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Case Report

Complete androgenin sensitivity syndrome presenting with primary amenorrhoea and inguinal mass: a case report

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ABSTRACT

Androgen insensitivity syndrome (AIS), also known as testicular feminization, an X-linked recessive disorder comprises a wide range of phenotypes that are caused by various types of mutations in the androgen receptor gene. AIs can be classified as complete, partial, or mild based on the phenotypic presentation. The clinical findings include a female type of external genitalia, 46-XY karyotype, absence of Mullerian structures, presence of Wolffian structures to various degree, and normal to high testosterone and gonadotropin levels. We report this case as an interesting and rare syndrome. The patient is a 15-year-old phenotypic female who presented with primary amenorrhea and normal-appearing external genitalia. Orchidectomy was done after proper counselling and proper psychological support was given to her.

Keywords: Androgen insensitivity syndrome, Androgen receptor gene, Testicular feminization

INTRODUCTION

Testicular Feminization, or the Androgen Insensitivity Syndrome, is a rare disease where a male, genetically XY, because of various abnormalities X chromosome, becomes resistant to the actions of the androgen hormones, which in turn stops the formation of the male genitalia and gives a female phenotype. The androgen insensitivity syndrome occurs in one out of 20,000 births and can be some physical characteristics of a woman, or even a full female phenotype.[1]

CASE REPORT

A 15 year old female patient of low economic status came to Gynecology department for primary amenorrhea, pain in the abdomen since 3 months and bilateral swelling of abdomen since 2 months with motion sickness. She had underwent a surgery at the age of 6 years on her right Inguinal region for mass removal. Her bowel and bladder habits were found to be normal but appetite was reduced since 10 days. On examination her vital signs were normal, height 151 cm, weight 45kg, Secondary sexual characters: breasts well developed, auxiliary and pubic hairs were absent.

On abdominal examination: There was swelling in the LEFT inguinal regions. Previous surgical scar+ on right inguinal region. Palpable swelling of 2x3cms size felt on left inguinal region. Vagina was present about 5 cm but ended blindly. Routine blood investigations were normal. USG of the abdomen showed absence of uterus and

ovaries, structures of homogenous echogenicity which were slightly hypoechoic in nature. Serum FSH and LH were 10.16 mIU/ ml and 37.46 mIU/ ml respectively. Serum testosterone was 4.71ng/ml. Her karyotyping has shown 46 XY. She was diagnosed as a case of androgen insensitivity syndrome.

As the inguinal swelling was gradually increasing in size, so decision was taken for excision. The left inguinal mass were excised and sent for histopathology. The examination of Orchidectomy specimen shows normal looking testis of 2.2X1.5 cm in size with thickened capsule and also there are thin cysts of <0.5cm in size in epididymal region.

Histopathological examination showed seminiferous tubules with reduced diameter lined by predominately sertoli cells with a few spermatogonia. The Leydig cells are increased in number. There is no evidence of spermatogenesis. Sections studied from epididymis show epididymal cysts. The patient is on regular follow-up. She has been prescribed with hormonal replacement therapy.

DISCUSSION

In 1953 American gynecologist Morris JM first described Androgen insensitivity syndrome.[2] Androgen Insensitivity Syndrome (AIS) was a condition that can be caused due to resistance to the androgens actions, effecting both the morphogenesis and differentiation of the body organs, and organ systems in which this hormone exerts its role. It depends on an X-linked mutation in the Androgen Receptor (AR) gene that is responsible for expressing a variety of phenotypes ranging from infertility in male to normal female external genitalia.[3]

This Androgen insensitivity syndrome based on the external genitalia at birth, abnormal secondary sexual development in puberty, and infertility in individuals with a 46, XY karyotype can be divided into 3 phenotypes: (1) complete androgen insensitivity syndrome (CAIS) with typical female genitalia; (2) partial androgen insensitivity syndrome (PAIS) with predominantly female, predominantly male, or ambiguous genitalia; and (3) mild androgen insensitivity syndrome (MAIS) with typical male genitalia .The incidence of AIS can be estimated to be 1:20,000-64,000 male births3.The risk of malignancy in AIS is considerably lower and occurs at a later age than with other intersex disorders. Typically, patients older than 30 year are at greatest risk.[4]

This is a complete androgen insensitivity syndrome because the phenotype is female in genetic male (46 XY). In neonates with complete androgen insensitivity syndrome (CAIS), the initial finding was unilateral or bilateral inguinal masses that are found to be testes during surgery. Associated hernias may or may not be present.[5] In adults, significant findings include amenorrhoea along with inguinal masses. Our patient also presented with this complaints but she had bilateral inguinal masses. In case of new born these masses may or may not be associated with hernias where as in adolescent patients no pubic and auxiliary hair, with scanty body hair, no acne were observed although breasts are normal due to peripheral conversion of testosterone to estradiol.[6] Our patient had all these features. Moreover, in patients with AIS, Anti-Mullerian Hormone (AMH) concentration is normal as the secretion and function of sertoli cell is not impaired.[7] So, they do not possess fallopian tubes, uterus or a proximal vagina.

The loss-of-functional mutation in the AR gene is considered as a primary etiology of androgen insensitivity syndrome that can cause a variety of functional defects, varying from a complete loss of cell surface receptors to changes in substrate binding affinity. So, in spite of normal level of androgen in the body, the typical post receptor events that mediate the effects of hormones on tissues do not occur. This results in the virilization of external genitalia, absence of pubic and auxiliary hair, lack of acne, and absence of voice changes at puberty.[8]

Endocrine features of CAIS are same as PAIS where we could observe normal or over production of serum luteinizing hormone (LH) and Testosterone during the first three months of new born. After this, LH and testosterone levels are in the normal range until puberty.[9] Later at puberty, serum levels of testosterone and of LH may be elevated, due to the androgen insensitivity and due to the lack of negative feedback by sex hormone on hypothalamus and hypophyxis. Then Testosterone itself is converted to estrogens.

Hence patients with CAIS are presented with higher levels of estrogens than normal with good development of breast. Patient had also elevated level of FSH, LH and testosterone. A pelvic ultrasound examination is frequently useful.[10] Identifying of any müllerian structures, such like uterus/fallopian tubes, is uncertain with a diagnosis of complete androgen insensitivity syndrome or partial androgen insensitivity syndrome. Final confirmation of disease in a suspected phenotypic female is by karyotyping. Androgen insensitivity syndrome, either complete or partial, has less risk of morbidity or mortality.[11]

However there is a theoretical risk of malignant transformation of testes (gonadoblastoma) and the risk estimate range from 0-22% in adults with complete androgen insensitivity syndrome.[12] Surgery was done in our case and the right lower abdominal mass was removed. For this reason the standard of care is an orchidectomy to prevent possible malignant changes of the testes.[4] The treatment for a patient with androgen insensitivity syndrome (AIS) includes hormone replacement therapy (HRT) and psychological support. Adult patients with androgen insensitivity syndrome require hormone replacement for prevention of

osteoporosis. She was prescribed with T. Lynoral 0.05mg OD. When the phenotypic females discover themselves to be genetic males they have psychosocial problems which range from identity issues to problems dealing with the gender perceptions of the outside world. Psychological support will probably the most important aspect as they become depressed and isolated.

CONCLUSION

Testicular feminization is a rare disease orchiectomy is to be done for the removal of Intra-abdominal testes, in order to avoid their malignant transformation. The medical management and psychological support for a woman with androgen insensitivity syndrome will be beneficial.

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