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# Case of a teenager patient complaining of amenorrhea found to have complete androgen insensitivity syndrome. A case report

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**Abstract**
Androgen insensitivity syndrome is the most common form of male hermaphroditism. Affected individuals have a male karyotype; however, sexual development is affected because of cellular resistance to androgens. The clinical manifestations of this disease are diverse. This case report discusses the complete type of androgen insensitivity syndrome, formerly known as "testicular feminization syndrome". These individuals have a karyotype of 46 XY. They have female external genitalia, male gonads, no uterus and fallopian tubes, and a short vagina, in this case the patient undergoes gonadectomy.

**Keywords:** Androgen insensitivity syndrome, hermaphroditism, gynecomastia, orchidectomy

## Introduction

Androgen insensitivity syndrome (AIS) is a rare X-linked genetic affecting androgen receptor (AR) [1]. It affects 1:20,000 to 1:64,000 male live births [2]. The presentation of androgen insensitivity syndrome (AIS) varies from a normal female phenotype to a male phenotype with gynecomastia, hypo masculinization and infertility [3]. Mutations in the androgen receptor (AR) gene cause alterations in AR synthesis, resulting in insensitivity of the receptors to circulating androgens [3]. John Morris was the first to describe this condition [4]. Here we present 15-year-old patient with female phenotype diagnosed as complete androgen insensitivity syndrome (CAIS). Who underwent orchidectomy.

## Case report

A 15-year-old female patient, who is medically free, presented to the clinic complaining of ammenohea. The physical examination showed a tall sature patient with inguinal swelling. Also, it showed well-developed external female parts, breast development (tanner 3–4), and scanty pubic and axillary hair. The uterus and both ovaries were absent from the MRI but the lower vagina was visible (Figure 1). Also, there were well defined oval-shaped enhancing masses with restrictive signals in proximal part of each inguinal canal (Figure 2) which is most like represent bilateral undescended testes. Laboratory and hormonal work were ordered, which included karyotyping. The results showed an increase in total testosterone (1275 ng/dl), and the FISH chromosome analysis revealed the presence of XY chromosomes. All the findings are consistent withcomplete androgen insensitivity syndrome. The patient underwent bilateral gonadectomy and continued to live as a female.

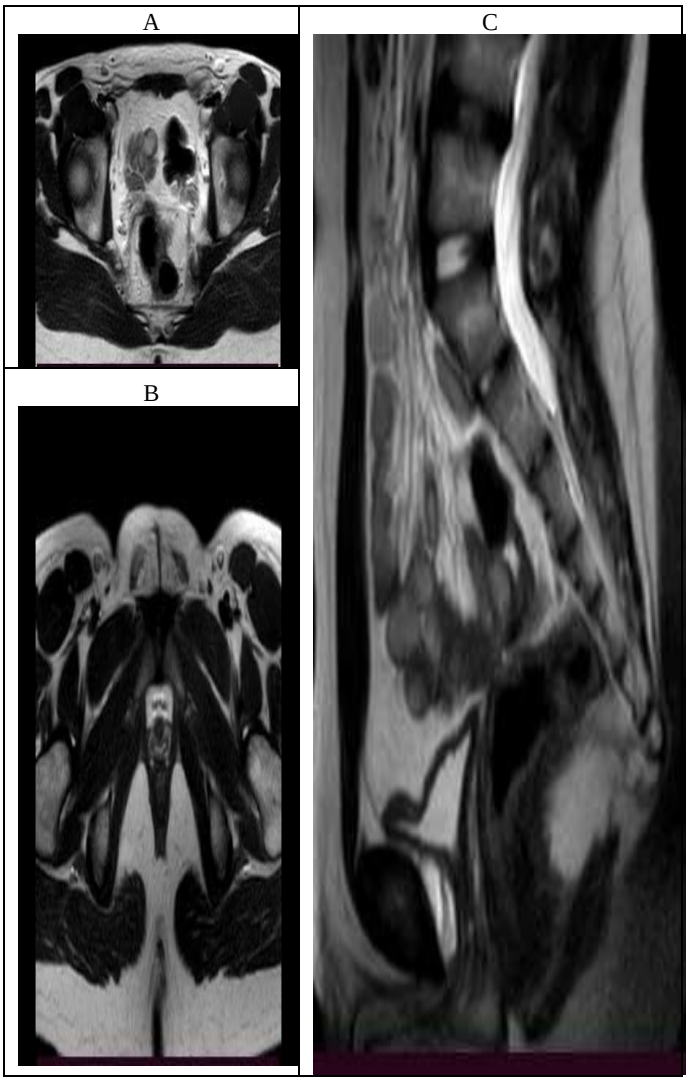


**Fig 1:** Pelvic MRI: T2 WI (A and B) axial cut and (C) sagittal cut. they show the absence of uterus, cervix and both ovaries with the presence of proximal vaginal canal.

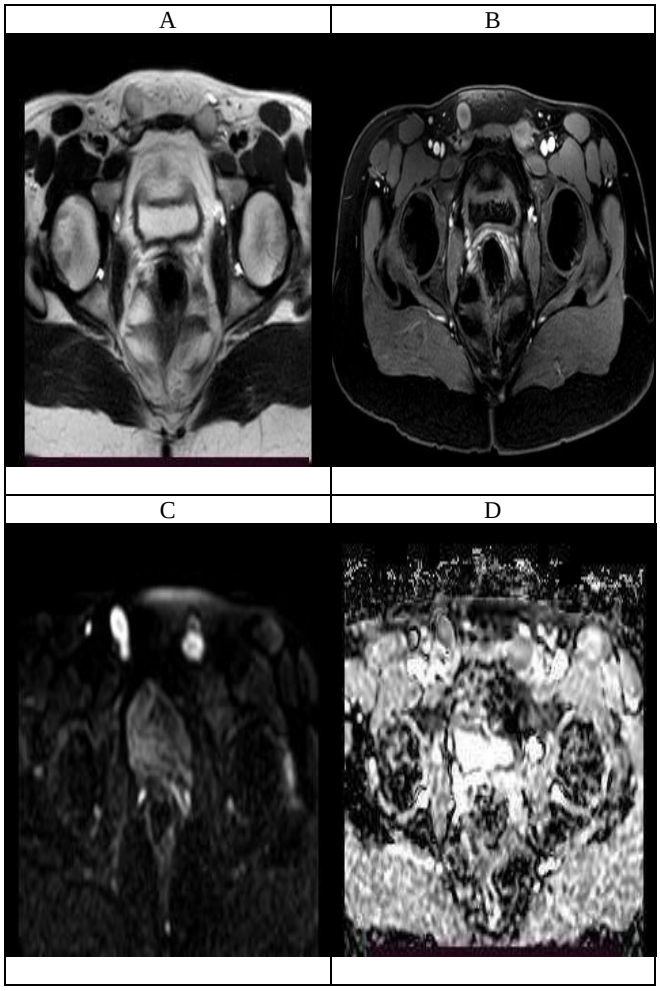


**Fig 2:** Pelvic MRI: (A) T2 WI axial cut (B) Post contrast image axial cut (C) DWI and ADC maps axial cuts. They show bilateral oval shaped structures seen in the proximal part of each inguinal canal which exhibit heterogenous signal intensity slightly hypointense in T2WI(A) restricted pattern in DWI and ADC maps (C and D) and heterogenous enhancement on post contrast images which mostly represents bilateral undescended testes.

## Discussion

In the 6th week of the gestation testicular differentiation happens. The sex determination Y (SRY) gene located on the Y chromosome plays a role in this process. The presence of the sexdetermining Y gene (SRY gene) initiates development toward the male phenotype. Deletion or inactivation of the SRY gene results in a female phenotype [8]. The sex determing region (SRY) of the Y chromosome encodes the testis determining factor (TDF). TDF promotes male development by initiating the transformation of undifferentiated gonadal tissue into testes. Testes secret hormones important for the growth and differentiation of males and females [10]. Sertoli cells produce anti-Müllerian, a peptide that inhibits the growth of the Müllerian ducts. This inhibits the development of the male uterus and fallopian tubes. Leydig cells secrete testosterone, which is then converted to dihydrotestosterone (DHT) by target cells. Testosterone stabilizes the Wolffian ducts and promotes their development into the epidedymis, vas deferens and seminal vesicles, while dihydrotestosterone (DHT) promotes prostate formation and the differentiation of the urogenital swelling, genital tubercles and urethral folds into the penis. The fact that testosterone and DHT bind to androgen receptors, a mechanism essential for sexual development, shows how important androgen receptors are for the proper functioning and release of the androgen [9-11]. In addition, testicular descent is androgen dependent [12]. Mutations in the AR gene cause cells to become unresponsive to male hormones during fetal development, thus preventing the masculinization of the male genitalia. It also prevents the development of secondary male sexual characteristics during puberty [12]. According to the phenotype, androgen insensitivity syndrome (AIS) is categorized as complete androgen insensitivity syndrome (CAIS), partial androgen insensitivity syndrome (PAIS), and mild androgen insensitivity syndrome (MAIS) [1]. Other names given to the different manifestations of AIS include Reifenstein syndrome, Rose-Water syndrome, Aiman syndrome, GilbertDreyfus syndrome, Lubs syndrome, Goldberg-Maxwell syndrome, and Morris syndrome [14]. The diagnosis of androgen insensitivity syndrome usually occurs at a young age, when the patient first presents with amenorrhea, (as in our case). Prenatal diagnosis can be made by comparing the amniotic fluid karyotype with the genetic sex confirmed by ultrasound. Sometimes patients are diagnosed with infertility later in life. There are no standard criteria for diagnosing AIS, but karyotyping, high testosterone levels, normal or high serum FSH, LH and estrogen levels, pelvic X-rays and genetic molecular testing to detect mutations in the AR gene AIS are used. The latter is very important because it helps distinguish Androgen Insensitivity Syndrome (AIS) from other diseases such as Klinefelter disease (47, XXY), Turner disease (45, XO), mixed gonadal agenesis (45, XO; 46 XY) and tetragametic mosaicism (45, XO; 46 XY) [15]. In women with CAIS, the vagina is shorter and there is no opening at the tip. In addition, organs derived from the Wolffian duct, such as the epididymis, vas deferens or seminal vesicles, and the prostate are absent. Many authors [17-19] have shown that CAIS rarely shows structures formed by the Müllerian ducts. The symptoms of this disease indicate the presence of a fully female phenotype from birth. An important factor that makes the diagnosis correct is the normal growth of the breast at an advanced age, with little or no growth of pubic and axillary hair, as in our case [16]. Early diagnosis of complete androgen insensitivity syndrome (CAIS) can be made by revealing a 46, XY karyotype in maternal amniocentesis. However, obstetric ultrasound or clinical examination at the time of delivery shows the presence of female external genitalia [20, 21]. Another diagnosis that can be suggested for the diagnosis of CAIS is the presence of unilateral or bilateral inguinal hernia in female patients (as in our case) [22]. Patients with PAIS exhibit different clinical phenotypes depending on the degree of hypomasculinization. Quigley *et al*. classify PAIS is into five grades [16]: Grade 1 is a normal female genital phenotype, while Grade 2 is a female phenotype with mild clitoromegaly or slight posterior labial fusion.

Grade 3 has undifferentiated phallic structures in the middle of the clitoris and penis, along with a urogenital sinus with a perineal orifice and labioscrotal folds.

Grade 4 is mostly male and has perineal hypospadias, a small penis, cryptorchidism, or a bifid scrotum.

And Grade 5 has isolated hypospadias and/or a micropenis.

Clinically, the new PAIS variants resemble MAIS. For example, they may present as coronal hypospadias or prominent raphe on the scrotum [23]. During puberty, MAIS patients may experience changes in spermatogenesis and

fertility, but this is not universal [24, 25]. However, impotence and gynecomastia are frequently seen. Complete androgen insensitivity syndrome (CAIS) and partial androgen insensitivity syndrome (PAIS) show the same endocrine profile: in the first three months of life, serum concentrations of luteinizing hormone (LH) and testosterone (T) are very normal or high. After that, LH and T levels remain in the normal range until puberty [26]. Later, during puberty, we see more testosterone and luteinizing hormone in the blood. This is because androgens are insensitive, so the hypothalamus and pituitary gland do not receive any negative feedback from sex hormones. This phenomenon was also observed in our patients. Aromatase converts testosterone to estrogen, and CAIS patients have higher estrogen levels and breast enlargement than men. Also, AIS patients have normal antiMüllerian hormone (AMH) because their supporting cells and Leydig cells are still functioning normally [13].

Symptomatic therapy is the mainstay of treatment. There is currently no specific treatment for AR gene mutations. After evaluation, the patient and their parents should be informed and make a decision. Orchidectomy should be done for undescended testis, as we do in our patients, to reduce the risk of testicular cancer. Several studies show that approximately 3.6% are at age 25 and 33% at age 50. In rare cases, some women choose to undergo vaginoplasty to create a functional vagina. Sex reassignment surgery may be beneficial for those who wish to identify as male. Patients are encouraged to have regular DEXA scans to measure bone density and to take hormone replacement therapy, calcium, and vitamin D supplements [26, 27].

## Conclusion

Complete Androge Insensitivity Syndrome (CAIS) is a rare syndrome. A proper diagnosis is critical for patients with sexual development abnormalities in order to provide appropriate care and further interventions. A multidisciplinary approach is essential in the management of patients with CAIS, encompassing paediatric endocrinology, urology, gynaecology, and clinical psychology. Key elements of counselling include discussions on spontaneous puberty, gonadectomy post-puberty, subsequent hormone replacement, and potential future infertility.

## References


1. Chang C, Yeh S, Lee SO. Androgen receptor (AR) pathophysiological roles in androgen-related diseases in skin, bone/muscle, metabolic syndrome and neuron/immune systems: lessons learned from mice lacking AR in specific cells. Nucl. Recept. Signal,2013:11:001.
2. Hurme T, Lahdes-Vasama T, Mäkelä E, *et al*. Clinical findings in prepubertal girls with inguinal hernia with special reference to the diagnosis of androgen insensitivity syndrome. Scand J Urol Nephrol, 2009:43:42-46. doi: 10.1080/00365590802299247.
3. Sultan C, Philibert P, Gaspari L, *et al*. Androgen insensitivity syndrome. In: New MI, Lekarev O, Parsa A, Yuen TT, O'Malley B, Hammer GD, *et al*. Genetic Steroid Disorders. Cambridge, MA: Academic Press, 2014, 225-237.
4. Morris JM, The syndrome of testicular feminization in male pseudohermaphrodites, American Journal of Obstetrics and Gynecology,1953:65(6):1192–1211, 2-s2.0-33747640635.
5. Allen L. Disorders of sexual development. Obstet Gynecol Clin North Am,2009:36(1):25–45. doi: 10.1016/j.ogc.2009.02.001. [PubMed: 19344846].
6. Anık A, Çatlı G, Abacı A, Böber E. 46, XX male disorder of sexual development: a case report. J Clin Res Pediatr Endocrinol,2013:5(4):258–60.
7. DeFalco T, Capel B: Gonad morphogenesis in vertebrates: divergent means to a convergent end. Annu Rev Cell Dev Biol,2009:25:457-482. 10.1146/annurev.cellbio.042308.13350.
8. Yamada G, Suzuki K, Haraguchi R, Miyagawa S, Satoh Y, Kamimura M. *et al*. Molecular genetic cascades for external genitalia formation: an emerging organogenesis program. Dev Dyn,2006:235:1738-1735. 10.1002/dvdy.20807.
9. Hiort O Clinical, molecular aspects of androgen insensitivity. Endocr Dev,2013:24:33-40.
10. Gottlieb B, Lehvaslaiho H, Beitel LK, *et al*. The androgen receptor gene mutations database. Nucleic Acids Res,1998:26:234-238.
11. Sultan C, Philibert P, Gaspari L, *et al*. Androgen insensitivity syndrome. In: New MI, Lekarev O, Parsa A, Yuen TT, O'Malley B, Hammer GD, *et al*. Genetic Steroid Disorders. Cambridge, MA: Academic Press, 2014, 225-237. [Google Scholar]
12. Hurme T, Lahdes-Vasama T, Mäkelä E, *et al*. Clinical findings in prepubertal girls with inguinal hernia with special reference to the diagnosis of androgen insensitivity syndrome. Scand J Urol Nephrol,2009:43:42-46. doi: 10.1080/00365590802299247.
13. Galani A, Kitsiou-Tzeli S, Sofokleous C, Kanavakis E, Kalpini-Mavrou A. Androgen insensitivity syndrome: clinical features and molecular defects. Hormones, 2008:7(3):217–229.
14. Ahmed SF, Achermann JC, Arlt W, Balen A, Conway G, Edwards Z. *et al*. Society for Endocrinology UK guidance on the initial evaluation of an infant or an adolescent with a suspected disorder of sex development (Revised 2015) Clin. Endocrinol,2016:84(May (5)):771–788.
15. Brown CJ, Goss SJ, Lubahn DB. Androgen receptor locus on the human X chromosome: regional localization to Xq11-12 and description of a DNA polymorphism. Am. J. Hum. Genet,1989:44(2):264–269.
16. Quigley CA, De Bellis A, Marschke KB, El-Awady M K, Wilson EM, French FS. *et al*. Androgen receptor defects: historical, clinical, and molecular perspectives, Endocrine Reviews,1995:16(3):271–321.
17. Ulloa-Aguirre A, Mendez JP, Chavez B, Carranza-Lira S, Angeles A, Perez- Palacios G. *et al*. Incomplete regression of müllerian ducts in the androgen insensitivity syndrome, Fertility and Sterility,1990:53(6):1024–1028.
18. Dodge ST, Finkelston MS, Miyazawa K, Testicular feminization with incomplete müllerian regression, Fertility and Sterility,1985:43(6):937–938.
19. Swanson ML, Coronel EH, Complete androgen insensitivity with persistent müllerian structures. A case report, The Journal of Reproductive Medicine,1993:38(7):565–568.
20. Stephens JD, Prenatal diagnosis of testicular feminisation, The Lancet,1984:2:8410.

21. Hiort O, Huang Q, Sinnecker GH G, Sadeghi-Nejad A B, Kruse K, Wolfe HJ. *et al*. Single strand conformation polymorphism analysis of androgen receptor gene mutations in patients with androgen insensitivity syndromes: application for diagnosis, genetic counseling, and therapy, Journal of Clinical Endocrinology and Metabolism,1993:77(1):262–266.
22. Grumbach MM, Conte FA, JD Wilson, DW Foster, Disorders of sex differentiation, Williams Textbook of Endocrinology, Saunders, Philadelphia, Pa, USA, 1991, 853–951.
23. Melo KFS, Mendonca BB, Billerbeck AEC, Costa EM F, Inácio M, Silva FAQ. *et al*. Clinical, hormonal, behavioral, and genetic characteristics of androgen insensitivity syndrome in a Brazilian cohort: five novel mutations in the androgen receptor gene, Journal of Clinical Endocrinology and Metabolism,2003:88(7):3241–3250.
24. Cundy TF, Rees M, Evans BAJ, Mild androgen insensitivity presenting with sexual dysfunction, Fertility and Sterility,1986:46(4):721–723.
25. Pinsky L, Kaufman M, Killinger DW, Human minimal androgen insensitivity with normal dihydrotestosterone-binding capacity in cultured genital skin fibroblasts: evidence for an androgen-selective qualitative abnormality of the receptor, American Journal of Human Genetics,1984:36(5):965–978.
26. Fulare S, Deshmukh S, Gupta J. Androgen insensitivity syndrome: A rare genetic disorder Int J Surg Case Rep, 2020:71:371–3.
27. Hines M, Ahmed SF, Hughes IA. Psychological outcomes and gender-related development in complete androgen insensitivity syndrome Arch Sex Behav, 2003:32:93–101.