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Bilateral inguinal masses or hernias in a female teenager with delayed menarche: Think of Complete Androgen Insensitivity Syndrome (CAIS), a case report

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ABSTRACT

INTRODUCTION: Complete Androgen Insensitivity Syndrome (CAIS) is a rare sexual development disorder with X-linked recessive inheritance. It is prevalent in 1:20400 to 1:99000 of female phenotypes, yet characterized by an XY genotype. Cases of CAIS usually present with primary amenorrhea together with unilateral/bilateral inguinal hernias.

CASE PRESENTATION: A previously healthy 19 year old sexually inactive girl presents to our clinics for delay in menarche and bilateral palpable inguinal masses 3 years ago. She has normal female habitus, tanner stage 3 and external female genetalia with sparse pubic hair. She has a family history of 2 aunts (mother side) having infertility with Bilateral inguinal hernias surgery. Hormonal tests showed male range testosterone levels. MRI showed bilateral inguinal masses with Mullerian structures agenesis and a misdiagnosis of Mayer-Rokitansky-Küster-Hauser syndrome (MRHKS) was interpreted. While karyotype showed XY genotype. She is then planned for bilateral orchiectomy. Final pathology of the 2 specimens taken showed testicular tissue correlating with CAIS.

DISCUSSION: CAIS patients presents with near normal female external genetalia, absence of Mullerian structures, taller status than regular females and testosterone levels equal or higher than male levels. Different imaging types together with karyotyping are crucial in diagnosing and differentiating CAIS from other entities such as MRHKS and Swyer syndrome. Treatment debates include prepubertal or postpubertal gonadectomy correlating with the age related malignancy rate and site of testis followed by Hormonal replacement therapy. CAIS management needs a multidisciplinary approach and decisions by the patient or his family sometimes.

CONCLUSION: CAIS must be suspected in any case of young females with bilateral inguinal hernias as in our case, and precise diagnostics tests such as MRI and Karyotyping must be done followed by biopsy or excision for diagnosis and then adequate treatment. Hormonal therapy must be continued after gonadectomy that is best to be postpubertal.

1. Introduction

Formerly known as "testicular feminization syndrome", CAIS is a rare sexual development disorder with X-linked recessive inheritance involving an androgen receptor mutation [1,2]. It is prevalent in 1:20400 to 1:99000 of female phenotypes, yet characterized by an XY genotype [3,4]. It is defined by completely indifferent androgen receptors in the whole body to the androgenic stimulations [2]. There are several types of androgen receptors mutations that led to sexual and phenotypic differentiation failure; Partial AIS, mild AIS and CAIS with varying degrees of androgen hormone resistance and masculinization [5]. Cases of CAIS usually present with primary amenorrhea together with unilateral/bilateral inguinal hernias [6].

Here we present a case of an adolescent XY genotype with female habitus having a palpable bilateral inguinal masses and delay in menarche, reported in Line with SCARE criteria [7].

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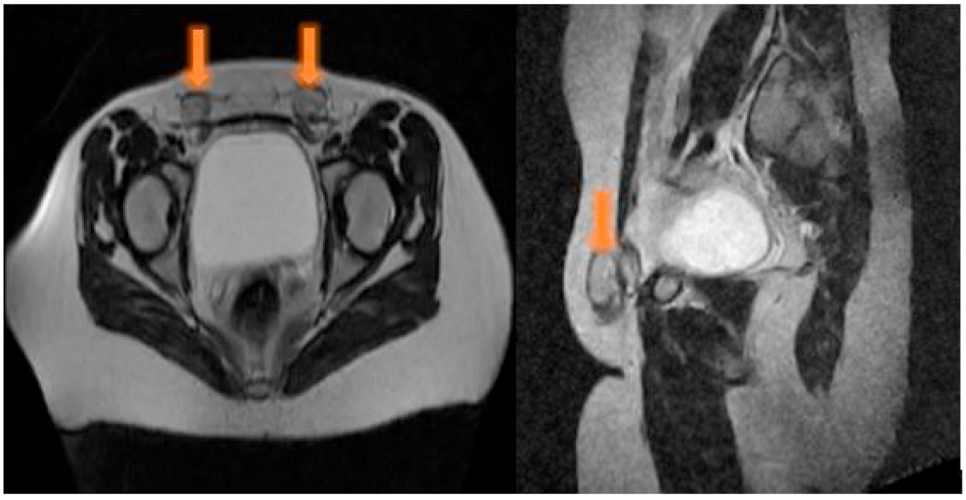


Fig. 1. MRI ABDOMEN PELVIS t2 weighted showing the testicles annotated by orange arrow (axial and sagittal cuts) and complete absence of uterus, ovaries, cervix and internal vagina.

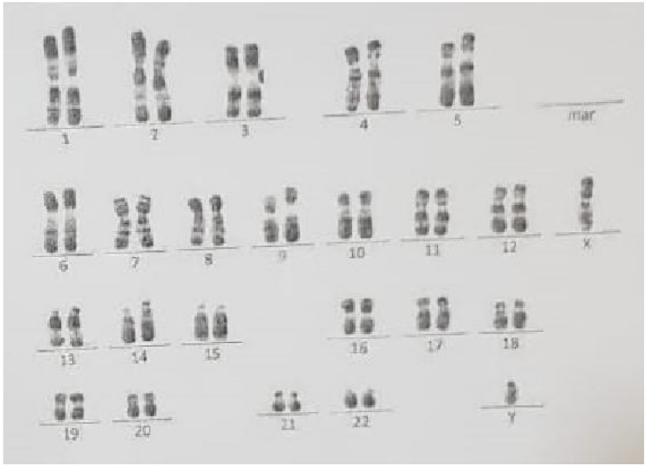


Fig. 2. Karyotyping showing an XY genotype.

2. Case description

This is a case of 19 year old sexually inactive girl, with a previously healthy medical history and a surgical history of a right eye unknown cyst surgery. She visited a gynecologist at the out clinics department of our hospital center for delay in menarche and bilateral palpable inguinal masses since she was 16 years old.

As a physical examination, she has normal female habitus and voice, normal intelligence, overweight BMI 27.2, well nourished, Tanner stage 3 breasts, normal female external genitalia and sparse pubic and axillary hair. Her abdominal exam showed no scars, non-distended, and palpable bilateral inguinal masses (around 3 cm) mildly tender presumed to be inguinal hernias. In the review of systems, she stated a history of intermittent dry eyes managed by artificial tear drops from time to time. Looking at her family history, she stated her 2 aunts (sisters of mother) having infertility and primary amenorrhea and had undergone inguinal surgeries bilaterally. Hormonal tests and MRI were ordered, and a general surgeon was consulted for inguinal masses/hernias assessment.

Hormonal tests are summarized in Table 1 showing male range free and total testosterone and elevated DHEAS.

MRI showed congenital agenesis of the uterus and vagina, bilateral inguinal masses 3 cm at external inguinal ring, short vaginal length 2.5 cm which is blind ended and a diagnosis of MRHKS (Fig. 1) was interpreted.

Table 1
Hormonal tests and normal ranges (M: Men, W: Women).

Tests	Results	Normal values
FSH	6.5	M: 1.5–12.4 mLU/mL W: Follicular phase: 2.9–12.5 mlU/mL Luteal phase: 1.5–7.7 mlU/mL Menopause: 17–130 mlU/mL
LH	23.27	M: 1.1–8.6 mLU/mL W: Follicular phase: 1.5–12 mlU/mL Luteal phase: 0.2–11 mlU/mL Menopause: 7.7–58 mlU/mL
Estradiol	28.18	M: <62 pg/mL W: Follicular phase: 24–400 pg/mL Luteal phase: 29–300 pg/mL Menopause: <58 pg/mL
Progesterone	0.1	M: <0.3 pg/mL W: Follicular phase: 0.3–1.1 pg/mL Luteal phase: 1.8–21 pg/mL Menopause: <0.3 pg/mL
17-OH progesterone	1.1	M: 0.54–2.3 ng/mL W: Follicular phase: 0.2–1.3 ng/mL Luteal phase: 1–4.5 ng/mL Menopause: 0.2–0.9 ng/mL
Prolactin	10.78	1.3–25 ng/mL
Testosterone	**4.48***	M: 2.41–8.27 ng/mL W: 0.15–0.7 ng/mL
Free Testosterone	**0.08***	M: 0.05–0.224 ng/mL W: 0.001–0.007 ng/mL
Dehydro-epiandrosterone sulfate (DHEAS)	**510.7***	M: 100–300 µg/mL W: Follicular phase: 70–320 µg/mL
TSH	1.27	0.27–5 µUI/mL

Karyotyping was done showing an XY karyotype (Fig. 2).

Echo pelvis was done in order to watch for an increase in size of the pre-seen inguinal masses, showed 3 oval solid formations measuring around 4 cm, 1.4 cm and 0.8 cm in both inguinal regions, uterus and ovaries weren't detected (Fig. 3).

She was planned for bilateral orchiectomy after she got a well preoperative clearance.

On the day of surgery, she was kept NPO, Scrubbing and draping done in usual manner, bilateral 5 cm inguinal incisions done by the primary surgeon, dissection through layers reaching the external oblique Apo neurosis and finding the inguinal mass situated at the external inguinal ring, its outer capsule was dissected until 2 whitish masses were encountered, excised and sent to pathology for analysis. External ring was repaired by absorbable Vicryl zero interrupted sutures, then closure layer by layer and dressing (Fig. 4A–D).

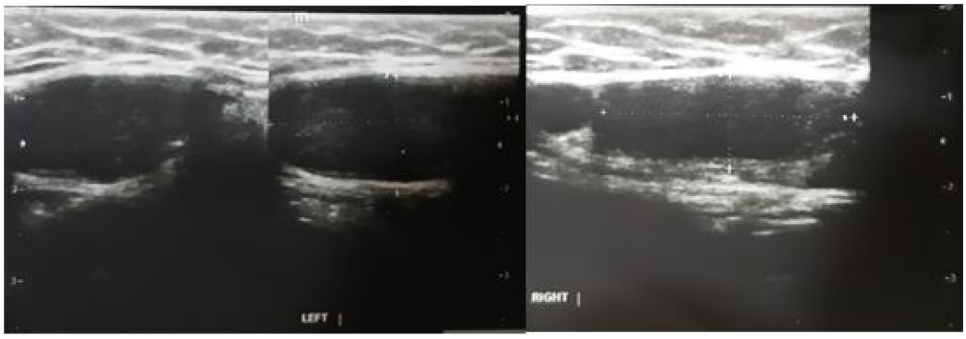
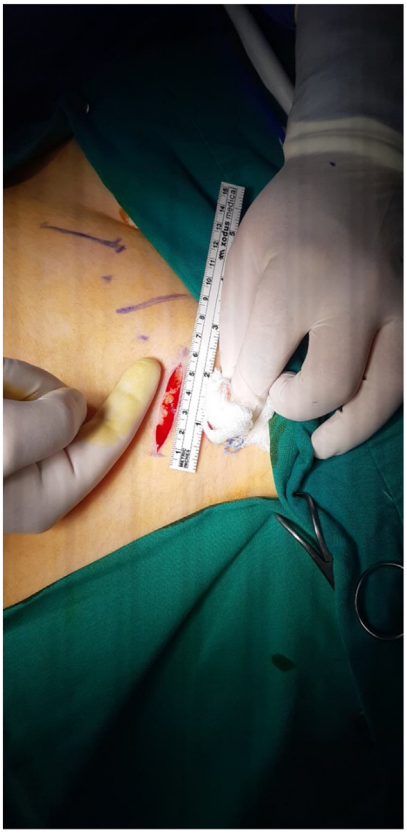
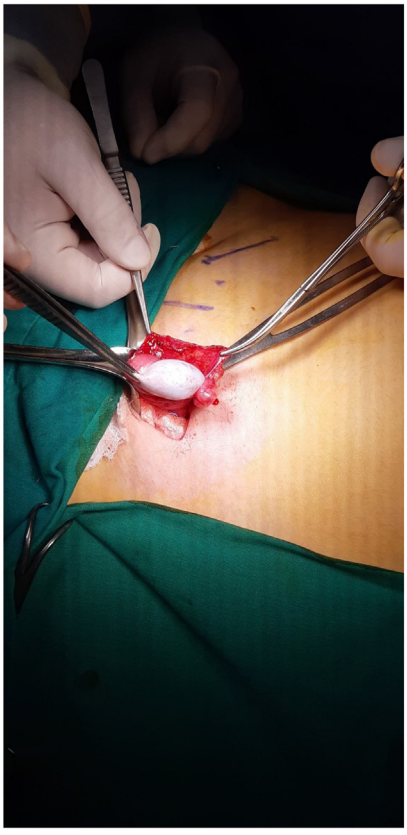


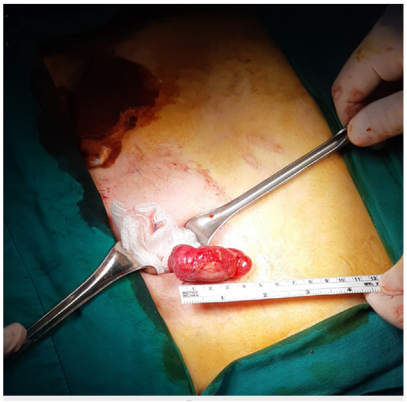
Fig. 3. Ultrasound pelvis showing bilateral inguinal solid masses.



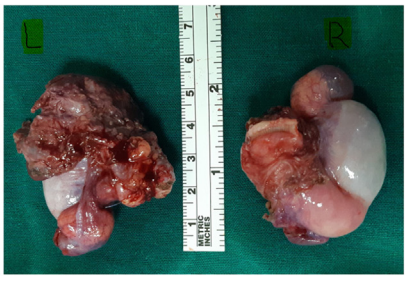
A 5cm Incision



B Right Testis



C Left Testis



D Specimens

Fig. 4. A 5 cm Incision; B Right Testis; C Left Testis; D Specimens.

Total operative time was 1 h and 15 min, minimal blood loss noted, patient was discharged on day 1 post the procedure, then followed up in 10 days having a clean and healing wound. Pathology result came after several weeks showing testicular specimen with definite diagnosis of CAIS.

3. Discussion

CAIS is a rare Sexual differentiation disorder in an XY-genotype individual defined by an inherited or sporadic major mutation in the AR rendering it completely insensitive to the androgenic stimuli hence failure of Wolfian ducts to differentiate into epididymis, seminal vesicles and vas deferens. The role of Mullerian Inhibitory Factor (MIH) that is released by the testicles due to the presence of y-chromosome is preserved and it prevents the development of females' internal genital organs [5]. Clinically, Individuals are characterized by: 1) possessing a near normal female external genetalia where the vagina may vary from being a perineal dimple or a blind ended sac with normal vaginal length along with the absence of male secondary sexual characteristics and Mullerian structures [8], 2) having a higher height than regular females but still lesser than normal males, where their testosterone levels are above or equal to the normal males range, and 3) suffering from a low density of minerals in bones yet they don't have a higher risk of fractures, due to the lower levels of estrogens than else female populations but it can managed by estrogens hormonal replacement paired with Calcium and Vit D supplement [5,8].

Suspecting and screening for CAIS may be simple via an easy physical exam by having an inguinal hernia in a young female and evident short vaginal length, it is confirmed by doing a transabdominal US to mark the absence of ovaries, fallopian tubes and uterus [8], by karyotyping or by biopsy of the gonad [5]. Through being operator dependent, Abdominal US may fail in CAIS diagnosis that may be more delicate necessitating MR Imaging that is said to be 100% accurate in noting the absence of Mullerian structures, assessing the precise vaginal length, delineating the presence of testicles, detecting their correct site and size, and looking for heterogeneity in testicular tissue that may be suspicious for malignancy [5,8,9].

Besides the PAIS and MAIS, Swyer syndrome is one of the CAIS differentials that is identified by an XY genotype but no secretion of MIF by testicles, leading to the presence of Mullerian structures and the uterus become more evident and developed by hormonal therapy [6]. Furthermore, Mayer-Rokitansky-Kuster-Hauser syndrome is considered as one of the differential diagnosis list, it is illustrated as having a normal female external genetalia, normal ovaries and normal female karyotype, but aplastic uterus and upper vaginal part [8].

According to the level of testosterone affecting the testicular descent [4], the site of the testicles in patient with CAIS ranges from being intra-abdominal or pelvic (62–70%) [10] and rarely in inguinal/labial region bilaterally [5]. Some studies stated that the rate of malignant transformation, with seminoma being the most common malignant tumor in CAIS [2], is higher in abdominal sited testicles [4] due to earlier presentation of the inguinal/labial testis [2].

Furthermore, Gonadectomy is a controversial event in management of CAIS. There are two issues to take into consideration. First is when to do the surgery; most studies shows that orchiectomy surgery is preferable in the early adulthood or postpubertal phase so that the patient can benefit from the aromatization of testosterone into estrogens for his puberty phase [2], otherwise he will use hormonal replacement therapy earlier [5,11]. Second is why to do the gonadectomy; reports showed that pre-pubertal malignant transformation is rare (0.8%) [8] relatively to the post pubertal, and it increases with age reaching 33% at age of 55 years old [4,12]. Gonads may be biopsied either subcutaneously or laparoscopically in order to feel any malignancy and to prepare for future decisions that are required by the patients and their parents [5]. It is difficult to understand the surgical anatomy of inguinal hernias, but once the surgical exploration is performed, surgical repair is simple [13].

At last, CAIS is a heavy impact diagnosis on the patient and his family, it needs decisions for management to be held from both sides and deep perception of infertility so that they may need to adopt children if they wish to have ones, and necessitates interference of a multidisciplinary team: a psychologist, an endocrinologist, a general surgeon, a gynecologist, a urologist for possible vaginal reconstruction surgeries, and an ophthalmologist as the CAIS can lead to dry eyes and Meibomian gland disease as in our case [5,11,14].

This patient was diagnosed having CAIS after the final pathology result post resection, there was no signs of malignancy. Her family history encouraged the family and the attending physician to go for surgery and refrain from biopsy.

4. Conclusion

CAIS must be suspected in any case of young females with bilateral inguinal hernias, and precise diagnostics tests such as MRI and Karyotyping must be done sooner followed by prompt further to biopsy or to excise after adequate discussions with the patients and families wishes depending on the patient age. Hormonal therapy must be continued after gonadectomy that is best to do just after puberty, and follow up and management needs gathering ideas and efforts of several specialty physicians.

Patient perspective

The patient was sad for the diagnosis and its outcome on her fertility, but in contrast they were grateful for the proper diagnosis which was failed to reach with her aunts.

Declaration of Competing Interest

The authors report no declarations of interest.

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Ethical approval

The study type is exempt from ethical approval.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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

Author contribution

Writing the paper, Study Concept: Houssam Khodor Abtar, Jad J Terro, Etienne El-Helou.

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Supervision: Houssam Khodor Abtar.

Registration of research studies

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Guarantor

Dr Houssam Khodor Abtar.

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