CASE REPORT

Subfertile couples with inv (9) (p11q13): Report of two cases

Nasrin Ghasemi, M.D.*  Abbas Aflatoonian, M.D.†
Seyed Mehdi Kalantar, M.D.*  Naeimeh Tayebi, M.D.‡

Departments of Medical Genetics and Obstetrics and Gynecology; Infertility Research and Clinical Center, Yazd Shahid Sadoghi Medical Sciences University, Yazd, Iran.

ABSTRACT

This paper reports two cases of inversion chromosome 9 in one of partners from two subfertile couples. The first case was the woman with idiopathic recurrent spontaneous abortion in the first trimester of her pregnancy, which referred to genetic counseling clinic. Cytogenetic examination showed that her karyotype was 46 XX, inv (9) (p11q13), and her husband’s karyotype was normal (46 XY). The second couple referred for idiopathic infertility to genetic counseling clinic. The woman's karyotype was normal (46XX), but she did not have any pregnancy in 5 years of marriage. Her husband's karyotype was 46XY, inv (9) (p11q13). His semen analysis showed low motility, but sperm count and morphology was normal. The abnormal karyotype of these cases, 46 XX, inv (9) (p11q13) and 46 XY, inv (9) (p11q13) could be acknowledged as a reason of infertility during evaluation of unknown infertile couple.

Key words: Inversion chromosome 9, recurrent spontaneous abortion, idiopathic infertility

INTRODUCTION

Chromosomes aberrations are found in 2-7% of couples with fertility problems (1). Carriers of balanced structural aberrations appear to have an increased risk of progeny with unbalanced karyotype resulting spontaneous abortion in 1st and second trimester. Pericentric inversion of the chromosome 9, inv (9) (p11q13), is such a common occurrence that some cytogeneticists would consider them as normal variants.

The incidence is said to be about 1% to 1.65% in the general population. Despite being categorized as a minor chromosomal rearrangement which does not correlate with abnormal phenotypes, many reports in the literature raised conflicting views regarding the association with subfertility and recurrent pregnancy loss, abnormal clinical conditions, as well as chromosomal abnormalities arising as a result of having this inversion (2).

CASE REPORT

This paper describes two infertile couples with inv (9) (p11q13). In each couple, one of partners was heterozygote for inv (9); 46, XX, inv (9) (p11q13) and 46, XY, inv (9) (p11q13) (Fig 1). The first case was the 35 years old woman with 5 spontaneous idiopathic abortions referred to genetic counseling clinic. She admitted that she was
unsuccessfully trying to get pregnant within the last 10 years. Hysterosalpingography showed that her fallopian tubes were patent. Serial sonography showed that her ovulations were normal. Both patient and her partner were offered a cytogenetic examination.

Lymphocytes of the woman and her partner were cultured, pretreated and fixed according to the standard cytogenetic procedure (3). The karyotypes were analyzed by use of the conventional banding technique (GTW-banding).

Cytogenetic examination revealed that her karyotype was 46 XX, inv (9) (p11q13), but her husband's karyotype was normal (46 XY).

In addition, she was homozygote for V leiden factor mutation. The etiology of miscarriage in this case could not be V leiden factor mutation, because this woman did used heparin during pregnancy. Her husband has normal semen analysis. In her familial pedigree, her father's karyotype is 46XY, inv (9) (p11q13), but he had four healthy children.

The second couple referred for idiopathic infertility to genetic counseling clinic. The woman had normal ovulations using serial sonography, and her fallopian tubes were patent by laparoscopy. Her karyotype was normal (46XX), but she did not have any pregnancy in 5 years of marriage. Her husband's karyotype was 46 XY, inv (9) (p11q13).

His semen analysis showed low motility, but sperm count and morphology was normal (Table 1).

**DISCUSSION**

Carriers of balanced aberrations have an increased risk of unbalanced progeny due to imbalances and delays in meiosis (4). The couples presented in the current study have pericentric inversion. The pericentric inversion of chromosome 9 inv (9) (p11q13) is recognized as a normal variant of chromosome 9. The inverted region contains only the centromere and centromeric heterochromatin, so it seldom results in aberrant chromosomes after crossing-over (4).

Nevertheless, Gardner and Sultherland (1996) claim that some patients carrying inversion have an increased risk of unbalanced progeny, ranging from 1 % to 10 % (5). Colls et al (1997) investigated semen of a man with karyotype 46XY, inv (9) (p11q13). Inv (9) was found in 48.7% of analyzed cells and disomic sperm cells for chromosome 9 and 21 were not more frequent than in men with the normal karyotype. They concluded that inv (9) (p11q13) does not cause defects in spermatogenesis (6). Some authors observed an increased risk of progeny with trisomy of chromosome 21 in carriers of inv (9) that contains additionally an enlarged heterochromatin region (7,8,9,10).

Those findings contradict the hypothesis that heterochromatin does not take part in crossing over. Ameil et al (2001) found an increased number of disomic (chromosome 9) sperm in such a carrier (11).

<table>
<thead>
<tr>
<th>Table 1. Result of the sperm analysis and processing in case with inv (9) (p11q13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Microscopic finding</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Results</td>
</tr>
</tbody>
</table>
Srebniak et al (2004) presented a subfertile couple with two chromosomal inversions in one of partners. The man's and woman's karyotype was 46 XY, inv (2) (p11q13), inv (9) (p11q13) and normal respectively. In this case report, they recognized this abnormal karyotype was as a possible reason of spontaneous abortion (12).

According to Kaiser (1988) the risk of further miscarriages is high, but the risk of progeny with abnormal karyotype is rather low. Small inversion may lead to recombinant with lethal deletion or addition of large fragment. It is presumed that the women could have some undetected miscarriages in early pregnancy. Many of her embryos may have had balanced karyotype, which made them unable to develop (4). Maybe in this second couple, miscarriage could be happened before positive pregnancy test.

In contrast, Gardner and Sutherland (2004) described inv (9) as normal variant chromosomes, and they do not mention subfertility in discussion about clinical consequences of chromosomal aberration (13).

The abnormal karyotypes of these case reports 46 XX, inv (9) (p11q13) or 46 XY, inv (9) (p11q13) could be acknowledged as a reason of fertility problems in these investigated couples. Rule out of other reasons for infertility or abortion in them make these possibility stronger. Balanced rearrangements such as, a reciprocal or Robertsonian translocation or an inversion, will be found among parents of unbalanced rearrangement and couples with recurrent fetal loss or infertility (14). This inversion could cause some silent or mild problem in some one, which cause severe problem in his/her children or grandchildren. So the evaluation of this chromosomal abnormality is important in infertile couples.

REFERENCES


Received on August 21, 2006; revised and accepted February 8, 2007