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Pathology

INTERSEX STATE WITH TESTICULAR FEMINIZATION SYNDROME: A CASE REPORT AND REVIEW OF LITERATURE.

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ABSTRACT Intersex state is a state in which intermingling of characters of both sexes present to varying degrees, including physical form, reproductive organs and sexual behavior. Testicular feminization, or the androgen insensitivity syndrome, is a rare disease. Because of various abnormalities of the X chromosome, a male, genetically XY, has some physical characteristics of a woman or a full female phenotype.

KEYWORDS :

Introduction

Intersex state is a state in which intermingling of characters of both sexes present to varying degrees, including physical form, reproductive organs and sexual behavior. It results from some defects in the embryonic development. It can be divided into four groups:

1. Gonadal Agenesis: (Testes or ovaries never developed)
2. Gonadal Dysgenesis: External sexual structures are present but at puberty the testes or ovaries fail to develop.
   a. Klinefelter'sSundrome: in this condition, the anatomical structure is of male but nuclear sexing is of female (XXY). There is delay in onset of puberty, behavioral disorders and mental retardation. Axillary and pubic hairs are absent and hair on chest and chin are reduced. Gynaecomastia, azoospermia, low levels of testosterone, sterility, increased urinary gonadotropins; signs of eunachoidism and increased height are common. Testicular atrophy with hyalinization of seminiferous tubules is seen histologically.HypergonadotropicHypogonadism is seen.
   b. Turner Syndrome: it is the most common sex chromosome abnormality of human females with incidence 1 in 2500 newborn. In this condition, the anatomical structure is of female but nuclear sexing is of male (XO). The ovaries do not contain primordial follicles (Ovarian dysgenesis).
3. True Hermaphroditism: This is very rare condition of bisexuality in which an ovary and a testicle or two ovotestis are present with external genitalia of both sexes.
4. Pseudo Hermaphroditism: in this condition gonadal tissue of only one sex is seen internally but external appearance is ofthe opposite sex.

A. MalePseudo Hermaphroditism / Testicular feminization syndrome: also called as Androgen insensitivity syndrome (AIS) is a rare disorder in individuals with karyotype XYbut sex organs and characteristics deviate to female form because of testicular feminization.It is a X-linked recessive androgen receptor (AR) disorder caused by mutation affecting the androgen receptor gene Xq 11-12 resulting in decreased peripheral responsiveness to circulating androgens.[1]The name testicular feminization syndrome was coined by John McLean Morris of Yale University in 1953. The first description of this syndrome dates back to 1817, as quoted by Morris [2]. It is the third most common cause of primary amenorrhea after gonadal dysgenesis and Müllerian agenesis [3].

It is characterized by Primary amenorrhea, female external genitalia, normal size breasts, scanty or absent axillary and pubic hairs. Testes are in abdomen or inguinal canal. 5-a reductase deficiency occurs.

AIS areclassified as complete, partial, or mild AIS.Complete AIS (CAIS) ischaracterizedbycomplete resistance to the actions of androgens and presented as female appearance and normal breast development, absence of uterus and ovaries, bilateral undescended testis, and elevated testosterone levels. AR signaling is associated with glucose homeostasis and lipidmetabolism.[4,5]

B. Female Pseudo Hermaphroditism: Nuclear sex is XX, but deviation of sex organs and sexual characters towards male are seen, due to adrenal hyperplasia. 21 Hydroxylase deficiency is most common.

We report a case of complete Androgen insensitivity syndrome in a 13 years old girl with primary amenorrhea. From this observation, we present the clinical and pathological aspects of the case.

Case report

We report a case of a 13 year old girl who came to surgery department for right inguinal swelling. Detailed history revealed that patient had primary amenorrhea. Clinical examination revealed a female phenotype: the breasts were normally developed, however, the labia was small, with absent axillary,pubic and groin hair . Sexual hormones in blood were measured: Gonadotropins were found normal (FSH 6.64 mUI/mL, LH 26.65 mUI/mL), so the progesterone (6.89 nmol/L) and estradiol (58 pmol/L), nevertheless the testosterone 2G was high for a woman (58.61 ng/mL). The pelvic MRIrevealed the absence of uterus and ovaries, hypoplastic vagina, and soft tissue lesion at superficial inguinal ring,likely testicular tissue . The inguinal swelling was dissected and removed .Histopathology revealed testicular tissue with atrophic seminiferous tubules containing only Sertoli cells, associated to a Leydig cells hyperplasia. No signs of testicular cancer were identified .

Discussion

Androgen insensitivity syndrome is typically characterized by evidence of feminization (ie, undermasculinization) of the external genitalia at birth, abnormal secondary sexual development in puberty, and infertility.The incidence of androgen insensitivity syndrome is estimated to be 1:20,000-64,000 male births [6].

The present case is a complete androgen insensitivity syndrome because the phenotype is female with genetic male and minimal Wolffian structures. However, the definition of CAIS itself is controversial, with different authors expressing different views. Griffin et al [7] define CAIS as completely female external genitalia, paucity of axillary and pubic hair, and absent Wolffian duct derivatives. Quigley [8] defines CAIS as completely female external genitalia without pubic hair, but states that remnants of Wolffian duct derivatives may be found. The presence of any amount of pubic hair is held as evidence of some degree of androgen responsiveness and thus classified as PAIS [9]. In the classification of Sinnecker et al [10], CAIS is a female phenotype with scant pubic and axillary hair (type a) or a female phenotype with absence of any androgen-dependent structures such as pubic and/or axillary hair (type b). No comment is made on the development of Wolffian duct derivatives.

The diagnosis of AIS in individuals is based on the following clinical findings: undermasculinization of the external genitalia, impaired spermatogenesis with otherwise normal testes, absent or rudimentary Müllerian structures, evidence of normal or increased synthesis of testosterone . In the present case, the diagnosis was established by undermusculinized external genitalia, intraabdominal testis without

any spermatogenesis, raised testosterone levels, and normal gonadotropin levels.

CONCLUSION

AIS is a rare disease.Close collaboration between gynecologist, endocrinologist and psychologist is essential for proper management of complete insensitivity syndrome androgen. Due to the risk of degeneration of the gonad, castration should be performed.

It is extremely distressing to the individual and to the family. It is associated with numerous psychosexual issues. So, systematic disclosure of the diagnosis should be done in an empathic environment, with both professional and family support .

Microphotographs

Figure 1-Section from the inguinal swelling showing histological features of testis i.e. seminiferous tubules and leydig cells(H&E,x100)

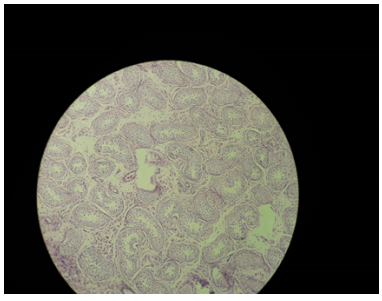
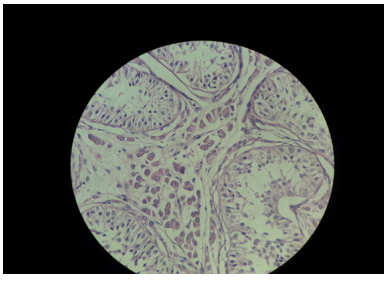


Figure 2:-Section shows seminiferous tubules containing only Sertoli cells along with Leydig cells hyperplasia. (H&E, X400)



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