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Testicular Adrenal Rest Tumors in Congenital Adrenal Hyperplasia: A Case Report

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Abstract **Case Report**

Testicular Adrenal Rest Tumors (ISIT) are rare benign tumors observed in hormone adrénocorticotrope hypersecretion syndromes, particularly in congenital adrenal hyperplasia (CAH). They originate from aberrant adrenal cortical cells that descend with the testes during embryogenesis. It is the most common cause of infertility in adult men. The diagnosis relies on ultrasound and histological criteria, which help distinguish them from Leydig cell tumors. We report the case of bilateral TARTs in patient with CAH due to a 21-hydroxylase enzyme deficiency. The testicular ultrasound revealed multiple bilateral testicular nodular formations measuring 32**20**38.6 mm on the right and 40**24.4**54 mm on the left, compatible with the diagnosis of TARTs. The patient was treated with a suppressive glucocorticoids 1 mg of Dexamethasone daily. The early detection of TARTs in men with CAH enables timely interventions to preserve fertility before testicular function declines.

Keywords: Testicular Adrenal Rest Tumors (TARTs), Congenital Adrenal Hyperplasia (CAH), 21-hydroxylase deficiency, Infertility, Glucocorticoid treatment (Dexamethasone).

INTRODUCTION

Testicular Adrenal Rest Tumors (TARTs) are rarely observed in men with congenital adrenal hyperplasia (CAH). They are benign tumors originating from aberrant adrenal cortical cells that descend with the testes during embryogenesis [1]. CAH is a group of autosomal recessive diseases characterized by enzymatic defects leading to decreased cortisol and aldosterone levels. The absence of negative feedback from cortisol stimulates the pituitary gland to secrete excessive adrenocorticotropic hormone (ACTH), which in turn causes adrenal hyperplasia. More than 90% of cases of CAH are due to 21-hydroxylase enzyme deficiency. TARTs presents a differential diagnostic challenge with other malignant tumors, especially Leydig cell tumors. Although TARTs are benign, these tumors can compress the seminiferous tubules, leading to obstructive azoospermia and irreversible damage to the surrounding testicular tissue, consequently causing impair testosterone production and infertility. We report the case of an 7-year-old patient with CAH due to 21-hydroxylase deficiency who presented TARTs in both testes.

CASE PRESENTATION

A 7-year-old patient was referred for evaluation of early puberty. Clinical examination revealed an advanced growth pattern and Tanner stage G5P5. Additionally, a heterogeneous mass was detected in the left testicle. Bone age assessment indicated significant advancement at 17 years. Hormonal analysis showed cortisol and ACTH levels of 3.02 µg/dl and 365.0 ng/l, respectively. Gonadotropins (FSH and LH) were suppressed, whereas testosterone was markedly elevated at 9.74 ng/dl. Cytogenetic analysis confirmed a 46XY karyotype. Ultrasound identified an enlarged testicle and multiple nodular formations, measuring 32×20×38.6 mm on the right and 40×24.4×54 mm on the left, with a heterogeneous echostructure suggestive of adrenal testicular inclusions. A diagnosis of CAH complicated by precocious puberty and testicular adrenal inclusions was established. Initial treatment consisted of gradually increasing hydrocortisone to 40 mg/day, with monitoring of 17-hydroxyprogesterone (17OHP) levels, which reached 775.9 nmol/l. The patient was subsequently placed on dexamethasone at a dosage of 1 mg/day. No surgical intervention was indicated as the patient was asymptomatic. Follow-up was planned, including a control ultrasound.

DISSCUSSION

The pathophysiology of TARTs is related to the hypersecretion of ACTH. They are primarily found in patients with congenital adrenal hyperplasia (CAH) due to complete or partial 21-hydroxylase deficiency. They have also been described in other conditions such as Nelson's syndrome, Cushing's disease, Addison's disease and in deficiencies of 11-hydroxylase or 18-hydroxylase [1-3]. Manon Engels et al. reported that elevated ACTH levels cause hyperplasia of pluripotent cells present in TARTs [4]. This hypothesis is supported by the high concentration of ACTH receptors found in these tumors, as well as the higher prevalence of these tumors in classical forms of CAH compared to the non-classical form [4].

Ultrasound typically shows well-defined, hypo-echoic images, often multifocal, bilateral, and possibly confluent. In Color Doppler, they display regular vascular architecture. According to Manon Engels et al.'s study, 83% of TARTs were described as hypo-echoic, 7% as hypo-echoic with hyper-echoic foci, 6% as hyper-echoic, and 4% as isogenic [4]. MRI has not yet proven useful in characterizing TARTs, with its only advantage being better visualization of the tumor boundaries [5], which could guide a possible partial orchidectomy [6]. Most teams have abandoned the practice of biopsy due to the histological challenges in differentiating TARTs from Leydig cell tumors. Biopsy is reserved for nodules that continue to grow despite well-conducted treatment, and several options are available, some teams opting for biopsy other for orchidectomy initially [2].

Histologically, TARTs consists of hypertrophied steroidogenic adrenal cells grouped in clusters within normal testicular parenchyma [2]. They appear as large polygonal cells with abundant eosinophilic cytoplasm arranged in cords or strands separated by fibrous septa [7]. They are differentiated from Leydig cell tumors by two elements: the absence of Reinke crystals and the presence of seminiferous tubules. Reinke crystals are never found in TARTs, but they are present in 40% of Leydig cell tumors [7]. On the other hand, seminiferous tubules are always present in TARTs, whereas they are often absent in Leydig cell tumors [2]. Immunohistochemistry confirms the diagnosis with strong positivity for CD56, negative reactivity for androgen receptors, and strong focal or diffuse reactivity for synaptophysin [8].

The treatment involves intensifying glucocorticoid therapy to suppress ACTH. According to Li Ma *et al*., regression or disappearance of TARTs was observed in 64% of lesions after corticosteroid treatment [9]. However, D'Avila *et al*., reported that TARTs can remain stable, increase or decrease in size, or even regress under restraint treatment during sonographic follow-up. These size variations can be significant and may occur rapidly, in this study cohort, these changes were not correlated with short-term clinical control, as assessed by 17-hydroxyprogesterone levels [10]. The early diagnosis of testicular adrenal rest tumors (TARTs) in men with congenital adrenal hyperplasia (CAH) enables timely interventions to preserve fertility before significant testicular dysfunction occurs. Semen cryopreservation can be promptly offered to individuals at high risk of infertility, ensuring fertility preservation before testicular function deteriorates [11]. Regular scrotal ultrasound screening is essential for male patients with congenital adrenal hyperplasia (CAH) to prevent infertility. It is recommended that screening be conducted at least every two years in early childhood and annually during the peripubertal period, with continued monitoring into adulthood [12].

CONCLUSION

Testicular Adrenal Rest Tumors (TARTs) are benign tumors observed in young boys with CAH. Ultrasound helps guide the diagnosis, while biopsy is only indicated in cases of suspected malignancy. These tumors regress or stabilize under glucocorticoid replacement therapy. Ultrasound monitoring is crucial to detect the independent development of new nodules within otherwise stable TARTs. The discovery of these tumors also requires the assessment of infertility by performing a spermogram.

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