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CASE REPORT II OPEN ACCESS

A Rare Case of Adrenocortical Carcinoma Presenting as Cushing's Syndrome

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Abstract

Background: We report a case of adrenocortical carcinoma presenting with atypical features of Cushing's syndrome in a young 20 year old female with duration of symptomatology of four months. It is imperative to consider malignancy as differential diagnosis for etiology of Cushing's syndrome with acute to subacute presentation.

Key words: Adrenocortical carcinoma, Cushing's syndrome, Hypercortisolism, Secondary hypertension.

Introduction

A 20 year old unmarried female, from far western region of Nepal, was referred from another center with the presenting complaints of generalized body swelling, fatigue and decreased appetite for last four months. She was apparently well till four months back when she gradually noticed puffiness of face and bilateral lower limb oedema. She gave history of retrosternal burning sensation and on off vomiting with feeds. There was no history of exertional dyspnea, decreased urine output or passage of frothy urine, no history of palpitations, headache, visual disturbances, diaphoresis, anxiety, tremulousness or lower limb weakness though she gave history of occasional lower limb cramps. The patient also gave history of recent appearance of acne over her face and upper back with increased facial hair. However, she denied any history of significant hair loss, change in voice or increased muscle bulk. Her menstrual cycles were regular. She didn't have significant past medical history or family history of any diseases.

On examination, the patient had body mass index of 20kg/m2. She had bilateral mild pitting oedema, was hypertensive with blood pressure of 150/100mmHg on bilateral arms and had regular pulse rate of 90 beats per minute. There was no buffalo hump or purplish abdominal striae. Skin was dry and appeared thinned out. Her face appeared puffy with grade 2 acne, facial hair was present, localized mainly over chin and preauricular area. Modified Ferriman Gallwey score was 15 suggestive of moderate hirsutism. Chest, cardiovascular and per abdominal examination was normal. Clitoromegaly was absent.

Routine blood investigations revealed hypokalemia with potassium levels in range of 2.8-3.2meq/L. Spot urine potassium was 36.7meq/L suggestive of urinary potassium loss. Serum magnesium, calcium and thyroid function test were normal. Chest Xray, electrocardiogram and echocardiography were normal. Upper gastrointestinal endoscopy was done in view of persistent symptoms of vomiting which came out to be normal.

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Contrast enhanced computed tomography of the abdomen (Figure 1) was done at the primary referring center that had revealed an infiltrating 8.5×7.5×7.5cm left suprarenal mass with areas of heterogenous enhancement and necrosis without separate visualization of left adrenal gland. Contralateral adrenal gland appeared normal. Biochemical investigations were then sent in line of an adrenal mass that are listed in Table 1.

Table 1: Biochemical test done in the patient after diagnosis of the adrenal mass.

Biochemical test	Value	Reference value
8am serum cortisol (test repeated)	>61.6µg/dl	5.2- 35µg/dl
8am serum cortisol (after 1mg overnight dexamethasone suppression test)	16µg/dl	< 1.8µg/dl
8am Adrenocorticotrophic hormone (ACTH)	13.3pg/ml	< 46pg/ml
24-hour urinary cortisol excretion	1980µg/day	58-403µg/day
Dihydroepiandrosterone sulphate (DHEAS)	386.5µg/dl	25.9-460.2µg/dl
Plasma free metanephrine	31.1pg/ml	<65pg/ml

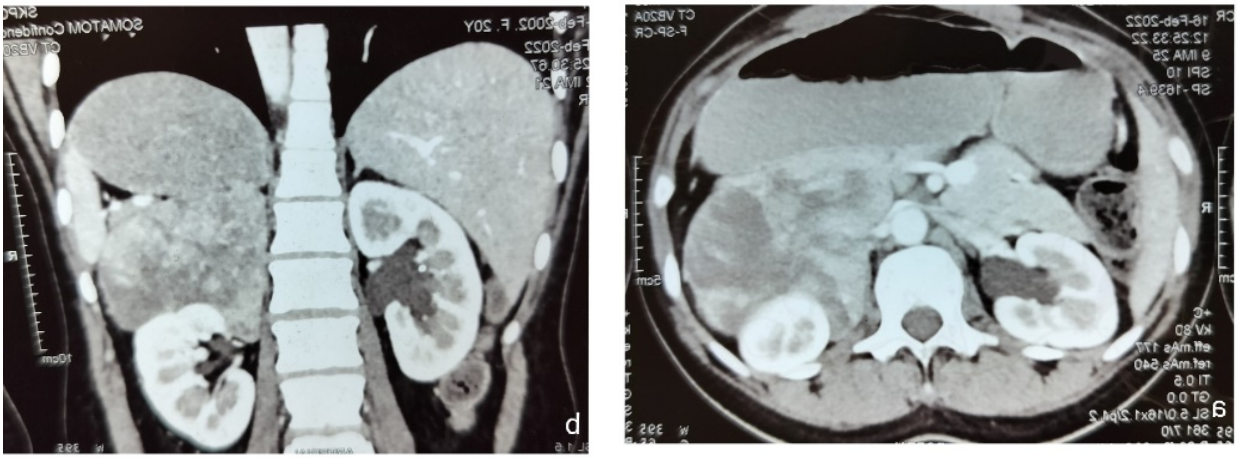

Figure 1: CECT abdomen of the patient. Panel (a) axial view. Panel (b) coronal view showing a necrotic heterogenous left suprarenal mass that had abutted superior pole of left kidney inferiorly and body and tail of pancreas superiorly, mass had extended into paraaortic region encasing left renal vessels medially and had extended into the splenic hilum laterally.

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Non-suppressed serum cortisol levels and high 24-hour urinary cortisol confirmed the diagnosis of Cushing's syndrome. In view of ACTH level being more than 5 pg/ml, dynamic contrast magnetic resonance imaging of the pituitary was done that revealed normal pituitary gland. The patient was provisionally diagnosed as a case of ACTH independent Cushing's syndrome due to left adrenal mass leading to secondary hypertension and hypokalemia. She was managed with antiemetics, iv fluids, antihypertensive (amlodipine), iv potassium supplements and planned for resection of the adrenal mass. Since surgery was already planned, aldosterone renin ratio was not sent considering financial constraints of the patient. However, patient delayed surgery for another two months due to personal/financial reasons despite counselling. The case was readmitted in urosurgery for resection of adrenal mass. Ultrasound abdomen was repeated prior to the planned procedure which revealed a 13.8×10.7×9.2cm left suprarenal mass with indistinct superior pole of left kidney. Size of mass had increased as compared to CECT done two months back.

Intraoperatively, a mass measuring 13×9cm was found in place of left adrenal gland which was abutting but not infiltrating the surrounding structures. Surgery was done with steroid coverage perioperatively in view of suppressed ACTH due to the cortisol secreting tumor. Postoperative period was uneventful. Potassium normalized and she was off antihypertensive medication. The patient was discharged on fifth postoperative day with daily steroid supplement equivalent to 7.5mg of cortilone. Histopathology (Figure 2) confirmed the specimen to be adrenal tissue composed of hyperchromatic, pleomorphic tumor cells with atypical mitosis and areas of necrosis (Weiss criteria of more than three) suggestive of adrenocortical malignancy. Customized immunohistochemistry (IHC) showed immunoreactivity for melanin A, patchy inhibin, calretinin, synaptophysin and negative for chromogranin suggestive of adrenocortical origin. IHC revealed disrupted reticular staining and high Ki67 of 35 to 40% that also favored the diagnosis of a malignant adrenocortical neoplasm.

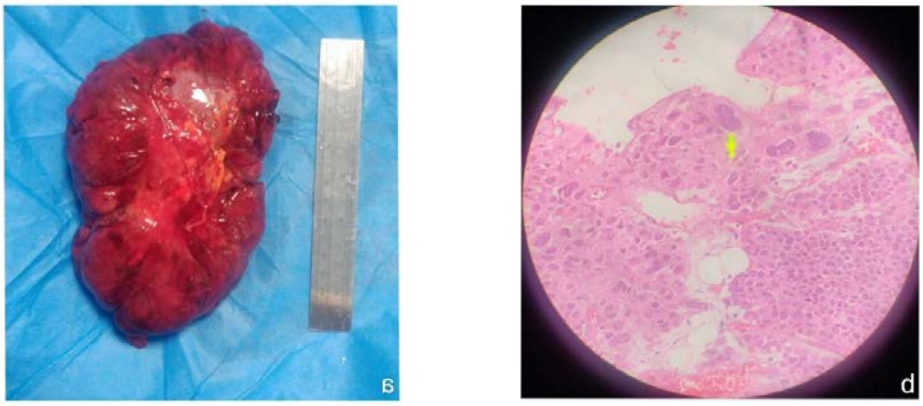

Figure 2: Panel (a) gross specimen of the resected tumor that showed reddish, friable tumor with yellowish areas towards the center. Panel (b) histologic slide showed intermediate to large sized tumor cells with marked pleomorphism, hyperchromatic nuclei and abundant eosinophilic cytoplasm. Multiple bizarre looking tumor cells are also seen (arrow). Mitotic figures (33/10HPF) and large areas of necrosis were seen. However, vascular and capsular invasion was not seen.

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Final diagnosis of the patient was made as a case of Cushing's syndrome secondary to left adrenocortical carcinoma (Stage II – T2N0M0 ENSAT classification). The patient came four weeks after the operative procedure for first follow up. She said that her clinical symptoms had dramatically improved with no episodes of vomiting, improved appetite and gradual resolution of body swelling and facial acne. Daily steroid supplement was continued and hypothalamopituitary axis was planned to be re-evaluated in a couple of weeks. The case was further referred to medical and radiation oncology for further management.

Discussion

Adrenocortical carcinoma (ACC) is a rare endocrine tumor with an incidence of 1-2 cases/million/ year.[1] It has bimodal age distribution affecting patients in 1st or 4th decade of life with females (59%) being more affected than males (41%).[2] 40 to 60% of ACCs are functional that secret endocrine hormones with hypercortisolism leading to Cushing's syndrome being the commonest presentation (50 to 70%).[3] Other endocrine manifestations may be androgen excess leading to virilization in females (20-30%), estrogen excess leading to feminization in males (5%) or mineralocorticoid excess leading to secondary hypertension (2-3%). 30 to 40% cases present with non-specific abdominal complaints whereas 10 to 15% cases are diagnosed during workup of an incidentaloma.[3] Cushing syndrome with short duration of symptoms without typical cushingoid features usually suggest malignant etiology.[4] Our case had symptomatology of only four months and typical findings of hypercortisolism like cushingoid striae, central obesity, buffalo hump were absent. Rather, the case presented sub acutely with hypokalemic secondary hypertension and abdominal complaints. There needs to be high degree of clinical suspicion and low threshold to assess cortisol axis and do relevant imaging to diagnose such cases. ACC is a tumor with grim prognosis with overall 5-year survival ranging from 16 to 38%.[5] Thus, the case needs aggressive follow up with regular imaging, screening for hormone secretion and oncological management.

Consent for publication

Consent for publication of the patient's data has been obtained from the patient herself

Competing interests

The authors declare that they have no competing interests.

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