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# A chromosomal study on 22 cases of congenital neural tube defects

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**Abstract.** A chromosomal study was conducted on 22 cases of congenital neural tube defects, including 20 cases of spina bifida and 2 of cranioschisis. Out of the 22 cases, 18 cases had normal karyotypes, 2 had normal variations, and 2 had abnormal karyotypes. Abnormal karyotypes were identified as 46, XY, del(2) (q35q36) and 46, XY, ins(22)(p13 ; p11.2p11.2)mat. Both were the cases of spina bifida.

Chromosomal Fragile sites were investigated on 20 cases. In 13 of the 20 cases fragile sites were found at 15 different sites. These sites were all common fragile ones, and no cases showing folic acid sensitive heritable fragile sites were found.

**Keywords**: Neural tube defects, Chromosomal abnormalities, Fragile sites

During a period from July 1993 to June 1998, a chromosomal study was conducted on 22 cases with congenital defects of neural tube for the purpose of exploring the causes of these disease. Out of the 22 cases, 14 cases were male and 8 were female. Their ages ranged from 11 months to 20 years. These cases included 20 cases of spina bifida and 2 of cranioschisis.

Chromosomal slides were prepared according to the standard blood culture procedures using Eagle's MEM medium (Nissui Pharmaceutical Co., LTD.). Karyotype analyses were made on 22 cases with the application of conventional Giemsa and G-banding stainings. The fragile sites were investigated in 20 cases. The lymphocytes were cultured in Eagle's MEM medium without folic acid (Nissui Pharmaceutical Co., LTD.). The frequency of breaks and/or gaps was based on 50 cells per patient, and the break points were identified by the G-banding. The break points with the occurrence of 4.0% or more at same point were considered as the fragile sites.

As a result of these studies, 18 of the 22 cases had normal karyotypes, 2 had normal ones with variations and 2 had abnormal ones showing an incidence of 9.1% (Table 1). Two cases of spina bifida had abnormal karyotypes which were identified as 46, XY, del(2) (q35q36)(Saito *et al.* 1994) and 46, XY, ins(22)(p13 ; p11.2p11.2)mat (Fig. 1).

In 13 cases out of the 20 cases chromosomal fragile sites were found out at 15 different sites. The fragile sites found out in this study were all common ones. The common fragile sites at 3p14 and 17q21 were frequently found in this study (Table 1). Folic acid sensitive heritable fragile sites were not found.

The congenital neural tube defects may be determined by both genetic and environmental factors. The defects may be caused by a teratogenic agent acting before neural tube closure, which occurs in the fourth week of gestation. Teratogens that are capable of inducing the neural tube defects in experimental animals and in human beings, include radiation, maternal hyperthermia, gestational diabetes mellitus, vitamin A deficiency or excess, d-mannose, excess glucose in embryo culture, valproic acid, and folic acid deficiency (Speidel 1973, Holmes *et al.* 1976, Layde *et al.* 1980, Pleet *et al.* 1981, Robert and Giubaud 1982, Shiota 1982, Freinkel *et al.* 1984, Miller *et al.* 1984).

In chromosomal study, it was reported that 13 trisomy and 18 trisomy often occurred the neural tube defects (Kenneth 1997). Congenital neural tube defects were recognized from spontaneous abortion showed high incidence of chromosomal abnormality(Coerdt *et al.* 1997). In the reports of long arm deletion of chromosome 2, only our case of del(2)(q35q36) had the neural tube defects. On the hydrocephalus, our case and another case of del(2)(q22q31) commented on by Nomoto (1996) also had it. The clinical features of del(2)(q35q36) distinguished from other cases of this study were arthrogryposis and peculiar countenance consisting of thick eye brows and small chin. At the severity of disease the case of del(2)(q35q36) was showed as moderate. The case of ins (22) had the same karyotype as his mother who was phenotypically normal. It was suggested from this result that prenatal environ-

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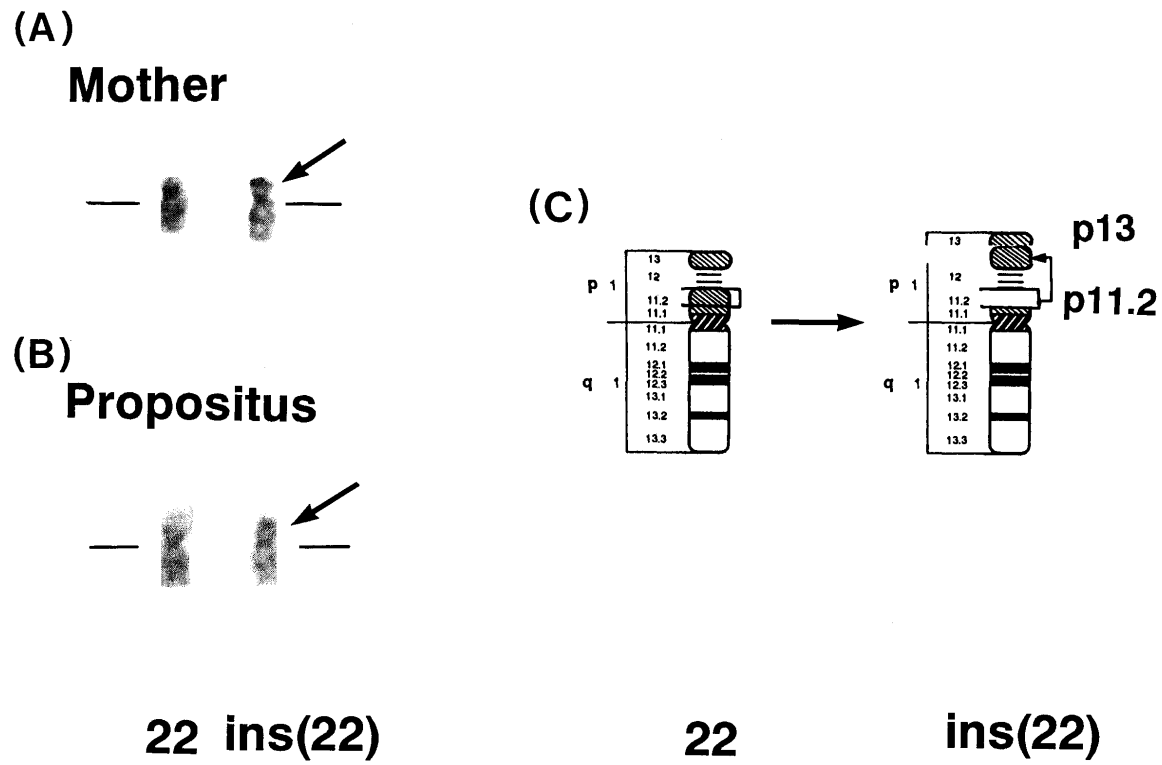


Figure 1. (A) shows the partial karyotype of the mother ; 46, XX, ins(22) (p13 ; p11.2p11.2) and (B) shows the partial karyotype of the patient ; 46, XY, ins(22)(p13 ; p11.2p11.2)mat. (C) shows the diagram of insertion. Arrow indicates the inserting segment.

Table 1. Karyotypes and fragile sites on 22 cases of congenital neural tube defects

〈Spina bifida〉

| Case | Age (y) | Karyotype | BP/CL | Break point (times) | Fragile site | Complication |
|---|---|---|---|---|---|---|
| 1 | 11 | 46, XY | 5/4 | 1q21 2q32 3p14(3) | 3p14 | MR(s), Hy-cep, NB |
| 2 | 12 | 46, XX, 1qh+ | 8/6 | 3p14(3) 5q15 6q26 7q31 10q25 11q21 | 3p14 | MR(s), Epi, Hy-cep, NB |
| 3 | 10 | 46, XX | 8/8 | 1p31 1q21 1q25 9q22 11q13 12q13 17q21(2) | 17q21 | Hy-cep, NB |
| 4 | 9 | 46, XY | 0/0 | | | Ptosis, Hy-cep, NB |
| 5 | 9 | 46, XY | 9/6 | 3p14(6) 5q3 6q15 17q21 | 3p14 | MR(m), Epi, Hy-cep, NB |
| 6 | 8 | 46, XY | 5/5 | 1q21 1q42 3p14 3q27 8q21 | | MR(m), Hy-cep, NB |
| 7 | 12 | 46, XY | 11/9 | 2q33 3p14(4) 4q33 9q22 13q21 17q21(3) | 3p14 17q21 | Hy-cep, NB |
| 8 | 7 | 46, XY | | not examined | | Hy-cep, NB |
| 9 | 2 | 46, XY, 9qh+ | 4/3 | 3p14(2) 6p21 Xp22 | 3p14 | Hy-cep, NB |
| 10 | 7 | 46, XX | 4/4 | 3p12 3q27 17q21(2) | 17q21 | MR(m), Hy-cep, NB, TOF |
| 11 | 12 | 46, XX | 4/4 | 1q21 3p14 4p14 5q31 | | MR(m), Hy-cep, NB |
| 12 | 9 | 46, XY, del(2) (q35q36) | 10/7 | 1p32 2p24 3p14(5) 4q31 5q31 11q13 | 3p14 | MR(mo), Hy-cep, NB, Arthrogryposis |
| 13 | 3 | 46, XX | | not examined | | MR(s), Epi |
| 14 | 8 | 46, XY | 8/8 | 1q12 1q13 2q21 2q31 7q22 9q12 11q13 12q21 | | MR(m), Hy-cep, NB |

| Case | Age (y) | Karyotype | BP/CL | Break point (times) | Fragile site | Complication |
|---|---|---|---|---|---|---|
| 15 | 11 | 46, XX | 11/6 | 3p14 6q21 9q12 11q13(2) 14q23 17q21(4) Xp11 | 11q13 17q21 | Hy-cep, NB |
| 16 | 5 | 46, XY, ins(22)(p13; p11.2p11.2) mat | 14/12 | 1q31 3p14(2) 3q13 3q27 4q23 6q26 10q22 12q13 14q23 16q23 16q22 17q21 19q13 | 3p14 | Hy-cep, NB |
| 17 | 11m | 46, XX | 7/7 | 1p22 2q31 4q27 6p21 17q21(3) | 17q21 | Hy-cep, NB, MR(mo) |
| 18 | 8 | 46, XY | 3/3 | 3p14 6q23 17q21 | | Hy-cep, NB |
| 19 | 1 | 46, XY | 4/4 | 1p21 1q25 3p14 6p21 | | Hy-cep, NB, MR(m) |
| 20 | 3 | 46, XY | 5/5 | 2p24 3p14(3) 16q23 | 3p14 | |
| 〈Cranioschisis〉 | | | | | | |
| 21 | 1 | 46, XY | 10/6 | 1p21 1p31 1q25 3q25 3q26 6q26 7(cp) 13q21 14q23 15q22 | | Hy-cep, Epi, MR(s) |
| 22 | 7 | 46, XX | 10/9 | 1p22 1p31 1p32 3p14(2) 6p21 6p25 10p13 11q14 17q21 | 3p14 | Hy-cep, NB, MR(mo) |

y : year(s), m : months, BP/CL : number of break point/number of cell with break point, NB : Neurogenic Bladder, Hy-cep : Hydrocephalus, Epi : Epilepsy, TOF : Tetralogy of Fallot, MR : Mental Retardation, (m) : mind, (mo) : moderate, (s) : severe

ments might participate in the developments of the fetus.

In chromosomal fragility, there was no case having a folic acid sensitive heritable fragile site. The studies of relationship between chromosome fragility and mental retardation had shown the high incidence of fragile X. But there has been few studies about the relationship between other neurological disease and chromosome fragility.

The result of this study is remarkable to investigate the etiology of the congenital neural tube defects. Further study is necessary to clarify the relationship between chromosomes and congenital neural tube defects. Chromosomal analysis is an important tool to explore the causes of congenital neural tube defects.

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