Pericentric inversion of chromosome 1 and 9 in a case with recurrent miscarriage in Egypt

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Abstract: We report phenotypically normal female carrying structural variants on both chromosomes 1 and 9. She was referred to the Recurrent Pregnancy Loss Clinic, National Research Centre, with a complaint of repeated miscarriage (5 consecutive first trimester miscarriages). Conventional cytogenetic study of the peripheral blood of the wife revealed 46, XX inv (1) (p32 q44) in all cells and inversion (9) (p12 q12) in 30% of the studied cells, while the husband was normal 46, XY. FISH study was done to confirm and clarify the findings. To the best of our knowledge, this is the first report of a phenotypically normal female carrying structural variant on both chromosomes 1 and 9 leading to recurrent miscarriage. Our study highlights the deleterious effect of pericentric inversion of chromosomes 1 and 9 on recurrent pregnancy loss. It also underlines the importance of performing cytogenetic studies for couples with such complaint. In such cases, a well informed genetic counseling should be given to the couple and prenatal diagnosis should be offered in future pregnancies. [Journal of American Science 2010;6(8):154-156]. (ISSN: 1545-1003).

Keywords: Pericentric inversion; chromosome; pregnancy

1. Introduction

Recurrent pregnancy loss is a serious health problem that affects many couples. Miscarriage occurs in up to 15% of pregnant women and is considered the most common complication of pregnancy [1]. Although 15% of clinically recognized pregnancies miscarry, total reproductive losses are closer to 50% [2]. It has been estimated that 2 to 5% of women have 3 or more miscarriages [1].

Recurrent pregnancy loss requires a multidisciplinary approach since genetic, endocrinologic, anatomic, immunologic, thrombophilic, infections and iatrogenic factors may require evaluation and management [3]. Structural chromosomal abnormalities are the single most common cause for pregnancy loss. Among first trimester abortions, 50 to 60% show chromosomal abnormalities [4, 5]. Published studies have shown a prevalence of chromosomal abnormalities that varies from 2 to 8% of couples with recurrent miscarriage [6, 7, 8].

In about 4% of couples with recurrent pregnancy loss, one partner carries a balanced reciprocal or Roberstonian translocation [9, 10]. Carriers of balanced reciprocal translocation are phenotypically normal, but 50 to 70% of their gametes are unbalanced, because of abnormal segregation at meiosis. The reproductive risk conferred by chromosome rearrangements is dependent on the type of rearrangement and whether it is carried by the female or the male partner [11].

Pericentric inversions have been described for all chromosomes. They are considered the less common structural aberrations in human and their incidence differs strongly from chromosome to chromosome [12]. The frequency of pericentric inversions in the general population vary from 0.089 to 0.34 [13, 14].

Pericentric inversion of chromosome 9 is usually a normal polymorphism and its incidence has been reported to be approximately 1 to 2% in the general population [15]. Although its clinical consequences remain unclear, studies have implicated it with recurrent miscarriages [16]. Demirhan et al., [17] indicated a correlation between pericentric inversions of 9 and recurrent miscarriages. Inversions in chromosomes 1, 8 and 16 are rare. A possible reason for such findings may be unequal recombination causing lethality and thus, limited detection [12]. Also, the additional genetic material from chromosome 1 leads to early termination of pregnancy and poor fetal development [18].

As inversions do not seem to influence female fertility to any noticeable degree apart from an increasing miscarriage rate [12], reproductive guidance for the management of recurrent miscarriage recommends chromosome analysis in both partners.

2. Material and Methods

Pedigree analysis of 3 generations of the couple having reproductive failure was performed in order to determine the presence of consanguinity or any other similar cases in the family.

Detailed medical and gynecologic evaluation was performed to exclude other causes for the pregnancy loss. This included: hysterosalpingogram (HSG) for anatomical evaluation, in addition to hormonal, immunologic and haematologic investigations.

Chromosomal analysis for the couple was done using G-banding technique according to the method described by Seabright [19] and Verma and Babu [20], a total of 25 metaphases were analyzed for each case. Structural or numerical anomalies were recorded and karyotyped according to the ISCN [21]. Fluorescence in situ Hybridization (FISH) analysis was used for further identification of the rearrangement type and the respective breakpoints.

3. Results

The female partner was of average height and weight (1.68 m and 72 kg respectively). Her basal hormone profile showed: FSH 6 mU/ml; LH 3.6 mU/ml; prolactin 19 ng/ml; progesterone 16 ng/ml (day 22 of the menstrual cycle) and her serum TSH was 2.8 mIU/ml. The results of lupus anticoagulant and anticardiolipin antibodies (Ig G and M) were negative. In addition, anatomical evaluation by ultrasonography and HSG revealed normal uterine cavity.

Semen analysis of the male partner revealed normal parameters with less than 20% abnormal forms.

The karyotype of the husband revealed normal male 46, XY, while that of the wife revealed 46, XX, pericentric inversion (1) (p32q44) in all cells and inversion (9) (p12q12) in 30% of the cells as shown in Fig. [1, 2].

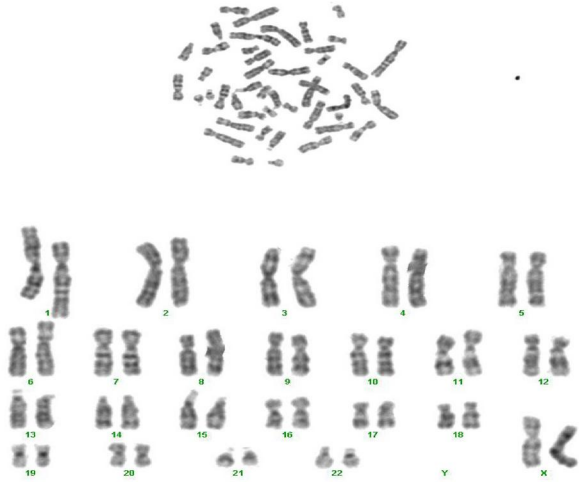

Fig. [1]: Karyotype of the wife revealed 46, XX, pericentric inversion (1) (p32q44).

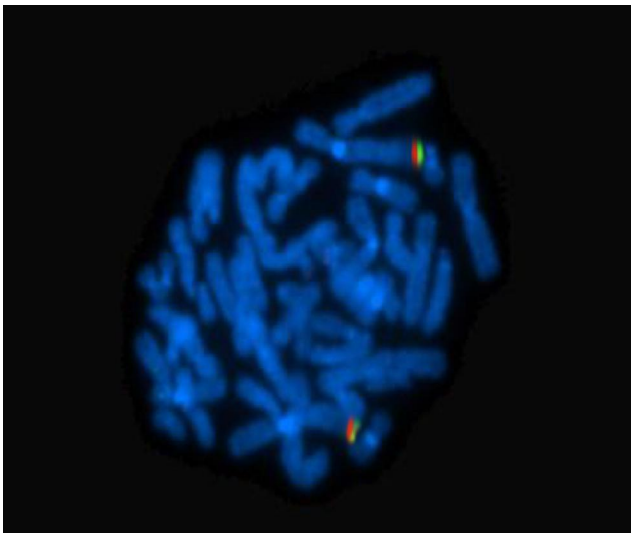

Fig. [2]: FISH using LSI p58 probe hybridized to band region 1p36 (spectrum orange) and band region 1p telomere (spectrum green) showing the involved break points.

4. Discussion

Chromosomal inversions are associated with a higher risk of pregnancy wastage; pericentric inversion 9 is considered a population variant [2]. There are a number of studies showing a correlation with reproductive failure. As previously hypothesized, the large amount of additional genetic material from chromosome 1 leads to a very early termination of pregnancy and poor fetal development [3, 4, 5].

To the best of our knowledge, this is the first report of a phenotypically normal mother carrying structural variants on both chromosomes 1 and 9 leading to repeated early miscarriage.

5. Conclusion

Genetic counseling is mandatory after the diagnosis of pericentric inversion of chromosome 1 and 9 and prenatal diagnosis should be offered in a subsequent pregnancy.

Competing interests

The authors declare that they have no competing interest

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