CASE REPORT

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A Very Rare Reason for Hyperandrogenism: Adrenal Tumor Case

Hiperandrojenizmin Çok Nadir Bir Nedeni: Adrenal Tümör Olgusu

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Abstract

Adrenal tumors are very rare causes of hyperandrogenism. Androgen-secreting adrenal tumors are usually malignant; however, benign tumors have also been described in women. Adrenocortical carcinoma is very rare with incidence of 1 2 million per year. The androgen secreting type of adrenocortical carcinoma can be presented with hirsutism, acne, alopecia and virilization symptoms such as cliteromegaly. This case was presented with hyperandrogenism and virilization symptoms and it was diagnosed as having a very rare cause, namely androgen secreting adrenal tumor. Because the symptoms are related to gynecological complaints such as menstrual irregularities and cliteromegaly, these patients would first need to apply to their gynecologists, who may play an important role in the early diagnoses of these rare diseases.

Keywords: Adrenal, adrenocortical carcinoma, adrenal tumor, andreogen excess, virilization

Öz

Adrenal tümörler hiperandrojenizmin çok nadir nedenleridir. Androjen salgılayan adrenal tümörler genellikle maligndirler, ancak kadınlarda benign tümörler de tanımlanmıştır. Adrenokortikal karsinom 1-2/milyon/yıl sıklığı ile çok nadirdir. Androjen salgılayan tipteki adrenokortikal karsinomlar hirsutizm, akne, alopesi ve kliteromegali gibi virilizasyon semptomları ile prezente olabilir. Bu olgu hiperandrojenizm ve virilizasyon bulguları ile başvurdu ve çok nadir bir neden olan androjen salgılayan adrenal tümör olarak teşhis edildi. Semptomlar adet düzensizliği ve klitoris büyüklüğü gibi jinekolojik şikayetlerle ilişkili olduğu için bu hastalar öncelikle jinekologlarına başvurabilirler. Jinekologlar bu nadir hastalıkların erken teşhisinde önemli bir rol oynayabilir.

Anahtar kelimeler: Adrenal, adrenal tümör, androjen fazlalığı, adrenokortikal karsinom, virilizasyon

Introduction

Hyperandrogenemia is an increased level of androgens in the blood and it can be presented by symptoms such as hirsutism, acne, androgenic alopecia, and virilization symptoms such as cliteromegaly. Polycystic ovarian syndrome (PCOS) is the main reason for hyperandrogenism in premenopausal women. The diagnosis of PCOS is made through the exclusion of other reasons for hyperandrogenism, such as non-classic congenital adrenal hyperplasia (NCCAH), hyperprolactinemia, Cushing's syndrome, and virilization tumors (1).

Androgen secreting tumors are very rare causes of hyperandrogenism originating from the adrenals. These tumors are generally malignant even though benign adrenal tumors also occur. In the studies published in the last 20 years, the rate of adrenocortical tumors was found to be 0.1% in patients investigated for clinical hyperandrogenemia (2). Adrenocortical carcinoma (ACC) is very rare, with incidences numbering 12 million per year (3). Approximately 60-80% of ACC is hormonally active. Of these, 30% are associated with glucocorticoids only, 20% with androgen-only hypersecretions, and less than 10% with hyperaldosteronism and feminization (4).

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17OH progesterone, androstenedione, DHEAS, and testosterone values occur at an increased level in most patients with ACC who secrete sex steroids (5). For all ACC cases, surgery with adrenalectomy is the treatment. Prognoses depend on the stage of the tumor and the feasibility of radical surgery (6).

Case Report

A 24 year old female patient presented with the complaint of not having had a menstrual period for eight months and an increase in hirsutism. She stated that her periods were regular prior to her complaints and she did not have any complaints of hirsutism. In ultrasonography, her uterus and ovaries were bilaterally normal. On examination, intense hirsutism (especially in the lower abdomen and chin) and cliteromegaly were present. Hormone test results of the patient showed hyperandrogenism and the other hormone results and tumor markers were normal (Table 1).

Hemogram, liver and kidney function blood test results were normal. Because the patient's androgens were very high, an upper abdominal ultrasound was requested to investigate possible adrenal tumor. A hyperechoic mass of 66×58 mm was observed in the right adrenal lodge. In a contrast-enhanced upper abdominal MRI, a tumoral lesion, which appeared to have pushed the right kidney inferiorly at the level of the right adrenal gland, had a size of 77×61 mm at its widest point (Figure 1). The lesion also appeared to have a well-contoured, distinctly heterogeneous internal structure, with local cystic necrotic areas being observed in T2 examinations. Intense heterogeneous contrast enhancements in the post-contrast examinations on T1 images (Figure 2) were observed. In the patient who was referred to the endocrinology department, catecholamine metabolites, adrenaline, noradrenaline, dopamine, metanephrine, normetanephrine, renin plasma activity, and aldosterone levels were measured in her 24hour urine. No pathological value was detected.

Whole body positron emission tomography (PET) was taken with the preliminary diagnosis of ACC. In the right adrenal gland, a mass lesion of 59×61×58 mm in size that is slightly heterogeneous increased the fluorodeoxyglucose (FDG) (12.45 mCi F18 FDG) uptake with smooth borders, with heterogeneous density being observed. Faintly circumscribed, locally hypodense, cystic necrotic foci is also observed. In this lesion, which was minimally hypermetabolic on PET examination, malignancies with low FDG affinity could not be excluded.

The patient underwent general surgery for a right adrenalectomy. Pathology results were evaluated as cortical adenomas. Focal necrosis was present with no significant capsular invasion. The patient's clear cell rate was less than 5%, and atypical mitosis was not observed. Her Weis score was reported as 3.

In the checks performed one month after the operation, androgen levels were found to be normal. Written informed consent was obtained from the patient.

Table 1. Hormone and tumor marker test results

Test	Result	Reference range
Beta HCG	0.1	0.15 IU/L
FSH	10.2	3.312.5 IU/L follicular phase
LH	4.36	2.412.6 IU/L follicular phase
Estradiol	22.73	26.7156 pg/mL follicular phase
Progesterone	4.11	0.21.5 ng/mL follicular phase
TSH	1.03	0.275.4 mU/L
Prolactin	35.1	4.7923.3 ng/mL
17OHprogesterone	13.2	0.150.7 ng/mL
Free testosterone	15	0.293.18 pg/mL
Total testosterone	4.69	0.0350.513 ng/mL
DHEAS	>1.000	148407 µg/dL
Cortisol	12.43	6.219.4 µg/dL
CA 199	7.5	033 U/mL
CEA	0.4	05 ng/mL non-smokers
CEA 125	14.4	035 U/mL

HCG: Human chorionic gonadotropin, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, TSH: Thyroid-stimulating hormone

Discussion

Hirsutism is usually a symptom of hyperandrogenism. The causes of hirsutism in 7080% of cases can be attributed to PCOS, 520% to idiopathic hirsutism, 4.2% to non-classical congenital adrenal hyperplasia and 0.2% of cases of hirsutism can be attributed to androgen-secreting tumors. In addition, Cushing's syndrome, acromegaly, hypothyroidism and rare incidences of hyperprolactinemia are also included in the differential diagnosis (7).

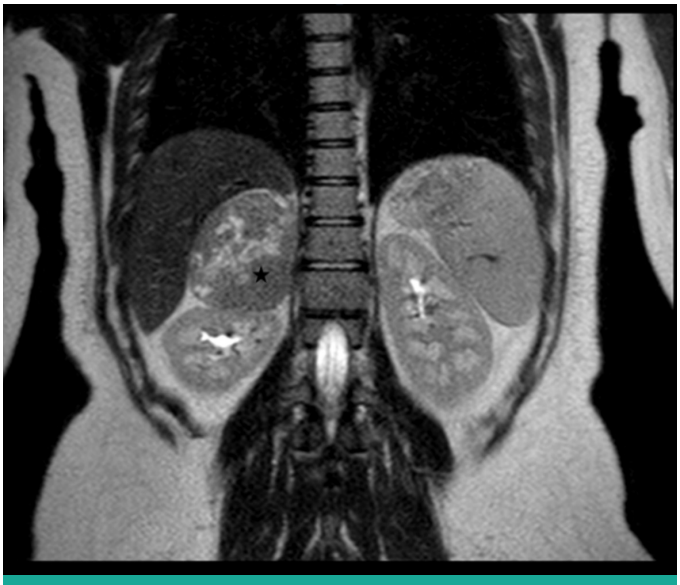

Figure 1. Adrenal tumor indicated by star. Tumor has well-contoured, distinctly heterogeneous internal structure. Local cystic necrotic areas were observed in T2 examinations

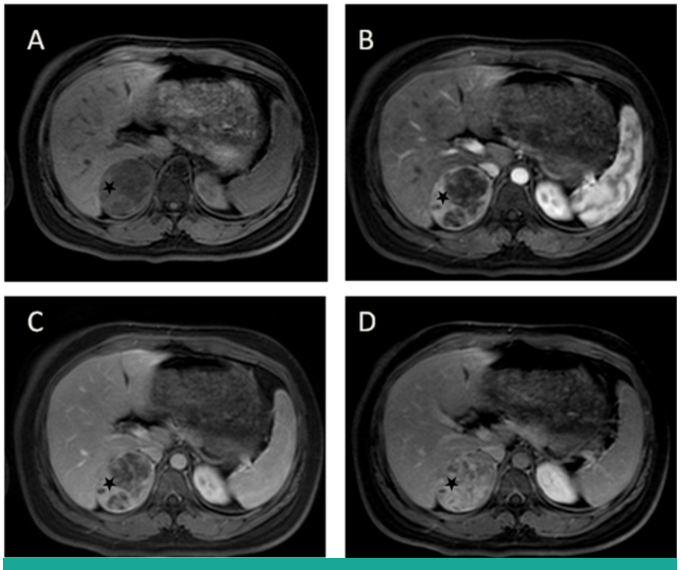

Figure 2. On pre contrast axial fat sat T1 A images, the lesion is hypointense, and on post contrast series (B-D), the lesion is observed to increase in contrast. The adrenal tumor is indicated by a star

If there is menstrual irregularity with hirsutism, there is usually an underlying endocrine disorder. Cases of hirsutism with a normal menstrual cycle are usually PCOS or idiopathic hirsutism and are unlikely to be serious.

Androgen-secreting adrenal tumors present with rapidly developing virilization, hirsutism, oligo-amenorrhea and androgenic alopecia (2).

Our case also presented with the complaints of hirsutism and secondary amenorrhea, which progressed rapidly in the last six months. In the examination, intense hirsutism and cliteromegaly were detected. The fact that the patient had regular menstrual cycles and did not have a complaint of hirsutism in addition to the presence of new virilization findings and the rapid exacerbation of her current complaints led us to conduct further research with the preliminary diagnosis of an androgen-secreting tumor.

Serum androgen levels were checked in patients presenting with hirsutism. In addition, if there is oligo-amenorrhea, pregnancy is excluded and ovarian and thyroid functions as well as prolactin levels are checked.

The most useful laboratory test in the evaluation of hirsutism is the total testosterone level. The upper limit of testosterone in women is between 0.45 and 0.6 ng/mL. Patients with mild androgen elevation, such as PCOS and NCCAH, have testosterone values above normal limits, but still below normal male levels. Women with testosterone values greater than three times the upper limit usually have evidence of virilization and androgen-secreting tumors, which should be investigated (8). In our patient, this value was 4.69, which is approximately ten times the upper limit.

DHEAS measurements are helpful in the investigation of adrenal hyperandrogenism. DHEAS may be elevated in both PCOS and adrenal tumors (9). In patients with a DHEAS value higher than 700 µg/dL, adrenal tumors should be excluded (7). In our patient, the DHEAS value was reported as >1.000.

17OHP measurements are important to rule out NC-CAH. In patients with 17OHP values of 210 ng/mL, the diagnosis of NC-CAH is made by performing the ACTH stimulation test (10). 17OHP is among the tests that should be investigated in ACC cases. In our case, a high value of 13.2 ng/mL was found.

It is recommended to investigate the symptoms and signs of pheochromocytoma, hyperaldosteronism, hyperandrogenism, and hypercortisolism in all patients with an adrenal mass (11). Laboratory studies were also

conducted in our patient. According to the results, it was determined that this adrenal mass secreted only androgens.

Among only androgen-secreting tumors, 75% were classified as adrenocortical cancer in histopathological examinations, while the others were adenomas (2).

Computed tomography and magnetic resonance imaging are important in diagnosis and surgical planning. FFDG PET is recommended for the evaluation of local recurrence and distant metastasis in ACC (5). In line with the clinical findings and hormonal changes in our patient, an adrenal tumor was suspected, and an adrenal mass was observed in the ultrasound. This was evaluated with magnetic resonance and FDG PET. No signs of metastasis or spread were detected.

In all ACC cases, surgical adrenalectomy is the treatment modality. Adjuvant Mitotane therapy is administered according to a post-operative evaluation and guidelines (6).

The Weiss score is very important in pathological evaluations. It includes nine criteria, such as proliferation, nuclear abnormality and tumor spread. A score of ≥3 is considered malignant. Tumors with a Weiss score of 23 may have ambiguous behavior (12). The Weiss score was evaluated as 3 in our patient.

Conclusion

Adrenal tumors are a very rare cause of hyperandrogenism with androgen-secreting tumors usually being malignant. Adrenocortical cancers are rare endocrine malignancies and have a poor prognosis. They can be detected incidentally or during investigations into the effects of the mass or hormonal disorders. 60% of ACCs are hormonally active and 20% of these are androgen-secreting tumors only. These patients may present in gynecology outpatient clinics with hirsutism, menstrual irregularity and virilization findings such as cliteromegaly. By making the differential diagnosis of hyperandrogenism, an early diagnosis can be made by a gynecologist. Early diagnoses positively affect the prognosis and surveillance of such patients. In addition, surgery is recommended for all androgen-secreting tumors.

Ethics

Informed Consent: Written informed consent was obtained from patient.

Peer-review: Internally and externally peer-reviewed.

Authorship Contributions

Concept: N.K.A., Design: N.K.A., Data Collection or Processing: N.K.A., G.G.P, Analysis or Interpretation: N.K.A., H.G., Drafting Manuscript: N.K.A., Critical Revisation of Manuscript: N.K.A., H.G., G.G.P., Final Approval and Accountability: N.K.A., H.G., G.G.P., Writing: N.K.A., H.G., G.G.P.

Conflict of Interest: No conflict of interest was declared by the authors.

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