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A Cytogenetic Study of Heavy Mental Retardates
I. A study on heavy mental retardates with cerebral palsy

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Key words: Chromosome abnormality, Mental retardation, Cerebral palsy

ABSTRACT

A cytogenetic study was made on heavy mentally retarded patients with cerebral palsy. The purpose of this study was to get a glimpse of the causes of mental retardation and cerebral palsy. As the results, chromosome abnormalities were found in 8.6% of the patients. By this study, it was revealed that chromosome abnormalities contribute significantly to the etiology of cerebral palsy.

The 58 cases examined in this study were admitted to National Sanatorium Kamo Hospital and Hiroshima Prefectural Handicapped Children's Hospital.

Chromosome slides were prepared in accordance with standard blood culture procedure. Karyotype analyses were made with the application of the conventional Giemsa staining and G-, C-, and Q-banding differential staining.

Of these 58 cases, 5 cases had abnormal karyotypes, showing an incidence of 8.6%. Of 5 abnormal karyotype cases, autosomal abnormalities were observed in 3 cases, and sex-chromosome abnormalities in 2 cases. And additional 4 cases had normal variations of no.1, 9, and Y chromosome. The clinical and cytogenetic findings of these patients were presented.

A chromosome study was conducted on 58 cases of heavy mental retardation with cerebral palsy. The patients were admitted to National Sanatorium Kamo Hospital and Hiroshima Prefectural Handicapped Children's Hospital.

The causes of cerebral palsy fall into three main groups: prenatal, perinatal, and postnatal factors, as related to the period. The purpose of this study was to get a glimpse of the causes of mental retardation and cerebral palsy, especially to know the proportion of the chromosome abnormalities among the prenatal causes of cerebral palsy.

In order to detect even minor chromosome abnormalities, banding techniques were employed routinely on all the cases.

PATIENTS

The 58 cases examined in this study consisted of 42 cases from Hiroshima Prefectural Handicapped Children's Hospital, and 16 cases from National Sanatorium Kamo Hospital.

All the cases had heavy mental retardation randing from severe in one case being 35-20 in IQ score to profound in 57 cases being under 20 in IQ score. And all the cases had cerebral palsy; dyskinesia, difficulty or inability in walking, muscular atrophy, palasis or hemiplegia of extremities, and speech disorders.

The chromosomal examinations were also performed on available relatives of karyotypically abnormal patients.

METHODS

The chromosomal preparations were made by

standard leucocyte culture procedure. Phytohemagglutin-stimulated peripheral blood was cultured in Eagle EME medium for 72 hr, and slides were made by means of the air-drying technique.

The conventional Giemsa staining and G-banding differential staining were routinely employed for chromosome identification.

Chromosome counts were made with about 25 well delineated metaphases. The karyotype was analysed in 6 cells by conventional Giemsa staining and G-banding saining.

In abnormal or ambiguous cases, C- or Q-banding satining were also employed as necessary, and the number of chromosome counts and of karyotyped cells was increased.

Table 1. Clinical and cytogenetic findings in 58 cases of heavy mental retardation with cerebral palsy

Case no.	Age	Sex	Karyotype	Clinical features
1	8 y.	F	46,XX	microcephalus, flat occiput, hypertelorism, dysplasia and malimplantation in teeth, hypoplastic thumb, hypotonia, Lennox's syndrome
2	6 y.	M	46,XY	Lecklinghausen's syndrome, dolichocephalia, low-set ears, dysplasia and malimplantation in teeth, hypoplastic thumb, hypotonia, hypoplastic extermal genitalia, coarse hair, nevus (left femoral region)
3	9 y.	F	46,XX	flat occiput, hypertelorism, hypoplastic thumb, club hands, club feet, calcaneous, hypotonia, seizure, hypothyroidism, kindney failure
4	26 y.	M	46,XY	microcephalus, flat occiput, hypertelorism, micrognathia, dysplasia and malimplantation in teeth, hypoplastic external genitalia, club hands, club feet, seizure
5	46 y.	F	46,XX	coarse hair, flat occiput, strabismus, seizure
6	12 y.	F	46,XX	flat occiput, club feet, seizure
7	2 y.	F	46,XX	flat occiput, strabismus, incurved index finer, seizure
8	34 y.	M	46,XY	microcephalus, flat occiput, strabismus, hypoplastic external genitalia, incurved fingers, seizure
9	10 y.	F	46,XX	head deformity, epicanthal fold, impaired vision, seizure, hypothyroidism, asthma
10	12 y.	F	46,XX	head deformity, hypotonia, seizure
11	7 y.	M	46,XY	flat occiput, ptosis of eyelid, hypoplastic external genitalia, hirsutism, seizure
12	44 y.	F	46,XX	exophthalmus, strabismus, dysplasia and malimplantation in teeth,
13	26 y.	M	46,XY	flat occiput, frontal bossing, hypoplastic external genitalia, incurved fingers, seizure
14	46 y.	M	46,XY	congenital cataract, seizure
15	23 y.	M	46,XY	hypertelorism, incurved thumb
16	13 y.	F	46,XX	microcephalus, flat occiput, dysplasia and malimplantation in teeth, seizure
17	17 y.	F	46,XX	seizure
18	18 y.	M	46,XX	Sanfillipp's syndrome, saddle nose, seizure
19	13 y.	M	46,XY	Sanfillipp's syndrome, saddle nose, nevus, high arched palate, varus
20	6 y.	F	46,XX	blindness, seizure
21	15 y.	M	46,XY	head deformity, strabismus, hypertonia, seizure
22	18 y.	M	46,XY	ornitin transcarboamidase deficiency, hypertelorism, seizure
23	48 y.	F	46,XX	hypertelorism, saddle nose, broad nasal base, upward slanted palpebral fissure
24	5 y.	F	46,XX	strabismus, behavior disorders
25	7 y.	M	46,XY	flat occiput, strabismus, behavior disorders
26	8 y.	M	46,XY	hypertelorism, strabismus, impaired vision, seizure
27	2 y.	M	46,XY	head deformity, strabismus, seizure
28	6 y.	F	47,XXX	blindness, prominent occiput, saddle nose, cleft palate, dysplasia and malimplantation in teeth, incurved thumb, seizure
29	16 y.	F	46,XX	hypertelorism, strabismus, saddle nose, cleft palate, hypertonia, athetosis

Case no.	Age	Sex	Karyotype	Clinical features
30	32 y.	M	46,XY	seizure
31	26 y.	M	46,XY	hypertelorism, flexion contracture of wrist, hypertonia
32	7 y.	M	46,XY	blindness, head deformity, strabismus, nystagmus, low-set ears, dysplasia and malimplantation in teeth, seizure, murmur
33	7 y.	F	46,XX	hypertelorism, hypotonia, athetosis, seizure
34	6 y.	M	46,XY	hypertelorism, upward slanted palpebral fissure, strabismus, saddle nose, hypotonia, Lennox's syndrome
35	7 y.	M	46,XY	Low's syndrome, congenital cataract, congenital glaucoma, flat occiput, upward slanted palpebral fissure, hypertelorism, epicanthal fold, dysplasia and malimplantation in teeth, seizure
36	42 y.	F	46,XX,inv(9)	hypertelorism, strabismus, upward slanted palpebral fissure, impaired vision, seizure
37	7 y.	M	46,XY	dysplasia and malimplantation in teeth
38	1 y.	F	46,XX	Cornelia dé Lange's syndrome, narrow high arched palate, impaired vision, seizure
39	10 y.	F	46,XX	head deformity, hypertelorism, athetosis, seizure
40	10 y.	F	46,XX	inverted epicanthus
41	10 y.	F	46,XX	flat occiput, seizure
42	15 y.	F	46,XX,1qh+	low nasal bridge, cleft lip, seizure behavior disorders
43	14 y.	M	46,XY	cataract, impaired vision, ataxia, behavior disorders
44	12 y.	M	46,XY	flat occiput, club feet, club hands, seizure
45	17 y.	F	46,XX	microcephalus, upward slanted palpebral fissure, seizure
46	13 y.	M	46,XY,9qh+	dolichocephalus, nystagmus, equino varus, seizure
47	18 y.	M	46,XY	ataxia, seizure
48	21 y.	F	45,X/46,XX/ 46,Xr(X)	short stature, microcephalus, hypertelorism, dysplasia and malimplantation in teeth, hypogonadism, hyporplastic external genitalia, webbed neck. equino varus, bilateral hypoplasia of fourth toe, seizure
49	16 y.	M	46,XYqh+	blue sclera, impaired vision, seizure
50	34 y.	F	46,XX	tuberous sclerosis, impaired vision, equino varus, hypertonia, adenoma sebaceum
51	13 y.	M	46,XY	impaired vision, seizure
52	10 y.	F	46,XX,inv(9)	micrognathia, seizure
53	18 y.	F	46,XX,1qh+	oxycephalus, seizure
54	12 y.	F	46,XX	flat occiput, seizure
55	27 y.	M	46,XY	microcephalus, seizure
56	15 y.	F	46,XX	exophthalmus, ptosis of eyelid, saddle nose, seizure
57	2 y.	F	46,XX,dir dup(7)	large forehead, frontal bossing, prominent occiput, hydrocephalus, almond shaped eyes, epicanthal fold, cleft palate, micrognathia, poorly shaped and low-set ears, short neck, congenital heart failure, hypotonia, simian crease
58	19 y.	M	46,XY	seizure

All the patients had mental retardation, dyskinesia, difficulty or inability in walking, muscular atrophy, palasis or hemiplegia of extremities and speech disorders.

RESULTS

The clinical and cytogenetic findings of all the cases are presented in Table 1. The abnormal karyotypes were found in 5 cases out of 58 cases, showing an incidence of 8,6%. Of the abnormal cases, autosomal abnormalities were seen in 3 cases, and sex-chromosome abnormalities were detected in 2 cases. And additional 4 cases showed normal variations on the long arm of no.1, 9, and Y chromosomes.

As the results f chromosomal examinations on relatives of karyotypically abnormal patients, the chromosome abnormalities, in this study, were found not to be transmitted through the parental line but to occur sporadically.

Abnormal karyotypes were seen in one case of a direct duplication of no.7 chromosome, 2 cases of a pericentric inversion of no.9, one case of triplo-X female, and one case of mosaic X chromosome with the phenotypically Turner's

syndrome.

Normal variations were seen in 2 cases of a long arm of no.1, one case of no.9, and one case of Y chromosome.

Details are given as follows.

CASE REPORTS

Cases of chromosome abnormalities

Case 1. (dir dup(7)) The patient was a 2-year-old girl, 5600 g in weight, 64 cm in length. She was born to a 27-year-old mother and a 28-year-old father as the first child. There was no history of abortion, stillbirth, congenital malformations, mental retardation, exposure to the atomic bomb, and consanguinity in this couple. Clinical examinations revealed that her parents were phenotypically normal.

The birth weight of the patient was 2230 g at the full term gestation. The remarkable clinical signs of this patient were large forehead with frontal bossing, prominant occiput, hydrocephalus, almond shaped eyes, epicanthus, slight strabismus, cleft palate, micrognathia, slightly low-set ears, poorly shaped ears, short neck, congenital heart defect, hypotonia, simian crease, severe growth and mental retardation.

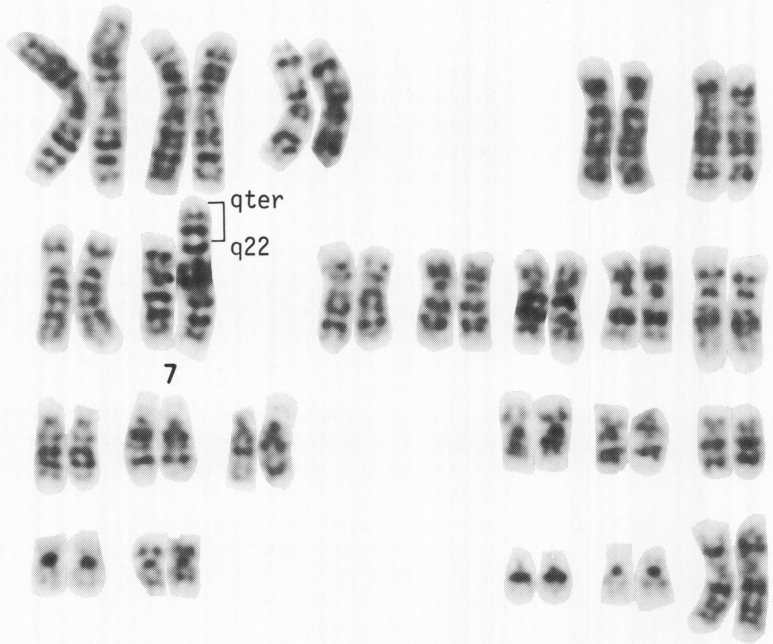


Fig. 1. G-banding karyotype of the patient, showing 46,XX,dir dup(7) (q22qter).

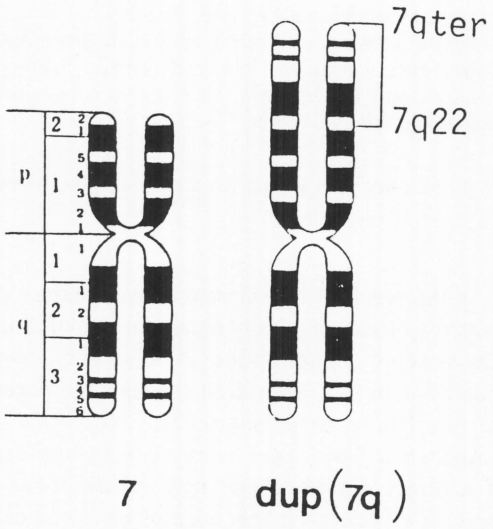


Fig. 2. Diagram showing the position of the duplication of no.7 chromosome

The chromosome constitution of the patient based on the conventional Giemsa specimen showed 46 chromosomes including a no.7 chromosome having an unusually elongated short arm. The G-banding analyses revealed that an unusually elongated element of the short arm of a no.7 chromosome corresponded to the duplication of the segments of 7(q22→qter)(Fig. 1). Then the chromosome formula of the patient was given as 46,XX,dir dup(7)(q22qter)(Fig. 2).

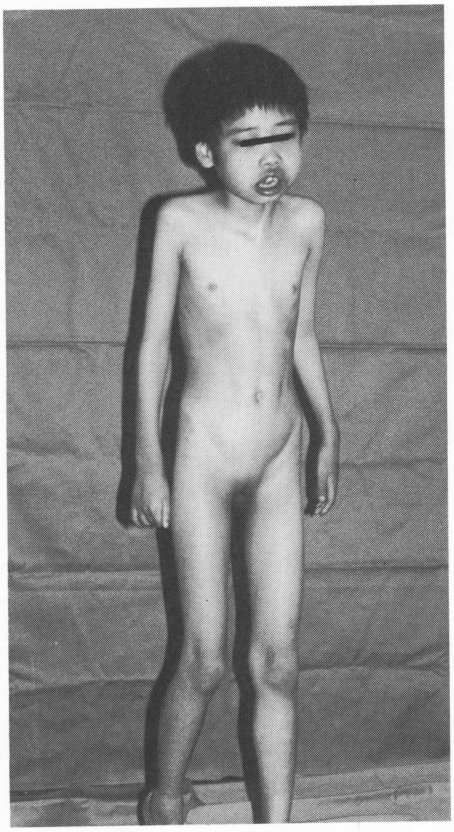
Her parents were chromosomally normal with no slight evidence for the aberration, based on 12 cells karyotyped in each.

Case 2. (inv(9)) The patient was an 11-year-old girl, 21,6 kg in weight, 130 cm in length. She was born to a 26-year-old mother and a 30-year-old father as the first child. There was no history of abortion, stillbirth, congenital malformations, mental retardation, exposure to the atomic bomb, and consanguinity in this couple. Clinical examinations revealed that her parents and her younger brother were phenotypically normal.

The birth weight of the patient was 2750 g and the head circumference was 32 cm at 37 weeks of normal gestation. Her neonatal period was not particular. She stood up at 10 months of age, and walked alone at 15 months of age. Her postnatal course seemed to be smooth and normal. At 3 years of age, she had a high temperature (39°C) and convalsions continuously for one week. The diagnosis of encephalitis was made.

The remarkable clinical signs of this patient were developmental disorder; 21,6 kg (-3,0 SD) in weight, 130 cm (-1,9 SD) in length, micrognathia, slight kyphosis, club foot, incurved III. and IV. fingers, at right side, hemiplegia at right side, hypotonia, difficulty in walking and in coordination, seizure, speech disorder, and behavior disorders; paraphagia, finger sucking (Fig. 3).

The chromosome constitution of the patient based on the conventional Giemsa specimen showed 46 chromosomes which included a no.9 chromosome having an unusually elongated short arm and shortened long arm. The G-and C-banding analyses revealed that one of the no.9 chromosome showed the pericentric inversion at p13-q21. Then the chromosome formula of this patient was given as 46,XX,inv(9)(p13q21)(Fig. 4). Her mother was Chromosomally normal with no evidence for the aberration. The chromosomal examination of her father and her younger brother were not cooperated.



Fig, 3. External picture of the patient.

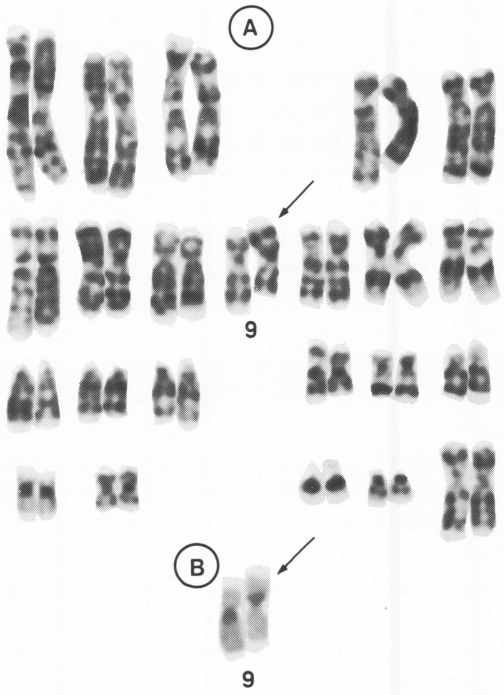


Fig. 4. G-banding karyotype(A) and partial C-banding karyotype(B) of the patient, showing 46,XX,inv(9) (p13q21).

Case 3. (inv(9)) The patient was a 4-year-old girl, 11,7 kg in weight, 92 cm in length. She was born to a 28-year-old mother and a 30-year-old father as the first child. There was no history of abortion, stillbirth, congenital malformations, mental retardation, exposure to the atomic bomb, and consanguinity in this couple. Clinical examinations revealed that her parents and her younger sister were phenotypically normal.

At the last period of the gestation, her mother suffered from toxemia, and she was delivered of the patient, who showed the condition of asphyxia, with forceps operation. The birth weight f the patient was 2725 g, the length was 50 cm, and the head circumference was 33 cm. During the early infancy, she was diagnosed as anoxic encephalitis.

The remarkable clinical signs of this patient were hypertelorism, strabismus, upward slanted palpebral fissure, impaired vision, seizure, palasis of extremities, inability in walking, and speech disorder.

The chromosome constitution of the patient based on the conventional Giemsa specimen showed 46 chromosomes which included a no.9 chromosome having an unusually elongated short arm and shortened long arm. The G-and C-banding analyses revealed that one of the no.9 chromosome showed the pericentric inversion at p11-q13. Then the chromosome formula of this patient was given as 46,XX,inv(9)(p11q13)(Fig. 5). Her mother was chromosomally normal with no evidence for the aberration. The chromosomal examinations of her father and her younger sister were not cooperated.

Case 4. (triplo-X) The patient was a 6-year-old girl, 14,0 kg in weight, 105,5 cm in length. She was born to a 24-year-old mother and a 26-year-old father as the second child. There was no history of abortion, stillbirth, congenital malformations, mental retardation, exposure to the atomic bomb, and consanguinity in this couple. Clinical examinations revealed that her parents and her elder sister were phenotypically normal.

At 7 months of the gestation, her mother suffered from toxemia, and she was delivered of the patient with forceps operation at 36 weeks of gestation. The birth weight of the patient was 2500 g, the length was 47 cm, and the head circumference was 30,5 cm. At 3 or 4 months of age, she was seized with a first cramp.

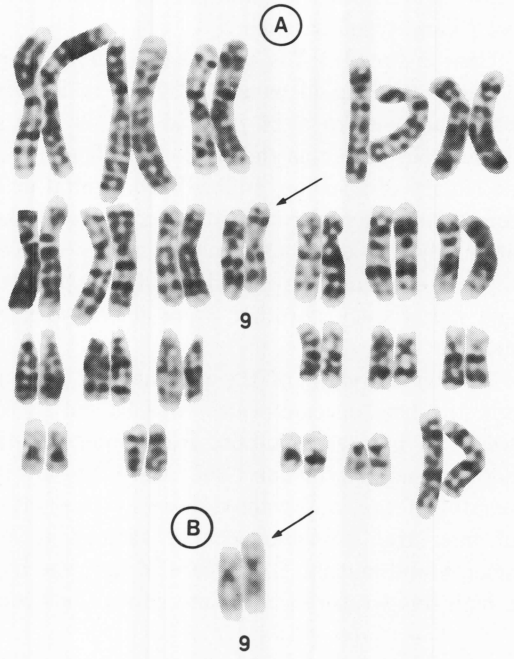


Fig. 5. G-banding karyotype(A) and partial C-banding karyotype(B) of the patient, showing 46,XX,inv(9) (p11q13).

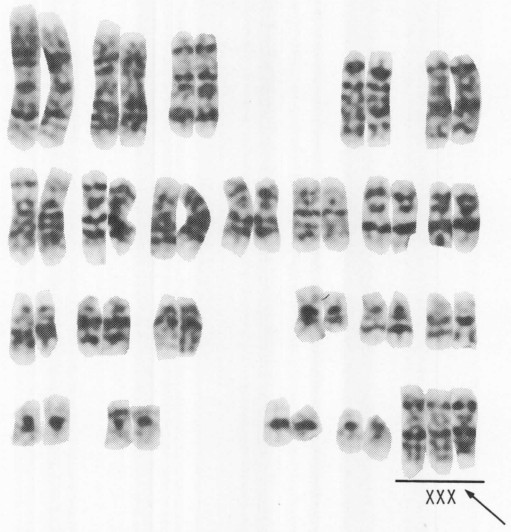


Fig. 6. G-banding karyotype of the patient, showing 47,XXX.

The remarkable clinical signs of this patient were prominant occiput, saddle nose, cleft palate, dysplasia and malimplantation in teeth, incurved thumb, blindness, palasis of extremities, inability in walking, seizure, and speech disorder.

The chromosome constitution of this patient based on the conventional Giemsa specimen showed 47 chromosomes which included an additional C-like chromosome. The G-banding analyses revealed that the additional chromosome was a X chromosome. Then the chromosome formula of this patient was given as 47,XXX(Fig. 6). The chromosomal examinations of her parents and her elder sister were not cooperated.

Case 5. (X/XX/Xr(X)) The patient was a 21-year-old girl. She was born to a 28-year-old mother and a 27-year-old father as the first child. There was one stillbirth at 9 months in the first pregnancy, but no history of spontaneous abortion, congenital malformations, mental retardation, exposure to the atomic bomb, and consanguinity in this couple. Clinical examinations revealed that her father was phenotypically normal. Her mother was already dead.

The birth weight of this patient was 1950 g at full term gestation. At 3 days she had a high temperature and hemiplegia at left side. At 6 months of age, she was diagnosed as cerebral palsy.

The remarkable clinical signs of this patient were growth retardation, especially short stature; 134 cm in length and 33 kg in weight, microcephalus, hypertelorism, saddle nose, dysplasia and malimplantation in teeth, webbed neck, hypoplastic external genitalia, talipes varus, hypoplasia of forth toes at both sides, hemiplegia at left side, difficulty in walking, seizure, and primary amenorrhea (Fig. 7).

The chromosome constitution of this patient derived from the conventional Giemsa-staining and G-banding technique showed 38 cells having 45,X, 14 cells having 46,XX, 2 cells having 46,Xr(X), and one cell having 44 with one marker chromosome. Then the chromosome complement of the patient was given as 45,X/46,XX/46,Xr(X)(Fig. 8).

The karyotype of her father derived from the conventional Giemsa staining and G-banding technique showed 4 cells having 45 chromosomes with randomly missed one, and 55 cells having 46,XY chromosome constitution. The chromosome aberrations; translocation, fragment, chromatid interchange, marker chromosome, were highly observed in her father's cells as shown in Table 2 and Fig. 9.

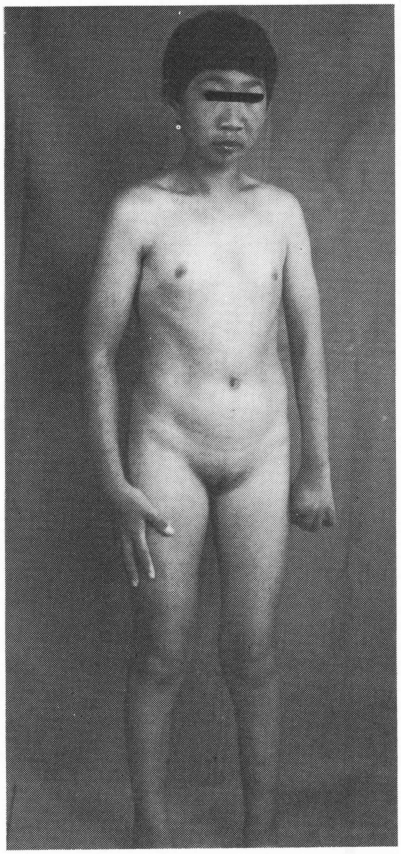


Fig. 7. External picture of the patient

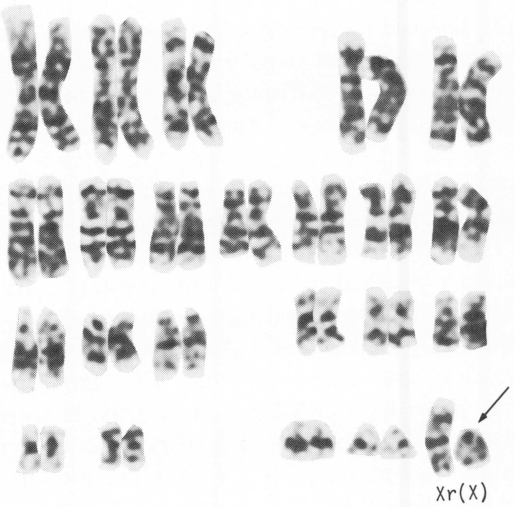


Fig. 8. G-banding karyotype of the patient, showing 46,Xr(X).

Table 2. Cytogenetic findings in the leucocyte cultures of the patient and her father

specimen	chromosome counts			total cells counted	chromosome aberrations					
	45	46	47		gap	break	t.	frag.	chr.inter.	mar.
patient	78	24	0	102	0	0	0	1	1	2
father	4	55	0	59	2	1	1	1	1	0

t.: translocation, frag.: fragment, chr.inter.: chromatid interchange, mar.: marker chromosome.

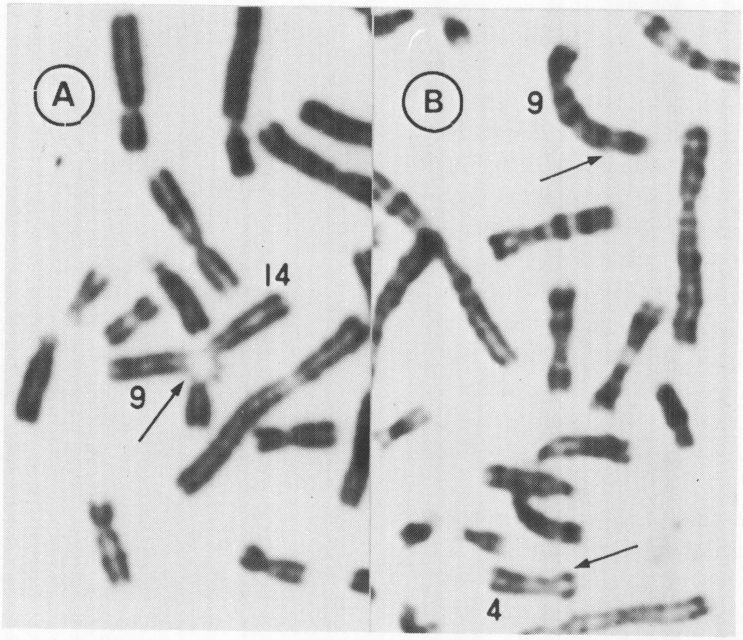


Fig. 9. Chromosome abberations observed in leucocyte cultures in the patient's father. (A). Chromatid interchange, (B). Translocation, t(9;4) (q21qter).

Cases of normal variations

Case 1. (1qh+) The patient was a 15-year-old girl. She had postencephalitic cerebral palsy. Her remarkable clinical signs were low nasal bridge, cleft lip, seizure, difficulty in walking, behavior disorders; excitement, wandering, and speech disorder. Her karyotype was given as 46,XX,1qh+. Her parents were phenotypically normal, and had the normal karyotypes.

Case 2. (1qh+) The patient was an 18-year-old girl. She had postmeningitic cerebral palsy. Her remarkable clinical signs were oxycephalus, seizure, hemiplegia at right side, difficulty in walking, and speech disorder. Her karyotype was given as 46,XX,1qh+. Her parents were phenotypically normal. The karyotype of her father was given as 46,XY. The chromosomal examination of her mother was not cooperated.

Case 3. (9qh+) The patient was a 13-year-old boy. He had cerebral palsy probably by perinatal cause which was asphyxia. His remarkable clinical signs were dolichocephalus, nystagmus, equino varus, seizure, hemiplegia at right side, inability in walking, behavior disorder; self injury, and speech disorder. His karyotype was given as 46,XY,9qh+. His parents and his younger sister were phenotypically normal, and had the normal karyotypes.

Case 4. (Yqh+) The patient was a 16-year-old boy. He had cerebral palsy probably by perinatal causes which were early rupture of bag and prolonged labor. His remarkable clinical signs were blue sclera, impaired vision,seizure, inability in walking, and speech disorder. His karyotype was given as 46,XYqh+. His parents were phenotypically normal. The chromosomal examinations of them, however, were not cooperated.

DISCUSSION

In this study, the incidence of chromosome ab-

normality was 8,6%, indicating higher incidence as compared to normal population; 0,3—0,5% (reviewed by Makino, 1975)[54].

Abnormal karyotypes were seen in one case of a direct duplication of no.7 chromosome (case 1), 2 cases of a pericentric inversion of no.9 chromosome (case 2 and case 3), one case of triplo-X female (case 4), and one case of mosaic X chromosome (case 5).

According to the reviews of partial trisomy for the long arm of no.7 chromosome (Al Saadi and Moghadam, 1976[2]: Alfi et al, 1973[1]: Bass et al, 1973[4]: Berger et al, 1974[5], 1977[6]: Carpentier et al, 1972[9]: Fryns et al, 1978[18]: Grace et al, 1972[23], 1972[24]: Kardon et al, 1983[48]: Klasen et al, 1983[51]: Morić-Petrović et al, 1975[56]: Newton et al, 1972[58]: Schinzel and Tönz, 1979[64]: Schmid et al, 1979[65]: Serville et al, 1975[66]: Turleau et al, 1976[73]: Vogel et al, 1973[76]: Vogel, 1977[77]; Wahrman et al, 1978[78]: Winsor et al, 1978[79], case 1 had almost typical clinical features; low birth weight, growth and mental retardation, large forehead, prominent occiput, flat nose, short neck, low-set ears, hypertelorism, and epicanthus. Of about 20 cases reported previously, almost all of the cases were paternal origin, but 4 cases including this case were sporadic.

The no.9 chromosome shows a high susceptibility for the structural rearrangement. In this study also, 2 cases (case 2 and case 3) had pericentric inversion. In reference to the previous reports on inversion of no.9 chromosome (Axelsson et al, 1981[3]: Boué et al, 1975[7]: Croquette et al 1979[11]: De La Chapelle et al, 1974[12]: Debevec and Canki, 1982[13]: Fällström and Wahlström, 1979[16]: Frydman et al, 1981[17]: Fuenmayor et al, 1981[19]: Hernandez et al, 1979[26]: Howard-Peebles and Stoddard, 1979[27]: Kadotani et al, 1981[34], 1984[36], 1985[38,39]: Kanata et al, 1985[42-44]: Karmon et al, 1978[49]: Kahn et al, 1978[40]: Kirillova et al, 1979[50]: Pescia et al, 1977[59]: Schinzel et al, 1974[63]: Shiraishi and Makino, 1977[67]: Sumitt et al, 1977[71]: Vine et al, 1976)[75], the features of the cases were various from phenotypically normal to phenotypically abnormal with multiple congenital malformations. Ghosh (1974)[22] mentioned, however, that the C-band heteromorphism including inversion was higher incidence in children with congenital malformations as compared to normal control.

The first report of triplo-X case was given by Jacobs et al (1959)[29]. Baar, Sergovich et al (1969) represented reports of 155 such females, 143 cases from the literature and 12 cases from their own studies. Polani (1970)[61] mentioned that this major chromosome abnormality does not produce an identifiable clinical syndrome, as there are no distinctive features of the 47,XXX female. German (1971)[21] reported that the patients are not perticularly abnormal and reproductive performance may be slight, although they may be dull and have psychological problems. Polani pointed out, however, that, in 47,XXX females as in 47,XXY males, there is a tendency to complex psychosocial maladjustments on the basis of deviate brain function which result in a degree of intellectual impairment.

It has been well known that the deletion of one out of two X chromosomes is Turner's Syndrome (Turner, 1938)[74], and many of X chromosome monosomy were reported (German, 1971[21]: Hayata, 1969[25]: Ikeuchi et al, 1968[28]: Makino et al, 1962[55], 1963: Nakagome et al, 1966[57]: Neu et al, 1968: Okada, 1968). The present case (case 5) was specific by reason that the patient, inspite of her typical Turner-like stiguma, had mosaic typed karyotype including the ring X. Further, the father of this patient had many cells showing the chromosome aberrations; translocation, fragment, chromatid interchange, marker chromosome. It is very suggestive that the recurrent occurrence of the patients with abnormal karyotype in the same family was reported (Kadotani et al, 1970: Kadotani and Watanabe, 1983[35]: Kondo et al, 1979[52]: Silengo et al, 1981)[68]. Those cases could be caused by a genetic tendency for nondisjunction or by mosaicism in one of the normal parents. In this case, however, the relationship between the cytogenetic findings of the patient and those of her father remains in the dark.

Four cases showed normal variations on the long arm of no.1, 9, and Y chromosome. In all of those cases, it was found that the elongation occurred at the area of constitutive heterochromatin. Although the elongated long arm of no.1, 9, and Y chromosome have been found in both normal persons and subjects with congeni-

tal abnormalities (Büchner et al, 1967[8]: Cooper and Hernis, 1963[10]: Donahue et al, 1968[15]: Jacobs et al, 1970[30]: Kadotani et al, 1980[33]: Kamaryt et al, 1972[41]: Lobitz et al, 1972[53]: Philip et al, 1965[60]: Prigozina et al, 1971[62]: Sofuni and Sandberg, 1967[69]: Ying and Ives, 1968[80]: Yunis and Gorlin, 1963)[81]:, more morphological variations of those chromosomes were found in abnormal population than in normal (Gardner et al, 1974[20]: Ghosh, 1979)[22]. Further, Soudek and Sroka (1979)[70] mentioned in the report of chromosomal variations in mentally retarded and normal men that increased size of 9qh+ seemed to be a factor with possible negative effect. Up to date, however, the significance of the variation of constitutive heterochromatin in relation to mental retardation and/or cerebral palsy is remained to be elucidated.

Although the chromosomal examinations were also performed on available relatives of karyotipically abnormal patients, in order to reveal whether the chromosome abnormalities were hereditary, the chromosomally abnormal relatives were not detected, in this study.

All the patients examined in this study had heavy mental retardation and cerebral palsy. Cerebral palsy is defined as any non progressive central motor deficit by the disease of brain, mainly motor center (Dephin and Speck, 1979)[14]. The causal brain disease occurs at prenatal, perinatal, or postnatal period. Untill now, peri-, and postnatal causes; asphyxia, forceps operation, pracenta praevia, inertia uteri, prolonged labor, severe jaundice, meningitis, encephalitis, and so on, have occupied the large proportion; 80—90%, and the proportion of the prenatal causes has been small. From now, however, according to the advance of medicine, peri-, and postnatal causes may be decreased. The prenatal causes include intrauterine infection, hereditary disease, chromosome abnormalities, and so on.

On the results of this study, it was confirmed that chromosome abnormalities contribute significantly to the prenatal causes of cerebral palsy, and that chromosome analyses are important to any mental retardate with cerebral palsy, even if the patient had another causal factor.

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