46XX Male with ambiguous genitalia - A case report

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Abstract

46 XX male is a very rare disorder of sexual differentiation presenting as an undervirilized male or with normal looking external genitalia and the absence of Y chromosome.This infant was diagnosed to be a 46XXmale based on clinical finding of microphallus, penoscrotal hypospadias, bifid scrotum, bilateral palpable gonads and karyotyping showing 46XX chromosomes.

Keywords: 46XX male, ambiguous genitalia, karyotype.

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Introduction

46 XX males as a clinical entity was first described by De La Chapelle [1] and is also known as De La Chapelle syndrome. It is a rare disorder of sexual differentiation wherein the testes and male genitalia develop in the absence of Y chromosome and possibly without the SRY gene. The incidence is around 1 in 20,000 to 1 in 25,000. This disorder has to be differentiated from true hermaphrodites as both these condition can have palpable gonads and possibly a XX peripheral karyotype. We describe here an infant who was born with a micro phallus, penoscrotal hypospadias and bilateral palpable gonads with a karyotype showing XX chromosomes.

Case Report

A 4 month old infant was brought with ambiguous genitalia as evidenced by microphallus, penoscrotal hypospadias, bifid scrotum and bilateral palpable gonads (Figure 1) for evaluation. He was born to non consanguineous parents by spontaneous vaginal delivery as a preterm infant at 34weeks of gestation with a birth weight of 1.35 kg, head circumference of 30 cms. The infant`s electrolytes during neonatal period were normal and was thriving well with appropriate weight gain and normal developmental milestones. Ultrasonogram revealed bilateral testes within the scrotal sac measuring 0.93×0.65 cm on the right and 1.02×0.55 cm on the left side.

There were patent processus vaginalis communicating freely within the peritoneal cavity without any other evidence of mullerian structures or ovaries. Hormonal proffile revealed a FSH level of 0.1 mIU/ ml (normal range 0.0-2.8 mIU/ml), LH level of 0.3 mIU/ml (normal range 0.0-1.6 mIU/ml), testosterone level of 58.8 ng/dl (normal range 10-20 ng/dl) and estradiol level of 82.9 pg/ml (normal <25 pg/ml). Karyotype revealed 46 XX genotype (Figure 2). There was no history of maternal intake of androgens and no other cause of virilization could be elicited from the history as well as physical examination on the mother.

Fig. 1: Showing microphallus, bifid scrotum with testes

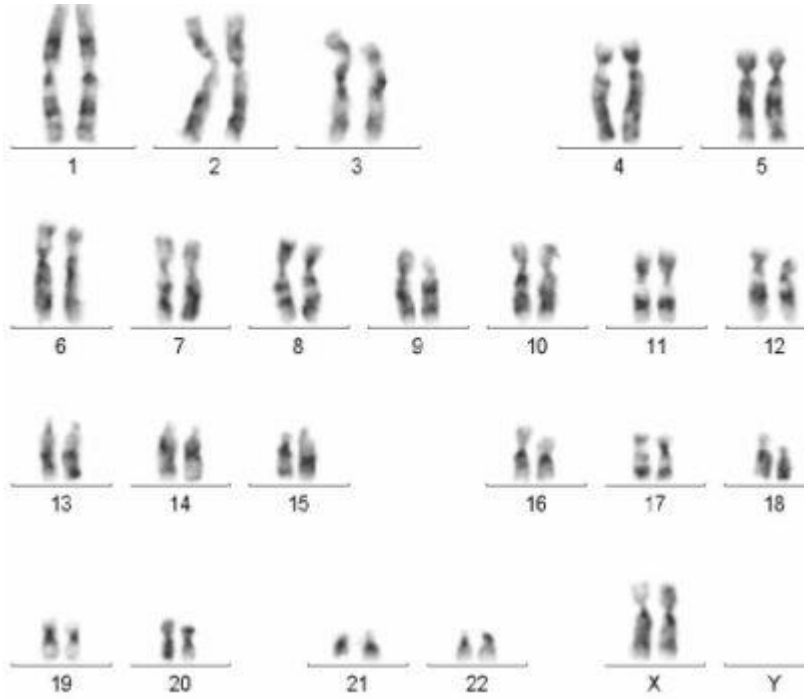

Fig. 2: Karyotype showing 46XX

Discussion

Males with 46 XX genotype have been described in literature as early as 1958 by Milner [2] and later by De La Chapelle. The discovery of SRY gene 3 decades later, further improved the understanding of genetic mechanisms involved in testicular differentiation. However it is still not clear whether other genes are also involved in the expression of male gonads and this problem is particularly highlighted by the finding of adults with male body habitus and male genitalia having 46 XX genotype. Possible explanations include an unequal crossover during meiosis resulting in the SRY GENEtranslocating to the X chromosome or other autosomes as identified by Fluorescent insitu hydridisation (FISH) technique and also referred to as SRY POSITIVE 46 XX males. Others suggest the presence of other autosomal genes like the Wilm`s tumor suppressor gene (WT1) and the SOX-9 that are capable of directing the differentiation of the bipotential gonads into that of males especially in SRY NEGATIVE 46 XX males. Majority of

these individuals have been identified during evaluation for infertility. Some of them present during the neonatal period with ambiguous genitalia and urethral abnormalities needing surgical reconstruction.

Varying degrees of hypospadias, microphallus, bifid scrotum, chordee and inguinal hernia have been described.

TRUE hermaphrodites are those who possess both ovaries and testes or ovotestes. The palpable gonads most of the time are ovotestes. However it could also be an unilateral ovotestis and a left sided ovary and rarely both ovary lying in their normal abdominal location with testes at various levels of descent either at the deep inguinal ring, inguinal canal or scrotum. The karyotype is most often 46 XX in 70% of the cases and in others, 46XY (10%) and 46XX/ 47XXY mosaicism may be seen. Some of these individuals are reared as males until they reach puberty when they start experiencing breast enlargement and even menstruation or cryptomenorrhoea depending upon the degree of development of mullerian structures. Though the ovaries in these individuals seem to be functional with some individuals even ovulating, the testicular tissues are generally atrophic, azoospermic and have the potential of malignant transformation and hence many authors advocate gonadectomy of testicular tissues. In an ovotestis, frozen sample biopsy will delineate testicular and ovarian tissues. The treatment of these individuals is removal of the gonad inconsistent to the sex of rearing along with plastic reconstruction of external genitalia.

In addition to the above mentioned differentials, there are case reports of families having both 46XX males and 46 XX true hermaphrodites in their own offsprings suggesting that both these conditions are caused by differential inactivation of the SRY bearing X chromosome rather than distinct clinical syndromes [3]. And an alternative theory explains the possible presence of cryptic gonadal mosaicism responsible for the variations.

In our case since the gonads were found to be testes both on palpation as well as by sonography and since ovaries and other mullerian structures were not visualized on serial sonography, the possibility of 46 XX male with ambiguous genitalia was thought of. In such individuals the SRY gene is usually absent [4] and hence the incomeplete development of male external genitalia.

References

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