Jpn J Human Genet 39, 201–204, 1994

Case Report

A FAMILY WITH PERICENTRIC INVERSION OF CHROMOSOME 12

Shigeki UEHARA, Shingo TANIGAWARA, Yoichi TAKEYAMA, Kunihiro OKAMURA, and Akira YAJIMA

Department of Obstetrics and Gynecology, Tohoku University School of Medicine, Seiryo-machi, Aoba-ku, Sendai 980, Japan

Summary A heterozygous pericentric inversion of chromosome 12 (inv(12)) was prenatally diagnosed. The breakpoints were localized to p12.3 and q14, resulting in more than one-third of the total length of the chromosome being inverted. The inversion was transmitted from the father whose phenotype was completely normal. The newborn also showed normal phenotype and grew without any clinical problems. The parents had no history of infertility. Based on these facts, it is indicated that pericentric inv(12) (p12.3q14) does not affect phenotype.

Key Words pericentric inversion, chromosome 12, phenotype, chromosome rearrangement

INTRODUCTION

Pericentric inversions are frequent chromosomal rearrangements. The incidence of pericentric inversion of chromosome 9 (inv(9)) is especially high. However, regarding pericentric inversions of chromosome 12 (inv(12)), only 13 families have been previously reported (Kim *et al.*, 1980; Prieto *et al.*, 1981; Poulsen *et al.*, 1981; Voiculescu *et al.*, 1986; Kleczkowska *et al.*, 1987; Watson *et al.*, 1987; Varela *et al.*, 1987; Haagerup and Hertz, 1992). In the report of Kim *et al.* (1980), the proband, the father and a sibling who were carriers of pericentric inv(12) were phenotypically normal. In the report of Prieto *et al.* (1981), a growth retarded female infant with inv(12)(p13q11) and another girl with trisomy 21 and inv(12)(p13q13) were observed. In the report of Poulsen *et al.* (1981), the carrier father was diagnosed as suffering from reduced fertility as shown by abnormal findings of sperm analyses, but his two offspring were normal. In the report of

Received November 18, 1993; Revised version accepted January 4, 1994.

Voiculescu *et al.* (1986), the carriers of inv(12)(p11.2q13) were phenotypically normal without noticeable fertility disturbance. Watson *et al.* (1987) presented a family of inv(12) including two male offspring with 46,XY,12q+. Varela *et al.* (1987) reported a girl with 46,XX,inv(12)/47,XX,i(Xq),inv(12). Haagerup and Hertz (1992) reported some families, including inv(12)(p13q13) carriers, with a birth history of Down syndrome offspring or reproductive failure. We recently experienced a Japanese family, including a female infant and her father, with heterozygous pericentric inv(12)(p12.3q14). The breakpoints in this family have not previously been reported. Therefore, we present the case and discuss the phenotype of the carrier having the rearrangement.

CASE REPORT

A healthy woman (3 gravity, 3 parity, 0 abortion) visited our clinic at Tohoku University School of Medicine for prenatal diagnosis of her fetal chromosomes because of her advanced age (39 years). Her previous three children (karyotypes not examined) were born after spontaneous labor and had grown without any problems after birth. Her husband was a 38-year-old businessman. His intelligence, physical condition and morphological phenotypes were completely normal. The couple was not consanguineous. Amniocentesis was carried out in the 16th gestational week and karyotyping revealed the fetus to be a heterozygote with inversion of chromosome 12 [46,XX,inv(12)(p12.3q14)] (Fig. 1). Based on the result of karyotyping, chromosomal examinations of the parents were then carried out. The karyotype of the father was 46,XY,inv(12)(p12.3q14) and that of the

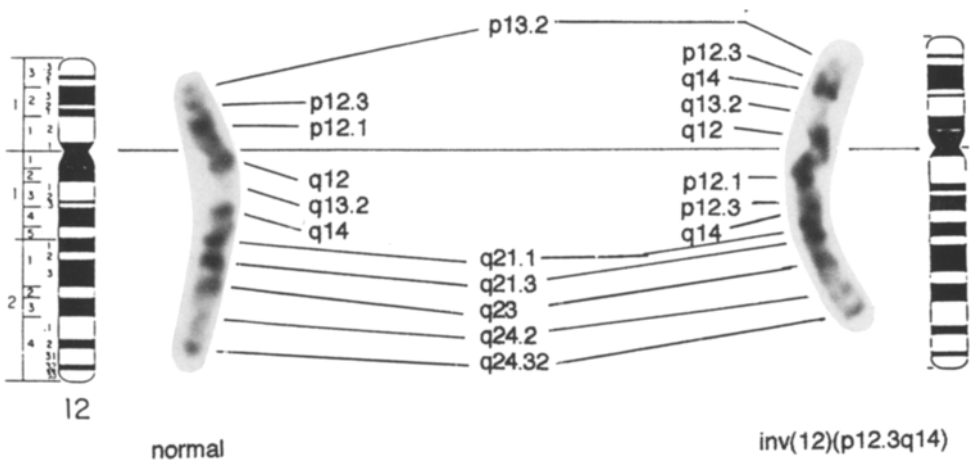

Fig. 1. High resolution banding of the fetal chromosome 12. The inverted chromosome 12 is shown on the right side and the normal chromosome 12 is shown on the left side. Idiograms are shown to indicate the breakpoints (p12.3q14).

mother was 46,XX. The mother had no specific problems during the pregnancy and delivered a female newborn after spontaneous labor on January 23, 1993. The newborn suffered no asphyxia. The birth weight was 2,838 g, the body height 48 cm, the head circumference 33 cm, the chest circumference 32 cm, and the abdominal circumference 32 cm. Those values were within the normal ranges. The weight of the placenta was 720 g. The newborn had no malformations, but a simian crease was found on the left hand. The results of neurological examination were entirely normal. The newborn was discharged after an uneventful perinatal period. She grew without any clinical problems thereafter.

CYTOGENETIC STUDIES

Chromosomal analyses were done by means of G-banding and high-resolution banding. The amniocytes were cultured in Ham F-10 media containing 10% fetal calf serum (FCS). The culture medium used for blood cells was RPMI1640, also containing 10% FCS. The cultures were carried out in 5% CO_2 in air at 37°C for 72 h. Four hours after colcemid treatment, culture cells were harvested, treated in hypotonic solution and fixed in Carnoy's solution.

DISCUSSION

The proband female infant and her father, both having inv(12)(p12.3q14), were phenotypically normal. The parents in this study had had no history of miscarriage. In the previous reports, most carriers were also phenotypically normal (Kim *et al.*, 1980; Prieto *et al.*, 1981; Poulsen *et al.*, 1981; Voiculescu *et al.*, 1986; Watson *et al.*, 1987; Haagerup and Hertz, 1992). Based on those reports and the present case, it is indicated that pericentric inv(12)(p11q13), (p12q13), (p13q13) and (p12.3q14) do not directly affect the phenotype. Some carriers, however, encountered growth retardation (Prieto *et al.*, 1981), infertility (Haagerup and Hertz, 1992) and birth of offspring with chromosomal abnormalities [trisomy 21 (Prieto *et al.*, 1981; Haagerup and Hertz, 1992); unbalanced karyotype (Watson *et al.*, 1987)]. However, since a proband girl having growth retardation (Prieto *et al.*, 1981) was born after preterm labor (7-month pregnancy) and her birth weight was 750 g, the immaturity might be related to the retardation of subsequent growth.

Kleczkowska *et al.* (1987) mentioned that pericentric inversions are related to the occurrence of unbalanced karyotypes, mentalr etardation, congenital anomalies, additional chromosomal abnormalities and infertility. Boue and Gallano (1984) described that couples with a pericentric inversion ascertained through an infant with unbalanced rearrangement can be considered to be a high risk group for unbalanced offspring. Although pericentric inv(9) is known to be a normal chromosomal variant which does not affect phenotype, this rearrangement has been reported to be related to infertility (Boue *et al.*, 1975; Uehara *et al.*, 1992) and a

increased risk of birth of offspring having Down syndrome (Serra *et al.*, 1990; Uehara *et al.*, 1992). Based on those previous reports, it is suggested that the carriers with pericentric inv(12) do not always suffer from clinical problems but have a relatively high risk of infertility or additional chromosomal abnormalities. However, further data and molecular biological analysis are required to investigate the mechanism involved in the manifestation of those clinical problems.

REFERENCES

Boué J, Taillemite JL, Hazael-Massieux P, Leonard C, Boue A (1975): Association of pericentric inversion of chromosome 9 and reproductive failure in ten unrelated families. Humangenetik **30**: 217–224

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

Haagerup A, Hertz JM (1992): Pericentric inversion of chromosome 12; a three-family study. Hum Genet **89**: 292–294

Kim HJ, Levy J, Roguero W (1980): Prenatal detection of pericentric inversion of chromosome 12. Diagn Gynecol Obstet **2**: 231–234

Kleczkowska A, Fryns JP, Van den Berghe H (1987): Pericentric inversions in man: personal experience and review of the literature. Hum Genet **75**: 333–338

Poulsen H, Mikkelsen M, Holmgren G (1981): Peri- and paracentric inversions in chromosome 12: prenatal diagnosis and family study. Prenat Diag **1**: 35–42

Prieto F, Badia L, Asensi F, Moya A, Figuera MJ (1981): Pericentric inversions of chromosome 12 in two families. Hum Genet **57**: 131–133

Serra A, Brahe C, Millington-Ward A, Neri G, Tedeschi B, Tassone F, Bova R (1990): Pericentric inversion of chromosome 9: prevalence in 300 Down syndrome families and molecular studies of nondisjunction. Am J Med Genet **7** (suppl): 214–217

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

Varela M, Wang N, Cerrillo M (1987): Prenatal diagnosis of a 46,XX,inv(12)pat/47,XX,i(Xq), inv(12)pat. Hum Genet **75**: 93–94

Voiculescu I, Barbi G, Wolff G, Steinbach P, Back E, Schempp W (1986): Familial pericentric inversion of chromosome 12. Hum Genet **72**: 320–322

Watson J, Ward G, Goldberg G (1987): Recombinant 12 resulting from a pericentric inversion of chromosome 12. Am J Hum Genet **41** (suppl): A89