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Diagnostic Challenges of an Extremely Large Testicular Adrenal Rest Tumor - a Case Report

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Abstract

Background: Congenital adrenal hyperplasia (CAH) is an autosomal recessive genetic disorder characterized by elevated levels of adrenocorticotropic hormone (ACTH) and overproduction of adrenal sex steroids. It is speculated that the correlation between CAH and testicular adrenal rest tumors (TARTs) is caused through ACTH-triggered progression of aberrant adrenal cells in testes.

Case Presentation: Here, we present a case of a nine-year-old boy with bilateral testicular masses referred to Ghaem hospital (Mashhad, Iran), in the summer of 2019. Laboratory studies revealed elevated ACTH and 17-hydroxyprogesterone confirming the diagnosis of CAH. Radiologic assessment showed bilateral multiple heterogeneous masses that had replaced the normal testicular tissue.

Conclusions: Due to the rare nature of TARTs and their manifestations, many of these patients, like ours don't get prompt detection. It seems crucial for urologists and radiologists to be familiar with this condition as a benign differential diagnosis of bilateral testicular tumors.

Key Words: Congenital adrenal hyperplasia; Sex steroid hormones; Testicular adrenal rest tumors.

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1- INTRODUCTION

Congenital adrenal hyperplasia is a genetic disorder that impairs steroid synthesis in adrenal glands. It has several subtypes. The most prevalent subtype (~ 95%), among them, is caused by mutations in CYP21A2 which lead to deficiency of 21-hydroxylase (P450c21); subsequently, the cortisol production is blocked and corticotropin (ACTH) overstimulation leads to the increased biosynthesis of sex hormones(1).

Testicular adrenal rest tumors are benign testicular masses sensitive to the circulating level of ACTH and can often be suppressed by administering exogenous corticosteroids (2). Although literature regarding the etiology of TARTs is not conclusive, it is speculated to be caused by overgrowth of ectopic adrenal tissue descended with testes during embryogenesis (3, 4).

Recent studies investigating the frequency of TARTs in children and adolescents with CAH have consistently reported a positive correlation between age and frequency of TARTs, noticeably around puberty (2, 5-7). In addition, there has been reports of TARTs in adult males presenting either as testicular mass or infertility (8, 9). Here, we presented a patient with extremely large bilateral testicles.

2- CASE PRESENTATION

A nine-year old boy presented with testicular enlargement and precocious puberty to Ghaem hospital (Mashhad, Iran), during the summer of 2019.

Initially, he was diagnosed with TARTs at age three when due to sizable testicles and suspicion for malignancy underwent a testicular biopsy; after two separate radiologists, he was mistakenly diagnosed with the testicular malignancy, in the ultrasound. He was prescribed with Fludrocortisone 0.1 mg (Aburaihan/Iran), and Dexamethasone 0.75 mg (Iran Hormone/Iran) daily. This treatment had alleviated his pain but did not lead to a reduction in the size of testicles (**Fig. 1, A**).

On examination, he had lumpy testicles and excess hair growth. In addition, his stature was larger in comparison to the usual stature of children in his age: 132 centimeters height and 32 kilograms weight.

Tumor markers were investigated which resulted in insignificant levels of AFP, BHCG and LDH. Abnormal laboratory findings are illustrated in **Table 1**.

An ultrasound scan of scrotal sac revealed extremely large testicles with multiple large heterogeneous hypoechoic masses (**Fig. 1, B and C**). Doppler investigation demonstrated high vascularity of the masses (**Fig. 1, D**). An abdominal CT-scan was also performed; no sign of adrenal mass or hyperplasia was found. It incidentally showed large non-homogenous testicles with multiple masses demonstrating avid enhancement (**Fig. 2**).

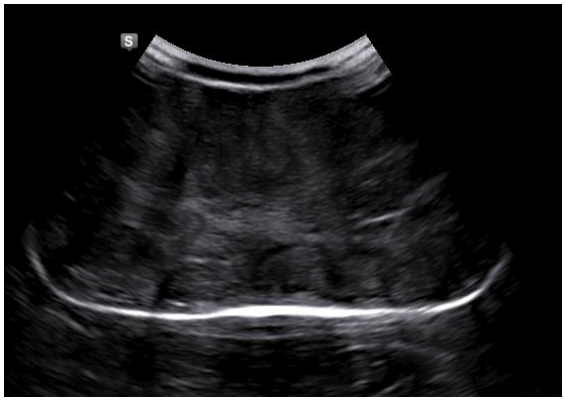
Magnetic Resonance Imaging (MRI) showed extremely large testicles with multiple bilateral masses that had replaced the normal texture of both testicles (**Fig. 3**). They were characterized by having well-defined irregular borders and being hypo-signal in T2 weighted images (**Fig. 3, A and B**). After contrast materials were administered, enhancement on T1 weighted axial images was evident (**Fig. 3, C and D**).

Written informed consent was obtained from parents for reporting this case.

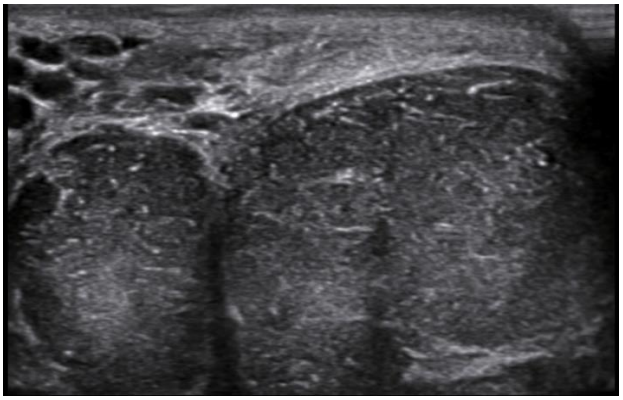
Table-1: Results of blood test

Biochemical test	Normal reference range	reported (at age3)
ACTH	7.2-63 pg/mL	>800 pg/mL (High)
17-Hydroxyprogesterone	0.5-2 ng/dL	2.4 ng/dL (High)
Testosterone	7-20 ng/dL	163 ng/dL (High)

Fig. 1: Grayscale ultrasound shows extremely large testicles (A) with multiple large heterogeneous masses in them (B and C). Color Doppler demonstrates the high vascularity of the masses (D)



(A)



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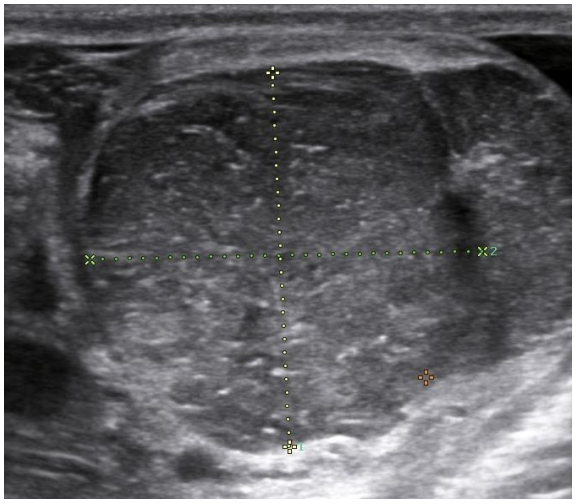
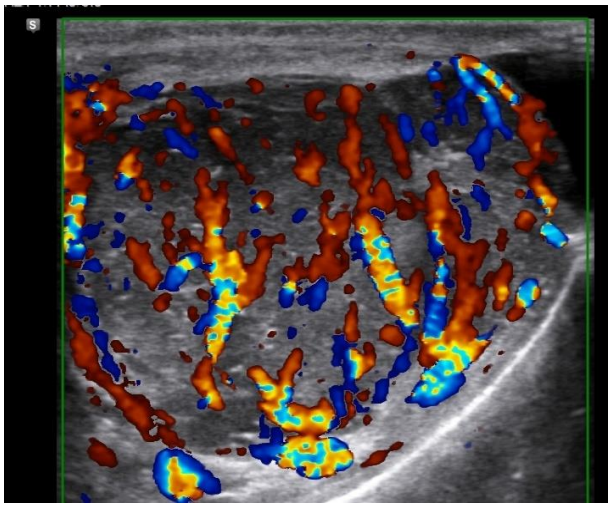
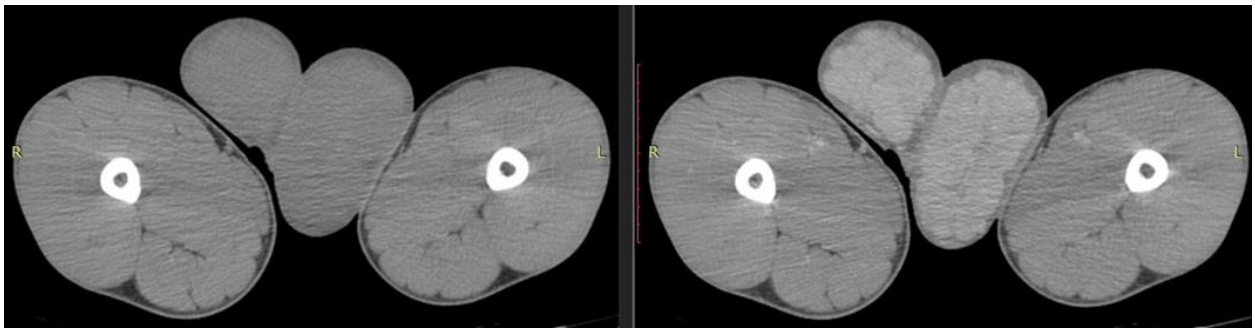


(C)



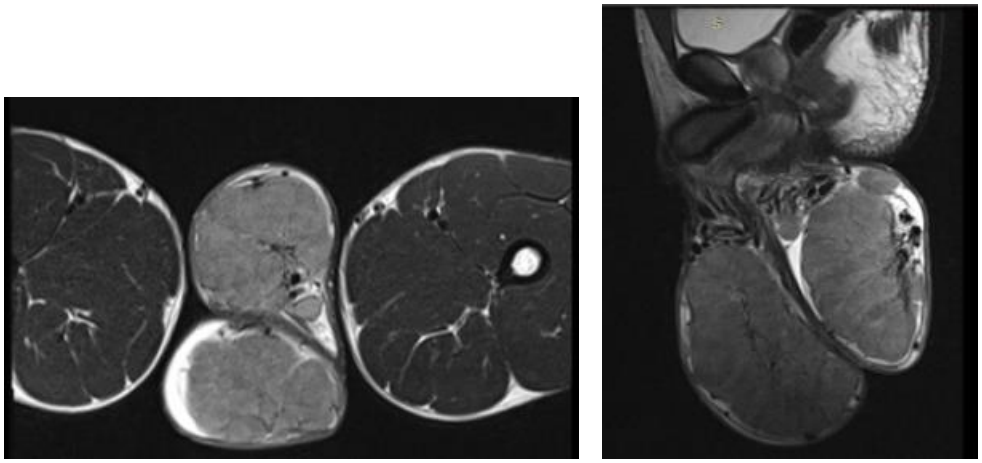
(D)

Fig. 2: Pre (A) and post (B) contrast CT scans show bilateral large testicles with multiple masses that enhances avidly after contrast administration

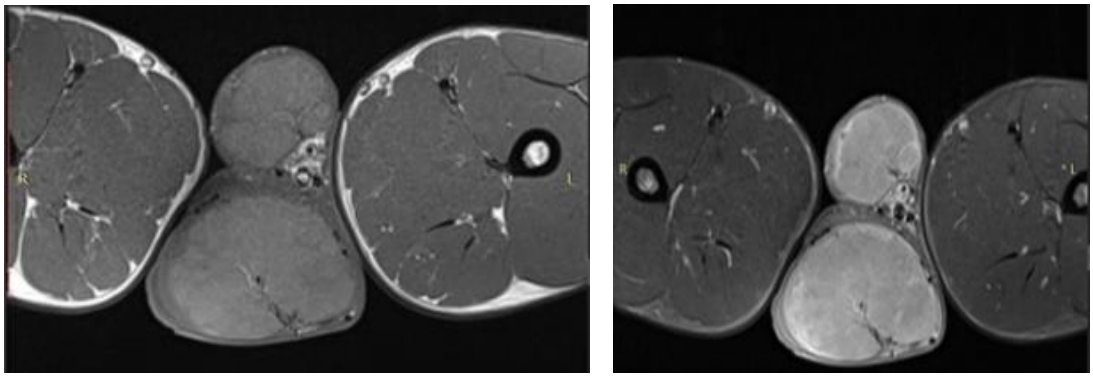


(A) (B)

Fig. 3: T2 W axial and sagittal MRI images (A and B) show extremely large testicles with multiple bilateral masses that replace the normal texture of both testicles.



(A) (B)



(C) (D)

The signal intensity of masses is lower than the signal of normal testis.
Pre(C) and post (D) contrast T1W axial images show enhancement of the masses

3- DISCUSSION

The recommended test for screening and diagnosis of CAH is measuring 17-hydroxyprogesterone. Currently more than 36 countries, not including Iran, screen neonates for CAH (1). Without screening, diagnosis of CAH in male patients with milder forms of the disease may not be established until adulthood when the patient is presented with testicular mass or infertility (9, 10). TARTs are mainly located at Rete testis and is thought to be induced by high levels of ACTH (3). Late diagnosis and treatment may lead to permanent damage of testes and infertility, probably due to longstanding obstruction of seminiferous tubules (11, 12).

Physical examination of tumors residing in rete testis is difficult, especially for the small ones (13). Thus, radiologic examination is necessary for early diagnosis. Both ultrasound and MR imaging has been used and reported to be valid. Yet lower cost and broader accessibility of ultrasound makes it preferable. Nuffer et al. have reviewed the sonographic findings of TARTs and discussed laterality, echogenicity, Doppler flow and location as most salient features. Existing evidence can summarize typical TART lesions as bilateral, hypoechoic masses, located adjacent to mediastinum testis without any calcification. Blood supply can vary significantly between lesions. They have also proposed a decision tree for differentiating TARTs from other testicular masses like germ cell tumors, sex cord stromal tumors, and lymphoma (14).

On MR, lesions are isointense on T1- and hypointense on T2-weighted images. It provides better resolution and thus the margins of lesions may be defined better; and can help with distinguishing a solitary large lobular lesion from multiple small, distinct lesions(15). Reports of CT scan images of TARTs are scarce, yet Li et al. have reported significantly enhanced masses similar to our finding (16).

As for the treatment, the conventional practice has been the augmentation of glucocorticoid therapy aiming to suppress ACTH level, cease and reverse tumor growth and improve testicular function. A classification has been proposed for TARTs constituting five stages from stage 1, a non-detectable presence of adrenal rests within the rete testis, to stage 5 irreversible damage of testicular parenchyma. Patients with tumors in stages 2 and 3 may probably benefit from intensifying the glucocorticoid therapy, whereas for patients in stage 4 testis sparing surgery has been proposed, and for patients in stage 5 a prior testicular biopsy to evaluate the presence of normal testicular parenchyma is suggested (3).

In our case, concerning extreme largeness of tumors, it seems improbable that glucocorticoid therapy may lead to significant effects. Yet as the patient is still a child, ethical consideration is in favor of a conservative approach preserving the small chance of fertility.

4- CONCLUSION

This report discusses a very rare manifestation (excessively large testicular tumors) of an infrequent etiology for testicular neoplasms (TARTs), and highlights the pitfalls in assessment and treatment of these patients. Due to the rare nature of adrenal rest tumor and its manifestations, many of these patients, like ours, may be subjected to unnecessary or inconclusive tests. Therefore, it seems crucial for urologists and radiologists to consider it as a benign differential diagnosis of bilateral testicular tumors, and by using radiologic investigation prevent unnecessary interventional procedures like biopsy or orchiectomy.

5- ABBREVIATIONS

ACTH: Adrenocorticotropic Hormone

TARTs: Testicular Adrenal Rest Tumors

CAH: Congenital Adrenal Hyperplasia

AFP: Alpha Fetoprotein

BHCG: Beta Human Chorionic Gonadotropin

LDH: Lactate Dehydrogenase

US: Ultrasonography

CT-scan: Computed Topography scan

MRI: Magnetic Resonance Imaging

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