Jpn J Human Genet 38, 319–328, 1993

Case Report

PARTIAL MONOSOMY 5p AND PARTIAL TRISOMY 5q DUE TO PATERNAL PERICENTRIC INVERSION OF CHROMOSOME 5

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Summary A male infant with partial monosomy 5p and partial trisomy 5q due to paternal pericentric inversion of chromosome 5 (46,XY,rec(5), dup q,inv(5)(p15.1q35.1)pat) is reported together with the oral findings. The phenotype was chiefly the cri-du-chat syndrome. Severe retardation of mental and motor development, microencephaly, cardiac malformation, crying and facial appearance unique to the cri-du-chat syndrome were observed. Perioral and intraoral findings included thin upper lip, down-turning corners of mouth, micrognathia, shallow palate, and cleft of soft palate. Anterior deciduous teeth were small and canine deciduous teeth were conic. The row of deciduous teeth showed a flat arch-like shape that was very wide but short in length. No abnormality was noted in the number of deciduous teeth or the timing of eruption.

Key Words pericentric inversion, recombinant chromosome, double aneuploidy, partial monosomy 5p, partial trisomy 5q

INTRODUCTION

Partial monosomy 5p and partial trisomy 5q originating from the parental pericentric inversion of chromosome 5 is a rare and complex chromosomal aberration, and only nine cases, namely, eight cases in six families (Faed *et al.*, 1972; Ebbin *et al.*, 1979; Beemer *et al.*, 1984; Miyazaki *et al.*, 1985; Schroeder *et al.*, 1986; Sonoda *et al.*, 1989) and one fetus (Martin *et al.*, 1988), have been reported since this condition was first reported by Faed *et al.* in 1972.

The authors encountered a male infant with partial monosomy 5p and partial trisomy 5q due to paternal pericentric inversion of chromosome 5. Detailed oral findings are reported.

Received March 4, 1993; Revised version accepted June 24, 1993.

CASE REPORT

The proband was a male infant born on February 4, 1988 by forceps delivery after 40 weeks of gestation. Nothing special was noted during the course of pregnancy. The body weight at birth was 2,580 g. The infant's father was 44 years old and the mother 25 at the birth of the infant. The infant was admitted to the NICU (newborn intensive care unit) of our university because of dyspnea and cardiac murmur. He was referred to us and examined for the first time on the 11th day after birth because of feeding difficulty.

Family history. The pedigree of the family is shown in Fig. 1. I-7, II-5, II-10, and III-1 were reported to be mentally retarded, and to have had a countenance similar to the present patient. II-10 died at the age of five years, and III-1 at the age of eight months.

The father (II-7) and his divorced wife (II-6) had a still-born girl (III-3) who had anencephaly, round face, ocular hypotelorism, flat nasal crest, median upper lip cleft, cleft palate, low-set ear, and simian line (Fig. 2). The karyotype was not tested.

Clinical symptoms. Microencephaly, round face, ocular hypertelorism, epicanthus, slanted-away ocular cleft, wide and high nasal crest, thin upper lip, down-turning corners of mouth, low-set ear, auricular fossula, and micrognathia were observed (Fig. 3). The fifth finger was inflexed. Concerning the dermatoglyphics, whorls were predominant in the fingerprint, and distant axial triradius was observed. Simian line was not observed. His cry was high-pitched and monotonous.

The infant had a congenital cardiac malformation including ventricular septal

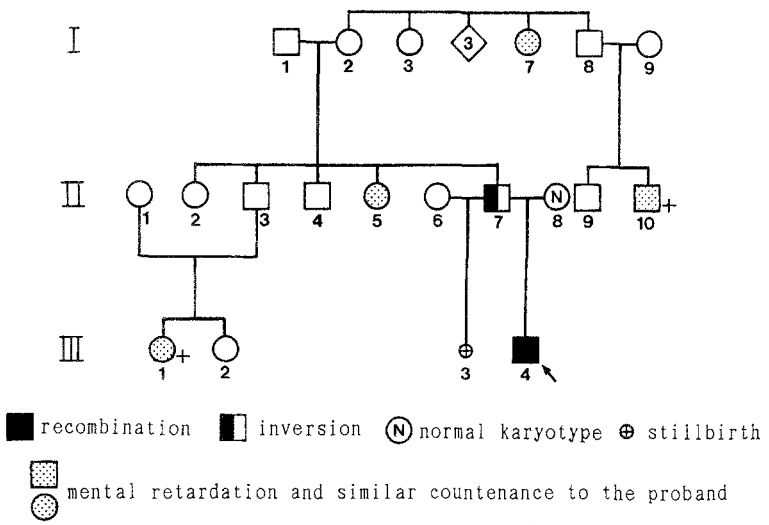


Fig. 1. Pedigree of family.

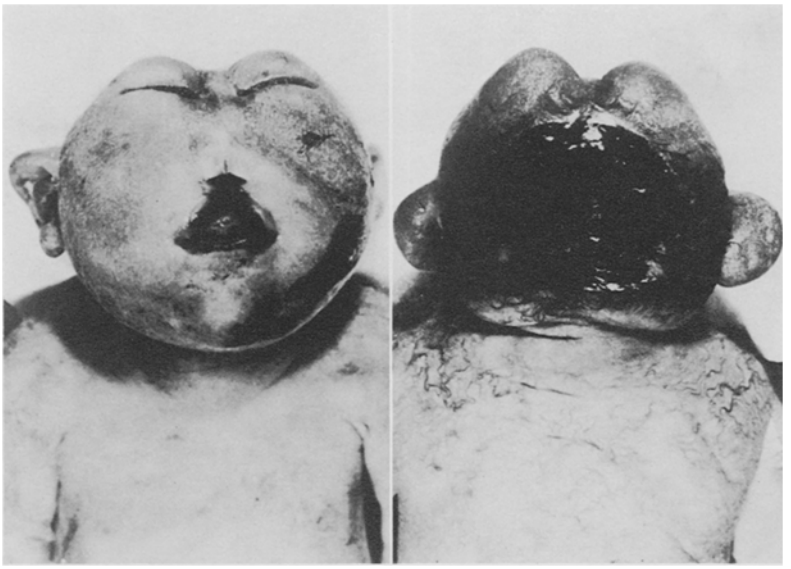


Fig. 2. Still-born sister of the proband born to the father and his divorced wife.

defect and patent ductus arteriosus. Ventricular septal defect spontaneously closed at the age of one year.

Oral observation (Fig. 4) revealed that the palate was shallow, and the depth from the occlusal plane to the deepest region of the hard palate was 10.0, 11.0, and 11.5 mm at the ages of one, two, and three, respectively. Thus, it was less than −2 S.D. (mean value from the report of Nagaoka, 1989). In addition, a relatively narrow soft palate cleft was observed.

Teeth (Table 1) and the row of teeth (Table 2) were examined after the eruption of deciduous teeth. The anterior deciduous teeth were small, and the canine deciduous teeth were conic. The maxillary dental arch demonstrated a flat arch-like shape that was very wide but short in length (Fig. 5). The number of teeth was normal, and no excess or defect of deciduous teeth was observed. No abnormality was noted during the period of eruption.

History of development. The respective body weights at birth and the ages of one month, six months, one year, one and a half years, two years, and three years were 2,580, 3,060, 4,440, 5,840, 7,500, 8,650, and 9,800 g. Thus, body weight was always −2 S.D. or less.

Developmental assessment conducted at the age of one year and five months by the Enjoji technique (Enjoji *et al.*, 1977) showed him to be at the seven-month level. According to the examination conducted at the age of two years and four months by the technique of Tsumori and Inage (1961), his developmental age was nine months and D.Q. 32. According to the KIDS (Kinder infant development scale) (Miyake *et al.*, 1989) conducted at the age of three years, his developmental

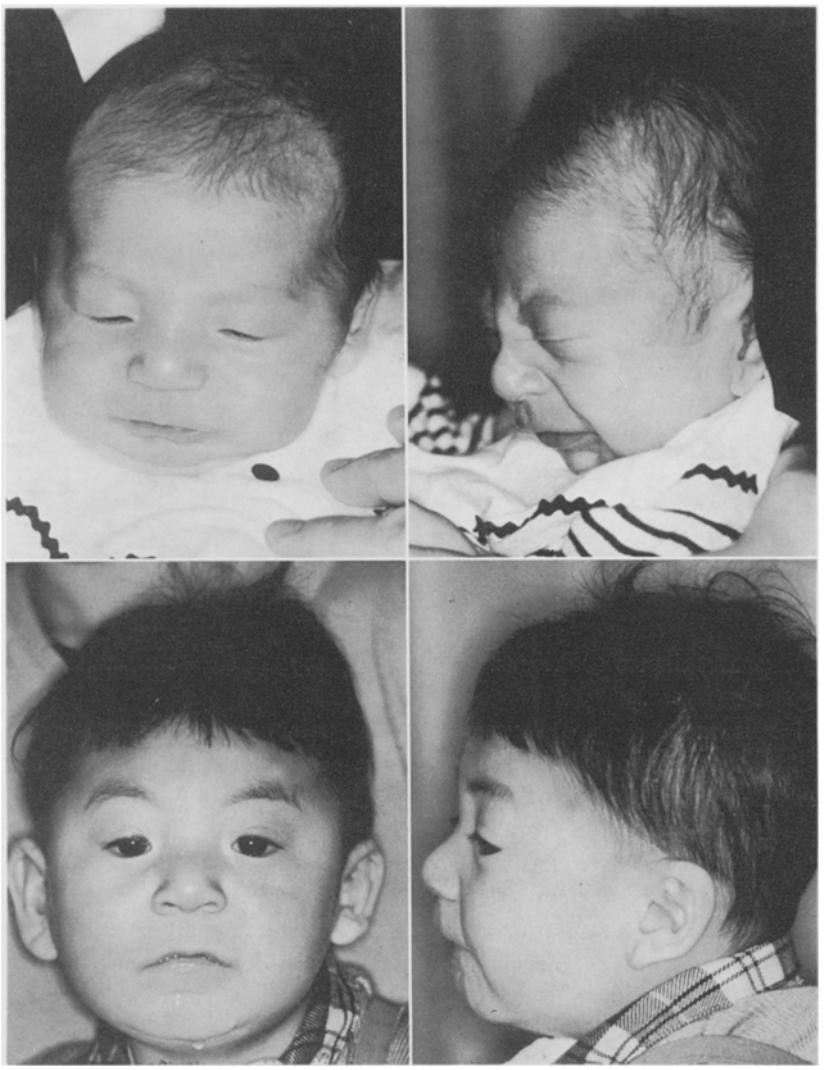


Fig. 3. Proband aged one month (above) and two years (below).

age was 10 months and D.Q. 28. Thus, severe retardation of mental and motor development was observed.

Chromosomal analysis. Monosomy of p15.1→pter, and trisomy of q35.1→qter were noted on chromosome 5 (Fig. 6). Pericentric inversion was observed in the father's chromosome 5. In the light of these findings, the infant is considered to have partial monosomy 5p and partial trisomy 5q due to paternal pericentric inversion of chromosome 5 followed by a crossing over within the inversion loop, and the karyotype can be expressed as 46,XY,rec(5),dup q,inv(5)(p15.1q35.1)pat.

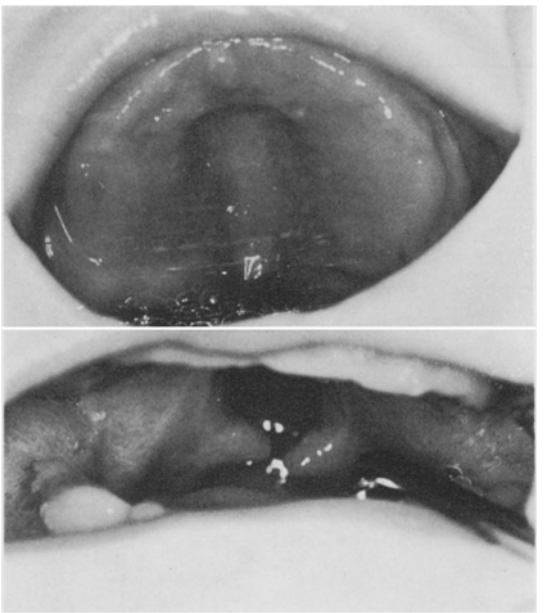


Fig. 4. Palate of the proband aged one month.

Table 1. Mesiodistal and labiolingual diameters of deciduous teeth crown. Mean values were taken from the report of Arai, 1937.

		Mesiodistal	mean ± S.D.	Labiolingual	mean ± S.D.
U	A	5.57(<2S.D.)	6.64 ± 0.41	4.71	4.84 ± 0.37
p	B	4.86	5.15 ± 0.58	4.25	4.39 ± 0.48
p	C	6.09	6.60 ± 0.26	5.58	5.66 ± 0.68
e	D	7.65	7.28 ± 0.54	9.08	8.78 ± 0.38
r	E	9.37	9.31 ± 0.61	10.54	10.07 ± 0.43
L	A	3.44(<2S.D.)	4.27 ± 0.26	3.36	3.74 ± 0.38
o	B	3.97(<2S.D.)	4.65 ± 0.26	4.10	4.10 ± 0.54
w	C	5.90	6.03 ± 0.34	5.11	5.36 ± 0.26
e	D	8.38	8.77 ± 0.49	7.18	7.00 ± 0.46
r	E	10.17	10.50 ± 0.59	9.17	9.01 ± 0.65

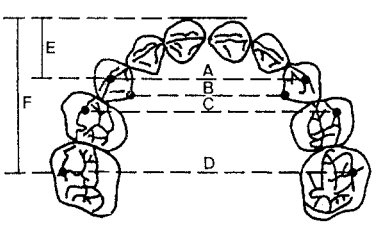
Unit: mm

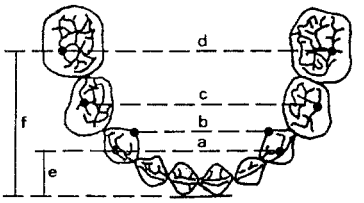
No abnormality was seen in the maternal chromosome.

Clinical course. Feeding difficulty was improved by using the Hotz type palatal plate (Hotz and Gnoinski, 1979) to the cleft palate. However, the infant suffered repeated upper airway inflammation, which was occasionally complicated

Table 2. Dental arch width and length aged three years. Mean values were taken from the report of Ono *et al.*, 1960.

		Dental arch width	mean ± S.D.
Upper	A	29.13	30.73 ± 1.71
	B	26.42	25.48 ± 1.65
	C	38.83	39.85 ± 1.68
	D	50.87 (>2S.D.)	46.48 ± 2.12
		Dental arch length	mean ± S.D.
	E	7.50	8.92 ± 0.95
	F	20.60 (<2S.D.)	23.40 ± 1.38
		Dental arch width	mean ± S.D.
Lower	a	25.78 (>2S.D.)	23.28 ± 1.21
	b	21.80	19.55 ± 1.40
	c	36.12	33.48 ± 1.73
	d	40.32	39.78 ± 1.86
		Dental arch length	mean ± S.D.
	e	5.60	5.51 ± 0.71
	f	18.43	19.59 ± 1.36





Unit: mm

with pneumonia. Accordingly, it was often necessary to relay on nutrition through tubes. At the age of three years, after the systemic condition of the infant had stabilized, palatoplasty was performed by double opposing Z-plasty (Furlow, 1986), in order to normalize food intake and prevent respiratory infection. Although the postoperative course has been satisfactory and the initial goal has been achieved, the patient is still unable to speak.

DISCUSSION

Our search of the literature revealed that partial monosomy 5p and partial trisomy 5q due to parental pericentric inversion of chromosome 5 have been reported in only 10 patients including the present case (nine patients in seven families and one fetus; Table 3) (Faed *et al.*, 1972; Ebbin *et al.*, 1979; Beemer *et al.*, 1984; Miyazaki *et al.*, 1985; Schroeder *et al.*, 1986; Martin *et al.*, 1988; Sonoda *et al.*, 1989). The aberration is more likely to be attributable to the father than the mother

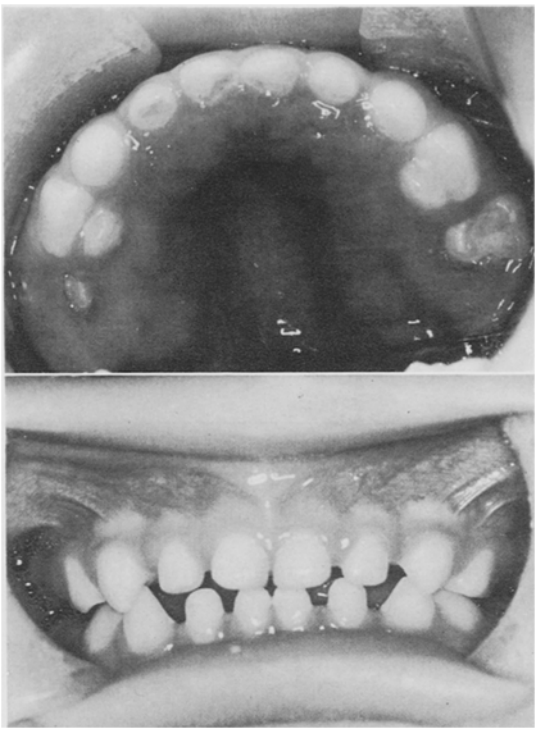


Fig. 5. Row of deciduous teeth aged three years.

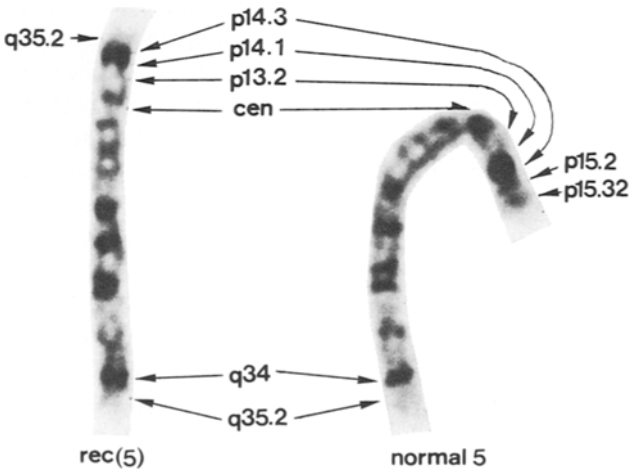


Fig. 6. Partial karyotype of the proband.

Table 3. Profiles of the present case and previously reported cases.

Authors	Carriers	Break points	Sex of probands	Phenotypes
Faed (1972)	Mother	p13 q33	1 Male	5p-
Ebbin (1979)	Father	p14.2 q33	1 Male	5p-
Beemer (1984)	Father	p15.1 q33.3	1 Male 2 Female	5p-, 5q+
Miyazaki (1985)	Father	p13 q35	1 Female	5p-
Schroeder (1986)	Father	p15 q32	1 Male	?
Martin (1988)	Mother	p13 q33	1 Male(Fetus)	?
Sonoda (1989)	Father	p15.1 q35.1	1 Male	5p-, 5q+
Present case	Father	p15.1 q35.1	1 Male	5p-

(the ratio is 6:2), and is more common in boys (7:3). The reason for the sex difference in the parents causing the aberration and the affected children is unknown. However, the higher percentage of fathers is considered to be explained by the fact that women with pericentric inversion are less likely to reproduce (Faed *et al.*, 1972; Martin *et al.*, 1988), and the higher incidence of partial monosomy 5p and partial trisomy 5q in males seems to be because the frequency of miscarriage and mortality in the early stage after birth are higher in females than in males (Sonoda *et al.*, 1989).

This chromosomal aberration is considered to be induced by recombination during the formation of the gamete (Faed *et al.*, 1972). In the other words, the inverse chromosome and the normal chromosome are combined at the homologous part in the process of reduction division and produce a loop in the heterozygote with pericentric inversion. Crossing within the loop induces recombination, generating a gamete with partial 5p defect and partial 5q duplication. Although it seems possible that a gamete with partial 5p duplication and partial 5q defect could be produced, partial 5p trisomy and partial 5q monosomy due to such a gamete has not been reported so far. It has been suggested that, because of the high mortality rate of gametes with partial 5p duplication and partial 5q defect or the heterozygote produced by it, and therefore, such cases are not encountered in the clinical setting (Martin *et al.*, 1988).

The phenotype of cases with partial monosomy 5p and partial trisomy 5q, which have two different abnormalities on the chromosome, can be classified into the following three types: 1) cases chiefly with the phenotype of partial monosomy 5p, as seen in the report by Faed *et al.* (1972); 2) cases with phenotypes of both partial monosomy 5p and trisomy 5q, as reported by Beemer *et al.* (1984) and Sonoda *et al.* (1989); and 3) cases in which symptoms such as holoprosencephaly are observed, but are difficult to attribute to either aberration, as reported by Schroeder *et al.* (1986). The phenotype of the present patient was considered to be mainly that of partial monosomy 5p.

In partial monosomy 5p, no association has been observed between the degree of 5p defect and clinical symptoms, and defect of the 5p15 band has been considered essential (Niebuhr, 1978). Because the chromosome was broken at 5p15.1 in the present case, manifestation of the symptoms of partial monosomy 5p is possible. On the other hand, Rodewald *et al.* (1980) classified the clinical features of trisomy 5q into three groups according to karyotype. Since the trisomic segment is small (5q35.1→ter) in the patient under study, their classification may not be applied. In cases of partial trisomy of 5q34→qter in their classification, in which duplication is noted in the most distal region, short stature, mild mental retardation, delayed pubertal manifestation, herniation, short flat forehead, high nasal crest, and hand malformation have been reported. Although short stature, mental retardation, and high nasal crest were noted in our patient, these manifestations can also be caused by partial monosomy 5p, and therefore, it is impossible to decide whether they were induced by partial trisomy 5q or partial monosomy 5p.

The points of breakages (p15.1q35.1) in our patient is identical to that in the patient reported by Sonoda *et al.* (1989) who had high-pitched crying, microencephaly, flat occiput, frontal hypertrichosis, ocular hypertelorism, slanted-away ocular cleft, flat nasal crest, malformed ear, auricular fossula, thin upper lip, micrognathia, high palate, inguinal hernia, small penis, inflection of the fifth finger, predominant whorls, simian line, distant axial triradius, and cardiac malformation. The body weight at the age of one year and six months was reported to be 4,290 g, and the development showed significant delay with all skills at the two to three months level. Some of the phenotypes differed between their patient and ours, and the degree of mental and physical retardation was obviously milder in our patient. The difference may be attributable to genetic background or environmental factors.

Although the karyotype of the patient's sister is unknown, her clinical features were similar to the case of Schroeder *et al.* (1986). Unlike many other patients with partial monosomy 5p and partial trisomy 5q, the symptoms of their case were severe, with scaphocephalism, round face, ocular hypotelorism, flat nasal crest, median upper lip cleft, and low-set ear. Organic malformations included malformation of the central nervous system (holoprosencephaly), tetralogy of Fallot, and esophageal atresia. Although our patient's sister was not personally examined, investigation of the photographs taken at autopsy and records of the autopsy suggested that she also had round face, ocular hypotelorism, flat nasal crest, median upper lip cleft and cleft palate, low-set ear and simian line, as well as the typical anencephaly. Judging from the phenotype, it is very likely that she had partial monosomy 5p and partial trisomy 5q.

Acknowledgments We would like to express our heartfelt gratitude to Dr. Kimiko Miyakawa of the Department of Pediatrics, Niigata City General Hospital, for her kind guidance and advice. We also thank Dr. Isamu Takahashi of the Department of Obstetrics and Gynecology of Niigata Cancer Center Hospital, for kindly providing the data on the patient's sister.

A summary of this article was reported at the 16th Annual Meeting of the Japanese Cleft Palate Association (In Kanazawa on July 16 and 17, 1992).

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