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Recurrent spontaneous abortion related to balanced translocation of chromosomes – A case report

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ABSTRACT

INTRODUCTION: Recurrent spontaneous abortion (RSA) is defined as three or more consecutive pregnancy losses before the 20th week of gestation. RSA is often idiopathic, but structural chromosomal abnormality is an important cause. An unbalanced karyotype in the conceptus of a couple when one partner has a structural chromosomal abnormality may result in failure to implant, miscarriage, or pregnancy of a fetus with an unbalanced karyotype.

CASE PRESENTATION: We report a rare case of RSA associated with balanced translocation of chromosomes. a woman who had four spontaneous abortions, all pregnancy loss happened before 12 weeks of gestation, no other known chronic diseases reported to the family nor medications taken during pregnancy. The karyotype was 46.XX, t(13p,21p) The abnormal karyotype was not found in any other chromosomes. Further spectral karyotyping was performed to rule out the involvement of any other chromosomal aberrations present in the genome.The cytogenetic analysis of the husband revealed a normal karyotype 46.XY.

CONCLUSION: Couples with more than three miscarriages should be referred to the genetist for chromosomal analysis for possible hereditary etiology and chromosomal abnormalities responsible for miscarriages to plan prenatal diagnostics and genetic counseling for subsequent pregnancies.

Keywords: Recurrent Spontaneous Abortion, Chromosomal Abnormalities, Cytogenetics Analysis, Karyotyping, Genetic Counseling.

INTRODUCTION

Chromosomal abnormalities are one of the genetic causes of reproductive abnormalities. Most of these abnormalities are numerical abnormalities (86%), and a low percentage is caused by structural abnormalities (6%) or other genetic mechanisms, including chromosome mosaicism (8%) [1].There are two main types of chromosomal diseases caused by abnormalities in chromosomal

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number, chromosomal structure, or both. These chromosomal abnormalities are among the important causes of infertility, spontaneous abortion, recurrent abortion, teratosis, stillbirth, oligospermia or no sperm, and other abnormal fertility problems in couples of childbearing age [2]. One of those abnormalities is a balanced translocation of chromosomes, which is a reciprocal exchange of genetic material between two nonhomologous chromosomes, Robertsonian (chromosomal rearrangement that in humans occurs in the five acrocentric pairs, namely chromosome 13, 14, 15, 21, and 22) [3]. Carriers of balanced reciprocal translocations are at risk of producing gametes with unbalanced forms of the re-arrangement following malsegregation of the translocation at meiosis, leading to infertility, recurrent miscarriage, fetal anomalies, and chromosomally abnormal offspring [4]. Should one of the partners of a couple have a balanced or unbalanced chromosomal structure abnormality, such as reciprocal or Robertsonian translocations, among others, the result may be a recurrent miscarriage or the presence of physical and/or mental disorder(s) in their descendants [5]. The percentage of chromosomal variations has been reported to be 5.5% in couples experiencing spontaneous abortion compared to 0.55% in the general population [6]. Among couples with recurrent miscarriages, about 60% of translocations are reciprocal and 40% are Robertsonian, with women being about twice more likely than men to have a balanced translocation [7]. Individuals with balanced translocations may be phenotypically normal, but their offspring may show chromosome duplications or deletions as a result of normal meiotic segregation. Here we report the first case of a rare case of recurrent spontaneous abortion (RSA) in a woman with balanced translocation of chromosomes in Rwanda.

CASE PRESENTATION

This was a 32-year-old woman who had a history of four spontaneous abortions, all of which occurred after 6 weeks but before 12 weeks of gestation. There was no history of chronic illness, medication use, exposure to toxic/harmful substances or radiation during the pregnancy. The patient had four siblings. There were no significant abnormalities in the phenotype and intelligence of her parents and siblings, and her younger sister had given birth to a daughter whose phenotype and intelligence fell into the normal range. The other sister and her younger brother were unmarried. The mother and sister had no history of spontaneous abortion.

The cytogenetic examination showed a female karyotype of 46.XX(13p,21p) (p) with the presence of balanced reciprocal translocation between the short arm (p) of chromosome 13 and short arm (p) of chromosome 21 (Figure 1). This balanced translocation with no loss and no gain is mostly associated with normal phenotypes and functions apart from fertility problems frequently characterized by miscarriages.

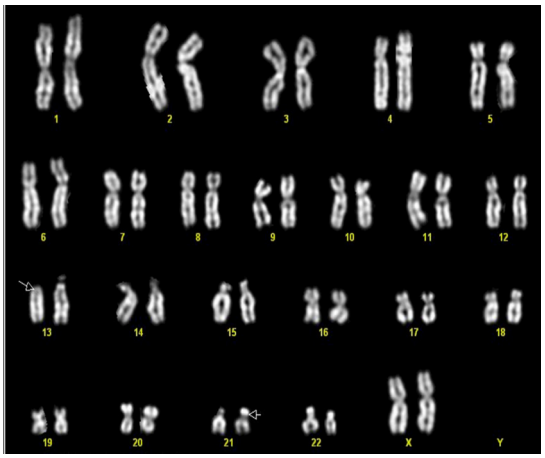

Figure 1: Karyotype showing balanced reciprocal translocation between the short arm (p) of chromosome 13 and short arm (p) of chromosome 21

DISCUSSION

Miscarriage is the most frequent pregnancy complication, and there are several recognized causes for RSA, such as structural uterine anomalies, endocrine disorders, prothrombotic conditions (e.g., antiphospholipid syndrome), and balanced translocation involving one of the parents [7]. Cytogenetic analyses have revealed a higher prevalence of chromosomal translocations in couples with recurrent miscarriages; consequently, an analysis of each translocation case is necessary to assess the risk of the woman for future miscarriage [8]. The case reported here involved chromosomal balanced translocations. Balanced translocation is the most common type of chromosomal structural abnormality. Although carriers of chromosomal abnormalities may have a normal phenotype in terms of body appearance and intelligence, they

may have reproductive disorders, such as repeated miscarriages, embryo growth discontinuation, teratosis, abnormal semen, and infertility, among others [9]. Of the many types of chromosome aberrations, equilibrium translocation is the most common. With equilibrium translocation, two non-homologous chromosomes break simultaneously, exchange without the centromere fragments, and form two newly derived chromosomes after conjugation. The carrier phenotype may be normal since only the relative position of the chromosome fragment is changed, and there is no deletion or duplication of genetic material. No obvious phenotypic or intellectual abnormalities were found in the case reported here. When one or both partners of a couple have balanced translocation, unbalanced gametes may be repeatedly produced, leading to repeated abortion or a stillborn child with deformity [10]. A Turkish retrospective study reported a total of 26 chromosome abnormalities in 600 individuals, of which there were 15 cases (57.7%) of structural anomalies and 11 cases (42.3%) of numerical chromosomal aberrations. And there were five cases of balanced translocations (33.3%) and four cases of Robertsonian translocations (26.7%) in the 15 cases of structural anomalies [11]. During the meiosis of parental heterozygotes, the partial deletion of a segment and partial duplication of another segment will occur if homologous pairing or exchange between the inverted chromosome and its normal homologous chromosome occurs within an inverted segment [12]. The length of the gene duplication and of the deletion fragments and the lethal effect of the genes contained in the fragments determine the genetic effects of these two recombinant chromosomes. In general, the duration of embryo survival produced by the union of unbalanced gametes to normal chromosomal gametes depends on the size of the unbalanced fragment and the nature of the gene contained. Usually, the smaller the non-equilibrium gene segment, the more likely an infant with deformities will be born; the larger the non-equilibrium fragment, the more easily abortion occurs after the formation of the zygote [13]. There are a few cases of balanced translocation and interarm inversion at the same time; in this scenario, the probability of giving birth to normal offspring is relatively smaller. Recurrent abortion caused by genetic factors causes physical and psychological damage. Some studies have compared the psychological characteristics of carriers of chromosomal structural abnormalities, and indicated that the self-rating anxiety scale and self-rating depression scale scores of women with structural chromosome abnormalities were significantly higher than those of females with normal karyotypes. These two scores of women with structural chromosome abnormalities were significantly higher than those of men with structural chromosome abnormalities. These results indicate that female carriers of structural chromosome abnormalities are more vulnerable to psychological distress and require psychological support [14]. As a hereditary factor, balanced translocation is the most common occurrence among couples with recurrent pregnancy loss. Researchers have reported the involvement of all autosome chromosome translocations in male or female factor infertility and recurrent miscarriages [15]. To identify the etiology and to intervene in reproductive and prenatal diagnosis as soon as possible and to reduce the occurrence of reproductive abnormalities due to genetic factors, the pain of multiple reproductive abnormalities to families, and the social burden of birth defects, we recommend that patients with a history of repetitive miscarriage should undergo routine genetic consultation. Karyotype analysis remains a powerful and cheap technology and continues to have wide applications in the field of medical genetics [16]. This technology can detect chromosomal translocations or deletions and is a valuable tool in genetic counseling for infertility and abortion or intrauterine fetal demise [17].

Scenario 1: *during fertilization, she can randomly give normal chromosome 13 and normal chromosome 21. In this case, the fetus will carry a normal karyotype [18].*
Scenario 2: *during fertilization, she can randomly give chromosome 13 missing short arm p and give chromosome 21 with an extra short arm from chromosome 13. In this scenario, there is no loss or gain. The fetus will be like the mother carrying balanced reciprocal translocation with normal phenotype but later will have fertility problems as expressed in her/his mother [19].*
Scenario 3: *during fertilization, she can randomly give chromosome 13, missing short arm, and normal chromosome 21. In this case, there is a loss of the short arm of chromosome 13 and the extra short arm of chromosome 21. It is called partial monosomy 13p and trisomy 21p and this, in most*

cases, results in a miscarriage [20].

Scenario 4: d*uring fertilization, she can randomly give normal chromosome 13 and give chromosome 21 with an extra short arm p of chromosome 13. In this case, there is an extra gain of the short arm of chromosome 13 and one copy of the short arm of chromosome 21. It is called partial trisomy 13p, monosomy 21p, and in most cases, it results in miscarriages [21].*

CONCLUSION

We described a rare case of reciprocal balanced translocation of chromosomes associated with recurrent abortion, referring the couple involved for karyotyping. Karyotype analysis will rule out or confirm the possible hereditary etiology and the source of chromosomal abnormalities in recurrent miscarriages.

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