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Caso Clínico

Complete Androgen Insensitivity Syndrome: Case Report

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A B S T R A C T

Complete androgen insensitivity syndrome (CAIS) is a condition characterized by insensitivity of the androgen receptor, despite normal hormone levels. This results in the development of a female phenotype, despite having a 46XY karyotype. We present the case of a 42-year-old female patient diagnosed with CAIS after consulting an endocrinologist. During the consultation, the patient exhibited a complete absence of pubic and axillary hair and complained of having a very high-pitched voice. A karyotype confirmed the 46XY. The patient underwent mastectomy initially and later underwent orchiectomy. After the CAIS diagnosis, the patient developed poorly controlled type 2 diabetes mellitus and weight gain, leading to a gastric bypass procedure. In patients with CAIS, early diagnosis plays a crucial role in managing this rare condition effectively and alleviating the significant psychological distress experienced by these patients.

Palavras-chave:
Síndrome de Insensibilidade aos Androgénios.

Síndrome da Insensibilidade Completa ao Androgénio: Relato de Caso

R E S U M O

A síndrome da insensibilidade completa ao androgénio (CAIS), é uma condição caracterizada pela insensibilidade do recetor androgénico, apesar dos níveis hormonais normais. Isso resulta no desenvolvimento de um fenótipo feminino, apesar de possuir um cariótipo 46XY. Apresentamos o caso de uma paciente do sexo feminino, 42 anos, com diagnóstico de CAIS após consulta com endocrinologista. Ao exame objetivo a paciente apresentava ausência completa de pelos púbicos ou axilares e queixava-se da voz ser muito aguda. Um cariótipo confirmou o genótipo 46XY. Paciente foi submetido inicialmente a mastectomia e posteriormente à orquiectomia. Após o diagnóstico, paciente evoluiu com diabetes *mellitus* tipo 2 mal controlado e ganho de peso, levando à realização de *bypass* gástrico. Em pacientes com CAIS, o diagnóstico precoce desempenha um papel crucial no tratamento eficaz desta condição rara e no alívio do sofrimento psicológico significativo vivenciado por esses pacientes.

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Introduction

Complete androgen insensitivity syndrome (CAIS), also known as Morris syndrome, was first described in 1953. It is a recessive disorder linked to the maternal X chromosome - locus Xq11-12 - that leads to a mutation in the androgen receptor (*AR*), resulting in an individual with a female phenotype but a 46XY karyotype and the presence of male gonads. This syndrome has a prevalence of approximately 1 in 40 000-60 000 births.[1]

In CAIS, tissue resistance to androgens is complete, even with normal or minimally elevated testosterone production.[2,3] The testicles are present but may be located in the inguinal canal, abdomen, or even the scrotal lip, with an increased risk of malignancy.[4] The estrogen receptor is normal, allowing for normal development of breast tissue and feminine adiposity, despite the absence of a uterus or ovaries, resulting in primary amenorrhea, and the presence of a hypoplastic vagina - short and blind-ending.[3]

The development of the Wolffian duct, which gives rise to the vas deferens and seminal vesicles, is interrupted. Consequently, individuals with CAIS have scant pubic and axillary hair and exhibit higher levels of luteinizing hormone (LH) and estradiol than the normal male level.[3] The simultaneous activity of anti-Müllerian hormone (AMH) impedes the development of the Müllerian duct and its derived organs, including the fallopian tubes, uterus, cervix, and part of the vagina, resulting in a recurrence of a hypoplastic vagina.[1] Another noteworthy finding in CAIS patients is an increase in body fat and elevated cholesterol levels.[1]

The investigation of pelvic organ pathologies is conducted through transvaginal ultrasound, magnetic resonance imaging, and computed tomography. Laboratory results indicate elevated levels of LH and testosterone. These results, combined with the female phenotype and male karyotype, strengthen the diagnosis of complete androgen insensitivity syndrome (CAIS).[1]

The aim of this report is to describe an original case of a patient with CAIS, diagnosed in adulthood, which has been sparsely documented in the literature and is relevant in the field of endocrinology.

Case Report

A 42-years-old patient, female, professional judoka, presented to the clinic with obesity and a desire for mastectomy. Was born with a female phenotype but currently identifies as a feminine homosexual.

During the consultation, she was accompanied by her wife and reported that she had never menstruated. She mentioned using estrogen in the past but had never sought treatment or a diagnosis for the cause of her primary amenorrhea due to not being concerned about fertility. In her medical history, she noted the absence of pubic and axillary hair, and breast growth occurred after the age of 18. She also had type 2 diabetes mellitus (DM2) and class III obesity.

Upon physical examination, her body mass index (BMI) was 47.08 kg/m^2, waist circumference was 141.0 cm, her thyroid was impalpable, and the external female genitalia were at Tanner stage P1. Her breasts were at Tanner stage M5. She denied any similar cases in her family.

The patient underwent a karyotype examination, which revealed a male genotype of 46XY, confirming the diagnosis of CAIS. General information about the syndrome, endocrinological follow-up, and a therapeutic plan for the removal of gonads were provided. Despite the diagnosis, the patient expressed the desire to be recognized as male and had already started the process of changing their social name. Throughout the clinical follow-up, the treatment for type 2 diabetes mellitus was optimized, and the patient achieved good control.

In the following year, the patient was referred for mastectomy and orchiectomy. The gonadal tissue was sent for histopathological examination, which confirmed the presence of testicular tissue, consistent with CAIS. Additionally, the patient began treatment with an otolaryngologist and speech therapist to address the voice alteration. Hormonal therapy was not used in the treatment. Despite the diagnosis and medical interventions, the patient and their partner adopted three children and continued their career as a judo teacher.

Additionally, approximately 2 years after the mastectomy and orchiectomy, the patient underwent gastric bypass bariatric surgery when they weighed 111 kg (BMI 40.77). Following the surgery, they lost approximately 70 kg. The patient continued with endocrinological and psychological follow-up care.

Discussion

The difficulty in establishing an early diagnosis of CAIS, as reflected in the presented case, hinders the patient from receiving the optimal therapeutic plan. In the case of orchiectomy, the treatment is conducted due to the increased risk of neoplasia; however, it is suggested to be performed after puberty since the risk of malignancy in childhood is low.[5,6]

Moreover, hormonal therapy is essential for patients who undergo bilateral gonad removal. Hormone replacement therapy not only maintains secondary sexual characteristics, well-being, and sexual function but also promotes bone health and cardiovascular protection.[7] The classic treatment plan consists of estrogen, with the dosage varying according to the individual patient. Another studied treatment approach is testosterone therapy, which improves the sexual health of CAIS patients, as some may experience drawbacks with estrogen use. Additionally, since CAIS patients do not have a uterus, the use of progesterone is unnecessary.[7]

Due to hormone insensitivity, patients with CAIS develop external female genitalia, despite having a male genotype, and also have well-developed breasts (Tanner stage V), resulting in a complete female phenotype. In the reported case, the patient received their diagnosis in adulthood, which may limit the approach to treatment. This highlights the importance of such presentations and the dissemination of knowledge about the syndrome, aiming for early diagnosis and, consequently, providing the best therapeutic options.

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EFZ and GCA: Conceptualization, data collection, writing original draft.
KPS: Supervision.
JCS and LCA: Translate, review and final approval.
All authors approved the final version to be published.

EFZ e GCA: Concetualização, recolha de dados, redação do projeto original.
KPS: Supervisão.
JCS e LCA: Tradução, revisão e aprovação final.
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