INTERSTITIAL DELETION OF THE LONG ARM OF CHROMOSOME 2: A CASE REPORT AND REVIEW OF THE LITERATURE

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Summary A girl with mental retardation and multiple anomalies was shown to have a *de novo* interstitial deletion of the long arm of chromosome 2 (2q23.3 → q24.2) by the use of high resolution banding technique. Review of the literature revealed that her clinical features resembled those of the previously reported cases with monosomy for the middle portion of 2q.

INTRODUCTION

Partial monosomy 2q is a rare chromosome aberration, and only 14 cases have been reported. The vast majority of them had an interstitial deletion of 2q. The recent technical advances leading to the improvement of banding resolution have facilitated the detection of subtle chromosome rearrangements. In this paper, we describe an additional case with a deletion of the short segment of the middle portion of 2q, which has been identified first by the high resolution banding technique. The published cases with a deletion of the long arm of chromosome 2 were reviewed.

CASE REPORT

The patient, an 8-year-old girl, was born to a 25-year-old mother and a 27-year-old father. They were unrelated and healthy. Her birth weight was 2,400 g. She had been cared for in an incubator during the first month of life. At that time, chromosome constitution was reported to be normal. Her psychomotor development was severely retarded: head control at 1 year and sitting without support at 3 years. Generalized tonic clonic convulsions had been noticed since 5 years and 2 months of age. At the age of 6 1/2 years, the body weight was 12.0 kg, length 95.0 cm and head circumference 44.0 cm (all far below the third percentile). She was found to have microcephaly with frontal bossing, thick eyebrows, antimongoloid

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Fig. 1. Present case.

palpebral fissures, left ptosis, external strabismus, congenital cataract, low-set ears, small nose with anteverted nostrils and flat nasal root, small mouth with bow-shaped upper lip, mild micrognathia, irregular dental arches and high-arched palate (Fig. 1, A and B). Hypertrichosis was noted over the forehead and the back. Thumbs were implanted proximally, and both fifth fingers were short (Fig. 1C). The first toes were bilaterally absent, the second toes were tibially incurved, and a large cleft between the first and second toes was seen on the right foot (Fig. 1D). Although no heart murmurs were audible, grade I A-V block was disclosed on electrocardiogram. Radiological examinations demonstrated open foramen parietalis, lumbar scoliosis, flat femoral head, hypoplasia of the middle and distal phalanges of the fifth fingers and absence of the proximal phalanges of the first toes (Fig. 2, A to D).

Fig. 2. Roentgenograms of the skull (A), spine and pelvis (B), hands (C) and feet (D).

Dermatoglyphic findings

Digital patterns were L^r, L^u, L^u, L^u, L^u on the right hand and W, L^u, L^u, L^u, W on the left (Fig. 3). A total finger ridge count was 114. The right and left hand formulae were $9.0.5'', 4-t'-T^u, O, O, O, L^d$ and $11.9.7.5'-t''-A^c, O, O, L^d, 0$, respectively (Fig. 3). There were supernumerary flexion creases on both thumbs and single flexion creases on both fifth fingers.

Cytogenetic findings

Cells in prometaphase and prophase were obtained from peripheral blood lymphocytes cultures, using the method of Ikeuchi and Sasaki (1979). High resolution banding analysis showed an interstitial deletion of the long arm of chromosome

Fig. 3. Dermatoglyphics of the case.

Fig. 4. Partial G-banded karyotypes. Arrows indicate breakpoints.

2 in all cells examined (Fig. 4). The karyotype was 46,XX,del (2) (pter → q23.3 : q24.2 → qter). Both parents had normal karyotypes.

Gene dosage studies

Red cell ACP, MDH and IDH activities were assayed according to the methods of Hopkinson *et al.* (1964), Bergmeyer and Bernt (1974), and Narahara *et al.* (1985), respectively. ACP₁ isozymes were separated on a starch gel as described by Harris

and Hopkinson (1976). In our case, the ACP₁ phenotype was BA, and the ACP₁ activity was normal (145.1 U/gHb; normal values of type BA (n=67), 157.3 ± 15.9 U/gHb). The MDH₁ and IDH₁ activities were also normal (MDH₁, 81.6 U/gHb; normal (n=20), 82.1 ± 12.5 U/gHb; IDH₁, 0.479 $\mu\text{mol}/\text{min}/\text{gHb}$; normal (n=100), 0.505 ± 0.103 $\mu\text{mol}/\text{min}/\text{gHb}$). The normal IDH₁ activity in our case excluded the IDH₁ locus from the region 2q23.3 $\rightarrow$ q24.2.

DISCUSSION

The published cases with partial monosomy 2q including ours differ considerably in deleted segments (Fig. 5) as well as in clinical features (Table 1). On the cytological basis, these cases can be classified into four groups: group 1 represents monosomy for the 2q1 band (case 2), group 2 monosomy for the 2q2 band (cases 1, 3, 4 and 6), group 3 monosomy for the proximal 2q3 band (cases 7, 8, 9, 10 and 11) and group 4 monosomy for the distal 2q3 band (cases 12, 13, 14 and 15). Case 5, in which a deletion involved the 2q2 and proximal 2q3 bands, is classifiable into both groups 2 and 3. Phenotypic delineation of group 1 is impossible, because no detailed clinical description of the case was given. Two cases with a terminal deletion in group 4 (cases 14 and 15) had some distinctive features such as acrocephaly and syndactyly, suggesting that the terminal deletion of 2q37 may be established as a clinical entity in future.

Fig. 5. Schematic representation depicting the segments deleted in the reported cases with partial monosomy 2q. 1: present case; 2: Antich *et al.* (1981); 3: Fryns *et al.* (1977); 4: McConnell *et al.* (1980); 5: Shabtai *et al.* (1982); 6: Moller *et al.* (1984); 7: Franceschini *et al.* (1983); 8: Buchanan *et al.* (1983); 9: Taysi *et al.* (1981); 10: Young *et al.* (1983); 11: Pai *et al.* (1983); 12: Narahara *et al.* (1985); 13: Warter *et al.* (1976); 14: Sanchez and Pantano (1984); and 15: Young *et al.* (1983).

Table 1. Clinical findings of the reported

Case No. ^a	1	2	3	4	5	6
Deleted segment	q23.3-q24.2	q12-q14	q21-q24	q22-q31	q23-q24	q24.2-q3105
Sex	F	M	F	F	F	F
Age at diagnosis	6 y	Newborn	Newborn	Newborn	20 y	4 y
Birth weight	2,400 g	ND	2,500 g	1,500 g	2,930 g	ND
Mental retardation	+	ND	+	+	+	+
Growth failure	+	?	?	?	+	+
Microcephaly	+	ND	—	Meningo-	—	+
Macrocephaly	—	ND	+	myelocele	—	—
Low-set/or malformed ears	+/-	+/+	ND ^b	+/+	+/+	+/+
Microphthalmia	—	ND	+	ND	+	—
Ptosis	+	ND	+	+	+	—
Cataract	+	ND	+	ND	+	—
Corneal opacity	—	ND	+	ND	ND	—
Antimongoloid slanting of the eyes	+	ND	ND	ND	+	+
Frontal bossing	+	+	+	+	ND	ND
Small upturned nose	+	ND	+	ND	+	+
Prominent nose	—	ND	—	ND	—	—
Cleft lip/or palate	high-arched	+	+	+	+	—
Microstomia	+	ND	+	ND	ND	ND
Macrostomia	—	ND	—	ND	ND	ND
Micrognathia	—	+	+	+	ND	—
Defective dentition	+	?	?	?	+	ND
Short neck	—	+	+	ND	ND	ND
Scoliosis	+	ND	ND	+	+	+
Cardiac defects	—	Murmur(+)	PDA	PTA ^c	Murmur(+)	ND
Hypoplastic nipples	—	ND	ND	+	+	ND
Flexion deformity of the fingers	—	+	+	+	+	+
Arachnodactyly	—	ND	+	ND	+	+
Large cleft between the 1st and 2nd toes	—	ND	+	+	+	+
Prominent calcanei	—	ND	ND	+	+	ND
Pes equinovarus	—	ND	ND	ND	ND	ND
Syndactyly of the fingers or toes	—	ND	—	—	—	—

^a The same numbers as in Fig. 4, ^b not described, ^c persistent truncus arteriosus, ^d coarctation of the aorta.

cases with a interstitial deletion of 2q.

7	8	9	10	11	12	13	14	15
q31-q33	q31-q33	q31-q33	q31-q33	q32(q31-q33)	q33.3-q35	q34-q36	q35-qter	q36-qter
F	F	F	M	F	F	F	F	F
11 y	Newborn	7 y	4 m	3 y	4 y	6 y	Newborn	8 m
ND	2,300 g	2,700 g	2,580 g	2,060 g	3,000 g	2,800 g	2,100 g	2,300 g
+	+	+	+	+	+	-	+	+
+	?	+	+	+	-	+	?	+
ND	+	+	ND	+	-	+	+	+
ND	-	-	ND	-	-	-	-	-
ND	ND/+	+/+	+/+	ND/-	-	+/+	+/+	+/+
+	+	-	+	ND	-	-	-	-
+	+	+	+	ND	-	-	-	-
-	-	-	-	ND	-	-	-	-
ND	+	ND	+	ND	-	-	-	-
+	ND	ND	ND	ND	-	-	+	+
ND	+	+	ND	+	-	ND	-	-
-	-	-	-	+	-	+	+	+
+	+	+	+	-	-	-	-	-
+	+	ND	ND	ND	-	-	high-arched	+
ND	+	ND	ND	-	-	-	-	ND
ND	-	ND	ND	+	-	+	+	ND
+	+	ND	+	+	-	ND	+	ND
ND	?	ND	?	ND	-	+	?	ND
ND	ND	ND	ND	+	-	-	ND	ND
ND	ND	ND	ND	ND	-	-	ND	ND
ND	CoA ^d +ASD	PS+PDA	-	ND	-	ASD	ND	ND
ND	ND	ND	ND	ND	-	ND	ND	inverted
+	+	+	ND	+	-	-	ND	ND
ND	+	ND	ND	Brachydactyly	-	-	ND	+
ND	+	+	ND	+	-	ND	ND	ND
ND	ND	ND	ND	ND	-	ND	ND	ND
ND	+	ND	+	+	-	-	ND	ND
+	-	-	+	-	-	-	+	+

Intriguingly, phenotypes of ten cases in groups 2 and 3 resembled each other. Clinical features shared by the majority of them included mental retardation, growth failure, microcephaly, low-set ears, ptosis, antimongoloid slanting of eyes, frontal bossing, micrognathia, cleft palate, cardiac defect, flexion deformity of fingers, arachnodactyly and large cleft between the first and second toes. On the other hand, cataract, small upturned nose, microstomia, scoliosis and prominent calcanei were more frequently observed in group 2, while microphthalmia, prominent nose, macrostomia, syndactyly and pes equinovarus were more frequently seen in group 3. The fact that all cases in the two groups had large cleft between the first and second toes in common indicates that a deletion of the segment 2q24.2→q31 may be related to this abnormality.

The phenotypic similarity between groups 2 and 3 in spite of the differences in the location and extent of deletions involved is difficult to explain. It may result either from the misinterpretations of the breakpoints in some cases in group 3 or from the existence of similar genetic materials both in the distal 2q2 and in the proximal 2q3 regions. The recent gene mapping data, however, make the latter explanation unlikely (HGM 7, 1983).

It should be noted that many clinical features seen in cases with monosomy for the middle portion of 2q (2q2 and proximal 2q3) are nonspecific. Further case reports are required to establish whether this chromosome abnormality constitutes a clinically recognizable syndrome.

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