

## A Subfertile Couple with Inv(9)(P11q13) had Spontaneous Pregnancies which was Prenatally Diagnosed as Having Inv(9)(P12q13),13p+ as Well as Polyhydramnios and Club Foot: Case Report

İnv(9)(P11q13) Taşıyıcısı Olan Subfertil Çiftin Spontan Oluşan Gebeliğinde, Prenatal Tanı Konulan ve Polihidramniyos ile Club Foot'un Eşlik Ettiği İnv(9)(P12q13), 13p+ Olgusu

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**ABSTRACT** The frequency of pericentric inversions among the most common chromosomal rearrangements is 1-2%. The pericentric inversion of chromosome 9 is one of the most common structural balanced chromosomal variations and has been found in both normal populations and patients with various abnormal phenotypes and diseases. We report the case of a subfertile couple with inv(9)(p11q13) who had spontaneous pregnancies that was prenatally diagnosed as having inv(9)(p12q13),13p+ as well as polyhydramnios and club foot. The incidence of inv(9)(p11q13) in patients with congenital anomalies was not only significantly different from the normal population but also been reported in various human diseases such as couples with repeated spontaneous abortions, bad obstetric history, infertility and congenital anomalies.

**Key Words:** Chromosome inversion; polyhydramnios; club foot; infertility

**ÖZET** Kromozomal yapının yeniden şekillendiği yapısal kromozomal anomaliler içerisinde en sık görülenlerden biri perisentrik inversiyonlardır ve perisentrik inversiyonların insidansı %1-2'dir. 9. kromozomun perisentrik inversiyonu ise en sık görülen dengeli yapısal kromozomal anomalilerden biri olup hem normal popülasyonda hem de çeşitli anormal fenotiplerin eşlik ettiği hasta grubunda izlenebilmektedir. Olgumuzda, inv(9)(p11q13) taşıyıcısı olan subfertil çiftin spontan oluşan gebeliğinde prenatal olarak tanı konulan ve polihidramniyos ile club foot'un eşlik ettiği inv(9)(p12q13),13p+ olgusu tartışılmıştır. İnv(9)(p11q13) karyotipe sahip bireylerde konjenital anomali insidansı normal popülasyona göre belirgin farklılık göstermemektedir. Bununla birlikte 9. kromozomun perisentrik inversiyonu, tekrarlayan gebelik kayıpları, kötü obstetrik öykü, infertilite ve konjenital anomali ile ilişkili olabilmektedir.

**Anahtar Kelimeler:** Kromozom inversiyonu; polihidramniyoz; çarpık ayak; infertilite

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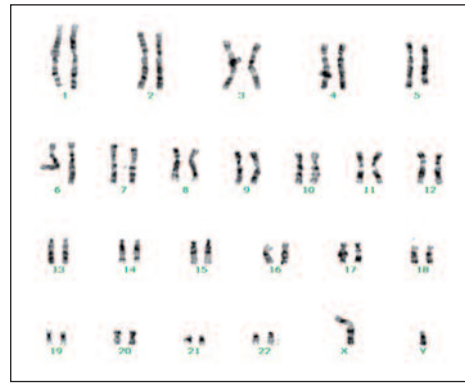
Constitutional chromosomal abnormalities are important causes of miscarriage, infertility, congenital anomalies, and mental retardation in humans.<sup>1</sup> Constitutional chromosomal abnormalities include numerical chromosome aberrations that cause aneuploidy and structural chromosome aberrations such as translocations, inversions, deletions, and

duplications.<sup>2</sup> The frequency of pericentric inversions among the most common chromosomal rearrangements is 1-2%. The pericentric inversion of the heterochromatic region of chromosome 9 [*inv(9)*], *inv(9)(p11q13)*, or *inv(9)(p12q13)*, is the most common pericentric inversion found in the human karyotype.<sup>3</sup> There is no phenotypic effect in the majority of pericentric inversion heterozygote carriers with balanced rearrangement. As the *inv(9)* has been found in -3.57% of human samples without apparent phenotypic consequences, *inv(9)* is considered to be a structural chromosomal variant in the general population.<sup>4</sup> However, in some of the previous reports, the clinical investigators had associated the pericentric inversion of chromosome 9 (*inv 9*) with various abnormalities which had included infertility, miscarriages, sub-fertility, birth defects, abnormal pregnancies like intrauterine growth retardation, etc.<sup>5,6</sup>

## CASE REPORT

A pregnant was a 37 year old and her 40 year old husband is her consanguineous first cousin. It was her first detected pregnancy. She admitted that she unsuccessfully was trying to get pregnant within the last 9 years. The subfertility of the couple was previously regarded as idiopathic. The wife and husband were phenotypically normal and had no relevant past medical history.

Fetal karyotyping was performed for reasons of advanced maternal age (more than 35 years of age) and bilateral club foot in ultrasound examinations of the fetus. The fetal karyotyping was carried out by means of cultured fetal cells obtained by amniocentesis. Amniocentesis was performed in 18th gestational week. The fetal karyotype was found to have a 46,XX,*inv(9)(p11q13)*,13p+. When *inv(9)* was detected in fetal cells, the parents were offered a cytogenetic examination and karyotyped using peripheral blood samples. The karyotypes were analysed by use of the conventional banding technique (GTG) at 400 band resolution. Twenty metaphases were counted and at least 5 metaphases were analyzed for each individual. The woman was found to have a normal karyotype, but her partner was found to have 46,XY,*inv(9)(p11q13)* (Figure 1).



**FIGURE 1:** A partial karyogram of the proband's partner; 46,XY,*inv(9)(p11q13)*.

Follow-up was carried out with regard to the general condition including phenotype after birth. The fetus had a polyhydramnios and polyhydramnios diagnosed at the 32th gestational week. The fetus was born in 39th gestation week spontaneous vaginally. The baby was available for direct chromosomal diagnosis at the age of 10 months. The presence of *inv(9)(p11q13)*,13p+ was then confirmed.

## DISCUSSION

The frequency of pericentric inversions among the most common chromosomal rearrangements is 1-2%. When pericentric inversions occur de novo, the phenotype usually is normal. If fertilization occurs in abnormal gametes, a risk for abnormal progeny arises. Parental karyotyping is indicated when a pericentric inversion is observed in a phenotypically abnormal child. The pericentric inversion of the heterochromatic region of chromosome 9 [*inv(9)*], *inv(9)(p11q13)*, or *inv(9)(p12q13)*, is the most common pericentric inversion found in the human karyotype.<sup>3</sup>

In comparison with the basic incidence, significant higher incidences were observed especially in the fetuses of couples whose offspring suffered various types of congenital clinical problems. Moreover, in the chromosomal examination of the parents whose fetuses were diagnosed as *inv(9)*, it was revealed that either parent might be the carrier.<sup>7</sup>

There is no phenotypic effect in the majority of pericentric inversion heterozygote carriers with balanced rearrangement. Because the inv(9) has been found in - 3.57% of human samples without apparent phenotypic consequences, inv(9) is considered to be a structural chromosomal variant in the general population.<sup>4</sup>

However, in some previous reports, the clinical investigators had associated the pericentric inversion of chromosome 9(inv 9) with various abnormalities which had included infertility, miscarriages, sub-fertility, birth defects, abnormal pregnancies like intrauterine growth retardation, etc.<sup>5,6</sup> Mozdarani et al. have investigated karyotypes of 300 infertile couples, and found the incidence of inversion 9 in males to be higher than that of normal population.<sup>5</sup>

A higher prevalence of inv(9) has been reported in couples with habitual abortion and a history of more than two spontaneous first trimester

abortions and aborted fetus.<sup>8</sup> Although no specific or common manifestations have been identified in these populations, a few studies have reported that inv(9) is sometimes associated with various clinical phenotypes related to fertilization, fetal development, morphogenesis and growth.<sup>9,10</sup> Salihu et al. reported that in more than 2000 high-risk pregnant women who underwent invasive prenatal procedures, fetal chromosomal or genetic anomalies were detected in 3.4%. In these fetuses single pericentric inversions of chromosome 9 were found to be 32% of all identified chromosomal or genetic abnormalities. In six of them, ultrasound findings were abnormal and hydramnios, anhydramnios, hydroureter, hydronephrosis, encephalocele or prune belly syndrome were observed.<sup>10</sup>

Although, inv(9) has been considered to be a normal variant, our observation implies a possible association between inv(9) and abnormalities.

## REFERENCES

1. McFadden DE, Friedman JM. Chromosome abnormalities in human beings. *Mutat Res* 1997;396(1-2):129-40.
2. Jeong SY, Kim BY, Yu JE. De novo pericentric inversion of chromosome 9 in congenital anomaly. *Yonsei Med J* 2010;51(5):775-80.
3. Kaiser P. Pericentric inversions. Problems and significance for clinical genetics. *Hum Genet* 1984;68(1):1-47.
4. Teo SH, Tan M, Knight L, Yeo SH, Ng I. Pericentric inversion 9--incidence and clinical significance. *Ann Acad Med Singapore* 1995;24(2):302-4.
5. Mozdarani H, Meybodi AM, Karimi H. Impact of pericentric inversion of Chromosome 9 [inv(9) (p11q12)] on infertility. *Indian J Hum Genet* 2007;13(1):26-9.
6. Akbas E, Senli H, Hallioglu O, Batmaz S, Eras Erdogan N. Association of pericentric inversion of chromosome 9 (Inv[9][P11q13]) and genetic diseases: case report. *LabMedicine* 2010;41(2):96-8.
7. Uehara S, Akai Y, Takeyama Y, Takabayashi T, Okamura K, Yajima A. Pericentric inversion of chromosome 9 in prenatal diagnosis and infertility. *Tohoku J Exp Med* 1992;166(4):417-27.
8. Kim JW, Lee JY, Hwang JW, Hong KE. Behavioral and developmental characteristics of children with inversion of chromosome 9 in Korea: a preliminary study. *Child Psychiatry Hum Dev* 2005;35(4):347-57.
9. Rao BV, Kerketta L, Korgaonkar S, Ghosh K. Pericentric inversion of chromosome 9[inv(9) (p12q13)]: Its association with genetic diseases. *Indian J Hum Genet* 2006;12(3):129-32.
10. Salihu HM, Boos R, Tchuinguem G, Schmidt W. Prenatal diagnosis of translocation and a single pericentric inversion 9: the value of fetal ultrasound. *J Obstet Gynaecol* 2001;21(5):474-7.