

A Chromosomal Study on 100 Cases of Cerebral Palsy

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KEY WORDS Chromosomal aberration; cerebral palsy; congenital anomaly; fragile site.

ABSTRACT A chromosomal study was conducted on the patients of cerebral palsy with congenital anomalies. One hundred cases were investigated on the chromosomal abnormalities and fragile sites. As a result of this study, 8 cases had abnormal karyotypes showing an incidence of 8.0%. Three out of the 8 cases had chromosomal aberrations transmitted from their parents showing an incidence of 37.5%. Only one case had a folic acid sensitive heritable fragile site at 12q13. Fragile X was not detected.

INTRODUCTION

It is well known that the chromosomal abnormalities are usually combined with congenital anomalies. And also the fragile site is very interesting subject for the study of clinical disorders. However, to date, the study combined with the chromosomal abnormalities and the fragile site in the patient having cerebral palsy with congenital anomalies has been still meager. This study was served to explore the relation to cerebral palsy with congenital anomalies and chromosomal abnormalities and also chromosome fragile sites.

MATERIALS AND METHODS

A chromosomal study was conducted on 100 cases of cerebral palsy with congenital anomalies who were admitted to Hiroshima Prefectural Rehabilitation Center for the Disabled, during the period from July 1993 to June 2000. These included 52 cases of cerebral palsy with central nervous system anomalies and 48 without central nervous system anomalies. Of the 100 cases, 58 were male and 42 were female. Their ages ranged from 3 months to 23 years old.

Chromosomal study was surveyed on chromosomal aberrations for 100 cases and on chro-

mosomal fragile sites for 85 out of the 100 cases. The chromosomal preparations were made by standard leucocyte culture procedures (Kadotani 1986). Phytohemagglutinin-stimulated peripheral blood was cultured for 72 hours in Eagle's MEM medium (Nissui Pharmaceutical Co., LTD) for chromosomal aberrations and in Eagle's MEM medium without folic acid (Nissui Pharmaceutical Co., LTD.) for fragile sites (Sutherland 1979; Sugio and Kajii 1985), and slides were made by means of the flame-drying technique. The conventional Giemsa and G-banding differential staining were routinely employed for chromosome identifications. In abnormal or ambiguous cases, C-banding, R-banding, high-resolution G-banding and/or Fluorescence *in situ* hybridization (FISH) technique were also employed as necessary (Takagi 1978; Ikeuchi 1984; Zhao et al. 1997). Chromosome counts were made with 62 well-delineated metaphases: 12 cells for chromosomal aberrations and 50 cells for fragile sites. The karyotype was analysed in 6 cells by conventional Giemsa staining and G-banding respectively. Regarding the survey of fragile sites, the break point with the occurrence of 4.0% or more at same point was considered as the fragile site (Takimoto et al. 1985; Sutherland and Matteti 1988).

RESULTS

Chromosomal Aberrations

Chromosomal aberrations were investigated in 100 cases of cerebral palsy with congenital anomalies: 52 cases were with central nervous system anomaly (CNS) and 48 cases were without CNS. Eighty-three out of the 100 cases had normal karyotypes: 46 cases were with CNS and 37 cases were without CNS. Nine cases had

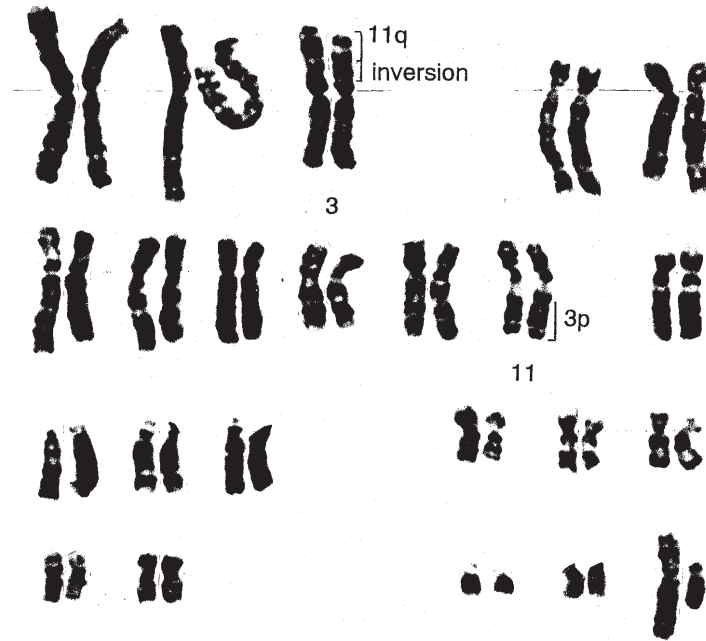


Fig. 1. The karyotype of the case of cerebral palsy with congenital anomalies: 46,XY,der(3)inv(3)(p13p21.3)t(3;11)(p21.3;q21)pat

normal karyotypes with variations: 4 cases were with CNS and 5 cases were without CNS, and 8 cases of 1qh+ and one case of 9qh+. And 8 cases had abnormal karyotypes showing an incidence of 8% (Table 1). In the 8 cases having abnormal karyotypes, two cases were with CNS and their karyotypes were 46, XY, ins (22) (p13; p11.2) mat and 46, XX, inv (4) (q27q31.3). And six cases were without CNS and their karyotypes were 46, XY, del (21) (p11) mat, 46, XY, der (3) inv (3) (p13q21.3) t (3;11) (p21.3; q21) pat (Fig. 1), 47, XYY, 46, XY, del (15) (q11q12), 46, XY, inv (9) (p11q13), and 46, XY, 1qh+, inv (9) (p11q13). Of the 8 cases, 3 cases had the chromosome aberrations transmitted from the parents: one case from paternal line and two cases from maternal line (Table 2).

Fragile Sites

Chromosomal fragile sites were investigated in 85 cases. Of the 85 cases, 32 cases had no fragile site, and 53 cases had the fragile sites. Out of the 53 cases, 29 cases were with CNS and had all common fragile sites, the incidence being 64.4%. Twenty-four cases were without

CNS, and 23 cases of the 24 had common fragile sites and one case had a folic acid sensitive heritable fragile site, the incidence being 60.0% (Table 3). So, 52 cases out of the 53 had common fragile sites. The folic acid sensitive heritable fragile site in one case was at 12q13. Some cases had two or three fragile sites and so total number of the fragile sites were 72. On the frequencies of each site, the site at 3p14 was found in 31; the incidence being 43.1%, the site at 17q21 was in 13; the incidence being 18.1%, the site at 6p21 was in 10; the incidence being 13.9%, and other sites were found in 18 (Table 4). On the frequencies of each fragile site at 3p14, 6p21 and 17q21 and of total fragile sites, the differences were scarcely recognized between in the cases of cerebral palsy with CNS and in

Table 1: Analysis of the karyotypes (cases)

	With CNS	Without CNS	Total
Normal	46	37	83
Normal variation 4 (1qh+:4)		5 (1qh+:4, 9qh+:1)	9
Abnormal	2	6	8
Total	52	48	100

CNS: Central Nervous System anomaly

Table 2: Chromosomal aberrations of cerebral palsy with congenital anomalies

Cerebral palsy	Total cases	Chromosomal aberration		
		Cases (%)	Transmitted	
With CNS	52	2 (3.8)	46,XY,ins(22)(p13;p11.2)mat	46,XX.inv(4)(q27q31.3)
Without CNS	48	6 (12.5)	46,XY,del(21)(p11)mat	47,XY
			46,XY,der(3)inv(3)(p13p21.3)	46,XY,del(15)(q11q12)
			t(3;11)(p21.3;q21)pat	46,XY,inv(9)(p11q13)
				46,XY,1qh+,inv(9)(p11q13)
Total	100	8 (8.0)	3 (37.5)	5 (62.5)

CNS: Central Nervous System anomaly

the cases without CNS. No fragile X was detected.

REMARKS AND CONCLUSION

The advances made in differential staining methods have contributed much to the incidence of knowledge in human cytogenetics. The application of many kinds of banding techniques had made it possible not only to detect the chromosome abnormalities but also to delineate the exact points of rearrangements. In order to detect even minor chromosome abnormalities, in this study, the banding techniques were routinely employed in all the cases.

As the result, out of 100 cases of cerebral palsy, 83 cases had normal karyotypes, 9 cases had normal karyotypes with variations, and the abnormal karyotypes were found in 8 cases. The

incidence of chromosome abnormalities in present study was 8%, which was relatively high as compared with the normal population: 0.3-0.5% (Makino 1979). On the abnormal 8 cases, chromosomal losses were found in 2 cases; one case of del(15) and one case of del(22)mat. The translocation-type abnormal karyotypes were found in 5 cases; one case of der (3) inv (3) t (3;11) pat, one case of inv (4), two cases of inv (9), and one of ins (22). The numerical abnormality was found in one case: 47, XYY. As a result of the chromosome analyses performed on the relatives of the cases having abnormal karyotypes, three cases were found to have the abnormalities transmitted through the parental line; one case from paternal and two cases from maternal.

The fragile sites are very interesting subjects for the study of clinical disorders. Especially, the fragile X chromosome has been well known as one of the causes of the mental retardation: fragile X syndrome (Sutherland 1983). In our study, the fragile sites were investigated in 85 cases of cerebral palsy with congenital anomalies and found in 53 cases out of the 85 cases. Of the 53 cases, 52 cases had common fragile sites, especially 3p14 was the most frequent fragile site: the incidence being 43.1%. Smeets et al. reported that 63 of the 70 investigated persons showed at least one gap or break at 3p14 and the

Table 3: The comparison of fragile sites (cases)

	Fragile site (%)		Total	No fragile site	Total
	Common	Heritable			
With CNS	29	0	29 (64.4)	16	45
Without CNS	23	1	24 (60.0)	16	40
Total	52	1	53 (62.4)	32	85

CNS: Central Nervous System anomaly
Common: Common fragile site, Heritable: Folic acid sensitive heritable fragile site

Table 4: The frequencies of fragile sites (%)

	1p36	1p21	1q12	1q21	1q25	3p14	5p14	5q31	6p21	6q21	7q22	7q32	9q12	11q13	11q23	12q13*	17q21	Xq22
With CNS	0	0	1	0	0	16(45.7)	0	0	5(14.3)	1	0	0	1	1	1	0	8(22.9)	1
Without CNS	1	1	0	1	1	15(40.5)	1	2	5(13.5)	0	1	1	0	2	0	1	5(13.5)	0
Total	1	1	1	1	1	31(43.1)	1	2	10(13.9)	1	1	1	1	3	1	1	13(18.1)	1

CNS: Central Nervous System anomaly, * : Folic acid sensitive heritable fragile site

most common fragile site in man was 3p14 (1986). In our study, a folic acid sensitive heritable fragile site was detected in one male case, which was at 12q13. Nevertheless, no fragile X was detected. Though the autosomal folic acid sensitive fragile sites among mental retardates were reported to be higher than that among normal populations (Sutherland 1985; Takahashi et al. 1988; Kadotani et al. 1994), the report on the fragile sites among cerebral palsy with congenital anomalies has been still meager. And also we cannot find any report on the chromosomal studies and fragile sites of cerebral palsy.

The present study has confirmed that chromosomal abnormalities contribute significantly to the etiology of cerebral palsy and that the chromosome analysis is an important tool to any congenital anomaly, especially when no obvious cause for the anomaly could be found.

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