Sapporo Med. J. **48** (2) 218~221 (1979)

Two Cases of 4p- Syndrome with Cleft Palate

Jun-ichi AZUMI

Department of Human Genetics, National Institute of Genetics
(Chief Director: E. Matsunaga)

Isao FURUTA, Masayuki IWAI, Gen-iku KOHAMA

Department of Oral Surgery, Sapporo Medical College
(Chief: Prof. G. Kohama)

(Received August 2, 1978 and accepted September 5, 1978)

1 INTRODUCTION

Since Wolf and his associates[1] described a case with partial deletion of the short arm of chromosome No. 4, some 50 cases have been reported. The identification of the deleted chromosome depended in most cases on the technique of autoradiography. Recently, with the advent of new banding techniques it has become possible to determine the structure of a deleted chromosome precisely.

During the course of a chromosomal survey in patients with cleft lip and/or cleft palate, we encountered two cases of 4p- syndrome with cleft palate[2~5]. In the present communication, cytogenetic and clinical features of these patients were described in detail. Chromosomes were examined in the light of the new banding technique.

2 CASE REPORTS

Case 1: The patient, a Japanese female infant, was the only child of a 21-year-old mother and 18-year-old father who were unrelated and in good health. The patient was born on July 14, 1973 after 42 weeks of gestation. She weighed 2000 g at birth. No family history of malformations or miscarriages were recorded. Fetal activity was noted to be weak and resuscitation was required at birth. The patient first arrived for examination at two years of age. At that time she weighed 7500 g, and was 74.3 cm in height and had a head circumference of 41.5 cm. Growth failure was prominent and psychomotor retardation was severe. Clinical features of this patient are shown in Table 1. Routine laboratory examinations were within normal limits. She died at two years and five months of age of pneumonia and severe seizures.

Table 1 *Summary of clinical findings in cases with 4p- syndrome*

Findings	Frequency*	Case No. 1	Case No. 2
Low birth weight (under 2500 g)	39/42	+	+
Severe growth retardation	46/47	+	+
Severe mental deficiency	41/41	+	+
Microcephaly	40/44	+	+
Seizures	27/34	+	+
Hypotonia	26/29	+	+
Hypertelorism	38/45	+	+
Strabismus	22/40	−	+
Epicanthal folds	10/27	−	−
Colobona iridis	16/41	−	−
Low-set ears	24/38	+	+
Broad or beaked nose	31/43	−	+
Cleft lip and/or cleft palate	28/45	+	+
Heart malformation	23/41	−	+
Hypoplastic dermal ridges	20/38	−	+

* Based on references 1, 4-15).

Case 2: The patient, a Japanese female, was born on March 12, 1976 after 41 weeks of gestation. Her birth weight was 2050 g. She first arrived for examination at one year and two months of age. At that time she weighed 4900 g, was 65.9 cm in height and had a head circumference of 39.7 cm. The father was 26 and the mother was 33 years at the time of her birth. The patient was the second child of healthy parents. Her elder sister was normal. The family history revealed no malformations or miscarriages. The pregnancy and the delivery were normal. She failed to thrive and there was severe psychomotor retardation. Seizures occurred once a day since the age of three months. Physical examinations revealed multiple abnormalities (Table 1). Routine laboratory examinations were within normal limits. The dermatoglyphic findings were characterized by arches (Ac) on both hypothenar areas with bilateral distal axial triradii (t"). Simian creases were not observed. There was a markedly increased frequency of whorls on the finger tips, but the total ridge count was not determined.

3 CYTOGENETIC FINDINGS

Cytogenetic examinations of the patients and their parents were carried out by the standard leukocyte-culture technique. Routine analyses disclosed the deletion of the short arm of a B-group chromosome in both patients. The amount of chromosomal loss in case 1 was slightly larger than that in case 2. In both of them, the deleted B group chromosomes were identified as No. 4 by the Q- and the G-banding techniques (Fig. 1). The karyotypes were designated as 46, XX, del (4) (p14) in case 1 and 46, XX, del (4) (p16) in case 2 based on the Paris Conference system[6].

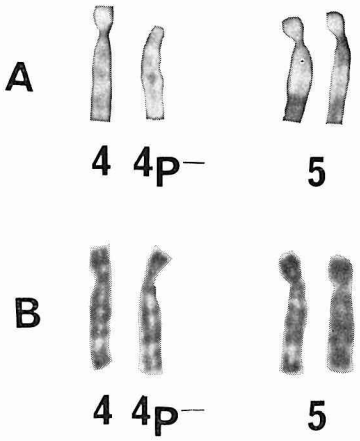

Fig. 1 A Q-banded and a G-banded partial karyotypes from cases 1 (A) and 2 (B). Two 4p- chromosomes represent a del (4) (p 14) and a del (4) (p 16), respectively.

4 DISCUSSION

Wolf *et al.*[1] described a paitent with partial deletion of the short arm of a group B chromosome in whom clinical features were different from that of the cri-du-chat syndrome[7]. The deleted chromosome was identified as No. 4 by autoradiographic studies. The phenotypic spectrum of 43 reported cases of 4p-syndrome were reviewed by Johnson *et al.*[8]. They can be distinguished from those with cri-du-chat syndrome by the absence of cat-like cry and the presence of coloboma of the iris, cleft lip and/or cleft palate, hypoplastic dermal ridges, malformation of the heart, genital abnormalities and delayed bone maturation, although distinction is not always easy[1,8~16].

In all reported cases, the parents showed a normal karyotype with only one exception. A cell with 4p- karyotype was detected in a mother with otherwise normal karyotype[17]. The size of the deletion varied from case to case. With the Q- and the G-banding techniques it is now possible to identify the breakpoint of an abnormal chromosome. Johnson *et al.*[8] suggested that the amount of chromosomal loss in cases of 4p- was not related in any way to the degree of mental retardation and the life span, as far as live-born cases were concerned.

He claimed that a larger deletion might have been lethal during fetal life. On the other hand, Centerwall *et al.*[18] suggested that the difference in the size of deletion could influence clinical features. Tanaka *et al.*[19] examined five patients with 4p- syndrome, and suggested that the loss of the most distal segment of 4p was a prerequisite for the expression of clinical features of the syndrome.

In the present study, it was not possible to delineate characteristic clinical features of the two cases, although the point of breakage was different in each case. Further studies are required before drawing any conclusions regarding this problem.

5 SUMMARY

Chromosomal studies were carried out on two Japanese infants with growth and mental retardation, hypotonia, seizures, microcephaly and cleft palate. Banding studies showed that their karyotypes were 46, XX, del (4) (p14) and 46, XX, del (4) (p16), respectively. Both parents had a normal karyotype. No difference was detected between the clinical features of the patients who showed breakpoints at different location.

ACKNOWLEDGMENTS

We are indebted to Dr. Naomi Takayanagi, Department of Pediatrics, Sapporo Medical College, Sapporo, and Dr. Tetsuo Shishido, Sapporo Municipal Hospital, Sapporo for the supply of clinical data in this study. We also thank Dr. Yasuo Nakagome, Department of Human Genetics, National Institute of Genetics, for his advice and improvement of this manuscript. This study was conducted by a grant in aid from the Ministry of Education (No. 148298).

References

1. Wolf, U., Reinwein, H., Porsch, R., Schroter, R. and Baitsch, H.: Defizienz an den kurzen Armen eines Chromosomes Nr. 4. Humangenetik **1**, 397–413 (1965).
2. Azumi, J., Kohama, G. and Sasaki, M.: Cytogenetic studies in patients with cleft lip and/or cleft palate (4) (Screening studies of chromosomes from August 1973 to August 1977). Jap. J. Human Genet. **23**, 161–166 (1978).
3. Sasaki, M., Azumi, J. and Igarashi, T.: Chromosome surveys in patients with cleft lip and/or cleft palate. (1) Date from December 1971 to June 1972. Chrom. Infor. Ser. No. 17, 15 (1974).
4. Sasaki, M., Azumi, J. and Igarashi, T.: Chromosome surveys in patients with cleft lip and/or cleft palate. (2) Screening date from July 1972 to July 1973 Chrom. Infor. Ser., No. 17, 16 (1974).
5. Sasaki, M., Azumi, J., Komatsu, Y. and Nishijima, K.: Chromosome surveys in patients with cleft lip and/or cleft palate. (3) Date from 43 patients and their relatives (1964–1972). Chrom. Infor. Ser., No. 18, 8 (1975).
6. Paris Conference: Standardization in human cytogenetics, Birth Defects, Orig. Art. Ser. 8 (7), The National Foundation, N. Y. (1971).
7. Lejeune, J., Lafourcade, J., de Grouchy, J., Berger, R., Gartier, M., Salmon, C. and Turpin, R.: Trois cas de delection partielle du bras court d'nm chromosome 5. C. R. Acad. Sci., Paris **257**, 3098–3102 (1963).
8. Johnson, V. P., Mulder, R. D. and Hosen, R.: The Wolf-Hirshhorn (4p-) syndrome. Clin. Genet. **10**, 104–112 (1976).
9. Hirschhorn, K., Cooper, H. L. and Firschein, I. L.: Deletion of short arms of chromosomes 4–5 in a child with defects of midline fusion. Humangenetik **1**, 479–482

(1965).
10. Arias, D., Passarge, E., Engle, M. A. and German, J.: Human chromosomal deletion: Two patients with the 4p- syndrome J. Pediat. **76**, 82–88 (1970).
11. Miller, D. A., de Capoa, A, Allderdice, P. W., Davis, J., Klinger, H. P., McGilvray, E. and Allen, F. H.: Partial deletion of the short arm of chromosome No. 4 (4p-). J. Pediat. **77**, 792–801 (1970).
12. Passarge, E., Altrogge, H. C. and Rudiger, R. A.: Human chromosomal defficiency: The 4p- syndrome. Humangenetik **10**, 51–57 (1970).
13. Guthrie, R. D., Aase, J. M., Asper, A. C. and Smith, D. W.: The 4p- syndrome. Am. J. Dis. Chld. **122**, 421–426 (1971).
14. Subrt, I. and Blehova, B.: Further observations on a previously reported case of 4p- syndrome. Humangenetik **15**, 361–363 (1972).
15. Fryns, J. P., Eggermont, E., Verresen, H. and van der Berghe, H.: The 4p- syndrome, with a report of two new cases. Humangenetik **19**, 99–109 (1973).
16. Mikelsaar, A. V. N., Lazjuk, G. J., Lurie, J. W., Tuur, S., Kaosaar, M. E., Mikelsaar, R. and Loolaid, V. E.: A 4p- syndrome. Humangenetik **19**, 345–347 (1973).
17. Taylor, A. I., Challacombe, D. N. and Howlett, R. M.: Short-arm deletion, chromosome 4, (4p-), a syndrome? Ann. Hum. Genet. **34**, 137–141 (1970).
18. Centerwall, W. R., Thompson, W. P., Allen, I. E. and Fobes, C. D.: Translocation 4p- syndrome. Am. J. Dis. Child. **129**, 366–370 (1975).
19. Tanaka, T., Yamamoto, Y., Matsui, I. and Kuroki, Y.: Clinical features and chromosomal loss in the 4p- syndrome. Cong. Anom. **17**, 169–175 (1977).

口蓋裂を伴った4p-症候群の2症例

安積順一　古田　勲
岩井正行　小浜源郁

Wolf ら (1965) が染色体 No. 4 の短腕の部分的欠損を有する1例を報告して以来，約50例の症例が報告されている．染色体の同定は，ほとんどの症例においてautoradiography を用いて行われた．近年，new banding 法が出現したことにより染色体の欠損部分の構造をより正確に決定することが可能になってきた．われわれは本法による唇顎口蓋裂患児の染色体の検索中に，4p-syndrome の2症例を経験し，その細胞遺伝学的特徴ならびに臨床的特徴について検討した．

これらの症例は，臨床所見として，成長および精神発育遅延，弛緩，発作，小頭症，口蓋裂を有していた．染色体分析では，1例は 46, XX, del (4) (p14)，他の1例は 46, XX, del (4) (p16) を示し，両者間の欠損部分に差異がみられた．しかし両者間の臨床的特徴の違いは明らかではなかった．