Chromosomal Translocation t (10;19) (q11.2;q13.4) in an Infertile Male

Infertil bir Erkekte t (10;19) (q11.2;q13.4) Kromozomal Translokasyonu

Murat Kara1, Askin Sen2, Esin Sakalli Cetin3, Kursat Kargun4
1Department of Medical Genetics, Mugla Sitki Kocman University Faculty of Medicine, Mugla, Turkey
2Department of Medical Genetics, Firat University Hospital Faculty of Medicine, Elazig, Turkey
3Department of Medical Biology, Mugla Sitki Kocman University Faculty of Medicine, Mugla, Turkey
4Department of Medical Genetics Laboratory, Firat University Hospital, Elazig, Turkey

Abstract
Chromosomal rearrangements are usually associated with male factor infertility. We report here a 34-year-old man suffering from primary infertility for 15 years. The cytogenetic analysis and investigation of Y-chromosome microdeletions were performed. A reciprocal balanced translocation t (10;19) (q11.2;q13.4) was found in oligozoospermic infertile men with no Y-chromosome microdeletions. In this case, we aimed to evaluate the 46,XY,t (10;19) (q11.2;q13.4) karyotype, which was detected through a cytogenetic analysis of a person referred to our genetic laboratory due to primary infertility, in the light of the literature.

Key Words: Chromosomal translocation, infertility

Introduction
Infertility means the inability to conceive after at least one year of unprotected intercourse. It effects around 15-20% of couples in their reproductive years [1]. Male factor infertility contributes to about 50% of all infertility cases among which chromosomal abnormalities varies from 2.2% to 15.2% [2, 3]. Robertsonian translocations and sex chromosome abnormalities are the most frequent chromosomal abnormalities in infertile men. Reciprocal translocations have been found in approximately 1% of infertile men, and are more common in azoospermic than in oligozoospermic males [4]. It is well known that chromosomal translocations in men can cause spermatogenesis failure due to meiotic impairment [5].

Y-chromosome microdeletions, also an important cause of male infertility, occur in 6-8% of severely oligospermic and in 3-15% of azoospermic men [6].

Here, according to what we know so far, this is the first report of a reciprocal translocation t (10;19) (q11.2;q13.4) in oligozoospermic infertile men.

Case Report
The patient was a 34-year-old male, who is married for 15 years with a 32-year-old female. The urology clinic referred him to our genetic counselling clinic for a karyotype analysis for infertility. The couple was not consanguineous. His history included bilateral varicocelectomy, and his physical examination revealed loss of vision in the right eye. Laboratory analyses using scrotal colour Doppler ultrasonography (USG) showed that the right testis was smaller than the left (right testis volume: 6.4cc, left testis volume: 5cc). Hormonal tests showed LH 9.97 mIU/mL (1.7-8.6), FSH 21.97 mIU/mL (1.6-11.0), and testosterone 1.73 ng/mL (2.18-9.05), with all other tests being normal. The spermiogram showed the number of spermatozoa in 1cc to be 100,000/mL, with a sperm motility of 40% per mL. The proband had 5 brothers and 1 sister and one of his brothers was unable to conceive for 4 years. There was an attempt of parental chromosomal analysis and siblings of the proband, however it failed as the parents and siblings lived in another city.
Cytogenetic analysis

Cytogenetic analysis was performed according to standard cytogenetic methods for karyotype analysis of the couple. The 72-hour cultured cells from peripheral blood were harvested. The trypsin GTG banded chromosomes of thirty metaphases were analysed according to the International System for Human Cytogenetic Nomenclature (ISCN) 2005.

Investigation of Y-chromosome microdeletions

For molecular genetic analysis, microdeletion analysis was performed by the multiplex polymerase chain reaction (PCR) method on DNA extracted from peripheral blood. In each case 8 markers in azoospermia factor (AZF) regions were tested: the Zinc finger Y-chromosomal protein (ZFY), sex-determining region Y (SRY), sY84, sY86 (AZFa); sY127, sY134 (AZFb); sY254, sY255 (AZFc).

Results

The male partner revealed a reciprocal translocation t (10;19) (q11.2;q13.4) with break points at 10 q11.2 and 19 q13.4 in all examined cells (Figures 1 and 2). The female partner’s karyotype was normal (46, XX). Other family members did not give consent for the karyotype analysis because they were living in another city. Molecular investigation did not detect any Y-chromosome microdeletions.

Discussion

Chromosomal rearrangements are observed in patients with azoospermia and severe oligospermia in autosomal and sex chromosomes, or both [7]. One of the most commonly seen chromosomal aberrations is the sex chromosome aneuploidies, which is also known as Klinefelter’s syndrome,
(47, XXY karyotype) [8]. The percentage of infertile men is higher since reciprocal and Robertsonian translocations are observed at 0.5-1/1000 in the newborns among the general population [9]. Spermatogenesis is negatively affected because of such irregularities in the chromosome and leading to the formation of unbalanced gametes. Therefore, it is very important to determine the underlying genetic factors in male infertility. Infertility cases associated with balanced translocations formed by different chromosomes such as t(13;19), t(3;5), t(9;11), t(7;16), t(6;12), t(8;13), t(18;21) were reported [5, 10-14]. To the best of our knowledge, this is the first report in the literature of balanced non-Robertsonian reciprocal autosomal translocation t(10;19)(q11.2;q13.4) associated with male infertility.

Translocations behave uniquely because of the chromosomes involved in the reorganization, the size of the translocated and the interstitial segments, and the presence or absence of recombination loci [15]. Depending on whether reciprocal translocations are present in a balanced or in an unbalanced form, they have different effects on carriers. Generally, carriers of unbalanced reciprocal translocation have phenotypic consequences of mental retardation and physical problems. Balanced forms do not have any phenotypic effect on the carriers, but these individuals are associated with reproductive problems such as infertility, repeated miscarriages and malformed offsprings due to chromosomally unbalanced gametes [4]. The mechanism of reciprocal translocation in male infertility is not understood so far. The reorganization of genetic material with reciprocal translocation may alter the normal progress of meiosis in two ways. First, the quadrivalent form of translocated chromosomes and their homologous can segregate in different ways during meiosis and this meiotic segregation is unique for each translocation carrier. Several factors such as the size of the intestinal and translocated segments, the morphological characteristics of the rearranged chromosomes and the distribution pattern of chiasmata during metaphase I (MI) are said to be determinant in the proportion of balanced and unbalanced gametes, which affect the final frequencies of normal and aberrant gametes [12, 16]. The other way is the increase of the aneuploidy frequencies of other chromosomes that are not related to the rearrangement. While sperm count is inversely correlated with the frequency of contact, oogenesis is relatively preserved in the presence of such chromosomal aberrations as seen in number of families with balanced chromosomal structural rearrangements associated with the female fertility [17]. A significant limitation of this case report is the non-availability of karyotype in other family members.

In conclusion, the case reported in the present study supports the relationship between chromosomal abnormalities and male infertility. Identification of the carriers of chromosomal anomalies may reveal the cause of infertility and fetal losses in married couples. Chromosomal analysis and Y-microdeletion screening are recommended when poor sperm production is suspected in male patients. In couples who admitted to visit genetic counselling clinics for infertility, it is important to diagnose infertility, identify the factors underlying infertility, and plan the treatment process accordingly. Therefore, when numerical or structural chromosomal anomalies are found in the patient, genetic counselling should be offered to the patient together with a recommendation of pre-implantation genetic diagnosis (PGT) and amniocentesis or chorionic villus sampling for prenatal genetic diagnosis. The person, who was identified as having reciprocal translocations, is very important for the calculation of the risks of its transmission to the unborn baby, if conception occurs after the treatment. To predict the risk of passing a genetic condition to future generations, cytogenetic analysis and genetic counselling have to be performed in cases of male infertility.

Informed Consent: Written informed consent was obtained from patients’ parents who participated in this case.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this case has received no financial support.

References

6. Walsh TJ, Pera RR, Turek PJ. The genetics of male infertility. Seminars in reproductive medicine 2009; 27: 124-36. [CrossRef]


9. Ioannou D, Griffin DK. Male fertility, chromosome abnormalities, and nuclear organization. Cytogenet Genome Res; 133: 269-79. [CrossRef]


