Brief Communication

Adrenal incidentaloma: A case of pheochromocytoma with sub-clinical Cushing's syndrome

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ABSTRACT

Adrenal incidentalomas (AIs) are a cluster of different pathologies, but AIs with dual functional aspects are very rare. We report a case of AI with the evidence of both pheochromocytoma and sub-clinical Cushing's syndrome. A 42-year-old female patient presented with the history of abdominal pain. Abdominal computed tomography revealed right adrenal mass suggestive of pheochromocytoma. On endocrine evaluation, she admitted history of intermittent headache and palpitations for 4 years and was on treatment for hypertension and diabetes. There were no signs and symptoms suggestive of Cushing's syndrome. The laboratory data demonstrated 10 times raised 24-h urinary fractionated metanephrines with non-suppressible serum cortisol after 2-day low-dose dexamethasone suppression test. She underwent right-sided adrenalectomy with subsequent resolution of both pheochromocytoma and hypercortisolism. Patient was discharged in good clinical condition.

Key words: Adrenal incidentaloma, Cushing's syndrome, pheochromocytoma

Introduction

An adrenal incidentaloma (AI) is defined as an adrenal lesion that is discovered when a radiological study is performed for indications other than suspected adrenal disease. All patients with an AI should be evaluated for hypercortisolism, pheochromocytoma and (if hypertensive) hyperaldosteronism.[1] A combination of pheochromocytoma and Cushing's syndrome due to pathology in same adrenal gland is extremely rare. There are few case reports suggesting the different etiologies for this association, namely, pheochromocytoma secreting adrenocorticotropin hormone (ACTH)[2] or its precursors,[3] corticomedullary mixed tumors[4] and focal adrenocortical hyperplasia.[5]

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Here, we report a case of AI with the clinical and biochemical evidence of both pheochromocytoma and sub-clinical Cushing's syndrome.

Case Report

A 42-year-old female patient was admitted under Department of Gastroenterology with abdominal pain for 1 week. Physical examination was unremarkable. Routine biochemical evaluation including complete blood count, renal function tests (including serum electrolytes) and liver function tests were normal. Abdominal computed tomography (CT) revealed a right supra-renal mass (40 mm × 39 mm × 40 mm), which was heterogeneously enhancing with multiple cystic areas and a homogenously enhancing solid component within the anterior limb of the right adrenal gland. Left adrenal gland was normal [Figure 1]. As per the CT findings, right-sided adrenal adenoma with the possibility of pheochromocytoma was suspected.

On endocrine assessment, she had a complaint of intermittent palpitations and headache for 4 years. There

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was no history of fractures, muscle weakness, easy bruisability, menstrual irregularity and hirsutism. She was on treatment for hypertension and diabetes for 4 years with an adequate control. She was not on any exogenous steroids. On examination, her height was 155 cm, weight was 60 kg, body mass index was 24.97 kg/m^2, blood pressure was 130/80 mmHg and pulse rate was 82/min. There were no cushignoid features and hyperpigmentation of skin [Figure 2].

Her endocrine investigations revealed raised 24-h urinary metanephrines and nor-metanephrines with value of 3268 μg/24-h (normal range 52-341) and 4591 μg/24-h (normal range 88-444), respectively; raised 8 a.m. serum cortisol with value of 80 μg/dl (normal range 5-25); and normal plasma aldosterone level of 32.84 pg/ml (normal range 34-273). She had non-suppressible serum cortisol of 56.91 μg/dl and 25.86 μg/dl after 1 mg-overnight dexamethasone suppression test (DST) and 48 h - 2 mg/day DST, respectively.

After pre-operative management with alpha and beta blockers, she underwent laparoscopic right adrenalectomy. During the post-operative period, she was watched for hypotension and hypoglycemia, but the entire course remained uneventful. Repeat 8 a.m. serum cortisol on 1st post-operative day was 11.20 μg/dl and she was started on intravenous hydrocortisone 50 mg tid.

The excised mass measured 4 cm × 3.5 cm × 3 cm with weight of 12 g. The Pathologist concluded that the lesion was pheochromocytoma staining positive for chromogranin and synaptophysin with hyperplastic adrenal cortex [Figure 2].

Patient was discharged on oral prednisolone 5 mg bid. Two weeks later, she was re-evaluated and her 24-h urinary fractionated metanephrines came out to be in normal range and fasting 8 a.m. serum cortisol level was 10 μg/dl (prednisolone stopped 2-day prior to testing). Prednisolone dose was tapered slowly over 2-month and presently; she is not on any medication and doing well.

Discussion

This patient represents a rare case of AI with evidence of both pheochromocytoma and sub-clinical Cushing's syndrome. Patient's condition improved with adrenalectomy of involved side and there was immediate fall in serum cortisol levels reflecting that the same adrenal gland was the source of excess cortisol.

Pheochromocytoma may secrete various substances such as somatostatin, enkephalines, calcitonin, vasoactive intenstinal peptide, neuropeptide-Y, renin, ACTH, parathyroid hormone, erythropoietin, adrenomedullin and dihydroxyphenylalanine (DOPA) in addition to catecholamines.[2] There are about thirty cases reported in the literature of Cushing's syndrome due to ACTH-secreting

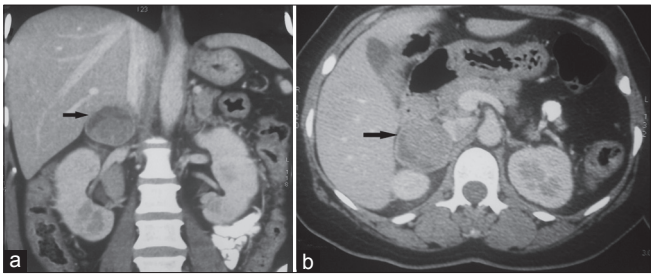

Figure 1: Computed tomography image of abdomen showing 4.0 cm × 3.9 cm × 4.0 cm heterogeneously enhancing right suprarenal mass (a) Coronal section and (b) Sagittal section

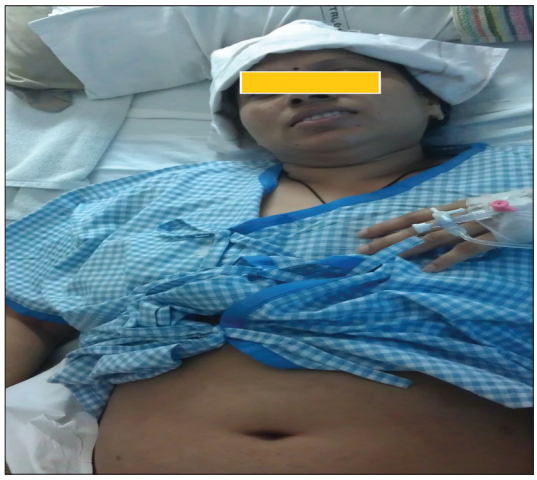

Figure 2: Absence of abdominal striae, moon facies and hyperpigmentation

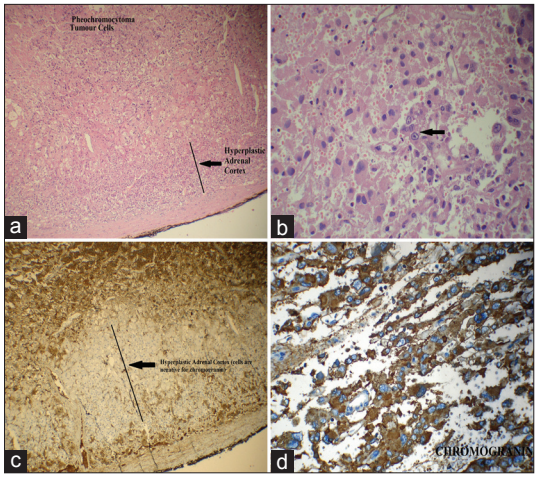

Figure 3: (a) H and E stain (low power) showing hyperplastic adrenal parenchyma with pheochromocytoma cells (b) High power view of tumor cells, arranged in nests, round to polygonal with scanty cytoplasm, vesicular nucleus and prominent nucleoli (c and d) Low and high power view of immunohistochemical staining showing tumor cells stained positive for chromogranin and absence of stain in the adrenal cortex

pheochromocytoma.[2] In some of these cases, there was pre-dominance of hyperpigmentation, hypokalemic alkalosis and evidence of contralateral adrenal gland hyperplasia on imaging, but these features were absent in our case.

Mixed tumors involving the cortical and medullary components of the adrenal gland are quite rare.[4] On histochemical staining, patient's tumor was not a corticomedullary mixed tumor, but a pure pheochromocytoma. There was prominent cortex showing hyperplasia on staining with no evidence of neoplastic changes [Figure 3].

In this case, we speculate that adrenocortical hyperplasia, which was possibly because of paracrine stimuli from the pheochromocytoma, was the source of autonomous cortisol production. Although, the possibility of ACTH-secreting pheochromocytoma cannot be completely ruled out as we do not have plasma ACTH levels. Furthermore, we have not observed until now such high levels of serum cortisol (8 a.m. value of 80 μg/dl), in cases of sub-clinical Cushing's syndrome without any cushignoid features.

The clinical aspects of this case suggest the importance of proper pre-operative recognition of the dual hormone secretion from adrenal mass, which, if goes unnoticed could lead to adrenal or hypertensive crisis in perioperative period. Hence, to conclude, we think all patients with adrenal mass should undergo evaluation based on the guidelines for management of AI.[1]

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