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Case Report

A Unique Case of Isolated Dehydroepiandrosterone-Sulfate Secreting Adrenocortical Carcinoma: A Case Report with Review of the Literature

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Abstract

Objective: Our objective is to report a case of isolated dehydroepiandrosterone-sulfate (DHEA-S) secreting adrenocortical carcinoma.

Case Presentation: A 52-year-old African American woman with a medical history of asthma for more than 10 years presented with shortness of breath, chest tightness, and cough. A diagnosis of acute asthma exacerbation with pleuritic chest pain was made, and a CT scan of the chest revealed an incidental left adrenal mass. The patient denied hyperandrogenic symptoms like deepening of the voice, acne, and excessive hair growth. The physical examination was normal, and there was no clitoromegaly. The endocrine workup was significant for increased DHEA-S 766 mcg/dl (15-170 mcg/dl), and the repeat DHEA-S was 829 mcg/dl. All other adrenal hormone levels were within normal limits. The CT scan of the abdomen and pelvis without contrast revealed a 5.5 cm left adrenal mass with Hounsfield units of 23. An open left adrenalectomy was done. Histopathology was reported as marked and diffuse nuclear atypia, necrosis, and atypical mitotic figures. The tumor was strongly positive for inhibin, synaptophysin, and melan-A. The Ki-67 immunostain showed 20-25% positive staining.

Discussion: Adrenocortical carcinoma (ACC) is a rare adrenal cortex malignancy. Both size more than 4 cm and radiographic appearance are significant predictors of malignancy. An isolated DHEA-S secreting ACC patient may have a DHEA-S level more than 3 times the normal upper limit.

Conclusion: Isolated DHEA-S secreting adrenocortical carcinoma patients may present without hyperandrogenic features like hirsutism and virilization.

Abbreviations

DHEA: Dehydroepiandrosterone; DHEA-S: Dehydroepiandrosterone-sulfate; ACC: Adrenocortical Carcinoma; ACTH: Adrenocorticotropic Hormone; DHT: Dihydrotestosterone; CT: Computed Tomography; FSH: Follicle-Stimulating Hormone; LH: Luteinizing Hormone

Introduction

Adrenocortical carcinoma is a rare adrenal cortex malignancy. It presents in as few as 1-2 per million of the population in the United States [1]. It accounts for 0.2% of annual deaths in the United States [2]. The tumors which are functional in nature often present with a clinical picture of Cushing's syndrome or a mixed hormonal pat-

tern. A smaller subset of patients present with purely androgen hypersecretion, which is more common in women than men [3,4]. The most commonly affected age group is adults in their fourth and fifth decades of life. However, the distribution is bimodal, also presenting in childhood [2,5]. Patients with functioning tumors account for approximately 60%, while patients with nonfunctioning tumors account for 40% of cases presenting with mass effect [6].

Case Presentation

A 52-year-old African American woman with a medical history of type 2 diabetes, obesity, status post-Roux-en-Y gastric bypass, hypertension, and asthma for more than 10 years, presented with shortness of breath, chest tightness, and cough. A diagnosis of acute asthma exacerbation with pleuritic chest pain was made and a CT scan of the chest revealed an incidental left adrenal mass. The Patient denied hyperandrogenic symptoms like deepening of the voice, acne, excessive hair growth on the face, back, and chest. The Physical examination was normal, and there was no clitoromegaly. The endocrine workup was significant for an elevated DHEA-S level of 766 mcg/dl (15-170 mcg/dl), and the repeat DHEA-S was 829 mcg/dl. All other adrenal hormone levels are included below.

ACTH- 6 pg/ml (6-50); Androstenedione- 25 ng/dl (20-75); DHEA- 3 ng/ml (<6); Total Testosterone- 7 ng/dl (2-45); free Testosterone- 2.1 pg/ml (0.1-6.4); Estradiol (post-menopausal)- 16 pg/ml (<31); FSH (post-menopausal)- 78.3 IU/L (>30); LH- 22.5 IU/L (1.4-7.7); Aldosterone- 6 ng/dl (3-16); Plasma Renin Activity- 1.98 ng/ml/hr (0.25-5.82); 24 hour urinary: Free Cortisol- 43.8 mcg/24 hrs (4.0-50); Epinephrine- 3 mcg/24 hr (2-24) Norepinephrine- 47 mcg/24hr (15-100); Dopamine- 236 mcg/24hr (52-480); Metanephrines- 516 mcg/24hr (224-832).

All Adrenal hormone levels, except DHEA-S, were within normal limits. FSH and LH concentrations were appropriately elevated for the post-menopausal state. The CT scan of the abdomen and pelvis without contrast revealed a 5.5 cm left adrenal mass with Hounsfield units of 23.

The patient underwent open left adrenalectomy based on the size and imaging phenotype. The adrenal mass was well encapsulated, and the patient tolerated the procedure without complications.

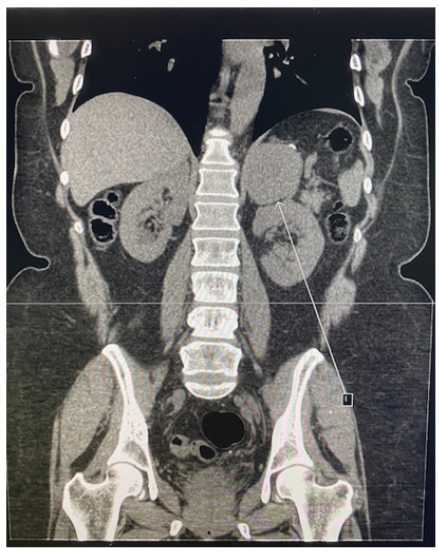

Figure 1: CT scan of abdomen and pelvis without contrast, coronal view revealed 5.5 cm left adrenal mass.

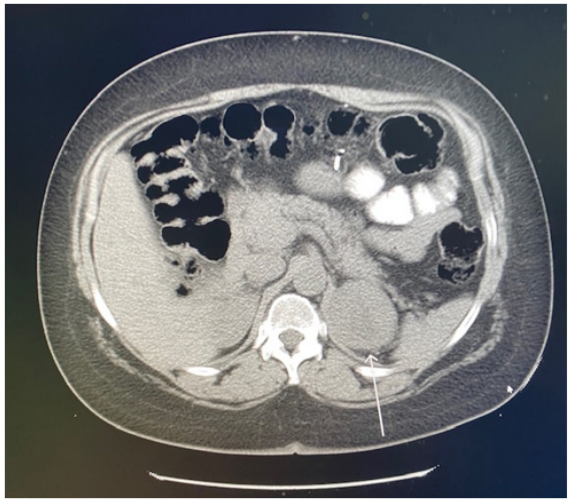

Figure 2: CT scan of abdomen and pelvis without contrast, transverse view revealed 5.5 cm left adrenal mass with Hounsfield units of 23.

Pathology revealed grossly, the specimen consisted of a 102-gram mass measuring 6.5 x 5.5 x 5.2 cm. Sectioning and inking revealed 6.6 x 5.2 x 5.1 cm tan-brown mass with focal areas of necrosis in the center of the lesion. Microscopically, hematoxylin and eosin staining showed marked and diffuse nuclear atypia, necrosis, and atypical mitotic figures. Immunohistochemical studies revealed that the tumor cells were strongly positive for inhibin, synaptophysin, and melan-A, which are the markers of adrenocortical carcinoma. It was weakly positive for S100 and negative for HMB-45. The Ki-67 immunostain showed approximately 20-25% positive staining. P53 staining showed less than 10% positive cells. The gross and immunohistochemical findings support the diagnosis of adrenocortical carcinoma.

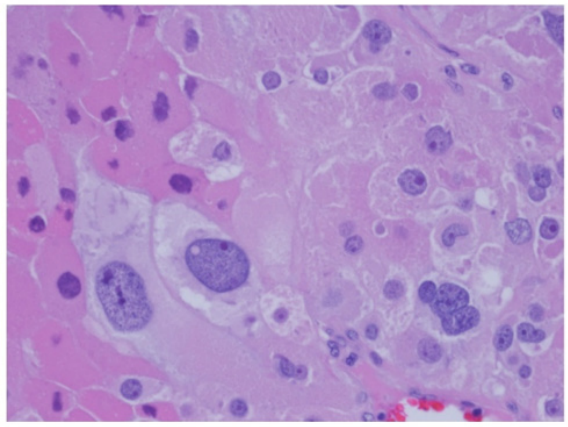

Figure 3: Left adrenal tumor H&E. The tumor showed marked nuclear pleomorphism with diffuse nuclear atypia.

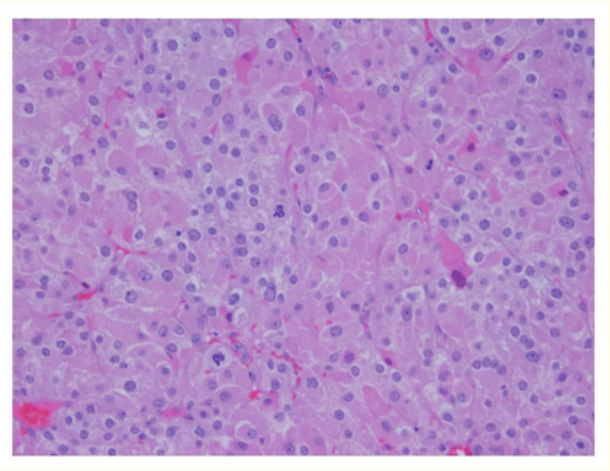

Figure 4: There was a high mitotic rate with atypical mitotic figures.

At one month post-adrenalectomy, serum DHEA-S concentration was less than 15 mcg/dl and remained normal. The patient was started on mitotane to prevent recurrence and was on treatment for 3 years and stopped. The patient is doing well and is being followed up with a yearly DHEA-S level that remained less than 15 mcg/dl without recurrence, and a CT scan of the abdomen reported as no recurrence.

Discussion

Our patient presented with symptoms of acute asthma exacerbation. A CT scan of the chest revealed an incidental 5.5 cm left adrenal mass and DHEA-S was more than 3 times the normal upper limit. All other adrenal hormone levels were within normal limits. The patient underwent a left adrenalectomy. Histopathology was reported as diffuse nuclear atypia and atypical mitotic figures. The tumor cells were strongly positive for inhibin, synaptophysin, and melan-A. So, a diagnosis of isolated DHEA-S secreting ACC was made.

ACC is found in approximately 4.7% of incidentally discovered adrenal masses, and 2.5% are metastatic upon presentation [7]. Both size and radiographic appearance are significant predictors of malignancy. Tumor size greater than 4 cm has reported a 90% sensitivity of predicting carcinoma but relatively low specificity of 24% [8]. According to the National Institute of Health consensus statement, tumors larger than 6 cm are highly suspicious for malignancy and should be removed [9]. Adrenocortical carcinoma has a relatively poor prognosis with an average 5-year mortality of 75-90% [10], and shows signs of relapse or metastasis in 70-85% [11].

DHEA-S, DHEA, and androstenedione may be considered prohormones, requiring conversion to testosterone or DHT to express androgenic effects such as hirsutism and virilization. DHEA-S level above 600 mcg/dl or more than 3 times the normal

upper limit of (15-170 mcg/dl) is diagnostic of adrenocortical carcinoma [12]. DHEA-S secreting adrenocortical carcinomas lose the ability to produce testosterone may be due to relative deficiency of 3-beta-hydroxysteroid dehydrogenase activity. So, their testosterone level will be normal, and patients may not present with hirsutism or virilization. However, adrenocortical adenomas produce excess testosterone, and patients present with androgenic effects.

In patients with ACC, tumor cells will be strongly positive for tumor markers such as inhibin, synaptophysin, and melan-A. ACC is treated with complete surgical resection in patients who are surgical candidates. Mitotane therapy is used for unresectable disease and disease recurrence. Radiation therapy is used for metastatic tumors.

Our patient presented with several predictive factors of malignant potential including tumor size and radiographic appearance, pathology of the mass showing high mitotic rate, and tumor necrosis has been related to a poor prognosis [13,14]. However, our patient is doing well and has been cured of ACC without recurrence through surgery and mitotane. The DHEA-S level remains less than 15 mcg/dl.

Conclusion

Isolated DHEA-S secreting adrenocortical carcinoma patients may present without hyperandrogenic features such as hirsutism and virilization.

Consent for Publication

Written informed consent to publish this case report and accompanying images has been obtained from the person described in the case.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Sources of Support

There are no sources of support.

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