CYTOGENETIC ANALYSIS REVEALED 47, XXY: A CASE REPORT

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ABSTRACT

Klinefelter's syndrome is a sex chromosomal aneuploidy caused by an addition of X chromosome in males (47, XXY).Variants of this syndrome with X and Y polygamy is of rare occurrence. Here we describe a rare case of 48, XXXY Klinefelter's variant from South India with a reported incidence of 1 per 17,000 to 1 per 50,000 male births. The presence of an extra X chromosome/s in these individuals has a great impact on the physical and cognitive functions, which could be attributed to Gene dosage effects and genes involved in neurogenic development.

Keywords:

Klinefelter's syndrome, Cytogenetic analysis, Genetic counseling, recurrent abortions,

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).The present study was carried out to find out frequency of chromosomal abnormalities & contribution of environmental, occupational factors in cases of male infertility. Klinefelter's syndrome (XXY) is the most common genetic disorder of human male infertility, in which there is at least one extra X chromosome. Males normally have an X chromosome and a Y chromosome (XY). But males who have Klinefelter syndrome have an extra X chromosome (XXY), giving them a total of 47 instead of the normal 46 chromosomes. After genetic counseling of patient attended to fertility and genetic clinic, during the clinical diagnosis we found the following complaints of loss of secondary sexual characteristics and infertility. Physical examination revealed breast development, thin built, small size testes, and absence of beard and pubic hairs. Karyotype and biochemical analysis were performed to detect chromosomal abnormality as well as hormonal level to confirm the diagnosis of Klinefelter's syndrome (XXY). Chromosomal analysis of the peripheral blood lymphocytes demonstrated the constitutional karyotype of 47, XXY. Using karyotype the presence of extra X chromosome was confirmed, supporting the cytogenetic finding. The 47, XXY syndrome is relatively uncommon and can be missed clinically because of its variable clinical presentations. Accurate diagnosis of this constitutional karyotype provides a valuable aid in the counseling and early management of the patients who undertake fertility evaluation. The present study reports the clinical and cytogenetic aspects of an uncommon non homologous chromosome X in a meal and female with spontaneous repeated abortions.

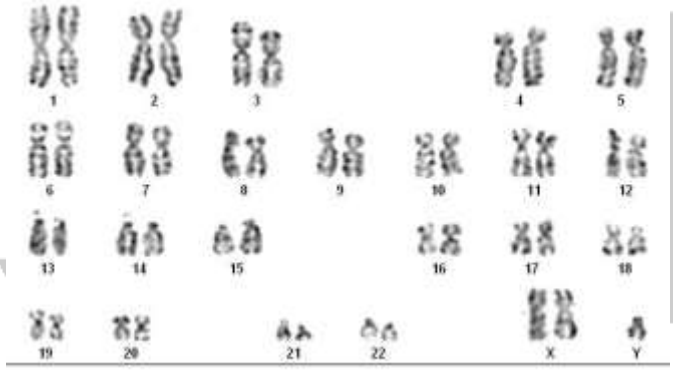
A Case Report:

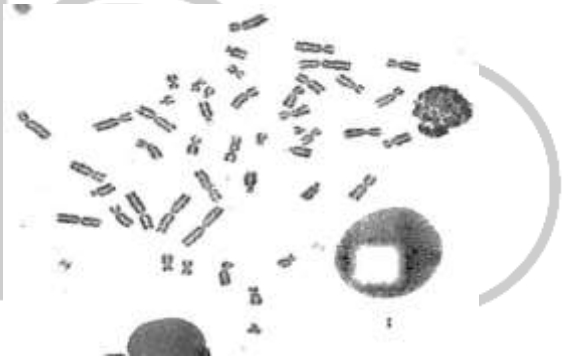
A couple with the complaint of repeated abortions was come to our hospital for cytogenetic evaluation. Chromosomal analysis of the couple revealed an abnormal karyotype in the male partner with 47, XXY.After counseling of couple who were referred for chromosome analysis because of a history of spontaneous abortions in the first-trimester. The female was 30 years old, and her husband 35 years. There was no known exposure to recognized teratogens. They were healthy and phenotypically normal (Male height- 172 cm and weight 66 kg, Female height- 155 cm and weight 45 kg). The present study information consent was obtained from the couple before investigation. Reproductive history of the female revealed three, first trimester miscarriages during the past 10 years, all being consecutive repeated abortions. The cause and genetic status of the miscarriages was not known. The

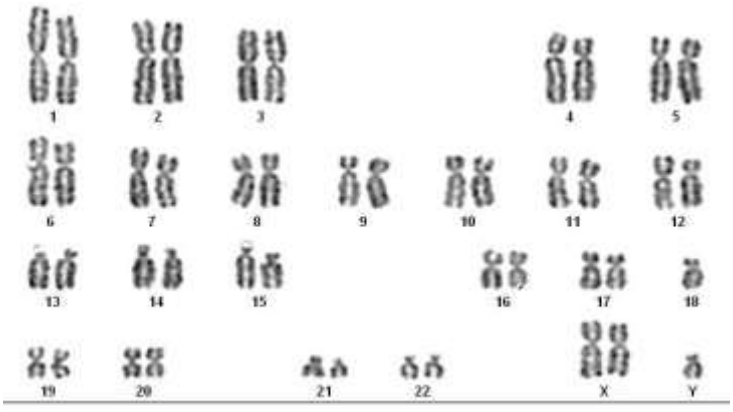
uterine cavity was evaluated by three dimensional ultrasonography and revealed normal size (6.0X3.5X3.0 cm) and echo pattern. Both the ovaries were found to be normal in size with right and left ovaries measuring2.2X2.0 cm and 2.1X1.8 cm respectively. The hormonal profile of the female partner demonstrated normal values for luteinizing hormone (LH) 5.5 mIU/ml (1.5–9.3 mIU/ml), Prolactin-8.5 ng/ml (3–21 ng/ml) and TSH 2.5 UIU/ml (0.35–5.5 UIU/ml). Follicle stimulating hormone (FSH) was determined on the 3rd day of the cycle and was in normal limits [8.5 mIU/ml (1.4–18.1 mIU/ml)]. Similarly, hormonal profile of the male spouse was within the normal range.

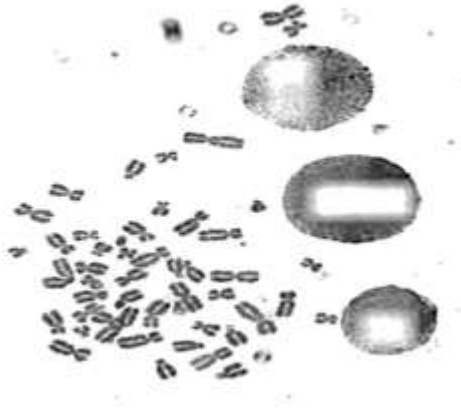
Materials and methods

Cytogenetic analysis was carried out based on phytohaemaglutinin- stimulated peripheral blood lymphocyte cultures, of the couple and parents of the female partner. Lymphocyte culturing and GTG-banding were performed following standard protocols using standard technique of Moorhead et al(1960)(Moorhead, 1960). A total of 50 metaphases were screened and normal karyotype was found in both the patients.









DISCUSSION

It is expected that 60 % of all spontaneous abortions in early pregnancies are a result of chromosomal aberrations during embryogenesis (Garcia et al. 2004). the common of pregnancy sufferers or neonatal deaths are reported to result by numerical chromosomal abnormalities especially Klinefelter's syndrome (XXY). The chromosomal aberrations can also be the cause of pregnancy loss and infertility. 47, XXY (or XXY) is a genetic condition caused when someone has two X chromosomes and one Y chromosome. Males normally have an X chromosome and a Y chromosome (46, XY), and females normally have two X chromosomes (46, XX).Because people with an XXY chromosome arrangement have a Y chromosome, they are considered genetic males. Most XXY individuals develop as males, often not knowing they have an extra chromosome. Some will develop the varied and often subtle characteristics associated with Klinefelter syndrome. And a small proportion will develop as intersex (between male and female) or female. Physical characteristics may appear around the time of puberty, when gender identity and sexual characteristics begin to take shape. Similar conditions are caused by additional X chromosomes (48, XXXY; 49, XXXXY), but they are much more rare. The more X chromosomes a person has, the stronger the physical characteristics and health problems tend to be, including intellectual disability.

Klinefelter's syndrome (XXY) is usually caused by what is called nondisjunction. Nondisjunction happens when a pair of sex chromosomes fails to separate during egg (or sperm) formation. When an egg (or sperm) with an extra X chromosomes joins with a normal sperm (or egg), the resulting embryo will end up with three sex chromosomes (XXY) instead of the normal two (XX or XY). As the baby develops, the extra chromosome is then copied in every cell. Nondisjunction leading to XXY is equally likely to happen in the mother's egg and the father's sperm. In about 10% of cases, chromosomes fail to separate when a cell divides very early in embryonic development, and only some of the baby's cells have an extra X chromosome. Such "mosaic" cases are usually mild and often remain undetected. 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.

REFERENCES

Ananthapur V, Avvari S, Tella S, Nallari P, Akka J. A Robertsonian Translocation rob (14;15) (q10:q10) in a Patient with Recurrent Abortions: A Case Report *(2010). J Reprod Infertil.;11(3):197-200.*

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.

Drugkar Amol Z, Gangane S.D, More Rakhi M Drugkar Swati . Cytogenetic Study In Male Infertility. *(2013). IOSR Journal of Dental and Medical Sciences (IOSR-JDMS): 2279-0853, p- ISSN: 2279-0861.Vol 5, Issue 2, PP 05-11.*

Eberhard Nieschlag. Klinefelter Syndrome (2013). *Dtsch Arztebl Int*; 110(20): 347−53.

Ina W. Kim, MD, MPH, Arjun C. Khadilkar, Edmund Y. Ko, MD,Edmund S. Sabanegh, Jr, MD.XYY Syndrome and Male Infertility*(2013)* Rev Urol. *15(4):188-196 doi: 10.3909/riu0580.*

Gorlin RJ, Cohen MM, Levin LS, Syndromes of the Head and Neck. New York, NY, Oxford,1990.

Moorhead PS, Nowell PS, Mellmann WJ, Battups DM, Hungerford DA,Chromosomal preparation of leukocytes cultured from human peripheral blood Exp. Cell Res, 20, 1960, 613-615.

Jejeebhoy, Shireen J. Infertility in India - levels, patterns and consequences: Priorities for social science research of Family Welfare. June 1998. 44(2). P. 15-24.
J.M. Pina-Neto, R.C.V. Carrara, R. Bisinella,L.F. Mazzucatto,M.D. Martins E. Sartoratto and R.

Yamasaki Somatic cytogenetic and azoospermia factor gene microdeletion studies in infertile men (2006). *Braz J Med Biol Re* : 39(4).

Mohammad T. Akbari, F. Behjati1, G. R. Pourmand2, F. Akbari Asbagh3, M. Ataei Kachoui Cytogenetic abnormalities in 222 infertile men with azoospermia and oligospermia in Iran (2014). *ijhg* (2014), IP: 49.206.214.217].

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.

Ponnudurai R, Srinivasan B, SumithaR, Teena Koshy, Solomon S. D. Paul, Thiruvikraman, Rani A. Klinefelter's syndrome (mosaic) with chromosome 9 inv and schizophrenia (2012). *Indian Journal of Psychiatry* 54(1),

Ramakrishnan v, Gowtham Kumar S, Radha Pandiyan. Klinefelter syndrome and its association with male infertility Asian Pacific (2014). *Journal of Reproduction* 77-79.

Sreenivasa G, Suttur S. Malini, Prasanna Kumari, Usha R. Dutta. Cytogenetic abnormalities in 200 male infertile cases in the southern region of India (2013) .Open *Journal of Genetics* 33-37.

Sullivan AE, Silver RM, LaCoursiere DY 2004. Recurrent fetal aneuploidy and recurrent miscarriage. *Obstet Gynaecol,* 104: 784-788.