Androgen Insensitivity Syndrome – A Case Report

Bangal V.B.*, Gavhane S.P **, Gupta K *, Gangapurwala S ****

* Professor, ** Assi.Prof ***Postgraduate student ****Postgraduate student Department of Obstetrics and Gynaecology of Rural Medical College, Loni,Maharashtra.413736

Abstracts: Androgen insensitivity syndrome (AIS), formerly known as testicular feminization, is an X-linked recessive condition resulting in a failure of normal masculinisation of the external genitalia in chromosomally male individuals. It affects 2 to 5 per 100,000 people who are genetically male. A case of Androgen insensitivity syndrome is reported in a 20 year-old married woman, who presented with a history of primary amenorrhea. Her karyotype report revealed a male karyotype (46XY). Transvaginal sonography revealed absence of cervix, uterus and ovaries. Ultrasound of abdomen pelvis reported – bilateral inguinal testes. Bilateral inguinal gonadectomy was done. Histopathology of the gonads revealed seminiferous tubules lined by germ cells exhibiting various stages of normal spermatogenesis. She was treated with hormonal replacement therapy.

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Key Words: Androgen insensitivity syndrome, Testicular feminization syndrome, Primary amenorrhoea

Author for correspondence: Dr. Bangal V. B , Department of Obstetrics and Gynaecology, Rural Medical College, Loni – 413736 . E- mail: vbb217@rediffmail.com

Introduction Androgen insensitivity syndrome (AIS), formerly known as testicular feminization, is an X-linked recessive condition resulting in a failure of normal masculinisation of the external genitalia in chromosomally male individuals. Androgen insensitivity syndrome (AIS) is now the accepted terminology for the syndromes resulting from unresponsiveness of the target cell to the action of androgenic hormones.[1].The failure of virilisation is either complete androgen insensitivity syndrome (CAIS) or partial androgen insensitivity syndrome (PAIS), depending on the amount of residual receptor function. It affects 2 to 5 per 100,000 people, who are genetically male.[1] Androgen insensitivity syndrome is the largest single entity that leads to 46,XY under- masculinized genitalia.[2] Individuals with partial androgen insensitivity, unlike those with the complete or mild forms, present at birth with ambiguous genitalia, and the decision to raise the child as male or female is often not obvious.[1,3,4]The main challenge for these individuals is to obtain a gender identity, failure of which can be very psychologically disturbing.

:tropeR esaC A 20 year-old young female came to Gynecology department with a history of primary amenorrhea with a married life of 3 years. She was second of the three girl children in the family. Her both sisters had normal onset of menstrual cycles .She did not have any other significant past medical or surgical history. She belonged to lower socio economic class and was educated till sixth class. She was staying away from husband due to some marital problems. On examination it was found that her height was 175cms. She had androgenic features .Her hands and feet had masculine features. She was brought up as female and had feminine psyche. There was no other evidence of genetic or endocrinal abnormality in general examination .Her vitals were within the normal limit. On local examination: there was sparse axillary and pubic hair. The breasts were under developed (Tanner stage II).[5] **(Fig 1,2).**

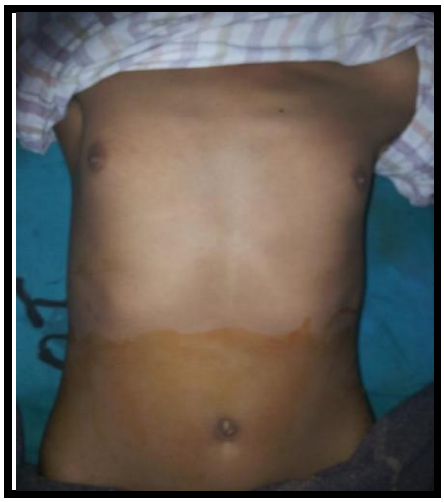


Fig. 1 -Underdeveloped Breast

Per abdominal examination revealed one swelling each, at the level of the external inguinal ring, approximately measuring 3x2x1 cm each .A normal vulva and vaginal introitus was seen. Per Vaginal examination through vagino-scope showed a blind vaginal pouch of 4cms depth .The uterus and cervix were absent. No other palpable pelvic masses felt in bimanual examination.

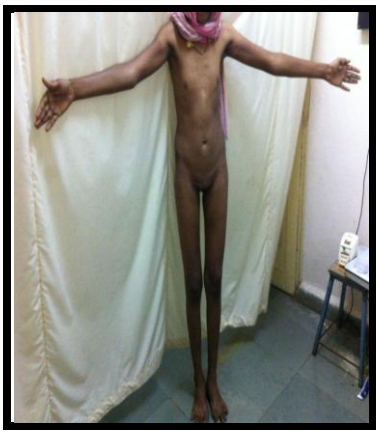


Fig .2 - Tall stature with sparse hair

Per rectal examination confirmed the absence of uterus. Routine blood investigations were normal. Trans-vaginal sonography revealed absence of uterus, cervix, fallopian tubes and ovaries. Ultrasound of inguinal region showed bilateral inguinal gonads(testes) measuring 2.5x 1.7x1.2 (volume approx 2.5–3cm), showing normal vascularity .The karyotyping report revealed a normal male karyotype (46XY). (Fig. 5) Bilateral inguinal gonadectomy was performed under general anaesthesia. (Fig.3,4).

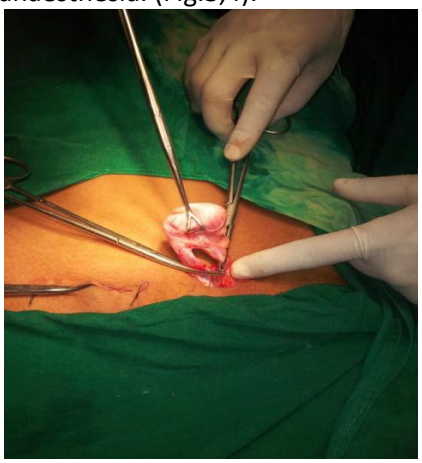


Fig.3 -Removal of inguinal gonads

Gonads were sent for histo-pathological examination.(Fig.6). Histopathology revealed seminiferous tubules lined by germ cells exhibiting various stages of normal spermatogenesis and spermiogenesis. The tubules shows sertoli cells, spermatogonia ,spermatids and sperms. In the interstitial spaces between the tubules, Leydig cells were present in groups. Patient had smooth postoperative period .She was discharged from hospital after 3 days with a advice to come for follow up visit after 8 days. She was counseled about the need for taking long term hormone replacement therapy .She was advised to take 0.625 mg of conjugated equine estrogen per day and to come for regular follow up in the hospital.

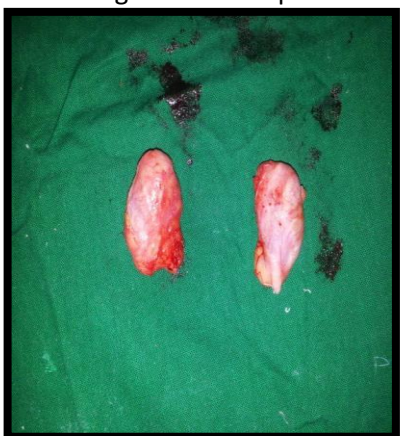
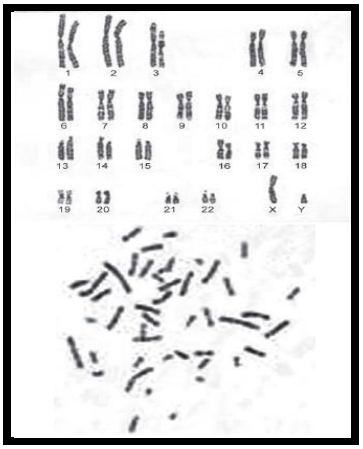


Fig. 4- Bilateral excised inguinal gonads



Fig,5- Karyo-typing -46 XY

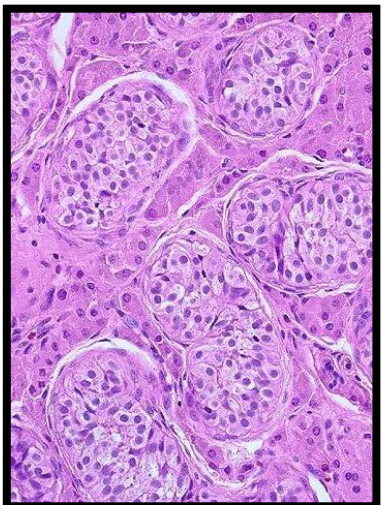


Fig.6- Histopathology –Testicular tissue

Knowing the facts about her gender, she opted to stay alone at her parents place and chose not to get re- married in spite of constant insistence by relatives.

Discussion: Androgen insensitivity syndrome (AIS) is a condition that results in the partial or complete inability of the cell to respond to androgens.[1,6,7] The unresponsiveness of the cell to the presence of androgenic hormones can impair or prevent the masculinization of male genitalia in the developing fetus, as well as the development of male secondary sexual characteristics at puberty, but does not significantly impair female genital or sexual development.[7,8] As such, the insensitivity to androgens is clinically significant only when it occurs in genetic males (i.e. individuals with a Y-chromosome, or more specifically, an SRY gene).[1]
.These cases are rarely diagnosed before puberty. They present with primary amenorrhoea or later on as a case of infertility. They are phenotypically and psychologically female but genetically male.They have enucoidal tendency with presence of long arms big hands and feet. The pubic and axillary hair are absent or sparse .Breast development may be adequate .Nipples are small. External genitalia looks female .Vagina is short and blind .Pelvic ultrasound will show absence of upper vagina ,uterus ,tubes and ovaries .Gonads are testes ,which are either placed in labia or in inguinal canal .The confirmation of the diagnosis is by karyotyping (XY) and gonadal biopsy .Serum LH and Serum LH values may be elevated. Serum testosteron values may be within average for normal males .Usually,this condition is not associated with any other anomaly.[9]
These cases should be reared up as girls .The ectopic gonads ie testes should be removed as there is risk of development of malignancy in the form of gonadoblastoma or dysgerminoma. Vaginoplasty can be done after the age of 18 years, when secondary sex characters are developed and growth is complete. After gonadectomy, these cases should be given long term hormone replacement therapy for prevention of cardiovascular complications and osteoporosis. Hormonal substitution therapy in the form of conjugated equine estrogen in the dose of 0.625 mg/day helps in maintenance of secondary sexual characters.[9]

Conclusion: Androgen insensitivity syndrome is a form of male hermophroditism .It is usually diagnosed after pubertal age. These individuals are infertile and have male gonads. Gonadectomy after development of secondary sex characters and hormone replacement therapy form the main stay of treatment. Proper counseling and emotional support help individual to cope up with this genetic abnormality.

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Patient's written consent - for publication of clinical photographs was obtained by the authors.

References:

1. Hughes IA, Deeb A."Androgen resistance". Best Pract. Res. Clin. Endocrinol. Metab. 2006; 20(4):577–98.
2. Ahmed SF, Cheng A, Hughes IA (April 1999)." Assessment of the gonadotrophin- gonadal axis in androgen insensitivity syndrome". Arch. Dis. Child. 80 (4): 324–9.
3. Köhler B, Lumbroso S, Leger J, Audran F, Grau ES, Kurtz F, Pinto G, Salerno M, Semitcheva T, Czernichow P, Sultan C (January 2005). "Androgen insensitivity syndrome: somatic mosaicism of the androgen receptor in seven families and consequences for sex assignment and genetic counseling". J. Clin. Endocrinol. Metab. 90 (1): 106–11
4. Bouvattier C, Mignot B, Lefèvre H, Morel Y, Bougnères P (September 2006). "Impaired sexual activity in male adults with partial androgen insensitivity". J. Clin. Endocrinol. Metab. 91 (9): 3310–5.
5. Puberty –Normal and Abnormal, In :Dutta DC .Textbbok of Gynaecology .6th ed. New Delhi. Jaypee Brothers. 2013; 49-56
6. Galani A, Kitsiou-Tzeli S, Sofokleous C, Kanavakis E, Kalpini-Mavrou A ."Androgen insensitivity syndrome: clinical features and molecular defects". Hormones (Athens) 2008;7(3):217–29.
7. Quigley CA, De Bellis A, Marschke KB, el-Awady MK, Wilson EM, French FS. "Androgen receptor defects: historical, clinical, and

molecular perspectives" .Endocr. Rev.1995;16 (3):271–321.
8. Giwercman YL, Nordenskjöld A, Ritzén EM, Nilsson KO, Ivarsson SA,Grandell U, Wedell A "An androgen receptor gene mutation (E653K) in a family with congenital adrenal hyperplasia due to steroid 21-hydroxylase deficiency as well as in partial androgen insensitivity". J. Clin Endocrinol. Metab. 2002;87(6):2623–8.
9. Amenorrhoea, In : Dutta DC. Textbbok of Gynaecology .6th ed. New Delhi. Jaypee Brothers. 2013;449-474

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