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Case Report

CHROMOSOMAL TRANSLOCATIONS IN MEN WITH AZOOSPERMIA

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Abstract: *Male infertility is liable for half of the genetic infertility cases. Robertsonian and Reciprocal translocations are the major chromosomal rearrangements in the infertile population. In this study, we aimed to submit a Robertsonian and two Reciprocal translocations in three couples with a history of male infertility with azoospermia. Chromosomal analysis of the one couple in the male partner appeared with an abnormal karyotype with 45,XY,rob(13;14) chromosomal constitution, while the female partner revealed normal 46,XX karyotype. The other two couple revealed in the male partner with reciprocal translocations, while the female partners showed normal 46,XX karyotype; one of the infertile males has karyotype with 46,XY,rcp(19;10), and another infertile male with 46,XY,rcp(6;14) chromosomal constitution. The cytogenetic analysis is mandatory to identify any probable chromosomal anomalies for couples with primer infertility. Couples with repeated abortions should be offered a prenatal diagnosis in the case of future pregnancies. Chromosome translocation carriers should be counseled to use advanced technologies such as assisted reproductive technology such as PGD.*

Keywords: *male infertility, chromosome abnormalities, oligozoospermia, azoospermia translocation*

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1. Introduction

Infertility is a disease-defined incapability to imagine within 12 months of regular and insecure sexual interaction. Men are responsible for only 20-30% of infertility cases, but 50% of total infertility cases are male infertility [1]. Male infertility is associated with genetic factors such as chromosomal structural abnormalities and specific genetic conditions (ie CFTR gene of cystic fibrosis, Y chromosome microdeletions) [2]. The q11 part on the long arm of the Y chromosome has AZF (AZFa, AZFb, AZFc) parts linked to sperm production. It is known that microdeletions in these regions cause oligospermia or azoospermia and thus cause fertility problems [3]. Therefore, microdeletion of a Y chromosome should be investigated by molecular genetic methods in patients with non-obstructive or harsh oligospermia. Translocation is one of the chromosomal abnormalities seen as the loss of a part of a chromosome or a part of it that breaks to another chromosome. If there is no loss of chromosome material during the exchange between chromosomes, it is called balanced translocation. These individuals are usually clinically normal. However, if chromosome material loss occurs during this change, it is called ‘unbalanced translocation and may present with serious clinical findings [4]. There are generally 2 types of translocation; Reciprocal and Robertsonian. Fragment exchange between non-homologous chromosomes is a chromosome abnormality called Reciprocal translocation. Two detached fragments of two different chromosomes are switched. Patients can be phenotypically normal when no genetic material gained or lost and if the breakpoints do not result in truncation of a gene. Reciprocal translocations are known to be a structural chromosomal abnormality that is common in the population

(1 in 600) [5]. Chromosomal reorganizations in the infertile males are about approximately 10 times as frequently as normal population [6]. The most widespread structural chromosomal anomaly observed in the population is Robertsonian translocations with a frequency of approximately 1.23 / 1000 live births [7]. These special types of translocation are formed by the centric fusion of the long arms of the acrocentric chromosomes 13, 14, 15, 21 and 22, and the long arms that fuse at the centromeric part and lose their short arms. Instantaneous loss of both short arms is usually observed [8]. This translocation transmitted by one of the parents or can be occurred de novo. Robertsonian translocation is one of the major chromosomal anomalies, with the pervasiveness of 1% of the infertile population and 0.1% of the general population. Because of oligoasthenoteratozoospermia men carrying this translocation have more frequent infertility problems (OAT). The most frequent type of translocations in infertile men are der(13;14) (0.97 per thousand), followed by der(14;21)(0.20 per thousand) [9]. In infertile men 5.3%) somatic chromosome abnormalities in the karyotypes have 10 times as high as in the general population. The incidence of male infertility with synaptic chromosome anomalies, which limited to the germ cell line and only visible by meiotic studies is 4–7.7 % [10]. Numerical and structural chromosome abnormalities play an important role in azoospermic and strictly oligoasthenozoospermic men [11]. In this study, we aimed to present a Robertsonian and two Reciprocal translocations in three couples with a history of male infertility with azoospermia. We believe that phenotype-genotype correlations of our cases provide important contributions to the literature.

2.Materials and methods

2.1.Case 1

A 35 year-old-male whose parents were non-consanguineous referred to our Medical Biology and Genetics laboratory for karyotype analysis because of primary infertility. According to information of his family, he had one sister who had died. He was married for 3 years and had no children. His 30year-old-wife had no apparent fertility problem. Physical examination showed male habitus with normal adult pubic and axillary hair. Either malformations or gynecomastia was not seen. Severe oligoasthenozospermia (sperm account $0.5*10^6$ ml, 10% normal morphology, and 90% continuous motility) was established in examinations. Laboratory examination of hormone tests as measured FSH: 8.74 mlU / ml, LH: 3.34 mlU / ml, Estradiol (E2): 35 pg / mL, Testosterone 4.41ng / mL, Prolactin 0.86 ng / ml within normal levels. The patient had never received hormone therapy. His Y chromosome microdeletion test was positive.

Lymphocyte culture performed in peripheral blood and 45,XY,rob(13;14) chromosomal constitution were found in all metaphases plates and diagnosed as Robertsonian Translocation. Karyotype indicated 45 chromosomes with deficient chromosomes of 13 and 14, together with an extra chromosome that did not suit into any group of the chromosomes in the karyotype. The banding pattern of the short and long arms of the extra chromosome was akin to chromosome 13 and 14, thus showing the existence of a non-homologous Robertsonian Translocation

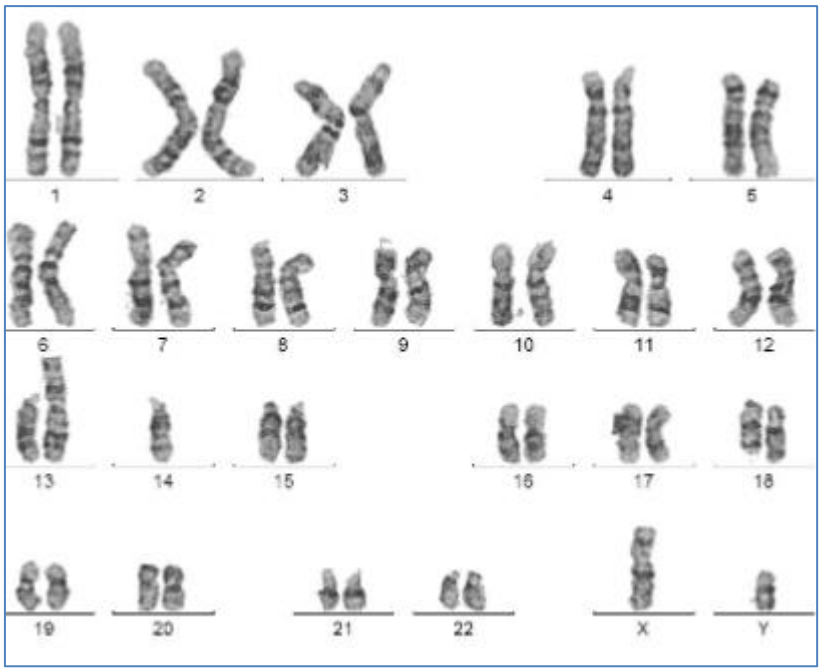

Figure 1. Robertsonian translocation karyotype analysis [45,XY,rob(13;14)]

2.2. Case 2

A 35-year-old man with fertility problems despite 14 years of sexual intercourse was referred to our Medical Biology and Genetics laboratory for karyotype analysis. His 32- year- old wife had no apparent fertility problem. The couple had one unsuccessful IVF trials. Laboratory examination of hormone tests as measured FSH: 21.97 mlU / ml, LH: 6.04 mlU / ml, Estradiol (E2): 15.56 pg / mL, Testosterone 1.73 ng / mL, Prolactin 4.18 ng / ml within normal levels. The patient had never received hormone therapy. His Y chromosome microdeletion test was positive. Semen analysis demonstrated normal volume azoospermia. Lymphocyte culture was performed in peripheral blood and an average of 2 preparations were made. Praperates were stained by Giemsa banding technique (GTG), [46,XY,rcp(19;10)] chromosomal constitution were found in 25 metaphases plates and diagnosed as Reciprocal Translocation. Karyotype analysis of mother, father, and sibling had done. Karyotyping of the mothers was normal (46,XX). The chromosome analysis of father also showed balanced Reciprocal translocation. Therefore, we considered the reciprocal translocation in the man transmitted from the father.

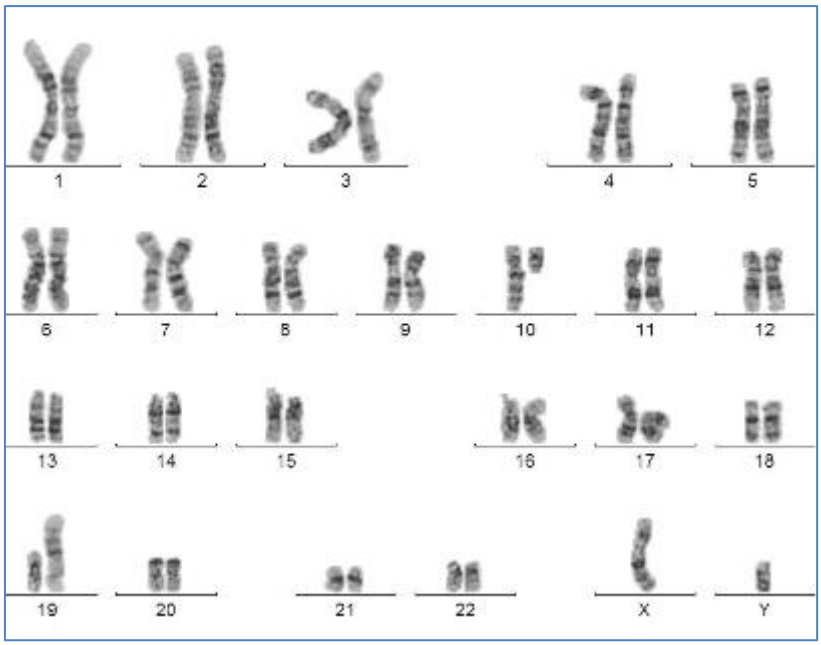

Figure 2. Reciprocal Translocation karyotype analysis [46,XY,rcp(19;10)]

2.3. Case 3

A 40-year-old male whose parents were consanguineous referred to our Medical Biology and Genetics laboratory for karyotype analysis after 6 years of sexual interaction without beginning his 33-year-old-wife had no apparent fertility problem. His brother was married for 25 years and had primary infertility problems. Semen analysis verified normal volume oligoasthenoteratozoospermia. His Y chromosome microdeletion test was positive. Laboratory examination of hormone tests as calculated FSH: 212.03 mlU / ml, LH: 5.34 mlU / ml, Testosterone 4.88 ng / mL, Prolactin 6.2 ng / ml within normal levels. Karyotype analysis revealed 46,XY,rcp(6;14).

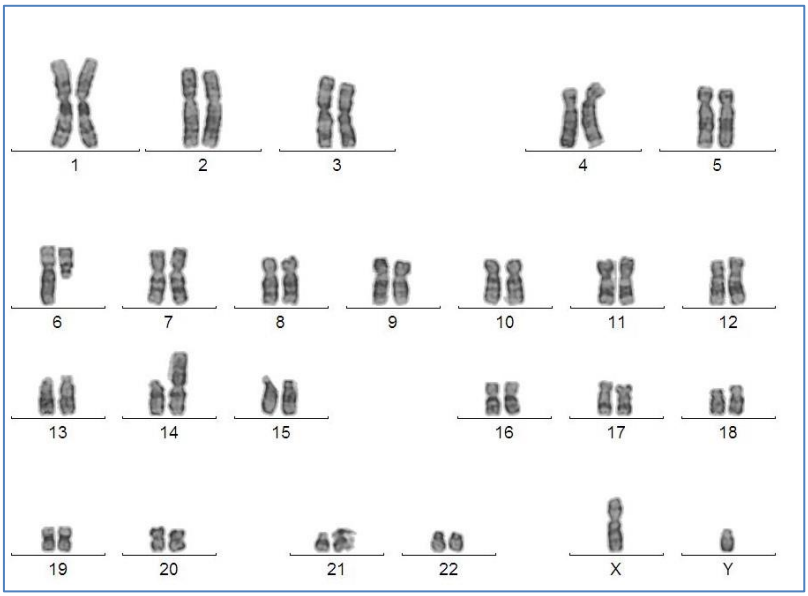

Figure 3. Reciprocal Translocation karyotype analysis [46,XY,rcp(6;14)]

3.Discussion

Infertile men have a higher frequency of structural chromosomal abnormality than the general population [12]. Loss of chromosome material in reciprocal translocation in the form of a balanced translocation and the clinical problem usually does not appear. However, although translocation carriers do not have any problems in themselves, they cause unstable chromosomal formations during parental gamete formation. Their infertility problems may be caused by more or less severe oligospermia [13]. In our infertile male cases with reciprocal translocation have a normal phenotype, but have troubles of infertility with azoospermia.

The number of chromosomes in Robertsonian translocation is 45. While most Robertsonian translocation is inborn from a parent, up to 40% can be de novo. We found that Robertsonian translocation had de novo. De novo translocations could be formed with rearrangements in meiosis. Robertsonian translocation linked to azoospermia is a rare condition [14]. Unlike the literature, karyotype analysis revealed 45,XY,rob(13;14) associated with azoospermia. Cytogenetic assessment should be a part of the evaluation of infertile male presenting to the reproductive clinic. Carriers of chromosome translocation should be counseled to utilize the diverse technologies obtainable through assisted reproductive technology, such as PGD.

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