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Case Report

PARACENTRIC INVERSION OF CHROMOSOME 14: A CASE REPORT

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Summary A new case of familial heterozygous paracentric inversion in the long arm of chromosome 14 [inv(14)(q22q32)] is presented. The rearrangement was first ascertained in a fetus examined due to advanced maternal age, and then detected in the father. The phenotypes of the newborn and the father were completely normal. The parents had no history of spontaneous abortion. With reference to previous reports, the risk of clinical abnormalities are discussed for both *de novo* and familial paracentric inversions of chromosome 14.

Key Words paracentric inversion, chromosome 14, phenotype, chromosome rearrangement

INTRODUCTION

We recently experienced a Japanese family having paracentric inversion of chromosome 14, inv(14)(q22q32), which is herein reported. With reference to previous reports, we discuss the possibility of clinical abnormalities in various types of inv(14).

CASE REPORT

The mother, a 39-year-old healthy Japanese, received a prenatal chromosomal examination at 15 weeks of gestation because of her advanced age. The father was a 41-year-old healthy Japanese. They were not consanguineous. This was the mother's second marriage. She had experienced one normal pregnancy with the present husband. The phenotype of the first child, a male, was normal. Prenatal cytogenetic analysis revealed a heterozygous paracentric inversion in the long

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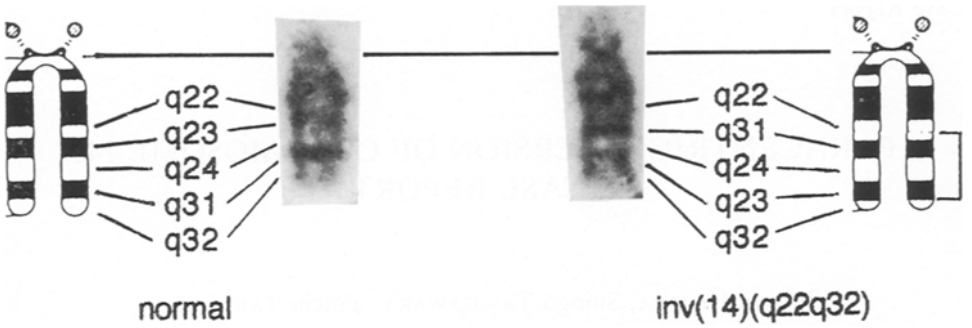

Fig. 1. G-banding of fetal chromosome 14. The inverted chromosome is shown on the right side and the normal chromosome is shown on the left side.

arm of chromosome 14 with breakpoints at q22 and q32, the karyotype being 46, XX,inv(14)(q22q32) (Fig. 1). Due to the fetal chromosomal rearrangement, cytogenetic analyses of the parents were performed. Although the mother had a normal karyotype, the father had the same chromosomal rearrangement as the fetus. Family history was negative with regard to miscarriages, mental retardation, and congenital malformations.

The mother spent an uneventful pregnancy and gave birth to a healthy female newborn after spontaneous labor in the 40th gestational week. The birth weight was 3,032 g, the body length 51.1 cm, the head circumference 33 cm, and the chest circumference 32 cm. The newborn had neither asphyxia nor malformations. The results of neurological examination were entirely normal. The newborn was discharged after an uneventful perinatal period and grew without any clinical problems thereafter.

DISCUSSION

Nineteen cases of heterozygous paracentric inversion in the long arm of chromosome 14 have been reported (Fryns and Van den Berghe, 1980; Jaeken *et al.*, 1980; Ridler and Sutton, 1981; Cox *et al.*, 1982; Boue and Gallano, 1984; Hecht *et al.*, 1984; Madan *et al.*, 1984; Mules and Stamberg, 1984; Groupe de Cytoegneticiens Francais, 1986; Leung and Hoo, 1986; Daniel *et al.*, 1989; Miller *et al.*, 1990; Turczynowicz *et al.*, 1992; Hales *et al.*, 1993). Out of the 20 cases including the present case, 14 cases were familial, five cases were *de novo* and one case was of unknown origin. In four out of the five *de novo* cases, the carriers suffered from clinical abnormalities, such as mental retardation, microcephaly, habitual abortion, or sterility (Fryns and Van den Berghe, 1980; Jaeken *et al.*, 1980; Groupe de Cytogeneticients Francais, 1986). Of the familial cases, seven cases were ascertained to have inversion because of their clinical abnormalities including microcephaly, mental retardation, neutropenia, hypospadias, habitual abortion, or chromosomal

recombination (Cox *et al.*, 1982; Mules and Stamberg, 1984; Groupe de Cytogeneticients Francais, 1986; Leung and Hoo, 1986; Miller *et al.*, 1990; Turczynowicz *et al.*, 1992). The other seven familial cases, including the present case, did not suffer from clinical abnormalities and were incidentally ascertained (Ridler and Sutton, 1981; Boue and Gallano, 1984; Madan *et al.*, 1984; Groupe de Cytogeneticients Francais, 1986; Daniel *et al.*, 1989).

Inversions, one type of balanced chromosomal rearrangements, often induce clinical abnormalities. As the mechanism of occurrence of abnormalities in *de novo* carriers, two explanations have been postulated: a breakpoint is located in a gene and the absence of the gene function may consequently induce abnormalities: such rearrangements cause a very small chromosomal deletion or duplication (Warburton, 1991). Referring to the previous reports of *de novo* paracentric inversion of chromosome 14, the incidence of morphological abnormalities observed in carriers is 2/5 [microcephaly observed in the two carriers of inv(14)(q13q24)], that of mental retardation is 1/5 (one patient with microcephaly complicated by mental retardation), and that of infertility is 2/5. Therefore, it must be emphasized that the risk of clinical abnormalities is remarkably high for a *de novo* carrier.

Since inversions are apparently balanced rearrangements of chromosomes, the risk of phenotypic abnormality has been thought to be low. For example, the risk of abnormalities is indeed very low in pericentric inversion of chromosome 9 (Uehara *et al.*, 1992) and the risk is relatively low in pericentric inversion of chromosome 12 (Uehara *et al.*, 1994). However, in contrast with those pericentric inversions, the risk in carriers of paracentric inversion of chromosome 14 is considerably high. Therefore, it is suggested that the risk seems to be different in various inversions. However, for better counselling for the carriers suffering from such chromosomal rearrangements, further accumulation of data and further molecular biological studies are necessary.

REFERENCES

Boue A, Gallano P (1984): A collaborative study of the segregation of inherited chromosome structural rearrangements in 1356 prenatal diagnoses. Prenat Diag **4**: 45–67

Cox DW, Markovic VD, Teshima IE (1982): Genes for immunoglobulin heavy chains and α_1-antitrypsin are localized to specific regions of chromosome 14q. Nature **297**: 428–430

Daniel A, Ernest B, Hook B, Wulf G (1989): Risks of unbalanced progeny at amniocentesis to carriers of chromosome rearrangements: Data from United States and Canadian laboratories. Am J Med Genet **31**: 14–53

Fryns JP, Van den Berghe H (1980): Paracentric inversion in man: Personal experience and review of the literature. Hum Genet **54**: 413–416

Groupe de Cytogeneticiens Francais (1986): Paracentric inversion in man. A French collaborative study. Ann Genet **29**: 129–176

Hales HA, Peterson CM, Carey J, Hecht BKM, Hecht F (1993): Prenatal detection of *de novo* paracentric inversion 46,XX inv(14)(q22q32.1) in a normal child: report and review of the literature. Am J Med Genet **47**: 848–851

Hecht F, Hecht BK, Berger CS (1984): Aneuploidy in recurrent spontaneous aborters: the tendency

to parental nondisjunction. Clin Genet **26**: 43–45

Jaeken J, Fryns JP, Standaert L, De Cock P, Van Den Berghe H (1980): *De novo* paracentric inversion in a microcephalic boy: 46,XY,INV(14)(q13q24). Ann Genet **23**: 105–107

Leung AKC, Hoo JJ (1986): A case of perineal hypospadias with paracentric inversion of chromosome 14. Eur J Pediatr **144**: 503–504

Madan K, Seabright M, Lindenbaum RH, Bobrow M (1984): Paracentric inversions in man. J Med Genet **21**: 407–412

Miller K, Raabe G, Schlesinger C, Schulze B (1990): Paracentric inversion 14. Ann Genet **33**: 225–227

Mules EH, Stamberg J (1984): Reproductive outcomes of paracentric inversion carriers: Report of a liveborn dicentric recombinant and literature review. Hum Genet **67**: 126–131

Ridler MAC, Sutton SD (1981): A case of paracentric inversion inv(7)(q11q22). Prenatal detection and counselling. Prenat Diag **1**: 81–84

Turczynowicz S, Sharma P, Smith A, Davidson AA (1992): Paracentric inversion of chromosome 14 plus rare 9p variant in a couple with habitual spontaneous abortion. Ann Genet **35**: 58–60

Uehara S, Akai Y, Takeyama Y, Takabayashi T, Okamura K, Yajima A (1992): Pericentric inversion of chromosome 9 in prenatal diagnosis and infertility. Tohoku J Exp Med **166**: 417–427

Uehara S, Tanigawara S, Takeyama Y, Okamura K, Yajima A (1994): A family with pericentric inversion of chromosome 12. Jpn J Human Genet **39**: 201–204

Warburton D (1991): *De novo* balanced chromosome rearrangements and extra marker chromosomes identified at prenatal diagnosis: clinical significance and distribution of breakpoints. Am J Hum Genet **49**: 995–1013