i	j	k	l	m	n	o	p	q	r	s	t	u	v	w
Sex	M	M	M	M	F	M	M	M	M	M	F	F	F	M	F	F	F	F	M	M	F	M	M
IUGR	+	-	?	-	?	-	+	?	?	+	-	+	+	-	-	?	?	+	?	+	-	-	-
Growth retardation		-	?	+	-	?	+	+	+	+	-	+	+	?	-	-	?	?	+	+	+	+	-
Microcephaly	+	+	?	?	-	?	-	-	?	+	+	-	+	+	+	+	?	?	?	-	?	-	-
Mental retardation	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Hypotonia	+	+	?	?	+	?	+	+	+	+	+	+	?	-	+	+	?	?	?	+	?	+	-
Facial dysmorphia	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+
Retinal abnormality		-	?	?	?	?	-	?	?	?	?	+	-	-	?	?	?	-	-	+	+	+	-
Strabismus		+	?	?	?	?	?	+	+	?	+	?	+	+	+	+	?	?	?	-	+	+	+
Malformed ears	+	+	+	+	?	+	+	+	+	+	+	+	-	+	+	+	+	+	+	+	?	-	+
Short neck																							

		+	?	?	+	+	+	+	+	+	?	+	?	?	+	+	+	+	-	+	?	+	+
Cardiac malformation	+	+	?	+	?	+	+	+	+	+	+	-	+	-	-	-	?	+	+	+	?	+	-
Hand abnormality		+	?	+	+	+	?	-	+	+	+	+	+	+	?	?	+	-	-	-	-	+	+
Foot abnormality		+	?	?	?	?	?	+	+	+	-	?	?	?	+	-	?	-	-	-	?	+	+

References: a: Ito *et al*., 1989; b: the present patient; c: Kueppers *et al.,* 1977; d: Golberg *et al.,* 1980; e: Fryns *et al*., 1986; f: Shen-Schwarz *et al*., 1989; g: Meng *et al*., 1992; h: Mikkelsen and Diggve, 1973; i: Milosevic and Kalicanin, 1975; j: Bartoshesky *et al*., 1978; k: Lieberfarb *et al.,* 1978; l: Rivas *et al*., 1986; m and n: Stevens *et al*., 1988; o and p: Oliveira-Duarte *et al*., 1990; q: Krassikoff and Sekhon, 1990; r and s: Valtat *et al.,* 1992; t: Meng *et al*., 1992; u: Hagemeijer *et al*. 1977; v: McLeod *et al*., 1990; w: Narahara *et al*., 1991.

Ocular anomalies such as retinitis pigmentosa (McLeod *et al.,* 1990) and macular degeneration (Hagemeijer *et al*., 1977; Rivas *et al.,* 1986) have been reported in these patients. McLeod *et al*. (1990) suggested that the smallest overlapping region for retinal changes is 6q26. Deletions in this area could permit the mapping of a locus for retinitis pigmentosa (Valtat *et al*., 1992). No ocular abnormality was detected in our patient carrying a 6q22 → qter deletion, probably due to clinical variability.

Congenital heart defect was present in eleven of the terminal 6q deletion cases (Mikkelsen and Dyggve, 1973; Bartoshesky *et al*., 1978; Liberfarb *et al*., 1978; Goldberg *et al*., 1980; Stevens *et al*., 1988; Shen-Schwarz *et al*., 1989; McLeod *et al*., 1990; Meng *et al*., 1992; Valtat *et al*., 1992), including our case. Atrial septal defect was present in two patients (Bartoshesky *et al.,* 1978; McLeod *et al*., 1990) and ventricular tetralogy of Fallot (Stevens *et al*., 1988), double outlet right ventricle (Liberfarb *et al.,* 1978), partial anomalous pulmonary venous return (Goldberg *et al*., 1980), atrioventricular canal (Shen-Schwarz *et al*., 1989), triatrial heart and ventricular septal defect and patent ductus arteriosus (Meng *et al.,* 1992) were present in one patient each.

The hand anomalies described consisted of digital hypoplasia, brachydactily, clinodactily, syndactily, and camptodactily. In one case, prenatal diagnosis was made based on nuchal cyst, intrauterine growth retardation, and bilateral diaphragmatic hernia (Shen-Schwarz *et al.,* 1989). Others with nuchal cysts were diagnosed only after birth (Krassikof and Sekhon, 1990; Valtat *et al.,* 1992).

Malformations such as corpus callosum agenesia, diaphragmatic hernia (Shen-Schwarz *et al*., 1989), multicystic kidney (Milosevic and Kalicanin, 1975) and congenital hydrocephalus (Narahara *et al*., 1991) have also been described.

Previous papers showed that the most frequent deletion incompasses the 6q25 → qter region. It seems that the smallest region of overlapping for the main clinical features on 6q deletion is band q25.

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RESUMO

Os autores descrevem um novo caso de monossomia parcial do braço longo do cromossomo 6 [46,XY,del (6)(q22 → qter)]. A ocorrência de retardo psicomotor severo é esperada em

função do paciente apresentar um dos maiores segmentos deletados além da banda 6q25.

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