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SEX REVERSAL SYNDROME: A CASE SERIES

Anatomy

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ABSTRACT

Background : Sex Reversal Syndrome (SRS) is a form of gender dysplasia that is characterized by an inconsistency between chromosomal and gonadal sexuality. The clinical types include 46,XY female SRS and 46,XX male SRS. A 46,XX male SRS is a rare clinical condition with a reported incidence of 1 in 20000 new-born males worldwide, but there is no exact data in our country.It most commonly occurs due to the translocation of the Y chromosome including the SRY gene on the X chromosome. Sexdetermining region Y (SRY) is the major factor for gonadal differentiation. Usually, genitalia development is normal and masculine features are obvious in SRY+ patients except cryptorchidism, small testis and hypospadias.. Clinical phenotypes are somehow similar to Klinefelter's syndrome. However, they are differentiated by their short stature, unlike those with Klinefelter's syndrome who are usually tall and pseudo-eunuchoid. Hypergonadotropic hypogonadism, azoospermia on semen analysis, 46,XX karyotyping and genetic analysis for the presence of the SRY gene help diagnose these patients. Fluorescence in-situ hybridization (FISH) and PCR can be used to identify the SRY gene. **Case series:** Here we report a case series of 8 patients with sex reversal syndrome. Most of them were referred with history of primary amenorrhea, for which the karyotyping was done. All these patients were phenotypically female and they genetically had 46,XY chromosome. Only one patient had phenotypically male features who genetically had 46,XX chromosome. **Conclusion:** Male sex reversal syndrome is a rare genetic cause of male factor infertility with a discrepancy between genotypic and phenotypic sex. Every physician either uro/andrologist or endocrinologist dealing with such cases should be oriented with clinical management and prognosis.

KEYWORDS

Sex reversal, Case series, Hypogonadism.

INTRODUCTION

Sex Reversal Syndrome (SRS) is a form of gender dysplasia that is characterized by an inconsistency between chromosomal and gonadal sexuality. The clinical types include 46,XY female SRS and 46,XX male SRS.[1] A 46,XX male SRS is a rare clinical condition with a reported incidence of 1 in 20000 new-born males worldwide, but there is no exact data in our country.[2] It most commonly occurs due to the translocation of the Y chromosome including the SRY gene on the X chromosome. Sexdetermining region Y (SRY) is the major factor for gonadal differentiation. [3] So, the amount of SRY gene present on the X chromosome and the degree of X chromosome activation determines the genital phenotypic variability. In SRYnegative patients, some other genes in the downstream pathway of testicular differentiation like SOX9, SOX3 and RSPO1 are responsible for gonadal differentiation.[2]

Usually, genitalia development is normal and masculine features are obvious in SRY+ patients except cryptorchidism, small testis and hypospadias.[4] Though testis morphology is normal in infancy, there is gradual hyalinization with azoospermia and reduced testosterone secretion leading to hypergonadotropic hypogonadism and infertility in adulthood.[5] Clinical phenotypes are somehow similar to Klinefelter's syndrome. However, they are differentiated by their short stature, unlike those with Klinefelter's syndrome who are usually tall and pseudo-eunuchoid.[6] Hypergonadotropic hypogonadism, azoospermia on semen analysis, 46,XX karyotyping and genetic analysis for the presence of the SRY gene help diagnose these patients. Fluorescence in-situ hybridization (FISH) and PCR can be used to identify the SRY gene.

Case series:

Here we report a case series of 8 patients with sex reversal syndrome. Most of them were referred with history of primary amenorrhea, for which the karyotyping was done, which revealed sex reversal syndrome. All these patients were phenotypically female and they genetically had **46, XY** chromosome. Only one patient had phenotypically male features who genetically had **46, XX** chromosome.

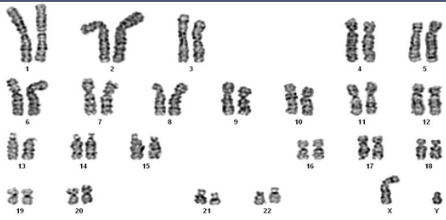

Fig no 1: Karyotyping of a female with XY chromosome with primary amenorrhea

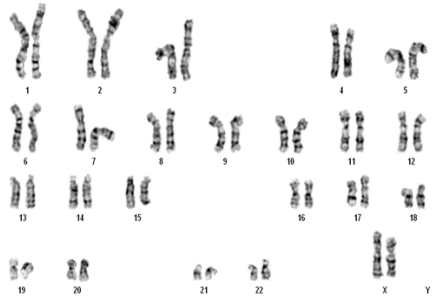

Fig no 2: Karyotyping of a male with XX chromosome

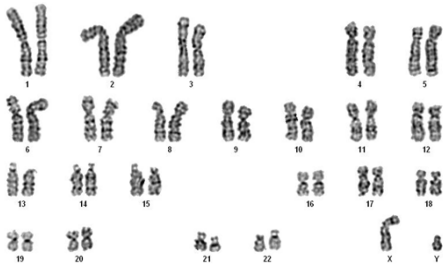

Fig no 3: Karyotyping of a female with XY chromosome with primary amenorrhea

DISCUSSION

The sex reversal syndrome (XX male) probably represents a variant of Klinefelter's syndrome, in which the patients are phenotypically and psychosexually normal males with small testes and a small-to-normal-sized penis. Affected patients are shorter in height than average. One-third of adults have gynecomastia. All are infertile; hypospadias occurs in 10% and cryptorchidism in 15%. The XX male patients are clinically indistinguishable from those with Klinefelter's syndrome.

Mohamed Ahmed Abd El Salam et al reported a case of male sex reversal syndrome (46, XX) with negative SRY gene. Genetic testing showed abnormal karyotyping (46, XX) in all examined cells, besides that FISH analysis for the SRY gene was found to be negative.[7]

Kishore Kumar Shil [8] et al reported a case of an SRY-positive 46,XX Indian male who presented with small testis and phallus, poor beard and mustache development and gynecomastia at the age of 24 years. He had 46,XX karyotype and Quantitative Fluorescence-PCR (QF-PCR) identified the SRY gene on the X chromosome. XUE DU et al [9] reported a 17-year-old girl with no menarche and continuous height growth. Peripheral blood chromosome analysis showed the 46,XY karyotype The patient was diagnosed with 46,XY female SRS, simple gonadal dysgenesis and unclear bilateral gonadal mass. Pasquini Neto R et al [10] reported a nine-year-old female patient was diagnosed with 46,XY DSD, and simple gonadal dysgenesis. The patient and her mother underwent counseling after diagnosis.

CONCLUSION:

Male sex reversal syndrome is a rare genetic cause of male factor infertility with a discrepancy between genotypic and phenotypic sex. Every physician either uro/andrologist or endocrinologist dealing with such cases should be oriented with clinical management and prognosis.

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