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Case Report

INTERSTITIAL DELETION OF THE SHORT ARM OF CHROMOSOME 10: REPORT OF A CASE AND REVIEW OF THE LITERATURE

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Summary The fifth patient with an interstitial deletion of the short arm of chromosome 10 is described. She showed most of the features observed in other known patients at age 20, including psychomotor retardation, distinct facial dysmorphism, abnormally shaped skull and cardiac malformation, while she did not show any growth retardation. The elevation of serum IgG level was observed from age 15, but she did not show DiGeorge syndrome. These differences would be explained by the differences in the amount of deleted segments using high resolution chromosome banding and molecular methods.

Key Words chromosome 10, short arm deletion, growth retardation, hypergammaglobulinemia, valproic acid

INTRODUCTION

Since the original observation by Elliot *et al.* (1970), about 20 patients with *de novo* partial deletion of chromosome 10p have been described. To date, there have been at least four patients reported to show an interstitial deletion of 10p (Juberg *et al.*, 1981; Danesino *et al.*, 1984; Obregon *et al.*, 1992). We report an additional case with an interstitial deletion of the short arm of chromosome 10.

CASE REPORT

The patient, a 20-year-old female, is the second child of healthy unrelated parents. The father and mother of the child at the time of birth were 29 and 25

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years old respectively. She was born at 42 weeks of uncomplicated gestation and her birth weight was 3,200 g. Family history was unremarkable. Her psychomotor development was retarded. It took 5 months for the acquisition of head control, 1 year and 8 months for walking alone. At age 7, a heart murmur was noticed and she was diagnosed as having an atrial septal defect for which she underwent surgery. At age 15, she had tonic convulsions and electroencephalogram (EEG) showed diffuse spike-waves at intermittent photo-stimulation. After valproic acid was started based on a diagnosis of epilepsy, convulsions were controlled and EEG findings normalized.

The major clinical features at age 20 included mild psychomotor retardation without growth retardation (height 157 cm, body weight 61 kg at age 20), downslanted palpebral fissures, ptosis, epichanthus, depressed nasal bridge, anteverted nostrils, micrognathia and small dysplastic ears. A CT scan of the head showed diffuse cortical atrophy and ventricular dilatation. Urinalysis and renal ultrasound revealed no abnormality. Laboratory investigations were grossly normal, including serum calcium concentration, parathyroid hormone level, IgA, IgM, IgG2, IgG3, IgG4 and lymphocyte responses to phytohemagglutinin and concanavalin-A, while elevation of serum IgG and IgG1 levels persisted from age 15 (IgG 2,467 mg/dl, IgG1 1,360 mg/dl at age 20).

CYTOGENETIC STUDY

Chromosome analysis of peripheral blood cells using G-banding showed an interstitial deletion of 10p11 to p13. The karyotype was 46,XX,del(10)(p11p13). We could not detect more precise breakpoints with high resolution G-banding technique (Ikeuchi, 1984). The deletion seemed to be 10p11.21 to p12.32 or 10p11.23 to p13 (Fig. 1). Her parents' karyotypes were normal.

DISCUSSION

We are aware of 22 patients with a partial deletion of the short arm of chromosome 10 (Elliot *et al.*, 1970; Juberg *et al.*, 1981; Oka *et al.*, 1983; Danesino *et al.*, 1984; Elstner *et al.*, 1984; Koenig *et al.*, 1985; Greenberg *et al.*, 1986; Monaco *et al.*, 1991; Kinoshita *et al.*, 1992; Obregon *et al.*, 1992; Shapira *et al.*, 1994). In 21 patients the imbalance was *de novo*: terminal deletion was found in 17 patients and interstitial deletion in four. One patient was derived from maternal reciprocal translocation (Genick *et al.*, 1983).

Table 1 shows a review of the clinical features of the patients with an interstitial deletion of 10p, including the present case, and a comparison with those of patients with 10p terminal deletion at the breakpoint p13 or p14. In all the 10p- cases, the skull shape was always abnormal with a prominent forehead. More than half of the patients had specific ocular anomalies, including downslanted palpe-

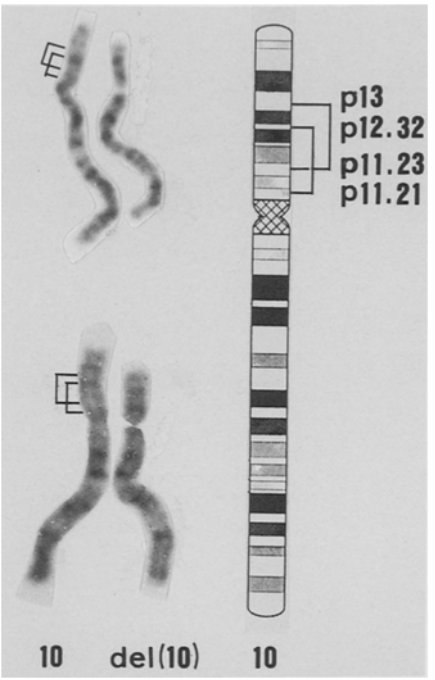

Fig. 1. Partial karyotype with GTG banding. The deleted chromosome 10 is on the right. Idiograms of normal and possible deletion patterns are shown.

bral fissures, epicanthal folds, hypertelorism and ptosis. In general, the nasal bridge was low and nostrils anteverted. Micrognathia and dysplastic ears were common features. Extremities showed heterogeneous abnormalities, including syndactyly, preaxial polydactyly, club hand and feet, clinodactyly, broad or proximally implanted thumbs, and hypoplastic distal phalanges. Half of the patients had congenital heart disease which was the major cause of death within the first months of life. Urinary tract anomalies were found in more than one third of the patients, which showed either aplastic, hypoplastic or dysplastic kidneys, hydronephrosis, duplicated ureters and urethral stenosis. Dilatation of cerebral ventricles and hypoplasia of brainstem, cerebellum or olfactory bulbs were documented in some patients. These pathological findings could be the cause of psychomotor delay and hearing disability, while there have not been reported the symptoms such as cerebeller ataxia or smelling disorder.

Elstner *et al.* (1984) suggested that monosomy of chromosomal material in 10p13 band might be what was necessary to produce the recognizable craniofacial features. We could not find clear-cut distinguishable features between interstitial deletion and terminal deletion from p13, both of which had a deletion of p13. However, terminal deletion from p14, which did not have a deletion of p13 by G-banding technique, also showed no clear-cut distinguishable feature from the

Table 1. Clinical features of partial deletion 10p.

Breakpoints	Interstitial deletion (a)						Terminal deletion (b)		Unknown (c)	Total
	1 p11p15	2 p12p14	3 p11.2p13	4 p11p13	Present case p11.21p12.32 or p11.23p13	Subtotal	p13	p14		
De novo	+	+	+	+	+	5/5	12/13	4/4	+	22/23
Sex	M	M	F	M	F	2F/3M	2F/11M	1F/3M	F	6F/17M
Age at evaluation	at birth	at birth	11 mo	at birth	20 yr					
Parental age						mean age	mean age	mean age		mean age
Maternal	19	34	28	34	25	28.0	25.9	24.0	27	25.9
Paternal	20	35	32	31	29	29.4	32.4	26.8	34	29.5
Small for gestational age	—	+	—	—	—	1/5	1/13	2/4	+	5/23
Phenotypic features										
Craniofacial										
Abnormally shaped skull	—	+	+	+	+	3/5	12/13	4/4	+	20/23
Down slanted palpebral fissures	+	—	—	+	+	3/5	11/13	2/4	—	16/23
Epichanthal folds	+	+	—	+	+	4/5	6/13	4/4	—	14/23
Ptosis	+	—	—	+	+	3/5	7/13	2/4	—	12/23
Low nasal root or bridge	+	+	—	—	+	3/5	10/13	2/4	+	16/23
Anteverted nostril	—	+	—	—	+	2/5	7/13	2/4	+	12/23
Cleft or high-arched palate	—	—	+	—	—	1/5	5/13	1/4	-	7/23
Micrognathia	+	+	+	+	+	5/5	9/13	4/4	—	19/23
Small, dysplastic ears	+	+	+	+	+	5/5	13/13	4/4		22/23
Trunk and extremities										
Wide-spaced nipples	—	—	—	+	—	1/5	8/13	1/4	—	11/23
Congenital heart disease	—	+	+	+	+	4/5	6/13	1/4	+	12/23
Urinary tract anomalies	—	+	—	+	—	2/5	5/13	2/4	+	10/23
Anomalies of hand and feet	—	+	+	+	—	3/5	10/13	3/4	+	17/23
Growth and development										
Growth retardation	D	D	+	+	—	2/3	10/11	3/4	D	15/18
Psychomotor retardation	D	D	+	+	+	3/3	9/9	4/4	D	16/16
Neurologic										
Convulsion	—	+	—	—	+	2/5	4/13	3/4	—	9/23
Ventricular dilatation/cortical atrophy	—	—	+	NA	+	2/3	1/4	2/2	+	6/10
Aplasia of olfactory bulb	—	+	NA	NA	NA	1/2	2/2	2/2	+	6/7
Hearing problem	D	D	NA	NA	—	0/1	2/2	2/2	D	4/5

Symbols used are: +, present; —, absent; D, patients died before assessment; NA, not applicable. (a) 1, Juberg *et al.*, 1981; 2, Danesino *et al.*, 1984; 3, 4, Obregon *et al.*, 1992. (b) Cited from the data by Oka *et al.*, 1983; Elstner *et al.*, 1984; Koenig *et al.*, 1985; Greenberg *et al.*, 1986; Monaco *et al.*, 1991; Kinoshita *et al.*, 1992; and Shapira *et al.*, 1994. (c) Elliot *et al.*, 1970.

others (Table 1). Our patient did not show any growth retardation but only manifested mild psychomotor retardation, while most patients had both kinds of retardations. Although the responsible region is unclear, its effect might work mainly on growth after birth, because only a few cases have intrauterine growth retardation. To clarify the genotype-phenotype correlation of the 10p- cases, it is necessary to perform more precise cytogenetical and molecular analyses at varied segments on the newly diagnosed cases and also on the reported cases.

Some patients with deletion of 10p had evidence of partial DiGeorge syndrome (DGS) (Koenig *et al.*, 1985; Monaco *et al.*, 1991; Obregon *et al.*, 1992). DGS is a heterogeneous entity in which thymic and parathyroid aplasia or hypoplasia, cardiac malformations, and dysmorphic features are manifested in different combinations and expressivity. Our patient had dysmorphic features and congenital heart disease, but she did not have hypocalcemia and the characteristic immunological abnormalities.

The elevation of the serum IgG level in our patient has been observed from age 15, at the age when valproic acid therapy was started. The relation between antiepileptic drugs and serum immunoglobulin levels has been reported (Lenti *et al.*, 1991), but the relation between hypergammaglobulinemia and valproic acid is unclear. In future, careful observation of the immunoglobulin levels after cessation of valproic acid treatment should be undertaken. This is important in order to establish whether the hypergammaglobulinemia is either a side effect of valproic acid or a genetic effect.

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