Jpn. J. Human Genet. **36**, 149–153, 1991

DE NOVO INTERSTITIAL DELETION OF 4q[46,XX,del(4)(q27q28.2)] WITH INTACT BLOOD GROUP-MN LOCUS, CONFINING ITS LOCUS TO 4q28.2-4q31.1

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Summary We report a malformed female infant with *de novo* interstitial deletion of 4q[46,XX,del(4)(q27q28.2)]. The MN blood type analysis of the family members showed that the patient had an intact blood group-MN locus. The locus of the gene responsible for the MN antigen activity is confined to a 4q28.2-4q31.1 segment on the basis of the result of this patient and the previous mapping data.

Key Words interstitial deletion of 4q, blood group-MN locus, glycophorin A, gene mapping

INTRODUCTION

An interstitial deletion of the middle portion of 4q is rare. There have been, to our knowledge, only 3 reported cases of an interstitial deletion involving the 4q28 band (Serville and Broustet, 1977; Mitchell *et al.*, 1981; Torrado *et al.*, 1982). The blood group-MN locus has been assigned to 4q28-4q31.1 (Divelbiss *et al.*, 1989). We describe here a malformed infant with an interstitial deletion of 4q27-4q28.2 and the intact blood group-MN locus.

CASE REPORT

The patient is the third child of a 41-year-old father and a 35-year-old mother, who are both healthy and nonconsanguinous. A 3-year-old elder brother is healthy and not malformed, but the second child was delivered as a stillbirth at the 36th week of pregnancy. The patient was born at 35th week of gestation by cesarean section because of breech presentation. Her birth weight was 2,580 g, length 43 cm and head circumference (OFC) 33 cm. She was complicated with neonatal asphyxia and referred to the neonatal intensive care unit of our medical center.

Received December 9, 1990; Accepted December 22, 1990.

The following anomalies were noticed: a narrow and hirsutulous forehead, hypertelorism, downward slanting of palpebral fissures, a suddle nose, a high-arched narrow palate, retrognathia with a pointed chin, large ears, a wide neck with redundant skin, wide-set nipples and hypoplastic nails (Fig. 1). Ventricular septal defect was noticed at birth by echocardiography, but it was spontaneously closed by age 9 month. Her developmental milestones were moderately retarded: head control at 5 months, sitting unsupported at 8 months and crawling at 11 months.

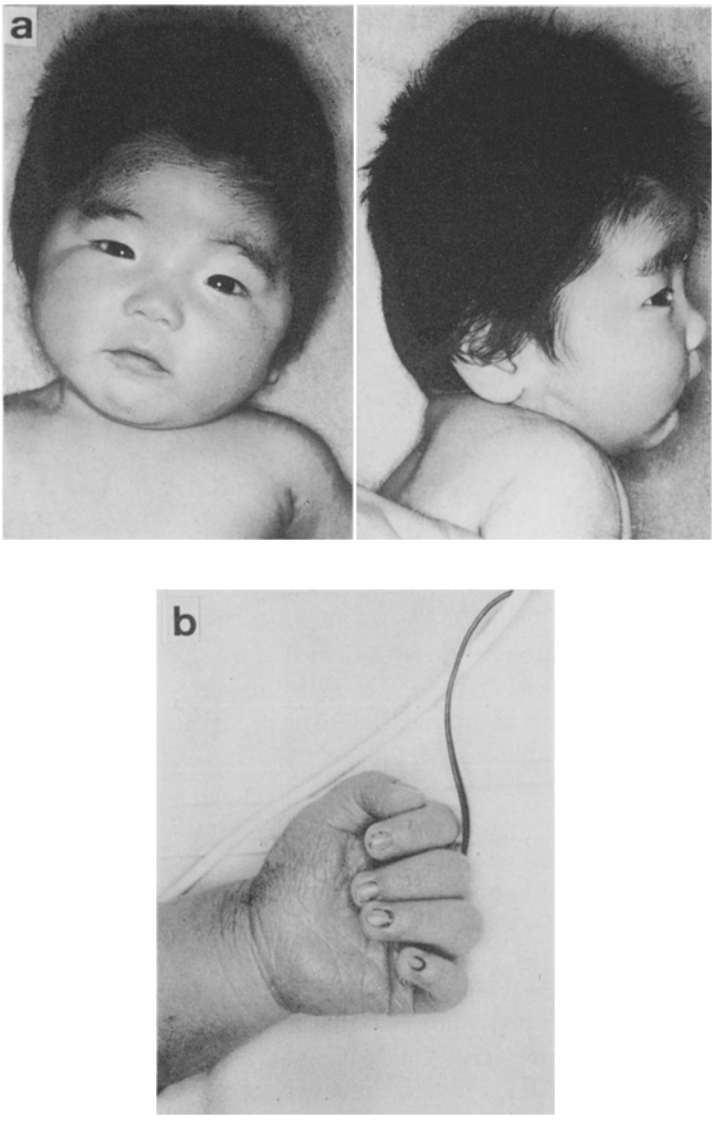

Fig. 1. (a) The patient at age 11 months. (b) Hypoplastic nails of the left fingers.

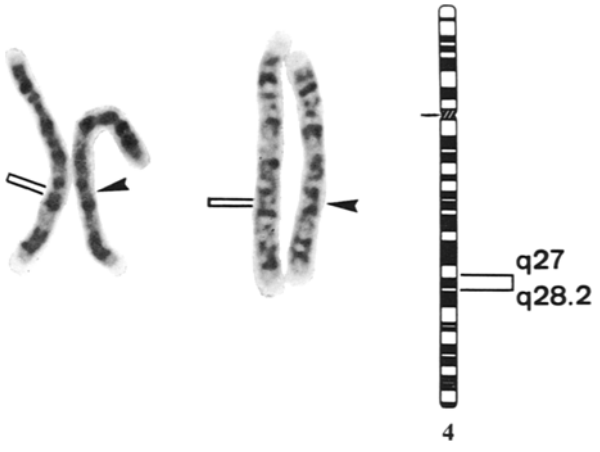

Fig. 2. High-resolution G-banded chromosomes 4 of the patient. Chromosome 4 on the right shows a deletion of bands 4q27 through 28.2.

Chromosome preparations were obtained from 3-day cultures of peripheral blood lymphocytes. Standard trypsin G-banding study showed imbalance of 4q. Prometaphase plates at the 850-band stage were collected, and chromosomes were GTG-banded. Special attention was focused on the chromosome 4 pairs. The patient had an interstitial deletion of 4q involving a segment from a distal part of band q27 to a proximal part of q28.2 (Fig. 2). The parents' chromosomes were normal. Thus, the karyotype of the patient was interpreted as 46,XX,del(4)(q27-q28.2) *de novo*.

MN blood types of the patient and her parents were analyzed by the saline method. The genotype of the patient was MN, the father MN and the mother MM, indicating the intact blood group-MN locus in the patient.

DISCUSSION

An interstitial deletion of the middle portion of 4q involving the 4q28 band has been reported only in 3 cases (Servilleand Broustet, 1977; Torrado *et al.*, 1982; Mitchell *et al.*, 1981). Deleted segments of these 3 cases varied: 4q24-4q32 in Serville and Broustet (1977), 4q27-4q31 in Torrado *et al.* (1982) and 4q27-4q31.22 in Mitchell *et al.* (1981). The present case has an interstitial deletion of 4q27-4q28.2, which is the smallest deletion of the long arm of chromosome 4. A case of Serville and Broustet (1977) had a larger deletion and the clinical findings quite differ from those of our case. Comparison of the clinical manifestations in the other 2 cases of 4q− with those in our case is shown in Table 1. Common manifestations among the 3 patients are not observed except for micrognathia, hypoplastic nails and mental retardation. These different phenotypes are likely due to differencies of their deleted regions.

Table 1. Comparison of clinical data of patients with interstitial deletion at the middle portion of 4q.

	Mitchell *et al.* (1981)	Torrado *et al.* (1982)	Present case
Deleted segments	q27-q31.22	q27-q31	q27-q28.2
Age (years)	2 6/12	11	11/12
Sex	Female	Male	Female
Maternal/paternal age (years)	31/32	21/27	35/41
Birth weight (g)/Gestational age (weeks)	2,260/38	3,100/40	2,580/35
Mental retardation (IQ)	severe	moderate (60)	moderate
Growth failure	+	+	−
Hypotonia	+		−
Brachycephaly		+	−
Large anterior fontanel	+		−
Narrow and hirsutulous forehead			+
Flat occiput	+		−
Prominent mid-face	+		−
Facial asymmetry		+	−
Prominent supraorbital ridges	+	+	−
Shallow orbital ridges		+	−
Down-slanted palpebral fissures	+		+
Epicanthus	+		−
Hypertelorism	+		+
Ptosis of eyelis	+		−
Deviated nose		+	−
Suddle nose			+
Depressed nasal bridge	+		−
Long philtrum		+	−
Small mouth		+	−
Micro-/retrognathia	+	+	+
Irregular placement of teeth		+	−
High-arched palate		+	+
Wide neck with redundant skin			+
Low posterior hair-line		+	−
Ears	small	small	large
Low-set ears	+	+	−
Hypoplastic helices	+		−
Posteriorly rotated ears		+	−
Widely spaced nipples		+	+
Hypoplastic nails	+	+	+
5th-finger clinodactyly	+		−
Simian creases	+	+	−
Pes valgus	+		−
Small testes		+	
Ventricular septal defect	+	−	+

MN blood type antigen activity is derived from the major sialoglycoprotein on the erythrocyte membrane, *i.e.*, glycophorin A (GYPA). The GYPA gene has been mapped by various techniques to 4q28-4q31 (Mattei *et al.*, 1987). Divelbiss *et al.* (1989) refined on the physical location of the gene to 4q28-4q31.1, based on the results of *in situ* hybridization study on a malformed patient with an apparently balanced translocation between 2q14.2 and 4q31.1. The MN blood type analysis of the present family showed MN in the father, MM in the mother and MN in the patient. These findings indicate that the blood group-MN locus is intact in the patient. Since the patient has an interstitial deletion of 4q27-4q28.2, the MN locus does not exist in this region. Thus, the blood group-MN locus is confined to 4q28.2-4q31.1.

Acknowledgments We are grateful to Prof. Norio Niikawa (Department of Human Genetics, Nagasaki University School of Medicine) for his helpful advice.

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