SRY- negative 46, XX male with complete virilization and infertility: A case report

Le male 46XX SRY- négative avec virilisation complète et infertilité: A propos d'un cas

Sonia Jellad[1], Mohamed Basly[2], Fethi Bougrine[3], Mounir Chibani[1], Rhadhouane Rachdi[2]

[1]*-Unit of Reproductive Biology/ Department of sterility exploration and PMA, Military Hospital Tunis / Faculté de médecine de Tunis*

[2]*-Department of obstetrics and Gynecology, Military hospital Tunis / Faculté de médecine de TUNIS*

[3]*- Laboratory of Pathological anatomy and cytology, Military hospital Tunis / Faculté de médecine de Tunis*

The 46 xx male syndrome(De la Chapelle syndrome or 46xx testicular disorder of sex development) is a rare cause of male infertility and a rare form of sex reversal with complex mechanisms leading to a large clinical features ranging from ambiguous genitalia to normal male phenotype combined with azoospermia. The Y chromosome, in particular, the sex- determining region Y gene (SRY), plays a major role in encoding a testis determining factor (TDF) [1]. The SRY gene is located near the pseudoautosomal boundary of the Y chromosome and it has many predicted properties of the TDF [1]. In addition, the gonad development is a result of the presence or absence of SRY. The sex differenciation is determined by the hormonal products produced by the gonads. Testosterone is required for Wolffian duct development while AMH (anti-Mullerian hormone) produced by sertoli cells, inhibits the development of Mullerian ducts promoting their regression. However, in some xx male individuals, the presence of Y chromosome material including SRY leads to testis determination and the development of a male phenotype. The majority of these individuals carry the SRY gene as a result of an illegitimate x/y chromosomal interchange during paternal meiosis [2]. Whereas, in xx males without SRY, testis development suggests the existence of other autosomal or x-linked sex determining genes that are associated with sexual development in humans [2, 3]. In fact, an autosomal recessive gene, termed « Z » has been identified and this gene's product inhibits SRY that normally is a repressor of the male pathway and x -linked locus dosage-sensitive sex reversal, which is a repressor of the male pathway [3, 4].

In this work, we will report a case of a man with a normal male phenotype who was presented for exploration of infertility and was found to be 46 xx male without SRY gene in the X chromosome.

Case Report

A 34 year old man was referred to our institution with a history of 2 years of infertility probably related to male factor. He is 168cm tall and he weights 70kg. The physical examination revealed that there were no dysmorphisms present except for a bilateral gynaecomastia. Facial, body, axillary, and pubic hair were of normal density and distribution. Also this examination revealed a normal penis size that was recorded to 9.8 cm on full erection and the external urethral meats was in the normal position. Both testes were palpable in the scrotum and appeared normal. Rectal examination revealed a normal sized prostate gland. Semen analysis showed azoospermia. Serum luteinizing hormone (LH) and follicle stimulating hormone (FSH) were estimated at 6.7 and 15.3mU/ml (normal range: 1.5-9.3 mU/ml and 1.4-18 mU/ml, respectively). The serum prolactin concentration was normal 5.3 ng/ml (normal range: 2 to 15 ng/ml) but the serum testosterone level was slightly lower the limit of normal range: 1.98ng/ml (normal range: 2.4 to10ng/ml). The testicular biopsy revealed germinal cell aplasia, fewer leydig cells without sertoli cells anomalies. At this stage the patient was diagnosed as non-obstructive azoospermia. The karyotype analysis of the patient showed 46, xx chromosome complement without evidence of mosaicism in peripheral blood cells. The polymerase chain reaction analysis and fluorescence in situ hybridization were performed in lynphocyte culture and also confirm the absence of Y chromosome sequences including any detectable SRY gene.

Conclusion

Throughout this report, we tried to highlight the important value of karyotyping all males with azoospermia or with severe oligozoospermia since the phenotypic sex does not always correlate with the genotypic one. Furthermore, chromosomal analysis can detect several anomalies including the number or the structure of sexual chromosomes and can also reveal discrepancies between phenotype and genotype.

References

1. Angelo V, Veronica B, Erika R, Paolo S. A 46, Xx Sry- Negative Man With Complete Virilization And Infertility As The Main Anomaly. Fertil Steril 2005; 83:216-219.
2. Abusheika N, Lass A, Brinsden P. Xx Males Without Sry Gene And With Infertility. Hum Reprod 2001; 16(4):717-718.
3. Temel Sg, Gulten T, Yakut T, Et Al. Extended Pedigree With Multiple Cases Of Xx Sex Reversal In The Absence Of Sry And Of A Mutation At The Sox9 Locus. Sex Dev 2007 ; 1 :24-34.
4. Ji Won Kim; Chong Won Bak, Mi Uk Chin, Dong Hyun Cha, Tae Ki Yoon, Sung Han Shim. Sry- Negative 46, Xx Infertile Male With Leydig Cell Hyperplasia: Clinical, Cytogenetic, And Molecular Analysis And Review Of The Literature. Fertil Steril 2010; 94(Suppl):753e.