Journal of Experimental and Clinical Medicine
Deneysel ve Klinik Tıp Dergisi

Case Report **doi:** 10.5835/jecm.omu.29.03.010

Recurrent miscarriages and balanced translocation t(4;9)(q21;q13)

Tekrarlayan düşükler ve dengeli translokasyon t(4;9)(q21;q13)

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ARTICLE INFO

Article History
Received 15 / 06 / 2011
Accepted 06 / 07 / 2011

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Keywords:
Balanced translocation
Recurrent abortions
Cytogenetic
Translocation carrier
Chromosomal rearrangement
Miscarriage

Anahtar Kelimeler:
Dengeli translokasyon
Tekrarlayan düşükler
Sitogenetik
Translokasyon taşıyıcısı
Kromozomal yeniden düzenlenme
Düşük

ABSTRACT

The structural chromosomal rearrangements are common in general population. Even balanced translocation carriers could have risk for having children with unbalanced chromosomes, they are phenotypically normal. Therefore, translocation can be observed with a higher incidence in couples with a history of recurrent abortions than the general population. In this study, we presented a 20 year old female patient referred to our laboratory from Department of Gynecology and Obstetrics. She had two abortions in the first trimester (12 and 8 gestational weeks). She does not have any living child. Her other past medical history and physical examination were unremarkable. The family history of proband revealed that her mother had three girls and three boys alive. The 40 year-old mother of proband's husband had a stilbirth. According to G-banding karyotype analysis, balanced translocation, 46, XX, t(4;9) (q21;q13), was diagnosed in the peripheral blood taken from her and her mother. Balanced translocation carriers could give unbalanced chromosomes to their newborn child. Also this observed situation shows an increase in the risk of abortion and physical anomalies. We concluded that the abortions in the family carrying balanced translocation might be due to the unbalanced distribution of chromosome translocation during gamete formation. Prenatal diagnosis should be recommended for their further pregnancies.
J. Exp. Clin. Med., 2012; 29:221-223

ÖZET

Yapısal kromozom yeniden düzenlemeleri genel toplumda yaygındır. Dengeli translokasyon taşıyıcısı bireyler fenotipik olarak normaldir fakat kromozomal olarak dengesiz gamet üretme yönünden anlamlı oranda artmış riske sahiptirler. Bu nedenle, translokasyon genel nüfusa göre tekrarlayan düşük öyküsü olan çiftlerde daha yüksek bir insidans ile izlenebilir. Bu çalışmada, Kadın Hastalıkları ve Doğum Bölümü'nden laboratuarımıza yönlendirilen 8 ve 12 haftalık iki ilk trimester düşük öyküsü olan 20 yaşında bir kadın olgu sunulmaktadır. Olgumuzun yaşayan çocuğu yoktur. Olgumuzun geçmiş medikal öyküsü ve fizik muayenesi normaldir. Probandın aile hikayesinde, annesinin üç kızı ve yaşayan bir oğlu olduğu görülmüştür. Probandın kocasının 40 yaşındaki annesinin bir ölüdoğum öyküsü vardır. Olgumuzun kocası ve kocasının annesinin periferal kanından elde edilen G-bant karyotip analizinde dengeli translokasyon 46, XX, t(4;9) (q21;q13) saptanmıştır. Dengeli translokasyon taşıyıcılığına sahip ailelerde meydana gelen düşüklerin gamet oluşumu sırasında dengeli translokasyonların dengesiz gametler oluşturabilmesi nedeniyle olabileceği sonucuna varılmıştır. Prenatal tanı dengeli translokasyon taşıyıcısı bireylerin sonraki gebelikleri için tavsiye edilmelidir.
J. Exp. Clin. Med., 2012; 29: 221-223

1. Introduction

Recurrent miscarriage (RM) or habitual abortion is defined as three or more consecutive pregnancy losses before 22 gestational weeks or more consecutive pregnancy losses before 22 gestational weeks or the spontaneous abortion of an embriyo/fetus weighing less than 500g (Carp et al., 2004). Although the patients with RM undergo multiple diagnostic tests to detect parental chromosomal anomalies, maternal thrombophilic, endocrine or immunological disorders, over 50% of the RM cases are classified as idiopathic. Balanced chromosome rearrangements are found in 3-6% of couples experiencing recurrent spontaneous abortions (Tunç et al., 2007). About

50% of all spontaneous abortions are caused by chromosomal abnormalities (Sanchez et al., 1999; Carp et al., 2004). Carriers of balanced chromosome rearrangements have increased risk of infertility, spontaneous abortion, mental retardation, stillbirth or the birth of a child with multiple congenital abnormalities (Carp et al., 2004)

2. Case

We present a couple with recurrent spontaneous abortions presented to our laboratuary for cytogenetic analysis. They were married for 3 years with a history of three consecutive first trimester pregnancy losses (12 and 8 gestational weeks). The 20 year-old patient and her 23 year-old husband were phenotypically normal and there were no consanguinity between them. Patient's obstetrical work-up including ultrasound and hysterosalpingography were normal. There were no systemic, endocrine, anatomic or environmental risk factors for miscarriage.

Cytogenetic analysis was performed using standart phytohemagglutinin-stimulated peripheral blood lymphocyte cultures. Metaphase chromosomes were banded by GTG banding technique and 25 metaphases analysed (Seabright,1971). Karyotypes were described according to the International System for Cytogenetic Nomenclature (ISCN 2005).

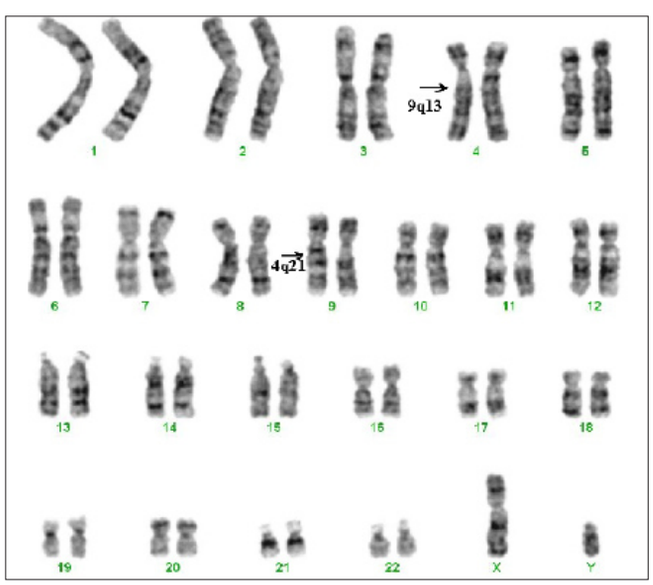

Fig. 1. G banding karyotype of t(4;9)(q21;q13)

The husband's karyotype was t(4;9)(q21;q13) (Fig. 1). Balanced reciprocal translocation between chromosomes 4 and 9 was observed. The break points were: t(4;9) (4→pter 4q21::9q13→9qter; 9pter→9q13::4q21→4qter (Fig. 2).

The husband's 40 year-old mother had a stilbirth. According to G-banding karyotype analysis, she had balanced translocation, 46, XX, t(4;9) (q21;q13).

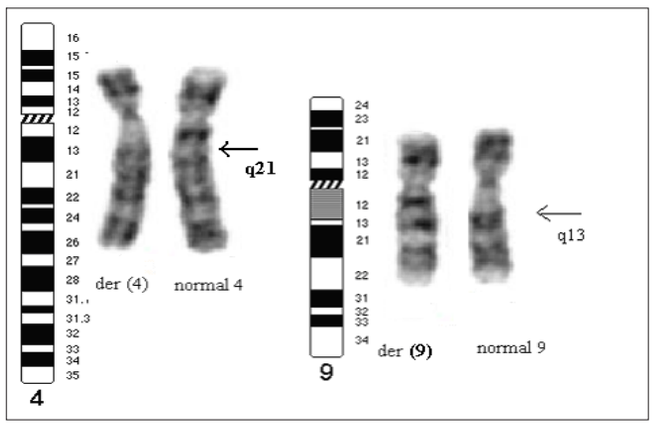

Fig. 2. G banding partial karyotype and schematic drawing of chromosomes 4 and 9 balanced rearrangement.

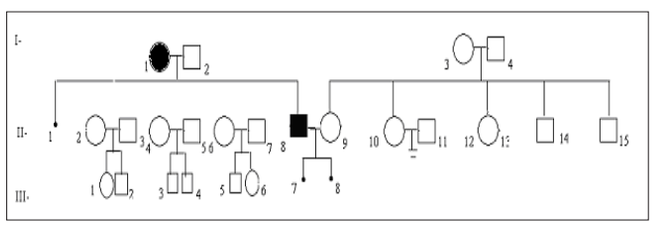

Fig. 3. The Pedigree of the family

3. Discussion

The balanced chromosome carrier is healthy but at a high risk of having a chromosomally unbalanced offspring, leading to a high rate of repeated spontaneous abortions (Gorski et al., 1988). The increased reproductive failures may result from the selective disadvantage of aneusomic gametes at fertilization or very early spontaneous abortions of unbalanced conceptuses. Adjacent segregation of interchromosomal insertions results in a deletion or duplication (Demirhan, 2006). It is interesting to consider the segregation of the quadrivalent at meiosis with reference to the present translocation. Theoretically, the expectation of balanced to unbalanced gametes is 1:2 due to the three modes of possible disjunction (Jalbert, 2004).

The recurrent abortions might result from the unbalanced distribution of translocation during gamete formation (Oral et al., 2006). A case had different break point t(4;9)(q34;p22) translocation Associated with Partial Epilepsy, Mental Retardation, and Dysmorphism (Striano, 2005) partial trisomies 9 and 4 resulting from maternal translocation t(4;9).

We suggest that an unbalanced translocation during gamete formation might be the cause of recurrent miscarriages in our case. Thus chromosomal analysis is an important etiological investigation in couples with repeated spontaneous abortions as it helps in genetic counseling and deciding about further reproductive abortions (Dubey et al., 2005).

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