Case Report

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Complete androgen insensitivity syndrome diagnosed after inguinal surgery in era of modern technology: a case report

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Introduction: Androgen Insensitivity Syndrome (AIS) is a rare X-linked recessive disorder of sexual development. It results from mutations in the Androgen Receptor (AR) gene located on chromosome Xq11–12. Affected individuals have a male genotype but a female phenotype.

Case presentation: A 20-year-old female presented to the emergency room with a history of pain in the bilateral inguinal region. In ultrasonography (USG), bilateral inguinal hernia was suspected. While performing an emergency operation for hernia repair, hernia was revealed as bilateral abdominal testis. Then, after a gynecology consultation, a bilateral orchidectomy was done. Postoperative karyotyping showed a male genotype. Then the patient was discharged on hormone replacement therapy to maintain normal bone mineral density and secondary sexual characteristics.

Discussion: AIS presents with primary amenorrhea in pubertal females. The growth spurt and secondary sexual characteristics are normal except for absent axillary and pubic hair. There is a short-blind vagina, but the uterus is absent, and the abdominal testis presents as an inguinal hernia. Serum gonadotropin level, karyotyping, and imaging studies are done to reach a diagnosis. Management includes gonadectomy, genitoplasty, and hormone replacement therapy.

Conclusion: The objective of this report was to make clinicians aware that AIS can present as a bilateral inguinal hernia. In acute presentations, it can be misdiagnosed as a strangulated femoral hernia only later to be identified as an undescended abdominal testis during surgery. An absence of proper clinical judgment and reliance on USG for imaging can often lead to misdiagnosis in acute settings.

Keywords: androgen insensitivity syndrome, androgen receptor mutation, case report, complete androgen insensitivity syndrome, disorder of sex development

Introduction

Background and rationale

A rare genetic disorder known as Androgen insensitivity syndrome (AIS) affects the sexual development of people with XY chromosomes[1]. The mutations in the androgen receptor gene on the X chromosome result in partial or total insensitivity to androgens in peripheral tissues[1,2]. The AR gene mutation is inherited as X-linked recessive, but some cases are due to spontaneous mutation[3]. When a child is born, they have female external genitalia but lack ovaries and internal genitalia and may have undescended or partially descended testes. Complete androgen insensitivity syndrome (CAIS), partial androgen insensitivity syndrome (PAIS), and mild androgen insensitivity syndrome (MAIS) are the three kinds of AIS that can be distinguished based on the degree of androgen receptor failure[3]. The CAIS patient typically presents as an adolescent female with primary amenorrhea or, in infants, as a bilateral inguinal hernia. They have proper breast and pubertal growth spurts at the appropriate age. Likely, the typical phenotype of PAIS is micropenis, severe hypospadias, and a bifid scrotum that might contain gonads, while MAIS presents in men as infertility but is not associated with genital anomalies[1,3]. While CAIS is extremely rare, it is often overlooked in cases of bilateral inguinal hernia;

HIGHLIGHTS

- Complete androgen insensitivity syndrome (CAIS) is rare X-linked disorder which can present as bilateral inguinal hernia.
- Detailed history and thorough clinical examination can lead to high degree of suspicion. Whereas, relying in ultrasonography finding can be misleading.
- Androgen Insensitivity Syndrome (AIS) are managed by gonadectomy, genitoplasty, and hormone replacement therapy along with psychiatric counseling.

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hence, we share our case of CAIS in a 20-year-old female who presented to the ER with a complaint of sudden onset of pain on bilateral inguinal hernia and later revealed it as bilateral undescended testis during operation.

Guidelines: SCARE 2023 paper

This case report is reported in line with Surgical CAse REport (SCARE) 2023 criteria[4].

Patient information: demographics and presentation

A 20-year-old South Asian female presented to the ER with pain over the bilateral inguinal region for 4 h. She has had bilateral inguinal hernia for 10 years, which was gradually increasing in size but was not painful. But since 4 h, she has complained of pain over the bilateral inguinal region, which was sudden in onset, sharp, localized, nonradiating, and aggravated during movement. There was no history of other constitutional symptoms. She also gave a history of the absence of menarche.

Past medical and surgical history

She had undergone appendectomy 10 years ago. No history of diabetes, hypertension, or thyroid disorders.

Drug and allergic history

There is no history of drug intake or any known allergy till date.

Family history

There is no history of similar illness in family members.

Social history

She does not smoke and does not consume alcohol.

Clinical findings

On examination, her general condition was fair. Her pulse was 88 beats per minute and regular. Her blood pressure was 120/80 mmHg, her respiratory rate was 12 breaths/min, and her temperature was 97°F. Her stature was above mid-parental height. On abdominal examination, there was swelling (3×3 cm) over the bilateral inguinal region, which was globular in shape, soft, nonreducible, and there was a presence of bilateral tenderness over the swelling in the inguinal region, but the cough impulse was negative. The overlying skin was normal, with no visible peristalsis. Her other abdominal examination was unremarkable. Her cardiovascular, respiratory, and neurological examinations were normal.

Diagnostic assessment and interpretation

Routine blood tests were within normal limits. Then ultrasonography (USG) of the abdomen and pelvis was done to screen and detect hernia content, which showed herniation of intra-abdominal content, reducible in the right and irreducible in the left, with a neck measuring 10 mm on both sides. An atypical femoral hernia (Laugier's hernia) was suspected.

A preoperative diagnosis of bilateral irreducible femoral hernia was made, and an operation was planned.

Intervention

During intra operative surgery, the hernia was found to be bilateral undecended testis (Fig. 1). Then a gynecology consultation was done intraoperatively. Per vaginal examination, a vaginal blind pouch was found, and the uterus could not be palpated. Though breasts were fully formed, axillary, and pubic hairs were absent. A decision was made for bilateral orchidectomy with consent from parents after counseling about the patient's condition. They were also advised for postoperative karyotyping and MRI.

The postoperative excision biopsy report of the testes showed bilateral testes with maturation arrest; spermatozoa were absent and negative for malignancy. A postoperative focused scan revealed the absence of Mullerian structure. Gonadotropins after surgery were high (LH: 52 mIU/ml, FSH: 8 mIU/ml) with a low testosterone level (0.3 ng/ml). Karyotype was 46 XY, consistent with the male chromosome. Finally, the patient was started on estrogen replacement therapy.

Outcome

The patient had no complaints after the operation and is being followed up in an outpatient clinic.

Discussion

CAIS is a rare X-linked recessive disorder of sexual development with an estimated incidence between 1:20 000 and 1:99 000 in genetic males. It is caused by mutations in the AR gene, which is located on chromosome Xq 11–12 and contains eight exons[1,3]. Till now, more than 500 mutations in the AR gene have been described. Different types of mutations include point mutations, frame shift mutations leading to premature termination of transcription, gross deletions, and small deletions or insertions scattered around the entire sequence of the gene[3,5]. Although most mutations are inherited, some are sporadic. According to the degree of androgen resistance, mutations in the AR gene cause androgen hormone resistance, which prevents the target tissue from recognizing and using testosterone. This results in a range of changes in genotypic males, from partial to full female phenotypes[5,6]. Three sorts of clinical phenotypes can be

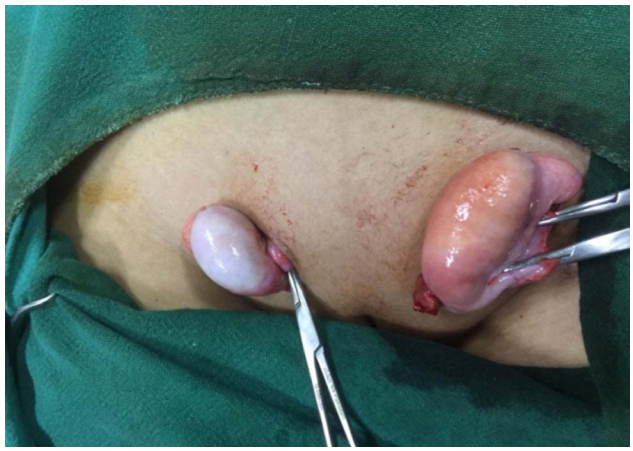

Figure 1. Intraoperative photo.

distinguished: total, partial, and moderate forms[7]. Affected individuals lack a uterus, fallopian tubes, or proximal vagina because their testes produce normal amounts of Müllerian-inhibiting factor[1,8]. There is another variant called AIS Type II, in which there are no mutations in the AR gene. Studies have suggested that unidentified cofactors of the AR are responsible for AIS Type II[9,10].

CAIS is consistently overlooked in infancy and is frequently diagnosed at puberty when the patient reports primary amenorrhea, while some patients also present in middle age and the elderly after the development of a testicular tumor. Despite being rare in female neonates, inguinal hernias are a well-known CAIS manifestation. In girls with inguinal hernias, the incidence of CAIS has been estimated to range from 0.8 to 2.4% in retrospective studies, whereas 50–80% of CAIS patients have a history of inguinal hernias[11,12]. Therefore, the presentation of inguinal hernia in a phenotypic female should raise the suspicion of CAIS[2,5]. Due to the aromatization of testosterone to estrogen, girls with CAIS experience a normal pubertal growth spurt and feminization at the time of predicted puberty. Axillary and pubic hairs are absent due to a lack of androgenic effects. The average height of females with CIAS is higher than that of normal girls but lower than that of normal boys in the same age range[13,14]. There may be a history of primary amenorrhea and inguinal hernia in siblings.

Serum testosterone, follicle-stimulating hormone, and inhibin concentrations are generally within or above normal limits, but the luteinizing hormone (LH) level is inappropriately increased. Excess testosterone is peripherally aromatized to estrogen, which, together with LH-induced direct secretion of testicular estrogen, results in serum estradiol concentrations higher than those noted in normal males but lower than those reported in normal females[1,3]. To screen for CAIS in prepubertal females with inguinal hernia, some clinicians advise karyotyping or biopsy of the testes within the hernial sac, while others advise measuring vaginal length[1,2]. While USG may be done for screening, sometimes diagnosis is missed, like in our case, so MRI is done to visualize internal female organs. In a resourceful setting, whole-exome sequencing (WES) is one of the most valuable tools for the detection of CAIS along with its mutations[5,6]. Genetic counseling is also needed to detect undiagnosed cases in family members.

As soon as the diagnosis is made, appropriate counseling is done about the patient's diagnosis and its consequences. The patient is reared as female, so knowing about her real gender as male and that she is going to be infertile is always devastating. After proper counseling, gonadectomy can be generally performed after puberty to allow a normal growth spurt and due to the increased risk of gonadal malignancy of 14% (range 0–22%) in adults with CAIS[12]. All gonadectomized people are required to take hormone replacement therapy. The development of secondary sexual traits and sufficient bone mass in females are the intended outcomes[13,15]. At 9–11 years of age, estrogen can be administered in low doses (one-fourth the adult dose), with this dosage being titrated every 6 months. It will take roughly two years for feminization to be complete. Alternative methods for replacing estrogen include transdermal or oral estrogen. The starting dose of 17β-estradiol is 0.25 mg/day, with the dose increasing every 6 months, taking the development of the breast into account. A regular dose (1–2 mg/day of 17β-estradiol continuously) can be introduced once breast growth is complete[2,16]. For affected patients who are phenotypic females, corrective plastic surgery with vaginal dilator therapy or vaginoplasty can be done[15]. After vaginal dilator or coital dilator therapy alone, 94–96% of patients can have satisfaction with their sexual life[17]. Diagnosing and managing CAIS correctly is crucial for the individual's well-being, ensuring appropriate medical care and ethical decision-making regarding gender identity. It also promotes greater societal understanding and acceptance of intersex variations.

Ethical considerations

The ethical considerations in managing CAIS revolve around respecting individuals' autonomy and well-being, encouraging sex identity exploration, and providing comprehensive care that addresses their physical and psychological needs while adhering to nondiscrimination and confidentiality principles. Ethical management of CAIS often requires a team-based approach, involving specialists in endocrinology, gynecology, genetics, psychology, and social work to provide comprehensive long-term care[11].

We report a case of complete androgen insensitivity in a 20-year-old female who presented to the emergency room with a history of pain in the bilateral inguinal region for 4 h and an inguinal hernia from childhood. USG was done, and the patient was suspected of bilateral inguinal hernia. While performing operation for hernia repair, bilateral abdominal testes were found. Then, after gynecology consultation and counseling, each testis was removed and sent for biopsy. Postoperative karyotyping was done, which showed a male genotype. Then the patient was discharged on hormone replacement therapy along with an appropriate psychiatric consultation.

Conclusion

To conclude, CIAS mostly presents in outpatient clinics, but sometimes it can present in emergencies with pain in the inguinal region, which can be frequently misdiagnosed as strangulated femoral hernia, like in our case. USG has low sensitivity, so MRI and karyotyping are used for a definitive diagnosis. Nevertheless, clinical judgment has paramount importance, and relying only on USG findings is often misleading. CAIS is managed by multidisciplinary teams like gynecologists, urologists, endocrinologists, and psychiatrists.

Ethical approval

Not applicable.

Consent

A written consent was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.S.: literature review, discussion writing, and discussion part; A.T.: presented the case; K.B.: editor of the article, case presentation writing, image collection, analysis, and revising of report; S.S.: editor of the article.

Conflicts of interest disclosure

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