PRINT: ISSN 0972-3757 ONLINE: 2456-6360
Int J Hum Genet, 3(3): 155-158 (2003)
DOI: 10.31901/24566330.2003/03.03.05

Chromosomal Study on Congenital Anomalies with Mental Retardation

Tetsuji Kadotani[1], Yoko Watanabe[1], Toshihide Saito[1] and Tomiko Kadotani[1]

1. The Kadotani Medical Research Foundation, 1248, Saijohigashi Saijo, Higashi-Hiroshima 739-0042, Japan, Fax: +81-824-23-2289

2. Department of Pediatrics, Hiroshima Prefectural Rehabilitation Center, 295-3, Taguchi, Saijo, Higashi-Hiroshima 739-0036, Japan, Fax: +81-824-25-1094

KEY WORDS Mental retardation; congenital anomaly; chromosomal abnormality

ABSTRACT Chromosomal study was carried out on congenital anomalies with mental retardation to explore the relation between mental retardation and chromosomal abnormalities. During a period from 1974 to 2000, 877 cases were referred for this study. These included 173 cases of central nervous system anomalies, 165 cases of epilepsy, 21 cases of muscular dystrophy, and 70 cases of Down syndrome. As a result, one hundred and fifty-four cases of the 877 had chromosomal abnormalities showing an incidence of 17.6% and 14 cases of the 144 had the abnormalities transmitted from the parents.

INTRODUCTION

The chromosomal abnormalities are usually combined with congenital anomalies. However it is still meager to study on chromosomal abnormalities and congenital anomalies with mental retardation. This study was served to explore the relation between congenital anomalies with mental retardation and chromosomal abnormalities on the patients with central nervous system anomalies, epilepsy, muscular dystrophy, Down syndrome and other congenital anomalies with mental retardation.

MATERIALS AND METHODS

Eight hundred and seventy seven cases of congenital anomalies with mental retardation were referred for this study and investigated regarding chromosomal abnormalities, during the period from 1974 to 2000. These included 173 cases of central nervous system anomalies: neural tube defect; microcephalus; hydrocephalus and other central nervous system anomalies, 165 cases of epilepsy, 21 cases of muscular dystrophy, 70 cases of Down's syndrome and other 499 cases of mental retardation. Some cases had two or more kinds of anomalies, for example having epilepsy and central nervous system anomaly.

The lymphocytes were cultured for 72 hours in the minimal essential medium supplemented with 5% calf serum. The slides were made by means of the flame-drying technique. The chromosome observation was made with 50 well-delineated metaphases. The conventional Giemsa and G-banding differential staining were routinely employed for chromosome identifications (Kadotani 1986). In abnormal or ambiguous cases, C- R-, Q-, or high-resolution G-banding and/or Fluorescence in situ hybridization (FISH) technique were also employed as necessary (Takagi 1987; Ikeuchi 1984; Zhao et al. 1997).

RESULTS

Chromosomal aberrations were investigated in 877 cases of congenital anomalies with mental retardation: 165 cases of epilepsy, 173 cases of central nervous system anomaly (CNS), 21 cases of muscular dystrophy, 70 cases of Down syndrome and 499 cases of other congenital anomaly (other-group) with mental retardation. Six hundred and eighty out of the 877 cases had normal karyotypes (Table 1). Forty three cases had normal karyotypes with variations which were normal variation: thirteen cases of epilepsy, ten cases of CNS, three cases of muscular dystrophy, no case of Down syndrome and twenty cases of other-group with mental retardation (Table 1). One hundred and fifty-four cases had abnormal karyotypes showing an incidence of 17.6% (Table 1). On the chromosomal abnormalities of each syndrome, fifteen cases were in epilepsy showing 9.1%, twenty-seven cases were in CNS showing 15.6%, one case was in muscular dystrophy showing 4.8%, seventy cases were

Table 1: Chromosomal analysis on each syndrome with mental retardation

Syndrome	*Case*	*Normal*	*Normal variation*	*Abnormal (%)*	*Transmit.**
MR	877	680	43	154 (17.6)	14
Epilepsy	165	137	13	15 (9.1)	2
CNS	173	136	10	27 (15.6)	4
Muscular dystrophy	21	17	3	1 (4.8)	0
Down syndrome	70	0	0	70(100)	0
Other mental retardation	499	423	20	56 (11.2)	8

MR: All cases of mental retardation, CNS: Central nervous system anomaly,
*: The abnormal transmitted from the parent.

Table 2: Chromosomal aberration on each syndrome (%)

Aberration	*MR*	*Epilepsy*	*CNS*	*Musc. dystrophy*	*Down sy.*	*Other MR*
Numerical aberration	91 (52.3)	2 (12.5)	12 (41.4)	0	67 (95.7)	10 (17.2)
Mosaic	9 (5.2)	0 (0)	3 (10.3)	0	0	6 (10.3)
Partial trisomy	20 (11.5)	3 (18.8)	5 (17.2)	0	0	12 (20.7)
Deletion	22 (12.6)	3 (18.8)	2 (6.9)	0	0	17 (29.3)
Inversion	12 (6.9)	5 (31.3)	1 (3.4)	1 (100)	0	5 (8.6)
Ring	6 (3.4)	1 (6.3)	2 (6.9)	0	0	3 (5.2)
Translocation	11 (6.3)	2 (12.5)	3 (10.3)	0	3 (4.3)	3 (5.2)
Insertion	3 (1.7)	0 (0)	1 (3.4)	0	0	2 (3.4)
Total	174	16	29	1	70	58

MR: All cases of mental retardation, Musc. Dystrophy: Muscular dystrophy, Down Sy: Down syndrome, Other MR: Other mental retardation

in Down syndrome showing 100% and 56 cases were in other-group with mental retardation showing 11.2%. The frequency of chromosomal abnormality was highest in the group of CNS except for Down syndrome. Of the 154 cases, 14 cases had the chromosomal abnormalities transmitted from the parents: two cases of epilepsy, four cases of CNS and eight cases of other-group with mental retardation. Of the 14 cases, nine cases were through the maternal line and five cases were through the paternal line (Table 3).

The chromosomal aberrations on each syndrome were shown in Table 2. Of the patient having chromosomal aberrations in all cases of mental retardation, 91 cases had numerical aberration showing 52.3%, 22 cases had chromosomal deletion showing 12.6%, and 20 cases had partial trisomy showing 11.5%. On the epilepsy, five cases had inversion showing 31.3%, three cases had partial trisomy and three cases had deletion, showing both 18.8%. On the CNS, twelve cases had numerical aberration showing 41.4%, and five cases had partial trisomy showing 17.2%. On Down syndrome, all cases had chromosome aberration: 67 cases of trisomy and 3 cases of translocation type. On other-group with mental retardation, deletion was most frequently in chromosomal aberrations, and next was partial trisomy.

Chromosomal abnormalities on each syndrome were shown in Table 3. Of the 14 cases having the chromosomal abnormalities transmitted from the parents, nine cases had the abnormalities through the maternal line and five cases had through the paternal line (Table 3).

REMARKS AND CONCLUSION

The application of some kinds of banding techniques had made 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. It has been reported on the chromosomal abnormalities in 877 cases of congenital anomalies with mental retardation. Of the 877 cases, 154 cases had chromosomal abnormalities, showing an incidence of 17.6%. The frequencies of chromosomal abnormalities were 9.1%, 15.6%, 4.8%, 100% and 11.2% in epilepsy, CNS, muscular dystrophy, Down syndrome and other-group with mental retardation each. These frequencies were relatively high as compared with the normal population: 0.3 - 0.5% (Makino 1979). As a result of the chromosome analyses performed on the relatives of the cases having abnormal karyotypes, fourteen

Table 3: Chromosomal abnormalities on each syndrome

Epilepsy		*Central nervous system anomaly*		*Muscular dystrophy*		*Down syndrome*		*Other mental retardation*	
46,XX,inv(4)(q27q31.3)	1	45,X/46,Xr(X)/46,XX	1	46,XY,inv(9)	1	46,XX,der(14;21)	2	45,X	1
46,XX,inv(9)	1	46,XX,13p+	1		**1**	46,XY,der(21;21)	1	45,X (XO-male)	1
46,XX,inv(9)(p13q21)	1	46,XX,7p+	1			47,XX,+21	26	45,X/46,Xdel(Y)(q11)	1
46,XX,r(22)(p11q13)	1	46,XX,der(14)t(10;14)(p11;p11)pat	1			47,XY,+21	41	45,X/46,Xr(X)	1
46,XX,t(1;17)(q23;q21.1)mat	1	46,XX,der(14;21)(q10;q10)	2				**70**	45,X/46,XX	1
46,XY,14p-	1	46,XX,der(15)ins(15;3)(p13;q22)mat	1					45,X/47,XXX	1
46,XY,del(4)(q31.2)	1	46,XX,inv(4)(q27q31.3)	1					45,XY,der(13;14)(q10;q10)	1
46,XY,del(5)(q11q13)	1	46,XX,t(7;21)(q31.2;q22.3)	1					46,ins(X;?)(q13;?)Y	1
46,XY,inv(9)(p11q13)	1	46,XX/46,XX,r(9)(p24q24)	1					46,X,der(Y)ins(Y;15)(p11;q11q13)pat	1
46,XY,der(3)inv(3)(p13p21.3) t(3;11)(p21.3;q21)pat	1	46,XY,del(2)(q35q36)	1					46,XX,15p+	1
		46,XY,del(4)(q31.2)	1					46,XX,1qh+,ins(17;1)(q25.3;q32.1q42.1)	1
46,XY,t(7;14)(q22;q32)	1	46,XY,der(18)t(9;18)(p22;p11.31)mat	1					46,XX,del(15)(q11q13)	1
47,XX,+mar	1	46,XY,ins(22)(p13;p11.2)mat	1					46,XX,del(18)(p11)	1
47,XXX	1	46,XY/47,XY,+mar	1					46,XX,del(22)(q12)pat	1
47,XY,+21	1	47,XX,+21	5					46,XX,der(14)t(8;14)(q22.3;q32.3)mat*	1
47,XY,+del(15)(q15)	1	47,XX,+E	1					46,XX,der(9)ins(9;X)(q13;q22q24)mat	1
	15	47,XY,+21	5					46,XX,dup(3)(q22q27)	1
		48,XXXY	1					46,XX,inv(9)(p11q12)	2
			27					46,XX,inv(9)(p11q13)	1
								46,XX,r(18)(p11q23)	1
								46,XX/46,X,del(X)	1
								46,XX/46,XX,r(22)(p11q13)	1
								46,XY (female)	3
								46,XY,12p+,21p-	1
								46,XY,1qh+,t(3;4)(q23;p14)	1
								46,XY,21p-	1
								46,XY,21p+	1
								46,XY,21p-mat	1
								46,XY,5p-	1
								46,XY,5p+	1
								46,XY,del(10)(p14pter)	1
								46,XY,del(15)(q11q12)	1
								46,XY,del(15)(q11q13)	1
								46,XY,del(5)(q15q31)	1
								46,XY,del(5)(q22q31)	1
								46,XY,del(9)(p21)	1
								46,XY,del(9)(q11q13)	1
								46,XY,der(1)ins(1;9)(q11;q12q13)mat	1
								46,XY,der(12)del(12)(q13.1q15)del(12)(q22q23)	1
								46,XY,der(4)t(4;X)(q35;p11.23)	1
								46,XY,dup(8)(q21.3q24.3)	1
								46,XY,inv(9)	1

Table 3: Cond....

Epilepsy	*Central nervous system anomaly*	*Muscular dystrophy*	*Down syndrome*	*Other mental retardation*	
				46,XY,inv(9)(p13q13)pat	1
				46,XY,t(7;14)(q11;q22)	1
				47,XX,+18	3
				47,XXX	1
				47,XY,+18	1
				47,XY,+22	2
				47,XY,+del(9)(q12)mat	1
				47,XYY	1
					56

cases were found to have the abnormalities transmitted from the parent, showing an incidence of 9.1%: nine cases through the maternal line and five cases through the paternal line.

The frequency of chromosomal abnormality was shown highest in the group of CNS except for Down syndrome. Next was in the group of epilepsy. On the chromosomal aberrations in each syndrome, inversion was most frequently in epilepsy, partial trisomy was most in CNS because ten cases out of the twelve cases having numerical aberration were the complex anomalies both CNS and Down syndrome, deletion was most in other-group with mental retardation (Table 2, 3).

In the present study, it has been confirmed that chromosomal analysis is an important tool to any congenital anomaly, especially when no obvious cause for the anomaly could be found.

A part of this paper was reported at the 30th Conference of the European Teratology Society in Hannover, Germany, 2002.

REFERENCES

Ikeuchi T 1984. Inhibitory effect of ethidium bromide on mitotic chromosome condensation and its application to high-resolution chromosome banding. *Cytogenet Cell Genet*, **38:** 56-61.

Kadotani T 1986. Cytogenetics and clinical application. *J Higashi-Hiroshima Med Assoc*, **9:** 2-30 (In Japanese)

Makino S 1979. *The Chromosomes-Human Cytogenetics*. Tokyo: Igaku Shoin LTD. (in Japanese).

Takagi N 1978. Senshokutai-hyouhon sakuseihou. In: Akira Tonomura (Ed.): *Senshokutai no bunsenhou, Senshokutai-ijou*. Tokyo: Asakura-shoten LTD pp.340-359 (in Japanese).

Zhao J, Saito T, Kadotani T, Watanabe Y, Tanaka T, Saito-Ohara F, Ikeuchi T. 1997. Reconfirmation of a previously reported *de novo* case of partial 7q trisomy by means of whole chromosome painting. *Chromosome Science*, **1:** 35-38.