

A 21/22 Translocation in a Female with Repeated Abortions: A Case Report

A. Venkateshwari¹, Ashrafunnisa Begum¹, A. Srilekha¹ M. Sujatha¹
Pratibha Nallari² and A. Jyothy¹

¹*Institute of Genetics and Hospital for Genetic Diseases, Osmania University, Begumpet,
Hyderabad 500 016, Andhra Pradesh, India*

²*Department of Genetics, Osmania University, Hyderabad 500 007, Andhra Pradesh, India*

KEYWORDS Repeated Abortions. Acrocentric Chromosomes. Robertsonian Translocation. Karyotype

ABSTRACT Robertsonian translocations (RT's) are present in 0.1% of the general population and 1% of the infertile population. Two types of RT's occur more frequently than all others, being 45,XX,rob(13;14)(q10;q10) and 45,XX,rob(14;21)(q10;q10) respectively. In the present report, an uncommon RT in a female with spontaneous repeated abortions is reported. Cytogenetic analysis of a couple with repeated abortions revealed the presence of 45,XX,rob(21;22)(q10;q10) chromosomal constitution in the female partner. The history of repeated abortions could be the outcome of unbalanced gametes (either monosomy or trisomy) resulting during the meiotic segregation of the balanced heterozygote female carrier.

INTRODUCTION

Chromosomal aberrations lead to reduced fertility in both men and women (Celep et al. 2006). About 15% of pregnancies end up in spontaneous abortions mostly in the first trimester. The most frequent cause being represented by chromosomal abnormalities, with an incidence of approximately 50 % in spontaneous abortions. (Sullivan et al. 2004).

Robertsonian translocation (RT) is recognized to be the most common structural chromosomal abnormality in the population with an incidence of 1.23/1000 live births (Nielsen et al. 1991). These chromosomal translocations are mainly observed in group D acrocentric chromosomes including 13, 14, 15 and group G including 21 and 22. The D/D translocation is the most frequent type with a high predominance of 13;14 translocation (Jacobs 1987). In RT, the pericentric regions of two acrocentric chromosomes fuse to form a mono or dicentric chromosome. The resulting balanced karyotype has only 45 chromosomes including the translocated chromosome. The meiotic segregation pattern of this translocation

heterozygote carrier results in trisomy or monosomy of the chromosomes (Pellerts 1990).

The present study reports the clinical and cytogenetic aspects of an uncommon non homologous Robertsonian translocation involving chromosomes 21 and 22 in a female with spontaneous repeated abortions.

CASE REPORT

A couple of age 35 years (male) and 30 years old (female) were referred to the Institute of Genetics, Hyderabad with a history of repeated abortions. Demographic history revealed a reproductive life of 16 years and both were related as first cousins. The reproductive performance showed that the first pregnancy during the third trimester resulted in an intrauterine death. Later, she had two spontaneous abortions with 3 months amenorrhea. There has been no previous history of such abortions in the family. She is a case of hypothyroidism and her TORCH profile revealed Ig M positive for Rubella.

Chromosome Analysis

Mitotic chromosome preparations were made from peripheral blood lymphocyte cultures of the couple following the standard method of Moorehead et al. (1960). Chromosome identification was carried out by means of G banding as per the protocol of Seabright (1971). Chromo-

Address Correspondence to:

Dr. A. Venkateshwari, Assistant Professor,
Institute of Genetics and Hospital for Genetic Diseases,
Osmania University, Begumpet, Hyderabad 500 016,
Andhra Pradesh, India
Telephone: 091-40-23403681,
E-mail: venkateshwari@yahoo.com

somal analysis of the female revealed a modal number of 45 chromosomes with two G group chromosomes missing and presence of an additional metacentric chromosome resembling the size of chromosome 16 in all the 50 metaphases screened. The banding pattern in the large and short arm of the additional metacentric chromosome was similar to G21 and G22, thereby indicating the presence of a non homologous RT. Thus, the karyotype was confirmed as 45, XX, rob (21; 22) (q10;q10) as depicted in Figure 1. Chromosomal analysis of the male partner showed normal 46, XY karyotype. Cytogenetic analysis was also performed in the lymphocyte cultures of the proband's parents and found normal.

DISCUSSION

It is estimated that 60 % of all spontaneous abortions in early pregnancies are a result of chromosomal aberrations during embryogenesis (Garcia et al. 2004). The majority of pregnancy losses or neonatal deaths are reported to result by numerical chromosomal abnormalities especially trisomies of chromosome 13, 18, 21 etc. The structural aberrations can also be the cause of pregnancy loss and infertility. Robert-

sonian translocations are the commonest structural aberrations of the acrocentric chromosomes, the most common are the non homologous forms i.e., those involving two different acrocentric chromosomes-either two different D group chromosomes (13, 14 and 15) or G group chromosomes (21 and 22) or a combination of D group and a G group chromosomes (Kim and Shaffer 2002).

A rare non homologous Robertsonian translocation between two G group chromosomes (21 and 22) in a female with repeated abortions is presented. The cytogenetic analysis revealed 45, XX, rob(21;22)(q10;q10) chromosome constitution in the female indicating the possible association of such anomaly with repeated abortions.

During pachytene stage in meiosis, homologous pairing of Robertsonian translocation is achieved by the formation of a trivalent. If alternate segregation occurs, then all gametes are potentially viable with balanced chromosomes. But, the adjacent segregation results in gametes nullisomic or disomic for one of the chromosomes involved in the rearrangement and consequently a zygote with trisomy or monosomy for one of the chromosomes involved (Table 1). Zygotes with monosomy are not compatible with

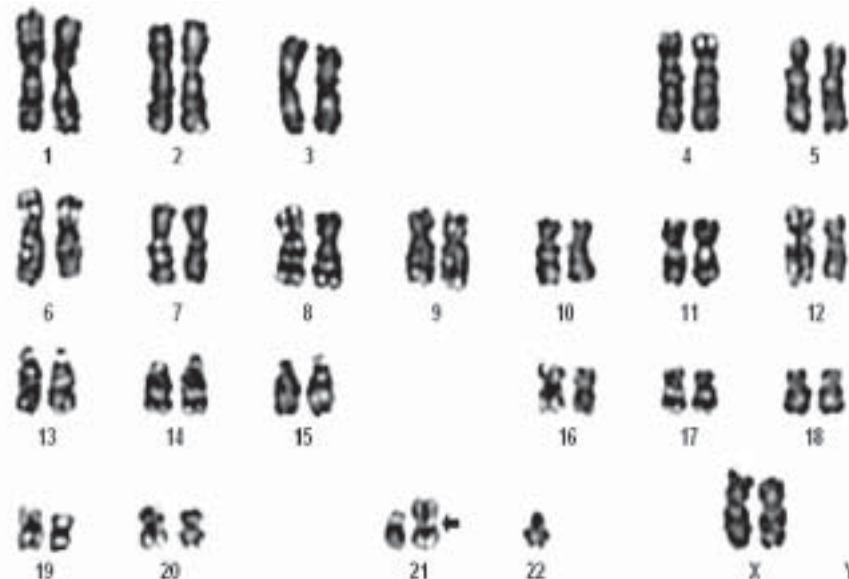


Fig. 1. Karyotype showing 45, XX, rob (21,22) chromosome constitution in a female partner with recurrent abortion.

Table 1: Segregation of gametes and the possible outcome from a female with balanced Robertsonian translocation (21,22)

Type of segregation	Possible gametes	Fertilization with normal sperm	Zygote	Status
Alternate	21,22	21,22	(21,22/21,22) Normal	Viable
	21/22	21,22	(21,22,21/22)Translocation carrier	Viable
Adjacent I	21	21,22	(21,22/21—)Monosomy 22	Non-viable
	22	21,22	(21,22/—22)Monosomy21	Non-viable
Adjacent II	21,21/22	21,22	(21,22,21,21/22)Trisomy21	Non-viable
	22,21/22	21,22	(21,22,21/22,22)Trisomy22	Non-viable

life and most translocated trisomy conceptuses are expected to result in early first trimester losses. However, some survive beyond the second trimester or up to term. Arab et al. (1999) estimated the risk of fetal abnormalities associated with maternally inherited Robertsonian 21; 22 translocation.

The major effect of RT in female carrier would be recurrent abortions while in male carrier, it may lead to infertility. As the parental karyotypes of the proband were found to be normal, it is suggested that the patient karyotype could be a de novo rearrangement that might have occurred at the post zygotic stage by the fusion of two non-homologous acrocentric chromosomes resulting in a balanced Robertsonian translocation. The association of this Robertsonian translocation in repeated abortions is expected as it results in the generation of unbalanced gametes, in accordance with the observations of previous reports (Anton et al. 2004, Biricik et al. 2004). Munne et al. (2000) also reported the formation of higher rates of unbalanced gametes in RT carrier females than in males during meiotic segregation.

Thus, cytogenetic analysis is a valuable tool for the reproducing couples with more than two spontaneous abortions to delineate chromosomal aberrations, if any. The early detection of chromosomal aberration helps for appropriate genetic counseling and allows parents to make an informed reproductive decision on subsequent pregnancies. Prenatal diagnosis offered to these couples on future pregnancies enables one to prevent social stigma of repeated abortions and implications of societal barriers.

ACKNOWLEDGEMENT

Authors thank Mrs.K.Veena and Mr. M.Panduranga Chary for the technical assistance.

REFERENCES

- Anton E, Blanco J, Eguzone J 2004. Sperm FISH studies in seven male carriers of Robertsonian translocation t(13;14) (q10;q10). *Human Reprod*, 19: 1345-1351.
- Arab S, Chitayat D, Gardner HA, Winsor EJT 1999. Mosaicism for a small marker chromosome from a familial Robertsonian translocation (21; 22). *Clin Genet*, 56: 362-366.
- Biricik A, Guney I, Berkil H, Benkhalija M, Kahraman S 2004. A male (15; 15) robertsonian translocation case with 11 previous consecutive recurrent spontaneous abortion. *Marmara Med J*, 17: 35-38.
- Celep E, Karaguzel A, Ozeren M, et al 2006. The frequency of chromosomal abnormalities in patients with reproductive failure. *Eur J Obst Gyn Reprod Biol*, 127: 106-109.
- Garcia – Enguidanrs A, Calle ME, Valero J, Luna S, Dominguez-Rojas V 2002. Risk factors in miscarriage a review. *Eur J Obstet Gynecol Reprod Biol*, 102: 111-119.
- Jacobs PA 1981. Mutation rates of structural chromosome rearrangements in man. *Am J Hum Genet*, 33: 44-54.
- Kim S, Shaffer CG 2002. Robertsonian translocations: mechanisms of formation, aneuploidy and uniparental disomy and diagnostic considerations. *Genet Test*, 6: 163-168.
- Moorehead PS, Nowell PC, Mellmann WJ, Battips DM, Hungerford DA 1960. Chromosomes preparation of leucocytes cultured from human peripheral blood. *Exp Cell Res*, 20: 613 -616.
- Munne S, Escudero T, Sandalinas M, Sable D, Cohen J 2000. Gamete segregation in female carriers of Robertsonian translocations. *Cytogenet Cell Genet*, 90: 303-308.
- Nielsen J, Wohlect M 1991. Chromosome abnormalities found among 34, 910 newborn children: Results from a 13 year incidence study in Arhus Denmark. *Hum Genet*, 87: 81-83.
- Pellestor F 1990. Analysis of meiotic segregation in a man heterozygous for a 13:15 Robertsonian translocation and a review of literature. *Hum Genet*, 85: 49-54.
- Seabright M 1971. A rapid banding technique for human chromosomes. *Lancet*, 11: 971-972.
- Sullivan AE, Silver RM, LaCoursiere DY 2004. Recurrent fetal aneuploidy and recurrent miscarriage. *Obstet Gynaecol*, 104: 784-788.