Short Communication

FAMILIAL PERICENTRIC INVERSION INCIDENTALLY DETECTED AT PRENATAL DIAGNOSIS

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Summary A case of familial heterozygous pericentric inversion of chromosome 1 [inv(1)(p13q23)] is presented. The inversion was incidentally detected in a fetus whose mother received prenatal chromosomal diagnosis due to her age (40 years old), and thereafter the same inversion was detected in the father whose phenotype was normal. No abnormalities were found in the phenotype of the newborn carrier. Semen analysis of the father revealed normal findings. The couple had no history of spontaneous abortion.

Key Words pericentric inversion, chromosome 1, prenatal diagnosis, semen analysis

Pericentric inversion of chromosome 1 is an extremely rare chromosomal rearrangement of which only 16 cases have been reported. Herein, we report a new case of a Japanese family having heterozygous pericentric inversion of chromosome 1, the breakpoints of which were p13 and q23. This is the first case in which pericentric inversion of chromosome 1 was prenatally diagnosed.

Case Report

A woman visited our clinic at Tohoku University Hospital for prenatal chromosomal diagnosis of her fetus because of her advanced age (40 years old). It was her first pregnancy. Phenotypes of her and her husband were normal.

Amniocentesis was performed at the 16th gestational week and the amniocytes were cultured in Chang's media under 5% CO₂ in air. The karyotype revealed the fetus to be a heterozygote with an pericentric inversion of chromosome 1 [46, XY, inv(1)(p13q23)] (Fig. 1). Based on the result, chromosomal examinations of the parents were consequently performed. Fetal blood cell karyotyping was carried out to deny any artifacts. Leukocytes of those samples were cultured in RPMI

Received March 6, 1995; Revised version accepted July 6, 1995.

Fig. 1. High resolution banding of fetal chromosome 1. The inverted chromosome is shown on the right. The inverted segment is almost 20% of the chromosome length. Idiograms are shown to indicate the breakpoints, p13q23.

1640 containing phytohemagglutinin under 5% CO₂ in air. The parental karyotypes revealed the father to be a carrier of the same inversion. Based on the facts that ultrasonography revealed no major malformation in the fetus, that the inversion was familial, and that the inverted segment was small (less than 20%), we concluded that the inversion had no adverse effect on the phenotype of the fetus. Therefore, the parents decided to continue the pregnancy.

The mother spent an uneventful pregnancy until the 39th gestational week, but ultrasonographic examination revealed that amniotic fluid to be high-echoic at the time of the onset of labor. The biophysical condition of the fetus was normal. Amniotic fluid obtained at amniotomy seemed to be chyle and its color was white. Microscopical observation revealed that the fluid contained many squamous cells, which probably originated in the vernix caseosa. Despite the abnormal amniotic fluid, she gave birth to a healthy male newborn after spontaneous labor in the 39th gestational week. The birth weight was 3,856 g, the body length 53 cm, the head circumference 35.5 cm, and the chest circumference 31 cm. The newborn had neither asphyxia nor malformations. Macroscopic observation of the placenta and the fetal membrane revealed no abnormal findings. The newborn was also normal in posture, appetite, and bowel movement, and results of the neurological examination and the congenital metabolic error screening were normal. The newborn grew without any clinical problems thereafter.

The father's parents, who had already died, had had no history of repeated spontaneous abortions. The father's four brothers are phenotypically normal and their spouses have not suffered from habitual abortions. Moreover, results

of semen analysis of the father showed no abnormalities in sperm count, morphology, and motility.

Discussion

There have been 16 previous reports in which the breakpoints of pericentric inversion of chromosome 1 were ascertained. The list of previous cases, the breakpoints, and the clinical problems of the carriers are shown in Table 1. Out of the 16 previous reports, the inversions were detected because of spermatogenic disturbances, such as azoospermia and oligozoospermia, in eight reports (Giraldo *et al.*, 1981; Toth *et al.*, 1982; Rivera *et al.*, 1984; Guichaoua *et al.*, 1985; Barros *et al.*, 1986; Gabriel-Robez *et al.*, 1986; Batanian and Hulten, 1987; Chandley *et al.*, 1987) and because of recurrent abortions in three reports (Lyberatou-Moraitou *et al.*, 1983; Johnson *et al.*, 1988; Martin *et al.*, 1994). In the other four reports, the probands of the inversion suffered from miscellaneous diseases, such as mucopolysaccharidosis (Lee *et al.*, 1974), Fanconi's anemia (Crippa and Ferrier, 1975), dwarfism (Char and Chueng, 1978), and Goldenhar's syndrome (Stahl-Mauge *et al.*, 1982). There was only one report in which the carriers had no clinical problems (Howard-Peebles, 1978). This is the seventeenth case of pericentric inversion of chromosome 1 in which the breakpoints were ascertained and the first report of a case which was prenatally diagnosed.

Table 1. Previous reports of pericentric inversions of chromosome 1.

References	Breakpoints	Clinical problem
The present case	p13q23	no problems
Martin <i>et al.</i> , 1994	p31q12	recurrent abortions
Johnson <i>et al.</i> , 1988	p36q32	recurrent abortions
Batanian and Hulten, 1987	p32q42	azoospermia
Chandley <i>et al.</i> , 1987	p31q43	severe oligozoospermia
Barros <i>et al.</i> , 1986	p36.3q12	severe oligozoospermia
Gabriel-Robez <i>et al.</i> , 1986	p32q12	oligoasthenoteratospermia
Guichaoua <i>et al.</i> , 1985	p32q21	oligozoospermia
Rivera <i>et al.</i> , 1984	p35q21	azoospermia
Lyberatou-Moraitou <i>et al.</i> , 1983	p12q23	recurrent abortions
Stahl-Mauge <i>et al.</i> , 1982	p13q21	Goldenhar's syndrome
Toth <i>et al.</i> , 1982	p34q23	azoospermia
Giraldo <i>et al.</i> , 1981	p13q25	azoospermia or severe oligozoospermia
Char and Chueng, 1978	p2q3	septo-optic pituitary dwarfism
Howard-Peebles, 1978	p13q23	no problems
Crippa and Ferrier, 1975	p13q21	Fanconi's anemia
Lee <i>et al.</i> , 1974	p13q23	mucopolysaccharidosis

The breakpoints of the present case were same as those of the cases of Lee *et al.* (1974) and Howard-Peebles (1978). Both the carriers in the present case and the one in the Howard-Peebles's case had no clinical problems. However, some chromosome inversions can give rise to abnormalities resulting from duplications and deficiencies of a recombinant chromosome. Recently, some recombinant chromosomes have been reported to be induced even by small inversions (Phelan *et al.*, 1993; Ayukawa *et al.*, 1994). However, the possibility of the occurrence of an offspring having a recombinant chromosome is higher in the carrier in which the inversion segment involves a minimum of 30% or one-third of the chromosome length than in the carrier in which the inversion segment involves less than 30% or one-third of the chromosome length (Winsor *et al.*, 1978; Trunca and Opitz, 1977). Although there has been no previous report directly describing a recombinant chromosome (chromosome imbalance) induced by pericentric inversion of chromosome 1, recurrent abortions complained of in two previously reported cases might have been caused by chromosome imbalance. A spermatogenic disorder in the carrier of an inversion seems to be due to recombinant chromosomes (Martin, 1991, 1993) or asynapsis (Miklos, 1974; Batanian and Hulten, 1987) observed in sperm samples. Moreover, based on the previous reports cited herein, spermatogenic disturbances seem to be induced by a relatively large inverted segment of chromosome 1, one of the breakpoints of which is mainly located in the p3 region. Since the inverted segment in the present case was smaller than those in the previous cases, the carrier offspring was able to avoid the formation of a recombinant chromosome. Additionally, based on the fact that the father's spermatogenicity was normal, the inversion of chromosome 1 of which breakpoints are p13q23 is seldom related to abnormal spermatogenicity. Therefore, it is expected that the male carrier newborn will have normal spermatogenicity.

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