

Case Report

Androgen Insensitivity Syndrome

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ABSTRACT

Background: Androgen insensitivity syndrome refers to an inability of the body to respond properly to male sex hormones (androgens) produced during pregnancy. This occurs because of a change (mutation) in a gene involved in the production of the protein inside cells that receives the androgen hormone and instructs the cells in how to use it. This is a genetic disorder that makes XY foetuses insensitive (unresponsive) to androgens, they are born looking externally like normal girls and Internally, there is a short blind pouch vagina and no uterus, fallopian tube or ovaries. There are testes in the abdomen or in the inguinal canal. The CAIS is usually detected at puberty when a girl should but does not begin to menstruate. They are at high risk of osteoporosis so should take oestrogen replacement therapy.

Case Report: PAIS results in micropenis with hypospadias and gynaecomastia. We report this rare case of 18yr old female patient with primary amenorrhea. Subsequent investigation including karyotyping revealed that the patient is phenotypically female but genotypically male with testes. Gonadectomy was done with proper counselling and patient was put on hormonal replacement therapy.

KEY WORDS: Androgen insensitivity, Primary amenorrhea, Pseudohermaphroditism.

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INTRODUCTION

Androgen insensitivity syndrome is a disorder where there is resistance to androgen actions influencing both the morphogenesis and differentiation of androgen responsive body structures. Adolescence is a time of enormous physical and psychological change for young women. Major gynaecological pathologies is rare at young age but the menstrual disturbances are common and poses psychological

disturbances. Menstrual cycle involves the co-ordination of hypothalamo-pituitary ovarian axis with influence of physiological and pathological changes occurring during reproductive life span. Embarrassment about discussing menstruation fear of disease, ignorance and fear of rejection after the facts are disclosed are main reasons for nondisclosure during early pubertal period. Psychological

support is very important when the phenotypic females discover themselves to be genetic males. This syndrome was first described by John Morris in 1953. The first description of this syndrome dates back to 1817. It is the 3rd most common cause of primary amenorrhea after gonadal dysgenesis and mullerian agenesis. The etiology of this syndrome is congenital insensitivity to androgens transmitted by means of maternal X linked recessive gene responsible for androgen intracellular receptors. The phenotype is a female despite 46XY karyotyping. Here we report a rare case of complete androgen insensitivity syndrome in 18yrs old female. The syndrome was detected on evaluation of a phenotypic female with primary amenorrhea [1,2,3].

Androgen insensitivity syndrome is an extreme form of male pseudohermaphroditism. In these individuals the genotypic sex is masked by phenotypic appearance which closely resembles the other sex called hermaphrodite. Male pseudo hermaphrodites have testes with a chromosomal complement 4xy but the external genitalia resemble that of female. Phallus remains rudimentary and looks like clitoris, scrotal swellings fail to fuse and gives an appearance of labia majora. The most important cause being the lack of androgens receptors so the androgens produced by foetal testes are ineffective in inducing differentiation of male genitalia. Androgen insensitivity syndrome is the largest single entity that leads to 46xy under masculinized genitalia. Inheritance is typically maternal and follows X linked recessive pattern. Individuals with 46xy karyotype express the mutant gene since they have only one X chromosome where as 46xy carriers are minimally affected. About 30% of the time the AR mutations is a spontaneous result and is not inherited. AR mutation may cause significant variations on the degree of masculinization. Such denovo mutations are the result of a germ cell mutation of germ cell mosaicism in the gonads of one of the parents or a mutation in the fertilized itself [4,5,6].

CASE REPORT

A young female 18yrs with low socioeconomic status visited obstetrics and gynec outpatient department of Rajarajeswari medical college and hospital. Her main complaint was primary

amenorrhoea and delayed development of secondary sexual characters. She was the only child for her parents and had no similar complaints in the family. She did not give history related to medical consultation before. On examination, her vitals were normal, general examination showed her height as 170cm, weight 43kg, arm span 17.9cm, umbilicus to head 56cm and umbilicus to toe 108cm. Breast development with tanner stage 3 with hair distribution minimal in axilla. Sparse pubic hair stage 3 and blind vagina.



Fig. 1: Testicular swellings in the left and right iliac fossa (Androgen Insensitivity Syndrome).

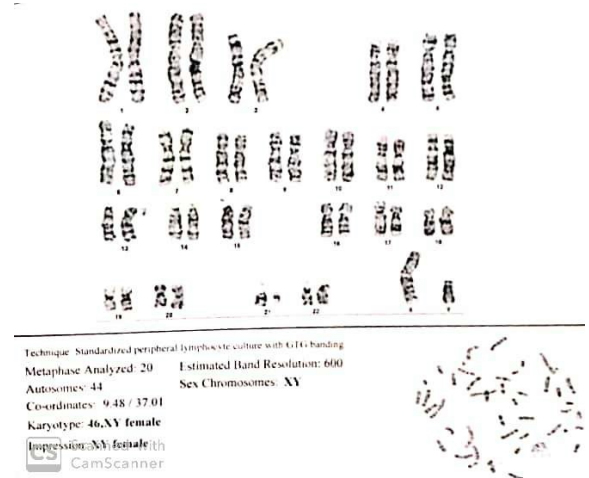


Fig. 2: Karyotype of patient (Androgen Insensitivity Syndrome).

Perabdominal examination showed swellings in the left and right iliac fossa. On local observation and examination we confirmed the swelling as testis. Right swelling measured 4.5x3x1.5cm and the left one measured 6x2.5x2cm. The swellings were hard in consistency but non tender. Per rectal examination revealed no uterus or cervix. Routine blood investigations were normal. Serum LH and FSH were 43.74mIU/ml & 9.59mIU/ml respectively. Prolactin was 8.21ng/ml and testosterone was 42ng/ml. Ultrasound abdomen and pelvis

revealed hypoplastic oval shaped structure in bilateral inguinal canal with echotexture similar to testis with absent uterus and ovaries. In USG uterus was not visualized. MRI abdomen and pelvis was done to diagnose the same. Which suggested a well defined oval shaped lesion in inguinal canal, absent uterus and ovaries with blind ending vagina, seminal vesicles seen bilaterally in rectovaginal pouch. Her karyotyping was done which said 46xy female. She was diagnosed as a case of androgen insensitivity syndrome/testicular feminization syndrome. Inguinal swellings were excised and sent for histopathology. Her postoperative recovery was uneventful. Histopathological examination of the gonad showed cyst on the surface of specimen measuring 1.5x1.0cm at lower pole and cord like structure of 2cm on right testis. Left testis also showed cord like structure of 2cm and its external surface was nodular and a grey brown structure with a lumen of 1.0x0.5cm (Figure 1, 2).

Microscopy of the specimen showed structure of immature testicular tissue with seminiferous tubular arranged in lobules separated by thick and thin fibrovascular septae. Leydig cell hyperplasia was noted at places. The patient was put on oestrogen oral replacement after counselling. In the present case diagnosis of androgen insensitivity syndrome was made undoubtedly by clinical features of delayed development of secondary sexual characters with bilateral testis at inguinal canal raised gonadotropins and normal testosterone. This was supported with USG & MRI findings and histopathology report of excised specimen which said atrophic testis with leydig cell hyperplasia. Atrophic uterus with hydrosalpinx on right side.

DISCUSSION

Androgen insensitivity syndrome is an x linked recessive disorder. The human androgen receptor (AR) is a protein encoded by a gene located on the proximal long arm of the X chromosome (locus Xq11-Xq12). Androgen insensitivity syndrome can be subdivided into 3 phenotypes 1) complete AIS with typical female genitalia 2) Partial AIS with predominantly female, male or ambiguous genitalia 3) mild AIS with typical male genitalia.

Individuals with a 46xy karyotype always express the mutant gene since they have only X chromosome, whereas 46xy carriers are minimally affected. About 30% of the cases, the AR mutation is a spontaneous result and is not inherited. At puberty serum levels of testosterone and LH gets elevated due to the androgen insensitivity and consequent lack of negative feedback by sex hormone on hypothalamus and hypophysis.

Our present case also showed elevated level of FSH, LH and testosterone. The partial or incomplete form of testicular feminization syndrome is associated with wide range of genital abnormalities and typically present at birth with genital ambiguity. AIS has little medical morbidity or mortality. However there is theoretical risk of malignant transformation of testis and risk estimate range from 0.22% in adults with CAIS. AIS prevention includes information about the condition and the woman's risk of having an affected child. Proper counselling regarding status and 50% chance of transmitting the mutated AR gene in carrier female during each pregnancy should be done in an empathetic environment with female and professionals support. Several case studies of fertile 46xy males with AIS have been reported. The present case was managed by Gonadectomy with oestrogen replacement [7,8,9].

CONCLUSION

Androgen insensitivity syndrome is a rare clinical condition in which affected individual is phenotypically female despite the presence of testes and 46xy chromosome complement. It is also called testicular feminization syndrome. It occurs in 1/20000 births due to a defect in androgen receptor mechanism. Androgen insensitivity syndrome is associated with numerous psychosexual issues. Therefore, systematic disclosure of the diagnosis of AIS should be done in an empathetic environment. Best option for management includes gonadectomy with hormonal replacement. Untreated patients have risk of developing seminoma and gonadoblastoma later.

Author Contributions

Shruthi B N: Concept and Design of the Case Report
Viviktha Venkatesh: Literature review

Vishnu Sri Manoj D R: Literature review

Bharathi D: Literature review

Angadi A V: Literature review

Shaik Hussain Saheb: Manuscript writing and Correspondence with Journal.

Conflicts of Interests: None

REFERENCES

- [1]. Tarafdar Runa Lailal, Sheik Salahuddin Ahmed. Androgen Insensitivity Syndrome- A Case Report. American Journal of Clinical and Experimental Medicine. 2015;3(4):133-136.
- [2]. Martha Hickey, Sari Lester. The management of menstrual disorders in early reproductive life. Review The Obstetrician and gynaecologist 2003;5:136-41.
- [3]. Adachi M, Takayang R, Tomura A. Androgen insensitivity syndrome as a possible co-activator disease. N Engl J Med. 2001;344(9):696.
- [4]. Adachi M, Takayanagi R, Tomura A, et al. Androgen- insensitivity syndrome as a possible coactivator disease. N Engl J Med. 2000;343(12):856-862.
- [5]. Gottlieb B, Beitel LK, Trifiro MA. Androgen insensitivity syndrome. In: Pagon RA, Bird TC, Dolan CR, Stephens K, eds, GeneReviews. Seattle, WA: University of Washington, Seattle; 1993-. National Center for Biotechnology Information, US National Library of Medicine Web site.
- [6]. Viner R, Teoh Y, Williams DM, Patterson MN, Hughes IA. Androgen insensitivity syndrome: a survey of diagnostic procedures and management in the UK. Arch Dis Child. 1997;77(4):305-309.
- [7]. Morris JM, Mahesh VB. Further observations on the syndrome, "Testicular feminization syndrome". Am J Obst Gynecol. 1963;15:731-45.
- [8]. Deans R, Creighton Sm, Liao LM, Conway GS. Timing of gonadectomy in adult women with complete androgen insensitivity syndrome(CAIS): patient preferences and clinical evidence. CLIN Endocrinol (oxf) 2012;76960:894-98.
- [9]. Negulici, Christodorescu D, Alexandru S. Psychological aspects of the testicular feminization syndrome. Psychosom Med. 1968;30(1):45-50.

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