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A middle-aged man with hyperandrogenic state

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ABSTRACT

Hyperandrogenism secondary to testicular cancer typically arises in patients in whom Leydig cell hyperplasia or neoplasia can be identified. Additionally, benign and malignant adrenocortical tumors can also present with signs and symptoms of hyperandrogenism. We report a case of a 40-year-old gentleman who experienced several months of weight gain, worsening gynecomastia, and mood changes secondary to high testosterone and estradiol levels. Workup initially was negative for testicular malignancy and positive for a benign-appearing lesion in the adrenal gland. Despite adrenalectomy, symptoms continued to persist and ultimately a testicular cancer without Leydig cell involvement was identified.

1. Introduction

Testicular cancer is the most common solid malignancy in younger men.[1] Men commonly present with a painless testicular mass. In very rare cases, however, men can present with signs and symptoms of hyperandrogenism, such as weight gain, body odor chances, and libido changes. In these cases, typically Leydig cell tumors or Leydig cell hyperplasia are typically suspected.[1] In this article, we present a very rare case of a hyperandrogenic man who presented with hyperandrogenism and was ultimately diagnosed with a non-seminomatous germ cell tumor without evidence of Leydig cell cancer or hyperplasia.

2. Case presentation

A 40-year-old male sought consultation for persistent weight gain despite calorie control and adequate exercise, gynecomastia, body odor changes, chest hair growth, migraines, depression, and a general feeling of being unwell over a period of several months. His medical history was notable for hypertension, obesity, and obstructive sleep apnea. There was no family history of endocrine disease. On examination, he was noted to be overweight and had facial flushing. The remainder of the exam was unremarkable, and no palpable mass was identified on the initial scrotal exam. Serum total testosterone and estradiol were elevated to 1011 ng/dL and 107 pg/mL, respectively, with undetectable levels of luteinizing hormone and follicle stimulating hormone. β-Human chorionic gonadotropin (β-hCG) was elevated at 33 mIU/mL; α-fetoprotein and lactate dehydrogenase were normal.

Initial scrotal ultrasound was found to be normal. Computed tomography demonstrated a 1.1 cm right adrenal mass consistent with adenoma. Functional workup of the adenoma was negative, however given clinical suspicion for malignancy in the absence of a testicular mass on ultrasound, the patient underwent adrenalectomy without any subsequent improvements in his hormone levels or clinical symptoms. Pathology report of the right adrenal gland revealed no evidence of neoplasm or adenomatous changes. Given diagnostic uncertainty, a repeat testicular ultrasound was performed several months later at our institution. This revealed a subtle 1.5 cm, ill-defined, hypoechoic lesion within the superior pole of the right testis with internal vascular flow (Fig. 1). Patient underwent a radical inguinal orchiectomy. Surgical pathology reported a mixed non-seminomatous germ cell tumor without any evidence of Leydig cell hyperplasia. Follow up labs demonstrated negative tumor markers, normal sex hormone levels, and recovery of pituitary gonadotrophs. The patient's clinical symptoms resolved and he subsequently lost 14 pounds within several months following his operation.

3. Discussion

Symptomatic androgen excess resulting from a germ cell tumor without Leydig cell hyperplasia, such as the case described herein, is rare but has been previously described.[2] There are two previously published cases of androgen-producing germ cell tumors without Leydig cell involvement described in the literature.[2] Androgen-secreting testicular tumors primarily arise from Leydig cells and Sertoli cells,

Abbreviations: β-hCG, β-human chorionic gonadotropin.

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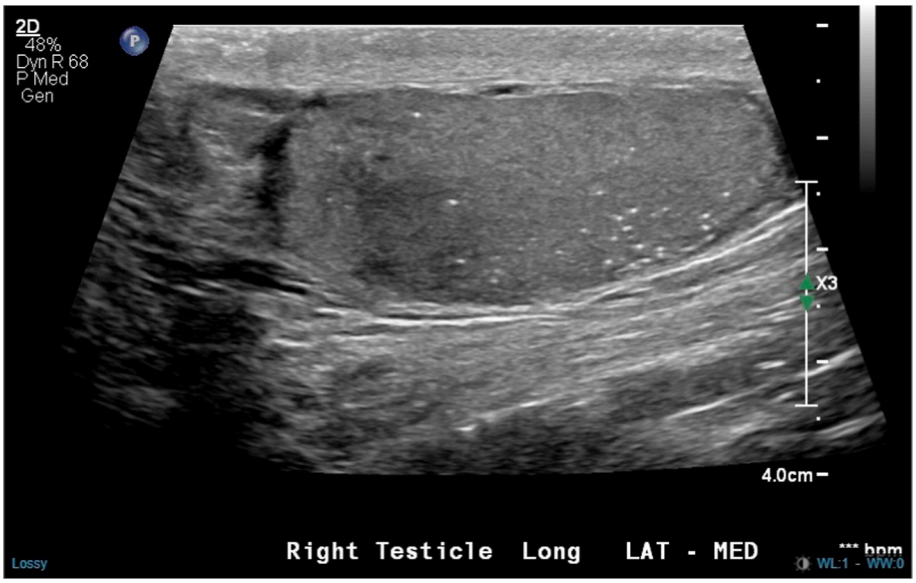

Fig. 1. Testicular Ultrasound (US). Longitudinal US of the right testicle demonstrates a lesion in the superior pole with indistinct borders.

the two hormone-producing stromal cells that support spermatogenesis. Leydig cells contain 17β-hydroxysteroid dehydrogenase and aromatase, enzymes important for testosterone production and estradiol formation, respectively. Leydig cell tumors produce large amounts of testosterone and estrogen and are the primary suspected diagnosis in individuals presenting with a testicular nodule and symptoms of hyperandrogenism, such as hair growth, body odor changes, and weight gain, among others.[3] This case is unusual and of clinical interest because primary germ cell tumors without stromal involvement do not commonly lead to signs and symptoms of hyperandrogenism.

Any solid nodule in the testis should be considered a germ cell tumor until proven otherwise. When testicular cancer is suspected, serum tumor markers should be drawn and a scrotal ultrasound with color Doppler evaluation should be performed prior to surgery.[1] Patients with lesions suspicious for malignancy should undergo radical inguinal orchiectomy. Sperm cryopreservation should be discussed prior to surgery, and postoperative follow up will differ based on clinical staging group, histology, and prognosis.[1] Partial orchiectomy is considered an alternative treatment option in highly selected men with small, well-demarcated testicular masses, particularly in whom there is a strong suspicion for a benign lesion, in whom tumor markers are normal, and in patients with single testicle to preserve fertility.[1] However, this option carries a higher risk of recurrence, for which additional adjuvant therapy (radiation therapy) may be required.[4] Radical orchiectomy was favored in this patient due to an elevation in serum β-hCG.

The other non-gonadal source of androgens is the adrenal gland, and both benign and malignant adrenal masses can lead to clinical androgen excess. This patient initially presented with high androgen state and negative testicular ultrasound. Radical adrenalectomy is indicated in cases of malignant tumors, functional adrenal tumors, and non-functional lesions with suspicion of malignancy.[5] Hence, despite the benign appearance of the adrenal mass, he underwent adrenalectomy with no improvements in his symptoms. This patent did have an elevated β-hCG that was noted early on in his workup. Given that androgen secreting adrenal lesions are not known to secrete β-hCG, this could have been an early sign to clinicians that the adrenal mass was not likely to be the source of androgen excess and could have prompted a higher clinical suspicion for testis mass.

4. Conclusion

Testicular cancers can rarely present with signs and symptoms of hyperandrogenism. Although Leydig cell involvement is often thought to be necessary for high circulatory androgen levels in testicular tumors, clinicians should be aware that, while uncommon, germ cell tumors can also produce symptomatic androgen excess.

Consent

Informed consent has been obtained from this patient for publication.

Author contributions

NMD and SVE conceived and supervised the research. RK wrote the original draft of the manuscript, and NMD and SVE edited and helped to finalize the manuscript. All authors contributed to the article and approved the submitted version.

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Declaration of competing interest

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