Complete Androgen Insensitivity Syndrome (CAIS) in a 15-Year-Old Female with Primary Amenorrhea: A Case Report

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Abstract

Androgen insensitivity syndrome (AIS) is a rare and common disorder of sex development, in which individuals present as phenotypic females despite having a 46, XY karyotype due to androgen receptor resistance. This case report describes the diagnosis and management of a 15-year-old female presenting with primary amenorrhea with normal breast development. Pelvic imaging of the patient revealed the absence of uterus and ovaries with a rudimentary vagina and undescended testes. Labs showed raised testosterone, and karyotyping was 46 XY, which confirmed the diagnosis of Complete Androgen Insensitivity Syndrome (CAIS). The patient and family were referred to a clinical psychologist, consented to identify as female, and were referred to a pediatric surgeon for gonadectomy to prevent gonadal malignancy. Postoperatively, the patient was sent to an endocrinologist for Hormonal replacement therapy. The report highlights the clinical presentation, diagnostic process, and considerations in managing CAIS, particularly in the context of adolescent care.

Keywords: *CAIS, AIS, PAIS, disorder of sex development, hormone replacement therapy (HRT).*

INTRODUCTION

Androgen Insensitivity Syndrome (AIS) is an X-linked recessive disorder where individuals with a 46, XY karyotype are phenotypically female due to the body's inability to respond to androgens. AIS can be complete (CAIS) or partial (PAIS). CAIS typically presents with primary amenorrhea and absent or scanty pubic and axillary hair in a phenotypically female adolescent. Although the androgen insensitivity syndrome is well recognized among clinicians, the disease remains uncommon, and the Office of Rare Diseases of the National Institute of Health still classifies CAIS as a rare disease [1]. Therefore, awareness among primary care physicians is important, as prompt diagnosis facilitates early specialist referrals, informed patient counselling, and coordinated multidisciplinary care, thereby improving the patient's physical and psychosocial well-being. This includes guidance on gender identity, psychological support, and legal considerations.

CASE PRESENTATION

A 15-year-old female child presented to the outpatient department with concerns of Primary amenorrhea. Otherwise, happy and healthy, no other issues. Attends school and Madrassa with a good educational record.

Clinical examination revealed a phenotypically female, well-nourished, developmentally appropriate for her age and sex, with long extremities. The patient had breast development at Tanner stage 4, fully developed normal female external genitalia, and sparse pubic and axillary hairs corresponding to Tanner stage 2.

There was no clitoromegaly (**Table 1**). The patient weighed 44 kg and was 150 cm tall, with a BMI of 19.6 kg/m2. The patient was normotensive, and other vitals were within normal limits. Family and past medical history were insignificant, with no known family history of

Table 1: Physical features of the patient.

Variables	Findings
Age (in years)	15
Symptoms	Primary amenorrhea
Thelarche	Tanner stage 4
Pubarche	Tanner stage 2
Labia	Well developed
Vagina	Rudimentary vagina
Male secondary sexual characters	Nil

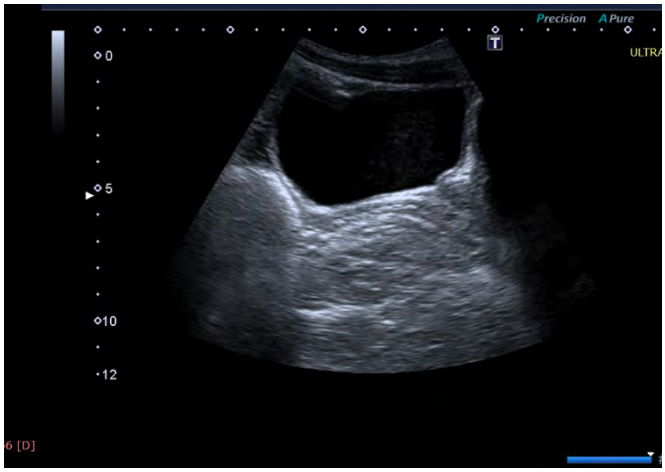

Fig. (1): Pelvic ultrasound: Absence of a uterus and ovaries.

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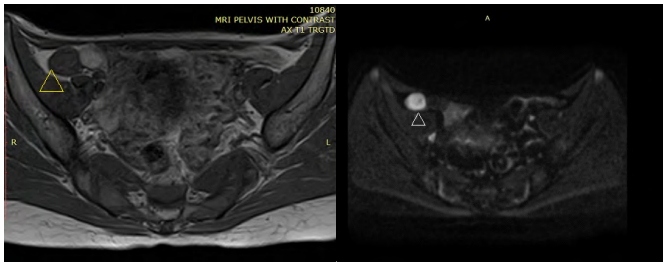

Fig. (2): MRI abdomen and pelvis. Absent uterus and ovaries with rudimentary vagina and undescended testes yellow and white triangle.

Table 2: Investigations performed on the patient.

Investigations	Results
Serum testosterone (ng/dl) (Normal: 20-80 ng/dl)	1051.83 Very high
Serum FSH (IU/L) (Normal: 5-20 IU/L)	3.8mIU/ml
Karyotyping	GTG banding 46, XY (20) male karyotype in phenotypic female confirmed.
Serum LH (IU/L) (Normal: 5-20 mIU/L)	34.13 mIU/ml
Cortisol (Normal morning: 5-25 µg/dL)	10.11
Thyroid profile (Normal TSH: 0.4-4.0 µIU/mL; Free T4: 0.8-1.8 ng/dL)	Normal TSH: 1.927 µIU/mL; Free T4:1.25 ng/dL
Progesterone ng/ml (Normal follicular: 0.1-0.8; luteal: 2-25 ng/mL)	0.99 ng/ml
MRI Abdomen and pelvis	Absent Uterus and ovaries with rudimentary vagina and undescended testes
Pelvic Ultrasound: Absence of a uterus and ovaries	Pelvic Ultrasound: Absence of a uterus and ovaries

delayed puberty or other similar conditions. Past surgical history was significant for bilateral inguinal repair, which was performed at another healthcare facility, where they did not investigate for disorder of sex development.

She was raised as a girl child. An ultrasound of the abdomen was performed, which showed the absence of a uterus and ovaries (**Fig. 1**), and an MRI was advised, along with a hormonal Profile. Findings of the MRI Pelvis were an absent uterus and ovaries with a rudimentary vagina and undescended testes. The right testis was located at the level of the right inguinal canal, and the left was not visualized (**Fig. 2**). Findings were consistent with disorder of sex development (DSD).

Laboratory investigations showed elevated serum LH, normal FSH, and significantly elevated serum testosterone levels, with normal thyroid profile, serum cortisol, estradiol, and blood glucose (**Table 2**). To confirm gender, given the above findings, chromosomal analysis was performed, which showed a GTG-banded 46, XY (20) male karyotype in a phenotypic female (**Fig. 3**).

The patient was referred to a clinical psychologist, the patient and the family consented to identify herself as a female, and she was referred to a pediatric surgeon for

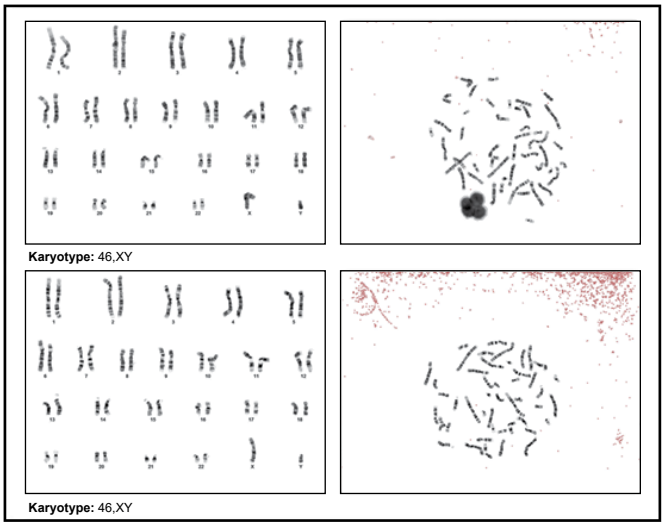

Fig. (3): GTG banding 46, XY [20]; Male karyotype in phenotypic female. Male chromosome complement was observed in all 20 GTG banded cells of a phenotypic female.

gonadectomy. The patient did right inguinal gonadectomy and with left laparoscopic exploration and gonadectomy, followed by left gonadectomy. Surgery was uneventful and was performed to prevent the risk of malignancy. On histopathological examination, both showed atrophic testicular tubules with intervening fibrosis and no spermatogenesis, and evidence of intratubular germ cell neoplasia or other neoplastic processes was noted. The patient was referred to an endocrinologist for further management and hormonal replacement therapy (HRT). She was started on Levonorgestrel (0.15 mg), Ethinyloestradiol (0.03 mg) once a quarter daily.

DIAGNOSIS

The combination of a phenotypic female with primary amenorrhea, normal breast development, sparse pubic hair, elevated testosterone levels, MRI findings, and a 46, XY karyotype led to the diagnosis of Complete Androgen Insensitivity Syndrome (CAIS). Although androgen receptor gene analysis or clinical exome sequencing can further confirm the diagnosis at the molecular level, such testing was not available in this case [2-4].

MANAGEMENT AND FOLLOW-UP

Medical care of patients with CAIS has two aspects, hormone replacement therapy and psychological support [5-7].

Psychological Support: The patient and her family were counseled about the diagnosis and its implications, including the genetic basis, fertility considerations, and psychosocial aspects. The counselling included discussion on gender identity, legal aspects, strategies for coping, family support, and future social considerations. Following counseling, the patient affirmed her female gender identity, with full family support.

Hormone Replacement Therapy (HRT): Post-gonadectomy, estrogen replacement therapy was

initiated to maintain secondary sexual characteristics and bone health [8].

Gonadectomy: Bilateral gonadectomy was performed after counselling regarding risks, benefits, and lifelong hormonal replacement therapy. Histopathology confirmed the presence of testicular tissue with no evidence of malignancy [9].

Long-term Care: Patient was referred to a multidisciplinary team, including endocrinologists, gynecologists, and psychologists, for ongoing management. Counseling was done regarding long-term health, hormone replacement therapy, fertility limitations, sexual health, and future marital considerations. Regular follow-up was planned to monitor bone density, cardiovascular health, and psychological well-being.

DISCUSSION

The etiology of complete androgen insensitivity syndrome is due to mutations in the androgen receptor gene (AR) on Xq11-12 [10]. These mutations can occur in the ligand-binding domain (LBD), DNA-binding domain (DBD), or the N-terminal Domain (NTD), and there is no straightforward genotype-phenotype correlation. The majority of them originate in the mother's germline, while in some cases, de novo mutations may also occur [10-12].

Endocrinologically, patients with CAIS typically have male-range or slightly elevated levels of testosterone, elevated LH, and normal FSH levels due to negative feedback of the hypothalamic-pituitary system.

Patients with CAIS are often taller than average. Excessive androgen at puberty is aromatized to estrogen, which leads to normal breast development. Nipple development depends on androgens; their nipples are poorly developed. Axillary and pubic hairs are scanty due to androgen insensitivity. Male external genitalia are absent due to the secretion of anti-Mullerian hormone by the testicles. Anti-Mullerian hormones inhibit the formation of the upper vagina, uterus, and fallopian tubes. The lower part of the vagina develops from the urogenital ridge. These patients have a short vagina, typically 2.5cm to 8 cm [12]. In clinical settings, inguinal hernia remained one of the most common presenting complaints of the CAIS, and the majority of the patients are diagnosed during infancy or early childhood [13]; however, some present later with primary amenorrhea, as in this case. In a female child with an inguinal hernia, the physician should consider karyotype [14]. The incidence of testicular malignancy increases with age, but is low before puberty [9].

In previous studies, the rate of testicular germ cell tumors in patients with CAIS was estimated at approximately 3.6% at age 25 and 33% at age 50 [9].

In a systematic review of 456 patients with CAIS who underwent testicular biopsy or gonadectomy, 6.14% had pre-cancerous findings. More than 82% were of post-puberty age, while 1.3% had malignancy. All occurring in post-pubertal or adult individuals [15].

Current consensus and expert recommendations emphasize shared decision-making regarding the timing of gonadectomy after completion of puberty. This process requires thorough counselling of the patient and family regarding the risks and benefits of gonadectomy. Gonadal retention with regular clinical and imaging surveillance is considered an acceptable alternative to surgery in selected post-pubertal individuals [5, 7, 9].

Long-term management of patients with CAIS requires hormone replacement therapy (HRT). HRT is essential for a patient's overall growth and metabolic well-being. It helps in maintaining secondary sexual characteristics, including breast development. In the pediatric age group with gonadectomy before adulthood, HRT ensures their height and breast development; it should be continued till they reach their peers' height. It is essential to monitor the patient's bone mineral density and bone muscle development. Physicians must pay attention to their psychosocial and sexual maturity.

Although CAIS is well described, delayed diagnosis still occurs, particularly in resource-limited settings, underscoring the relevance of this case.

This case emphasizes the importance of considering AIS in the differential diagnosis of primary amenorrhea in adolescents, especially when there is discordance between physical examination findings and hormonal profiles. Early diagnosis and appropriate management, including psychological support and surgical intervention, are crucial for improving the quality of life in individuals with AIS.

CONCLUSION

Complete Androgen Insensitivity Syndrome, though rare, is a significant cause of primary amenorrhea in adolescents. Multidisciplinary care is essential for managing the condition, addressing both its physical and psychological aspects. This case report provides a structured approach to documenting and managing a case of Androgen Insensitivity Syndrome in an adolescent.

PATIENT PERSPECTIVE

The patient was satisfied and expressed relief after knowing her diagnosis. She also reported satisfaction with her care and treatment. She identified herself comfortably as female and also appreciated the counselling provided to her and her family.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient and her parents for Publication of this case report.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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GENERATIVE AI AND AI-ASSISTED TECHNOLOGIES IN THE WRITING PROCESS

During the preparation of this work, the authors used ChatGPT (GPT-4, OpenAI) sparingly to generate language suggestions and perform minor proofreading in some parts of the manuscript. After using this tool/ service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

REFERENCES

1. Singh S, Ilyayeva S. Androgen insensitivity syndrome. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
2. Mongan NP, Tadokoro-Cuccaro R, Bunch T, Hughes IA. Androgen insensitivity syndrome. Best Pract Res Clin Endocrinol Metab 2015; 29(4): 569-80.
DOI: https://doi.org/10.1016/j.beem.2015.04.005
3. Ohba K, Hayashida Y, Hakariya H, Ichinose S, Naitou S. Case of complete androgen insensitivity syndrome. Hinyokika Kiyo Acta Urolo Japon 2009; 55(5): 277-80.
4. Oakes MB, Eyvazzadeh AD, Quint E, Smith YR. Complete androgen insensitivity syndrome: a review. J Pediatr Adolesc Gynecol 2008; 21(6): 305-10.
DOI: https://doi.org/10.1016/j.jpag.2007.09.006
5. Hughes IA, Davies JD, Bunch TI, Pasterski V, Mastroyannopoulou K, MacDougall J. Androgen insensitivity syndrome. Lancet 2012; 380(9851): 1419-28.
DOI: https://doi.org/10.1016/S0140-6736(12)60071-3
6. Bertelloni S, Dati E, Baroncelli GI, Hiort O. Hormonal management of complete androgen insensitivity syndrome from adolescence onward. Horm Res Paediatr 2011; 76(6): 428-33.
DOI: https://doi.org/10.1159/000334162
7. Chen MJ, Vu BM, Axelrad M, Dietrich JE, Gargollo P, Gunn S, *et al.* Androgen insensitivity syndrome: Management considerations from infancy to adulthood. Pediatr Endocrinol Rev 2015; 12(4): 373-87.
8. Ko JKY, King TFJ, Williams L, Creighton SM, Conway GS. Hormone replacement treatment choices in complete androgen insensitivity syndrome: an audit of an adult clinic. Endocr Connect 2017; 6(6): 375 9.
DOI: https://doi.org/10.1530/EC 17 0083
9. Barros BA, Oliveira LR, Surur CR, Barros Filho AA, Maciel Guerra AT, Guerra Junior G. Complete androgen insensitivity syndrome and risk of gonadal malignancy: systematic review. Ann Pediatr Endocrinol Metab 2021; 26(1): 19 23.
DOI: https://doi.org/10.6065/apem.2040170.085
10. Hiort O, Sinnecker GH, Holterhus PM, Nitsche EM, Kruse K. Inherited and de novo androgen receptor gene mutations: investigation of single case families. J Pediatr 1998; 132(6): 939 43.
DOI: https://doi.org/10.1016/S0022 3476(98)70387 7
11. Liu Q, Yin X, Li P. Clinical characteristics, AR gene variants, and functional domains in 64 patients with androgen insensitivity syndrome. J Endocrinol Invest 2023; 46(1): 151 8.
DOI: https://doi.org/10.1007/s40618 022 01894 4
12. Tyutyusheva N, Mancini I, Baroncelli GI, D'Elios S, Peroni D, Meriggiola MC, *et al.* Complete androgen insensitivity syndrome: from bench to bed. Int J Mol Sci 2021; 22(3): 1264.
DOI: https://doi.org/10.3390/ijms22031264
13. Kimizuka Y, Sato T, Nakano S, Ishii T, Hasegawa T. Potential risk of inguinal hernia in complete androgen insensitivity syndrome. Clin Pediatr Endocrinol 2023; 32(1): 76-8.
DOI: https://doi.org/10.1297/cpe.2022-0058
14. Chang SJ, Chen JY-C, Hsu CK, Chuang FC, Yang SS-D. The incidence of inguinal hernia and associated risk factors of incarceration in pediatric inguinal hernia: a nation-wide longitudinal population-based study. Hernia 2016; 20(4): 559-63.
DOI: https://doi.org/10.1007/s10029-015-1450-x
15. Liu AX, Shi HY, Cai ZJ, Liu A, Zhang D, Huang HF, *et al.* Complete androgen insensitivity syndrome and risk of gonadal malignancy: A systematic review. Int J Endocrinol 2021; 2021: 1-10.
DOI: https://doi.org/10.1155/2021/8879187