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Imaging characteristics of androgen insensitivity syndrome

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ABSTRACT

Androgen insensitivity syndrome (AIS), also known as testicular feminization, is a genetic disorder which leads to lack of response to androgens caused by a defect in the androgen receptor. It is relatively uncommon and is usually diagnosed through clinical symptoms, laboratory findings, physical exam, radiological imaging, and genetic analysis. Our case is a middle-aged woman with complete AIS and demonstrates the importance of the various imaging modalities that are implemented in initially diagnosing and assisting in surgical management.

1. Introduction

Androgen insensitivity syndrome (AIS), also known as *testicular feminization*, is a genetic disorder which leads to a partial or complete lack of response to androgens caused by a defect in the androgen receptor [1]. It is relatively uncommon and is usually diagnosed through the combination of clinical symptoms, laboratory findings, physical exam, radiological imaging, and genetic analysis. We present a case of a middle-aged woman with complete AIS in order to demonstrate the importance of the various imaging modalities that are implemented in initially diagnosing and assisting in surgical management. We discuss the role of imaging in AIS along with the relevant literature review.

2. History

A 49-year-old woman with a past medical history of amenorrhea presented to the emergency department with right groin pain. The patient was born in Guatemala and reportedly had ambiguous genitalia as a child. Upon further questioning, she reported having abdominal surgery as a child for resection of an enlarged clitoris and removal of testes but was then lost to follow-up. She reported having a small, but slowly enlarging mass in her right groin with associated right buttock and right upper thigh pain. Physical examination was significant for a small bulge in the right groin with a positive cough impulse. Labs revealed abnormally elevated testosterone levels with normal 5-dihydrotestosterone levels. Imaging was performed, including ultrasound of the pelvis and computed tomography (CT) of the abdomen/pelvis, followed by MRI of the abdomen and pelvis and a nuclear medicine testicular scan. Further workup included genetic chromosome analysis.

3. Findings

CT of the abdomen and pelvis demonstrated an ovoid-enhancing soft tissue mass in the right groin just above the superficial inguinal ring (Fig. 1a), best appreciated on the coronal projection (Fig. 1b). This mass was contiguous with the ipsilateral round ligament (vs. spermatic cord). There were no uterus and ovaries visualized in the expected normal location in the pelvis. These findings were concerning for an undescended testis or ovary, given the patient's history of ambiguous genitalia. Other differential diagnoses included an enlarged lymph node or an occult neoplasm.

Gray-scale ultrasound of the pelvis showed no uterus and ovaries in the pelvis. There was a tubular hypo-echoic structure near the right inguinal canal. Doppler flow imaging revealed minimal vascularity in the tubular structure (arrow in Fig. 2).

A testicular scan was also performed using Tc-99 m pertechnetate and demonstrated no uptake in the expected region of the scrotum on either side during dynamic and static phases (Fig. 3-b). There was a focus of faint radiotracer uptake over the right iliac vessel (arrow in Fig. 3b), which may correspond to the lesion seen on cross-sectional imaging.

MRI demonstrated a 2×7-cm solid, soft tissue mass adjacent to the right inguinal canal (Fig. 4a–d). The mass was hyperintense to the surrounding musculature on fat-suppressed T2 (Fig. 4a) and isointense on precontrast T1 (Fig. 4b). Following contrast injection, the mass showed mild enhancement at 20 s (Fig. 4c) and relatively homogenous, avid enhancement at 3 min (Fig. 4d). The differential diagnoses included undescended testis, enlarged lymph node, or a testicular neoplasm if

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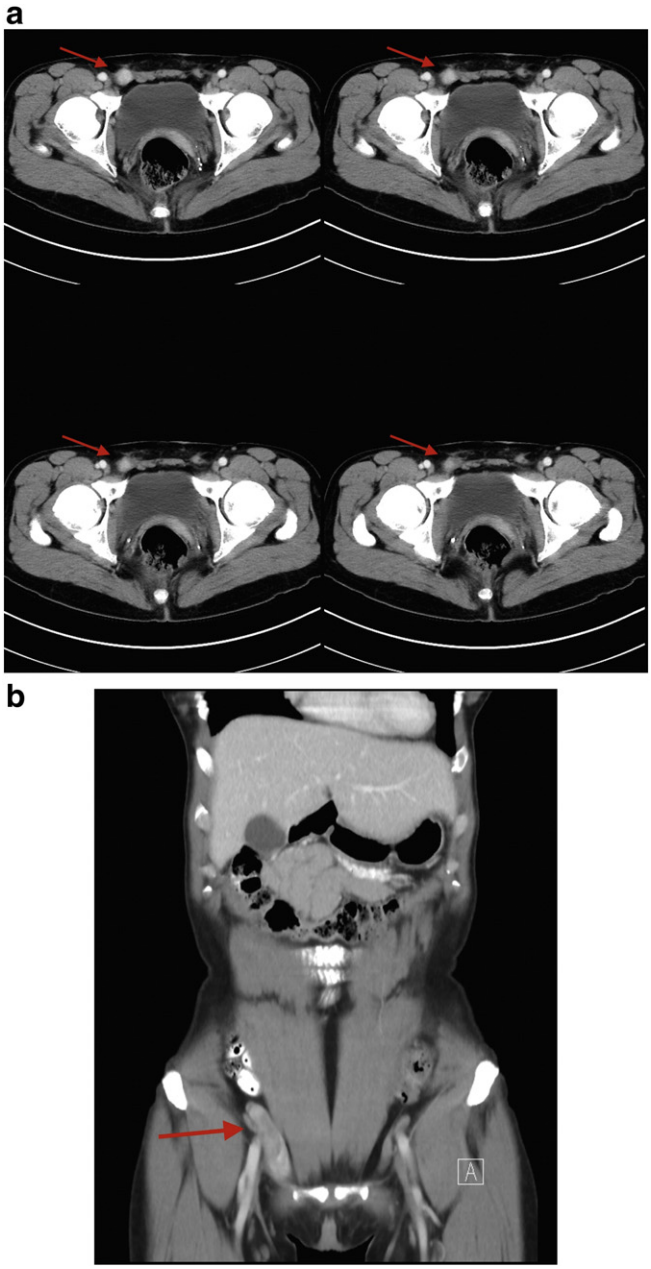

Fig. 1. (a & b) Forty-nine-year-old woman with right groin pain. Axial CT images demonstrate an ovoid enhancing soft tissue mass above the superficial inguinal ring (Fig. 1a), best appreciated on the coronal projection (Fig. 1b).

there was an incomplete resection of the previously resected undescended testis.

She underwent a right inguinal canal exploration with orchiectomy and repair of inguinal hernia. Pathology revealed testicular atrophy with Sertoli cell tubules and diffuse Leydig cell hyperplasia, consistent with testicular feminization and benign Leydig cell tumor. Genetic chromosomal analysis was remarkable for a 46 XY phenotypic female with a 2.3-Mb deletion in chromosome 9q21.11.

4. Discussion

AIS is a relatively uncommon disorder, with the prevalence estimated to be between 1 in 20,400 and 1 in 99,100 [2]. It is caused by mutations in the androgen receptor gene. AIS is divided into two variants, complete androgen insensitivity syndrome (CAIS) and partial androgen insensitivity syndrome (PAIS), depending on the absence or presence of virilization [3]. In the complete form, there are no functional androgen receptors, and therefore, the patient develops external female genitalia and secondary sexual characteristics. Because there are Sertoli cells in the testes secreting Mullerian inhibiting factor, there is regression of the internal female genital tract structures [4]. PAIS differs in that there is some functional androgen receptor activity, leading to partially masculinized genital tract structures. The typical phenotype in PAIS is a micropenis, severe hypospadias, and a bifid scrotum, which may contain gonads [2]. In either complete or partial AIS, the psychosexual gender of the patient is wholly female [4].

Clinically, patients present with different initial symptoms based on the age of presentation. In infancy, CAIS presents most commonly as an inguinal hernia or labial swelling [2]. Adolescent patients tend to present with amenorrhea and a palpable mass or hernia [3]. In all cases, the testes are incompletely descended and can be located in the abdomen, inguinal canal, or in the sublabial soft tissues [5]. It is well known that undescended tests are at a higher risk of undergoing malignant degeneration. The risk is low in prepubertal individuals, with an incidence of 0.18% [6]. Whereas in adults, the risk of malignancy is greatly increased and is estimated to be around 14% (ranging from 0 to 22%) [7].

The differential diagnosis in patients with ambiguous genitalia and undescended testis is cryptorchidism, germ cell tumors, and lymphadenopathy. Rarely, infection can have a similar appearance. In cases of CAIS, Mayer–Rokitansky–Kuster–Hauser (MRKH) syndrome is a possibility. MRKH is a congenital anomaly, which arises during embryogenesis with arrested development of the paramesonephric ducts during Week 7 of development [4]. There are two forms of MRKH, typical and atypical [5]. In both instances, there are normal female genitalia with absence of the uterus and upper vagina [5]. In typical MRKH, there are also normal ovaries and fallopian tubes, whereas atypical MRKH includes abnormalities of the ovaries, fallopian tubes, and kidneys [5].

In most instances, ultrasound is the first imaging modality ordered to locate the suspected undescended testes [1]. It has the advantage of being readily accessible at all hospitals and clinics, while providing excellent information regarding anatomy and blood flow in the area of interest. In addition, there is no radiation exposure, making it ideal in the pediatric population [8]. While it is sensitive in localizing testicular tissue, its efficacy is decreased when the testes are situated above the inguinal ring [9].

The most common imaging modalities implemented are cross-sectional imaging — CT and MRI. They both have the advantage of providing excellent anatomic detail, which is of utmost importance when used for preoperative planning. In addition, with the use of intravenous contrast, they can greatly help to narrow down the differential in certain cases. The drawbacks of CT are the use of ionizing radiation, while MRI is particularly sensitive to patient motion and sedation is often required in the pediatric population [8]. Radionuclide imaging can also be used to assess for scrotal disease. However, it is not as commonly used due to the poor anatomic detail, exposure to ionizing radiation, and need for sedatives in children [8].

AIS is a relatively rare disorder but should be in the differential in all patients with ambiguous genitalia. It is crucial that patients with AIS be followed up as there is a risk for developing malignancy without surgical intervention. Imaging is a crucial element in patient care, with cross-sectional imaging being the most important for both initial diagnosis as well as preoperative planning and treatment.

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