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Male infertility and 47,XYY syndrome: Case report

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ABSTRACT:
Background: 47,XYY syndrome is a sex chromosomal anomaly observed in humans with prevalence rate of 1 in 1000 male live births. This anomaly is frequently associated with male infertility. **Method:** A retrospective study was carried out on infertile male referred to our diagnostic laboratory for chromosomal analysis. In the current study, six cases of infertile male with azoospermia and oligospermia were studied in detail out of total 562 infertile males. The study was extended using FISH technique and confirmed presence of extra Y chromosome in all six cases. **Results:** Chromosomal analysis revealed nonmosaic karyotype of 47, XYY in all six cases. In these cases, presence of extra Y chromosome was confirmed in metaphase chromosome and interphase cell by FISH analysis using fluorescence labelled X and Y centeromeric probes. **Conclusion**: The 47,XYY syndrome is relatively uncommon and due to non-phenotypic abnormalities it can be missed. Accurate diagnosis with karyotype and FISH will be helpful in management of infertile males.

Key-words: 47,XYY syndrome, G-banding, Karyotype, FISH, Male infertility.

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INTRODUCTION

47,XYY syndrome is an aneuploidy of sex chromosomes in which male receives extra chromosome having 47,XYY karyotype. The occurrence is 1 in 1000 live male births in population[1]. Parental nondisjunction at meiosis II resulting in an extra Y chromosome produces a 47,XYY karyotype. Generally there are no phenotypic abnormalities in 47,XYY but they are at greater risk for behavioural problems, learning disability, tall statute, delayed speech or language development.[2] Several studies have shown increased chromosomal rearrangements for oligospermic (5-7%) and azoospermia (10-15%). There are several reasons of spermatogenic failures. In 47,XYY syndrome, main cause of hormonal disturbance in gonadal environment, which finally affects the normal function of human chorionic gonadotropin.[3]

METHODS

a) Patients: A retrospective study was carried out on infertile male referred to our diagnostic laboratory for chromosomal analysis. The written consent was obtained before taking blood. The 06 cases were identified out of 562 infertile males, who were having an abnormal non-mosaic karyotype of 47,XYY complement.

b) Cytogenetic and FISH analysis: The conventional cytogenetic analysis was performed on peripheral blood samples followed by GTG banding.[4] The karyotype was described according to ISCN.[5] Fluorescence in situ hybridization (FISH) performed using labelled X and Y centromeric probes (Vysis, Germany) according to manufacturer's recommendation.

c) Case presentation:

Case-1:

A 33- year old man referred for having infertility. The patient was non-consanguineous healthy male. He had normal phenotypic features and tall stature (height 182 cm and weight 58 kg). Hormonal levels demonstrated that FSH and LH were increased (22.3 mlU/ml and 14.3 mlU/ml) respectively and very low level testosterone 1.6 ng/ml was found. Seminal analyses showed severe oligospermia (sperm count less than 5 million sperm/ml).

Case-2:

A 35-year old male was referred to our laboratory for chromosomal analysis. The patient had non-consanguineous history. Physical examination revealed normal male with height of 185 cm and weight 69 kg. Measurement of serum hormone levels demonstrated that FSH and LH were increased (24.3 mlU/ml and 16.9 mlU/ml) respectively. The level of testosterone was 1.2ng/ml and seminal analyses revealed azoospermic (no spermatozoa).

Case-3:

A 24-year old man was approached us for peripheral blood cytogenetic investigation who had non-consanguineous family history. The results of physical examination revealed a tall stature (height 186 cm) and weight was (52 kg). Hormonal analyses of serum showed increased levels of FSH and LH (26.7 mlU/ml and 16.3 mlU/ml) respectively. The testosterone level was very low as 0.97 ng/ml. Seminal analyses revealed oligozoospermia with sperm concentration 1.3 10^6/ml.

Case-4:

A 30-year old man with infertility referred to us. There was no family history of similar affected members and born to non-consanguineous parents. The physical examination revealed a normal male with height 181 cm and weight 72 kg. Measurement of serum hormone revealed normal values for LH (4.6 mlU/ml) and testosterone (7.6 ng/ml) with elevated levels of FSH (24.7 mlU/ml). Seminal analysis was not available.

Case-5:

A 26-year old man was referred for cytogenetic analysis having history of infertility. The patient born to non-consanguineous parents. The physical examination revealed 176 cm height and 45 kg weight with normal phenotypic features. Blood serum levels of hormones showed increased in FSH and LH (29.3 mlU/ml and 15.3 mlU/ml) respectively. The level of testosterone was decreased as low as 1.03 ng/ml. The seminal analyses showed azoospermic (no spermatozoa).

Case-6:

A 30-year old man with 2 years of infertility married male referred for chromosomal analysis. He was born to non-consanguineous parents. Physical examination revealed normal male with a height of 187 cm and weight was 58 kg. The serum hormone levels showed increased in FSH and LH (21.7 mlU/ml and 16.4 mlU/ml) respectively. The testosterone level was very low (0.96 ng/ml). The seminal analyses showed oligozoospermia with sperm concentration 1.4 X 10^6 ml (8.2 X 10^6 ejaculate).

CYTOGENETIC RESULTS

The chromosomal analysis of GTG banding revealed non-mosaic 47,XYY karyotype (Fig.1) in all six patients. The presence of extra Y chromosome was confirmed in metaphase chromosome and interphase cell by FISH analysis using fluorescence labelled X and Y centeromeric probes (Figs. 2 & 3).

DISCUSSION

The 47,XYY chromosome variation is the most common sex chromosome anomaly after Klinfelter syndrome occurring in 1 in 1000 live male births[1]. It is interesting to note here that quite a few number of man with 47,XYY karyotype are

fertile in spite of their sex chromosome abnormalities. Few studies have pointed out that the extra Y chromosome is lost before meiosis.[3,6]

The diagnosis of 47,XYY syndrome often occurs later in life due to the lack of phenotypical characteristics compared to men with 46,XY. In the present study all six cases had increased FSH and LH levels. In contrast, the testosterone level was low in all six cases. Abnormal levels of hormone may be associated with infertility in males. Few studies have shown the correlation between FSH, LH and testosterone with infertility in man.[3]

The other important point hypothesised was that human subfertility may have a familial component. In the present study, it appears that reason may have other than genetic basis since all six cases come from families with non-consanguineous marriages. Therefore, 47,XYY is not inherited but usually occurs as a random error in chromosome separation during the formation of sperm cells with an extra copy of Y chromosome. It is also important to note that persistence of extra Y chromosome during meiosis can result in spermatogenesis impairment.[7]

CONCLUSION

It is essential to conclude that no systematic studies have been published showing that XYY syndrome is associated with increased frequency of infertility. On the contrary, few case reports of abnormalities of fertility have been published in males with XYY syndrome[8]. Therefore, six cases of abnormal karyotype (47,XYY) in infertile men in our report justifies the use of karyotyping to evaluate males with reproductive abnormalities especially in the case of those with non-consanguineous marriages in the Indian population.

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Conflict Of Interest: No conflict of interest

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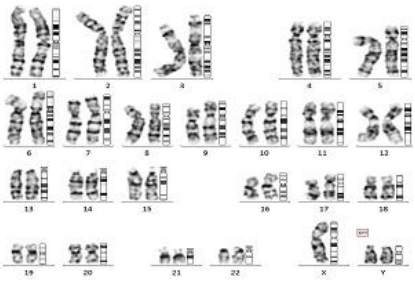

Figure: 1 G-banded karyotype of male (case-1) with 47,XYY syndrome

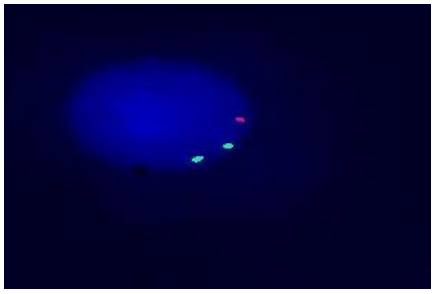

Figure 3: Interphase FISH showing two green signals and one red signals confirms karyotype 47,XYY

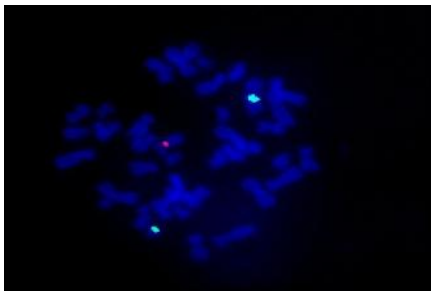

Figure 2: Metaphase FISH showing two green signals of the centromere of Y chromosome and one red signal of X-chromosome confirms karyotype 47,XYY

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