Case Report

# Complete Androgen Insensitivity Syndrome: Dilemmas for Further Management after Gonadectomy

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**Abstract**

Complete androgen insensitivity syndrome is a rare condition, wherein a genetic male is phenotypically female and is raised as a female. Treatement requires timely gonadectomy, need for long term hormonal replaceent therapy, psycological and genetic counseling. The type, dose, duration of hrt is not well studied. Reproductive issues also need to be addressed in these young woman. We report here a case of complete androgen insensitivity which posed a quandary for management of long term bone health. Review of literature for management is discussed. These cases are best managed by a multi-disciplenary team comprising of gynecologist, geneticist, endocrinologist and clinical psycologist or psychiatrist.

**Keywords:** *Complete androgen insensitivity syndrome, hormone replacement therapy, partial androgen insensitivity syndrome, testicular feminization syndrome*

## Introduction

Androgen insensitivity syndrome (AIS) is a disorder caused by a mutation of the gene encoding the androgen receptor (AR; Xq11–q12). The prevalence of AIS has been estimated to be one in 20,000–64,000 newborn for the complete AIS, while the prevalence for partial AIS is unknown.[1] The clinical presentation may vary from a complete phenotypically female with testes or completely normal-looking male with impaired spermatogenesis.[1,2,3]

## Case Report

A 28-year-old Indian unmarried educated woman came with primary amenorrhea. Her case records were reviewed, which revealed that she had a inguinal lump at the age of 7 years, her pelvic ultrasonography (USG) did not show any uterus like structure, and the biopsy of the lump tissue revealed testicular tissue, so karyotype was performed, which was XY. Her parents were advised that she should undergo gonadectomy after puberty.

She had a good height of 158 cm, well-developed breast, and absent axillary and pubic hairs. She had a blind vagina with no dimpling at the vaginal end.

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Her hormonal investigations showed follicle-stimulating hormone of 72 IU/ml, testosterone 20.3 (normal male range), and estradiol 170 pmol/l (equivalent to early follicular phase of menstrual cycle). USG pelvis revealed absent uterus and two lesions suggestive of gonads, one at ovarian fossa in pelvis and other at inguinal canal. All management options were discussed with her in details, and she opted for vaginoplasty and gonadectomy. Her postoperative stay was uneventful except for few outbursts of stress. Histopathology report (HPR) of the gonads revealed testicular tissue and no malignancy. She is still under follow-up.

## Discussion

AIS, earlier called as testicular feminization syndrome, is an X-linked recessive disorder leading to failure of a normal masculinization of external genitalia in a XY-karyotype individual. It could be partial or complete, resulting from amount of residual receptor function. Hence, even with normal androgen levels, due to absent/defective receptor function, external genitalia develop as phenotypically female. Normal breast

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development is either due to peripheral conversion of testosterone to estradiol or due to increased secretion from the testicular tissue.[2] These patients require management for sexual identity, as the knowledge of different sex genotype is generally contradictory to their upbringing till now. They require gonadectomy, to prevent development of malignancy. Fertility issues also need to be taken care of in managing these young women as well as there is need for hormones for bone health.

Bone mass progressively increases during childhood, with a rapid gain during puberty in both the sexes, though some gender differences in bone mass may be there. At birth and during prepubertal years, males and females have similar values of total body bone mass and bone mineral density (BMD) at lumbar bones; however, with age and under the effects of hormones, it may not remain so. In patients of AIS, gonadectomy may lead to significant change in BMD, and hence, these patients require hormones for their optimal bone health; however, the hormone type, dose, and duration have not been addressed well.

Orchidectomy in a male may cause alterations in BMD, suggesting the important role of androgens in bone mineralization[3,4] and optimal skeletal development. AIS patient in the presence of testes might achieve optimal bone mass by the end of puberty.[1,3] Contrary to this, it is also said that patients of AIS may develop osteopenia due to defective androgen action or estrogen deficiency or even a combination of both these.[4]

Patients of AIS require hormonal supplements with estrogens after gonadectomy. Generally, pregonadectomy circulating estradiol concentrations are low and postgonadectomy inadequate supplements lead to low estrogens and the adverse consequences on BMD.[1] Hormonal replacement therapy (HRT) in AIS is required for bone health as well as for maintenance of secondary sexual characteristics and preventive aspects of cardiovascular health. Pros and cons associated HRT must be taken into account as suggested by WHI study in US, with some increase risk of breast cancer and coronary artery disease, stroke, thromboembolism, and prevention or improvement in BMD, skin and connective tissue disorders. Nevertheless, HRT is recommended in women of premature menopause up to the age of natural menopause; however, the use of HRT in AIS is not been well studied. It has been proposed that in the absence of or for poorly developed secondary sexual characteristics, estrogen administration should be gradually increased until the desired breast and genital development is reached. The optimal dose of HRT in these women is not known. It is recommended that frequent checks for BMD should be done to offer the best dose with optimal effect. Calcium should be prescribed.

Alternatives to HRT for preventing osteopenia and osteoporosis can be bisphosphonates or selective estrogen receptor modulators (SERMs) after assessing the bone heath, long-term consequences, and the cost of drug; however, these drugs have not been well studied in AIS patients.[5,6] Raloxifene (SERM) may be given and has advantage of reduced breast cancer risk in women with osteoporosis. However, the risk of breast cancer in AIS is unknown.[4] Role of phytoestrogens and bisphosphonates is also not known in AIS.

Women with AIS are sterile. They require adoption or surrogacy with ovum or embryo donation. AIS is an X-linked recessive genetic disease due to mutations in the AR gene (Xq11–q12). Relatives are affected in 50% of cases if mother is a carrier of mutation. As AIS is a genetic condition, women may want preimplantation genetic diagnosis to see if the embryo is healthy.[7]

These patients will also require reinforcement of gender identity, genetic counseling, and psychological counseling for their well-being. Hence, a multidisciplinary management is recommended.

Our patient wanted HRT after some time; in the meantime, she was advised regular exercises, Vitamin D, and calcium.

## Prognosis

The prognosis for this condition is generally good, timely diagnosis, and gonadectomy and HRT usually give satisfactory short- and long-term results. However, it is necessary to follow these patients regularly to avoid long-term consequences of bone demineralization, adverse effects of HRT and for ensuring psychological well-being.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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