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

Raquel Boy 1, Márcia Mattos Gonçalves Pimentel 1, Ana Paula Hemerly 1, Maria do Perpétuo Socorro Silva 1, Ana Paula Barreiro 1, José Carlos Cabral de Almeida 2,3, and Juan Llerena 2

1 Serviço de Genética Humana, Departamento de Biologia Celular e Genética, Instituto de Biologia, UERJ, Rua São Francisco Xavier, 524 - PHLC, 2º andar, sala 205, Maracanã, 20550-013 Rio de Janeiro, RJ, Brasil. E-mail: pimentel@uerj.br. Send correspondence to M.M.G.P.

2 Centro de Genética Médica, Instituto Fernandes Figueira/ FIOCRUZ, Rio de Janeiro, RJ, Brasil.

3 Unidade de Citogenética Humana, Instituto de Biofísica Carlos Chagas Filho, UFRJ, Rio de Janeiro, RJ, Brasil.

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 Fallot’s 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 dysmorphism 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-Schwarz 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.

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<th>Deletion</th>
<th>q21→qter</th>
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<th>q24→qter</th>
<th>q25→qter</th>
<th>q26→qter</th>
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<td>Mental retardation</td>
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<td>Facial dysmophia</td>
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<tr>
<td>Malformed ears</td>
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<td>Short neck</td>
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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; LibeरfArk 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 encompasses 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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