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XY FEMALE WITH PARTIAL ANDROGEN INSENSITIVITY SYNDROME

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Abstract : Androgen Insensitivity Syndrome, previously called as Testicular feminisation syndrome, is an X-linked recessive rare disorder. It was initially described by Morris in 1953. It can be either complete (CAIS), mild (MAIS) or partial androgen insensitivity (PAIS) depending on the receptors response to testosterone. Partial androgen insensitivity syndrome describes a variety of disorders that result in androgen action less severe than those associated with complete androgen sensitivity. The individual is phenotypically female and genotypically male (XY) a male pseudohermaphrodite. The condition is suspected when the individual is evaluated for primary amenorrhoea, infertility, or when unilateral or bilateral inguinal hernia is diagnosed in females or lack of virilisation in males at puberty. Treatment is directed towards gender assignment, psychological support, gonadectomy, vaginoplasty and hormonal therapy. Here we present a case of a 25year old female with partial androgen sensitivity syndrome with primary amenorrhoea with normal secondary sexual characters with clitoromegaly and testis in labia majora. She was managed surgically by Reduction clitoroplasty with bilateral gonadectomy. Post operatively patient was started on estrogen replacement therapy with Tab.Premarin 0.625mg daily.

Keyword : Androgen Insensitivity Syndrome, pseudohermaphrodite, primary amenorrhoea, gonadectomy

INTRODUCTION:

Androgen receptor (AR) gene is located in X chromosome (Xq12). Mutation in genes that encodes androgen receptor can produce variety of phenotypes in males having normal testis and testosterone production. Till date, more than 400 different AR mutations have been identified. Collectively, these 46 XY disorders of sexual development are known as Androgen insensitivity syndrome. The genetics, pathophysiology, endocrinology of AR disorders are quite similar. The phenotype depends on whether AR are absent entirely, present but are functionally abnormal or normal but decreased in quantity. Patient with complete androgen sensitivity syndrome presents with primary amenorrhoea, normal breasts development, absent or scanty axillary and pubic hair, short vagina with absent cervix and uterus, serum testosterone in male range, with 46,XY karyotype, whereas patients with partial androgen insensitivity syndrome presents as phenotypic female with mild virilisation of external genitalia, well developed breasts with normal axillary and pubic hair, otherwise same as complete androgen insensitivity syndrome. Patients with mild androgen insensitivity syndrome (10%) present as under-virilised male with azoozpermia or with severe oligozoospermia, with normal internal and external genitalia with normally descended testis but exhibits spermatogenic arrest. Serum testosterone may be normal or elevated. Our patient present to us with hoarseness of voice, primary amenorrhoea with clitoromegaly with normally developed breasts, normal distribution of axillary and pubic hair and short vagina. USG revealed the absence of uterus and ovaries and presence of testis in labia majora. The karyotyping is 46, XY and the HPE of gonad is testicular tissue. Hence this patient is classified under Partial androgen insensitivity syndrome.

CASE REPORT:

A 25 year unmarried female, presented to the gynaecological OPD with history of not attained menarche. History revealed the development of secondary sexual characters and hoarseness of voice by 16 years of age. No history of any familial occurrence or exposure to any drugs in utero or operations on childhood. On examination, she was tall, well built and nourished with stable vitals. The figure is rather masculine with hirsuitism with enlarged breasts but the outlook and interests were feminine. Her details are as follows:

Height – 167 cms, Weight – 64kgs, BMI = 25, Arm span = 165cm Thyroid – clinically normal, Waist circumference =82cm, Waist / Hip ratio = 82/90 = 0.91. Secondary sexual characters: Axillary and Pubic hair – present, Breast – Tanner stage II Abdomen – soft External genitalia – Clitoromegaly with phallus present Both hernial orifices and renal angles free On per speculum examination – A 3cm long blind vaginal pouch was seen. A non-tender swelling on both sides of labia majora was felt on palpation. Sonography revealed absent uterus and ovaries, an oval hypoechoic structures on both sides of labia majora, all other abdominal organs were normal Diagnostic laparoscopy confirmed the absence of uterus and ovaries Chromosomal analysis showed XY pattern

Blood investigations:
Serum testosterone – 3.04ng/ml (male – 1.8 - 9.0ng/ml, female – 0.2 -1.2ng/ml) LH – 21.04mIU/ml (male – 1.5 – 9.3 mIU/ml) FSH – 2.53mIU/ml (male – 1.4 – 18.1mIU/ml) Serum estradiol – 55.17pg/ml (male – 11.6 – 42pg/ml)
All blood tests were in male range and in accordance with androgen insensitivity syndrome. After counselling, patient was posted for surgery. Reduction clitoroplasty with bilateral gonadectomy done. Intra operatively both gonads were present in labia majora. The histopathology report confirmed the testicular tissue. Post operative period was uneventful. Patient was discharged on 10th post operative day. Estrogen replacement therapy was given with Tab.Premarin 0.625 mg daily.

DISCUSSION:
Partial androgen sensitivity syndrome is only a tenth common as complete androgen sensitivity syndrome. These individuals may present at birth with ambiguous genitalia, or at puberty with lack of virilisation in a boy or signs of virilisation in a girl with primary amenorrhoea. They resemble women with complete androgen insensitivity, but have normal body hair, external genitalia exhibiting partial fusion of labioscrotal folds, with or without clitoromegaly. They have no mullerian structures (due to action of anti mullerian hormone), underdeveloped male internal genital organs and testis. Axillary and pubic hair are normal. Breast development, overall body habitus and gender identity are distinctly female. Clinical management of partial androgen insensitivity is directed towards appropriate gender assignment, psychological support, gonadectomy to prevent tumourigenesis (1-2%) in cryptorchid testis, reconstructive surgery and hormonal therapy. Whereas gonadectomy can be postponed until puberty in complete androgen insensitivity syndrome, earlier surgery is indicated to prevent further virilisation in patient with partial androgen insensitivity syndrome. This patient is reared as female and her psychological interests and outlook are feminine, we planned to proceed her with reduction clitoroplasty with bilateral gonadectomy and with estrogen replacement therapy. Patient surgical outcome was very good except for the voice change after 6 months. Vaginal dilators are adviced for stretching the length of vagina if she plans for marriage.

CONCLUSION:
Thorough history and examination, with high index of suspicion, will help us diagnose rare disease like Partial androgen sensitivity syndrome. The patient and the family members may not be able to understand this condition unless help is sought and provided well. Timely and appropriate intervention helped to provide a better life style for this patient.

Figure.1. External appearance of the patient

Figure.2.External genitalia Figure.3.Testis in labia majora

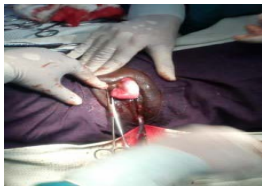

Figure.4. After surgery Figure.5.HPE of Gonad - Testis

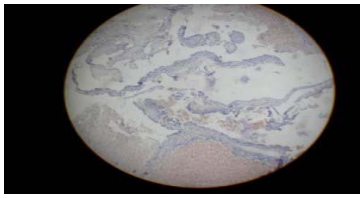

Figure.6. Follow up after 6 months

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