Case Report

The Robertsonian translocation of '21/22' in Nonobstructive Azoospermia: A Rare Case Report from India

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Abstract

Robertsonian translocation is a subtype of balanced translocation involving two acrocentric chromosomes. Individuals who are carrier of this abnormality are at increased risk of infertility or bad obstetric history. This case is reported with the aim to describe a male who presented with nonobstructive azoospermia at a tertiary care center. The individual was phenotypically normal but carrier of a Robertsonian translocation of two acrocentric chromosomes. With this literature, we emphasize that conventional cytogenetic is an essential diagnostic tool for screening genetic factors in infertility.

Keywords: *Azoospermia, cytogenetic, Robertsonian translocation*

Introduction

The World Health Organization defines primary infertility as a disease of the reproductive system wherein there is failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse.[1] Certainly, it is a common disability with worldwide variation, affecting from 3% to 15% of Indian couples based on their reproductive age groups.[2] Male factor contributes up to 50% in a couple-seeking medical attention. Different etiologies have been documented for male and female infertility, of which a fraction of cases have genetic predisposition, and a minority of this fraction carry demonstrable chromosomal aberration.[3]

The present study reports the clinical, hormonal, and cytogenetic profile of a male patient with azoospermia and a carrier of an uncommon Robertsonian translocation involving small acrocentric chromosomes 21 and 22. A careful Internet search was carried out, and to the best of our knowledge, no such case has been reported from India till date from India.

Case Report

Our patient is a 37-year-old male patient married for the last 8 years, with cohabitation of 7 years and presented to the infertility clinic of a tertiary care center. His height was 169 cm with obese build and BMI of 31 kg/m^2. The individual was also on regular medications for generalized tonic–clonic seizures for the past 3 years and recently diagnosed diabetes mellitus type 2. Systemic, genitalia examination, and ultrasonography of the scrotum were essentially normal. His hematological and basic biochemical parameters were normal. All viral markers were negative. Repeated semen analysis on three separate occasions revealed azoospermia. Hormonal profile revealed elevated gonadotropins (FSH & LH) whereas testosterone level was decreased [Table 1].

Cytogenetic profile

Somatic chromosomes study

After obtaining informed consent, conventional cytogenetic analysis (CCA) was performed on phytohemagglutinin-stimulated peripheral blood T-lymphocytes using GTG banding and standard cytogenetics protocol. Chromosomes analysis was done using image processor and software (Cytovision) version 7.2 build 147. Chromosomal abnormalities were reported according to the International System for Human Cytogenetic Nomenclature (ISCN, version: 2016) at band level of 500–550. All 20 analyzed metaphases demonstrated a Robertsonian translocation involving two nonhomologous "G" group acrocentric chromosomes, namely chromosome 21 and 22. This balanced

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translocation has resulted in a modal chromosome number of 45. The modal karyotype of the patient was 45, XY, rob (21;22)(q10;q10) [Figure 1]. There was no structural abnormality in the Y chromosome at the above band level. As an institutional policy, we also performed CCA on peripheral blood of the patient's wife which revealed a normal female karyotype (46, XX).

CCA of extended family members could not be performed as the couple is staying away from his family because of service conditions in armed forces.

Germ cell chromosomal study

Meiotic chromosomal study in this case could not be performed because of azoospermia.

Discussion

The prevalence of genetic abnormalities in male infertility varies from 4% to 13%, especially in men with defective sperm production.[4] Among these, the most common cytogenetic aberrations involve the gonosomes.[5] This can be seen in the form of a numerical or structural abnormality, involving X or Y chromosomes. Another category of chromosomal defects in such individuals may be due to structural or uncommon numerical abnormalities of autosomes (balanced reciprocal translocations and inversions or even presence of a supernumerary marker chromosome). In the former group, Robertsonian translocation involving acrocentric chromosomes of D and G groups are more common than other autosomes.[6]

Robertsonian translocation involving t (D; D) (translocation involving two long acrocentric chromosomes) and t (D; G) (translocations involving one long and one short acrocentric chromosomes) group of chromosomes is more common[7] than the t (G; G) (translocation involving both short acrocentric chromosomes group), which is involved in our patient, formed by fusion of long "q" arms of chromosome 21 and 22. This translocation resulted in formation of one chromosome resembling a short metacentric chromosome and loss of short "p" arm material which contains ribosomal RNA.

Although the gametogenesis in patients with balanced translocations is highly variable, oligospermia in our patient may be explained due to spermatogenic blockage of synapsis and recombination of sex chromosomes, the X-Y bivalent, by the unpaired/additional acrocentric chromosome [Figure 2]. Another mechanism which may impair gametogenesis is synapsis of homologous segments in normal and rearranged chromosomes. These mechanisms finally may cause spermatogenesis arrest at meiosis-I and apoptosis of germ cells due to genetic imbalances and reduced pairing.

Table 1: Hormonal profile

Hormone	Values	Interpretation
FSH	7.1 mIU/ml	Elevated
LH	9.7 mIU/ml	Elevated
Prolactin	6.02 mg/ml	Normal
TSH	1.48 µIU/ml	Decreased
Testosterone	1.31 ng/ml	Decreased

FSH=Follicle-stimulating hormone, LH=Luteinizing hormone, TSH=Thyroid-stimulating hormone

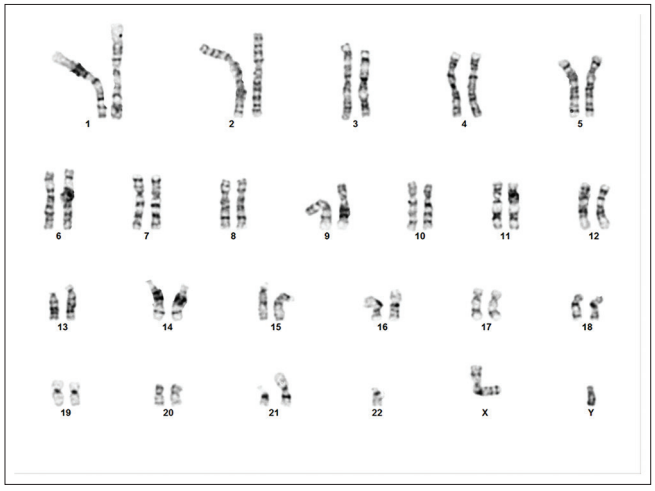

Figure 1: Robertsonian translocation involving acrocentric chromosomes 21 and 22. ISCN result: 45, XY, rob (21;22)(q10;q10)

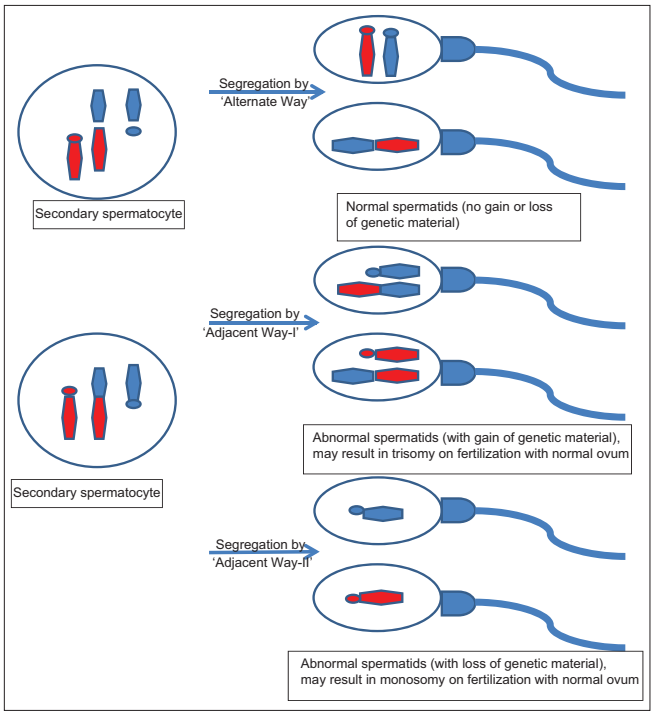

Figure 2: Meiotic behaviour in heterozygous carrier, six possible gamete formations by alternate and adjacent segregation methods

Males who are carrier of Robertsonian translocation usually have unremarkable phenotypic characters but may have certain reproductive problems in the form of infertility, spontaneous abortions or even have the history of children with congenital anomalies or birth defects either due to major genetic imbalances (monosomies or trisomies) or even uniparental disomy.

Management options for the carrier of such balanced translocations may be *in vitro* fertilization using intracytoplasmic sperm injection and prenatal genetic diagnosis or sperm donation and a detail genetic counseling.

Conclusion

Chromosomal aberration is an important etiology in infertility. Therefore, cytogenetic analysis is important not only from diagnostic point of view but also an essential tool for enlightening both the treating doctor and the patient for various pregnancy outcomes. Hence, affected couples should be counseled and advised accordingly for a happy and successful ending.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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