A CASE WITH A TERMINAL DELETION OF THE LONG ARM OF CHROMOSOME 7

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Summary A malformed female infant with a *de novo* 7q terminal deletion (q32→qter) resulting from interchange between chromosome 4 and 7 was described. Her phenotype had a close resemblance to those of the previously reported cases. A further delineation of clinical features of 7q terminal deletion syndrome was attempted.

INTRODUCTION

Up to date, 25 cases with partial monosomy 7q have been reported, and 10 out of those cases showed a terminal deletion 7q32→7qter. The clinical entity associated with this deletion has firstly been suggested by Harris *et al.* (1977). The clinical pictures of this syndrome, however, still await further elucidation.

CASE REPORT

The patient was born after 41 weeks of normal gestation. She was the first child of a 26-year-old mother and a 28-year-old father. The parents were unrelated. Family history was not contributory. The delivery was induced because of weak pains, and the Apgar Scores were 5 at 1 minute. At birth, she weighed 1,880 g and measured 41.2 cm, with her head circumference 29.5 cm. The following abnormalities were noted: microcephaly, bushy eyebrows, hypertelorism, exophthalmus, divergent strabismus, blue sclera, short nose with broad nasal tip and anteverted nostrils, long and prominent philtrum, thin upper lip, low-set ears with simple and round auricles, micrognathia, irregular alveolar ridge, systolic heart murmurs, sacral dimple, long slender trunk, small pelvis and cutis marmorata (Fig. 1). Dermato-glyphic patterns on fingertips, palms and soles were obscure due to ridge hypoplasia, but palmar flexion creases were found to be deep.

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Laboratory investigations including complete blood count, urinalysis, serum electrolytes, serum thyroid hormone values and urinary aminogram showed all within normal ranges. X-ray examination revealed that the skeletal system was normal, and computerized cranial tomography scan revealed slight enlargement of

Fig. 1. Appearance of the patient. Note bushy eyebrows, hypertelorism, exophthalmus, divergent strabismus, short nose with broad nasal tip and anteverted nostrils, long and prominent philtrum, and ear malformation.

the lateral ventricles. There was no serologic evidence for intrauterine infections (congenital toxoplasmosis, rubella, or cytomegalic inclusion disease).

Feeding difficulty and cyanosis on crying had been present since birth, and she had been failing to thrive. At 5 months of age, she weighed only 2,070 g. Her psychomotor development was also severely retarded. She died of congestive heart failure at 5 months. Autopsy disclosed ventricular septal defect and patent ductus arteriosus.

CYTOGENETIC FINDINGS

Cytogenetic studies were performed on cultured peripheral blood lymphocytes from the patient and her parents. Chromosome analyses using GTG, QFQ, and RHG-banding revealed that the patient had a chromosome count of 46. A complicated rearrangement involving chromosomes 4 and 7 was present in all of the cells studied (Fig. 2). Based on the examination of the G-banding patterns of

Fig. 2. Complete G-banded karyotype of the patient. Arrows indicate rearranged chromosomes 4 and 7.

chromosomes from early metaphases (Fig. 3a), the most pertinent interpretation of this rearrangement was as follows: the segment q311→qter of a chromosome 4 was transposed to p22 of a chromosome 7, and the segment p22→pter of the chromosome 7 rejoined with the broken end of the chromosome 4 (4q311), while the segment q32→qter of the chromosome 7 was deleted. Although there could be another interpretation that the segment 7p22→pter reunited with 7q32 instead

Fig. 3. Partial karyotype of the patient. a, G-banding; b, R-banding.

Fig. 4. Schematic representation of the process through which a three-break-event have produced 7q terminal deletion.

of 4q311, R-banding analysis was more consistent with our interpretation (Fig. 3b). Consequently, the patient was thought to be monosomic for the segment 7q32→qter.

Three breakpoints (4q311, 7p22, and 7q32) were identified in this arrangement. It appeared that the abnormal karyotype in the patient would be the result of a three-break-event involving the two chromosomes. The process, through which the three-break-event would have produced the terminal 7q deletion, could be speculated as shown in Fig. 4.

DISCUSSION

The previously reported cases with partial monosomy 7q can be classified into five groups based on cytogenetic findings: (1) An interstitial deletion 7q11→7q21 or q22 in 6 cases (Valentine and Sergovich, 1977; Seabright and Lewis, 1978; Klep-de Pater *et al.*, 1979; Crawford *et al.*, 1979), (2) An interstitial deletion 7q21→7q31 or q32 in 4 cases (Ayraud *et al.*, 1976; Higginson *et al.*, 1976; Franceschini *et al.*, 1978; Klep-de Pater *et al.*, 1979), (3) A terminal deletion 7q32→7qter in 10 cases (de Grouchy *et al.*, 1968, 1974; Shokeir *et al.*, 1973; Harris *et al.*, 1977; Kousseff *et al.*, 1977; Biederman and Bowen, 1978; Bernstein *et al.*, 1980), (4) An interstitial deletion 7q32→7q34 in 3 related cases (Nielsen *et al.*, 1979) (The possibility that the interstitial deletion involved the segment 7q32→q36 was also suggested by the authors.), and (5) A terminal deletion 7q35→7qter in 2 cases (Francke, 1978; Turleau *et al.*, 1979). As for the groups 1 and 2, there are still few consistent features. On the other hand, the group 3 appears to constitute a clinically recognizable syndrome, as has been suggested by Harris *et al.* (1977).

In order to make a further delineation of the phenotypic features of the terminal deletion 7q32→7qter syndrome, clinical findings of the cases in the groups 3, 4 and 5 were summarized in Table 1. The phenotype of the present case had a close resemblance to those of the group 3 cases. Characteristic craniofacial dysmorphism for terminal deletion 7q32→7qter consisted of microcephaly, hypertelorism, broad nasal tip, short nose, anteverted nostrils, long and prominent philtrum, and ear malformations. Frontal bossing, though less frequently found, seemed to be an important feature as well. The present case, in addition, exhibited exophthalmus and thin upper lip, which were also described in three other cases, respectively. Further case studies may be desirable before determining whether these symptoms represent additional features characteristic for 7q terminal deletion. Mental retardation and growth failure were always present. In male cases, genital abnormalities were also usual findings. Low birth weight was noticed in two thirds of the cases. Congenital heart disease was observed only in the present case. This malformation apparently had an unfavorable influence upon her life. All other cases were reported to be alive, and the absence of serious internal malformations was probably the reason for their good life prognosis.

Table 1. Clinical findings of the cases with distal 7q deletions.

	Present case	Group 3 del(7) (q32→qter)	Group 4 del(7) (q32→q34 or q36)	Group 5 del(7) (q35→qter)
Low birth weight	+	6/9	0/3	2/2
Growth failure	+	9/9	1/3	2/2
Mental retardation	+	9/9	3/3	1/1
Microcephaly	+	9/9	0/3	2/2
Broad nasal tip	+	9/10	3/3	2/2
Low-set and/or malformed ears	+	8/9	2/3	2/2
Anteverted nostrils	+	8/9	0/0	2/2
Short nose	+	6/7	3/3	2/2
Abnormal genitalia in males	/	5/5	0/1	0/1
Long and prominent philtrum	+	4/5	0/0	2/2
Hypertelorism	+	5/7	3/3	0/1
Frontal bossing	—	5/10	0/3	2/2
Simian lines	—	5/8	0/3	0/1
Hypotonia	+	4/8	0/3	0/2
Exophthalmus	+	3/6	0/3	0/2
Thin upper lip	+	3/5	0/3	1/1
Micro- and/or retrognathia	+	3/6	1/3	2/2
Inguinal hernia	—	3/10	0/3	0/2
Cleft palate and/or lip	—	3/10	0/3	0/2
Congenital heart disease	+	0/10	0/3	0/2

As shown in Table 1, the groups 4 and 5 had many features in common with the group 3. The comparison of phenotypes between the three groups permitted us to suppose that most of the basic features of this syndrome could be associated with monosomy for the segment 7q35→7qter. The failure to establish more precise correlations between each feature and specific segments may be ascribed in large part to the equivocal location of the distal breakpoint of the group 4. Except for certain features, however, the phenotype of the group 4 was similar to that of the group 5. This would suggest that the monosomic segments of these two groups may be indeed overlapping and the distal breakpoint of the group 4 was more likely to be at 7q36.

Finally, it should be noted that 7q32 was the most frequent breakpoint involved in cases with partial monosomy 7q, and terminal deletions 7q32→7qter had arisen *de novo* in all cases but one (Case 1 of Bernstein *et al.*, 1980). This would lead us to assume that 7q32 may be a region very liable to break.

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