

Hypokalemia associated with a solitary pulmonary nodule

A case report

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Abstract

Background: Differential diagnosis of hypokalemia and adrenocorticotropic hormone (ACTH)-dependent Cushing's syndrome often presents challenging in endocrinology and requires careful clinical, biochemical, radiological, and pathological investigations. Hypokalemia is a common abnormality and systematic approach is required to avoid delays in diagnosis of important underlying causes.

Case Summary: A 49-year-old woman presented with moderate hypokalemia. Further evaluation showed hypercortisolism due to ectopic ACTH secretion.

Chest computed tomography (CT) revealed a peripheral solitary pulmonary nodule. Excision biopsy of the nodule showed carcinoid tumor. After excision biopsy, all of the patient's symptoms improved and electrolytes and ACTH levels also became normal.

Conclusion: Carcinoid tumors should be considered as a differential diagnosis in patients presenting with hypokalemia and ectopic ACTH syndrome. Carcinoid tumor often present as solitary pulmonary nodule and excision biopsy can be curative.

Abbreviations: 5-HIAA = 5-Hydroindoleacetic acid, ACTH = adrenocorticotropic hormone, BMI = body mass index, CT = computed tomography, MRI = magnetic resonance imaging, PET = positron emission tomography.

Keywords: ACTH syndrome, ectopic, carcinoid tumor, case report, cushing syndrome, hypokalemia, neuroendocrine tumors, solitary pulmonary nodule

1. Introduction

Hypokalemia is a common and often benign electrolyte abnormality. But hypokalemia associated with metabolic alkalosis and hypertension is highly suggestive for overproduction of adrenocorticotropic hormone (ACTH).

Cushing's syndrome due to cancer was first described in 1928 in a patient with small cell carcinoma of the lung.^[1] In the 1960s ACTH was shown to be produced by nonpituitary tumors.^[2] Various tumors can secrete ectopic ACTH that small cell lung carcinoma, carcinoid tumors (especially of the lungs, thymus, and gastrointestinal tract), islet cell tumors, pheochromocytoma, and medullary thyroid carcinomas are the most frequent causes.^[3]

We describe a case with carcinoid tumor in lung periphery producing ACTH with unusual biochemical and imaging finding.

2. Case presentation

A 49-year-old woman with past medical history of diabetes mellitus and hypertension was admitted in the General Internal Medicine ward with chief complaint of abdominal pain, constipation, and malaise for 5 days. She also had history of unexplained weight gain since 2 months ago and denied any history of taking exogenous steroid or herbal medications. Family history was unremarkable.

Physical examination showed a body mass index (BMI) of 32 kg/m², blood pressure equal to 140/90 mmHg (on anti-hypertensive medications), abdominal obesity, decreased bowel sounds, and proximal muscle weakness of upper and lower extremities.

Routine laboratory results revealed modest hypokalemia (2.7 mmol/L), hyperglycemia (245 mg/dL), and a metabolic alkalosis. Twenty four hours urine free cortisol excretion showed significant elevation (403 µgr/24 h—normal range: 10–100) and overnight (1 mg) dexamethasone suppression test revealed a failure to suppress cortisol level (63.7 µgr/dl ≈ 2.3 mmol/L). The serum ACTH level was elevated (165 pg/mL—normal range: 8.3–57.8 pg/mL). Cortisol level suppressed more than 50% with high dose dexamethasone test after 2 mg dexamethasone every 6 hour for 2 days (baseline cortisol level of 65 µgr/dL decreased to 18.5 µgr/dL).

Hypothalamopituitary axis magnetic resonance imaging (MRI) with and without contrast was normal. To find the possible source of ectopic ACTH secretion, the spiral chest and

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Informed Consent: The patient signed informed consent for publication of this case report and any associated images.

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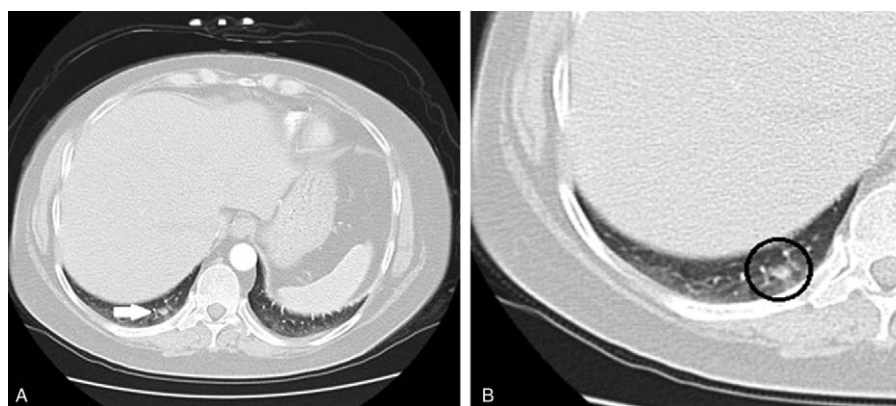


Figure 1. Chest computed tomography (CT) scan demonstrating a small 17 × 15 mm right lower-lobe peripheral pulmonary nodule in actual size (A, white arrow) and with magnification (B, black circle).

abdominal and pelvic computed tomography (CT) scan requested. The finding was only a 17 × 15 mm solitary peripheral pulmonary nodule in medial aspect of base of right lower lobe adjacent to the diaphragm (Fig. 1).

A 24-hour urine specimen for 5-HIAA (5-hydroxyindoleacetic acid) showed normal result (5 mg/day—normal range: 0–15 mg/day).

The functional imaging like positron emission tomography (PET) CT was not available. The pulmonary nodule was too small to biopsy. So, the patient underwent wedge resection with video-assisted thoracoscopic surgery as a diagnostic and possible therapeutic procedure. The nodule was excised with free margin. Histologic examination of the biopsy specimens showed carcinoid tumor.

One day after tumor resection the basal morning cortisol and plasma ACTH levels were significantly decreased to 8 μgr/dL (normal range: 5.5–28.7 μgr/dL) and 34.41 pg/mL (normal range: 8.3–57.8 pg/mL), respectively. Prednisolone was administered and tapered slowly in 3 months. Signs and symptoms of hypercortisolism (such as hypokalemia, proximal muscle weakness, skin darkening, and weight gain) recovered gradually.

Now after 6 months of operation she is well with no complaint, normal K levels, controlled blood sugar, normal suppression of serum cortisol level with low-dose dexamethasone suppression test, and normal chest CT.

3. Discussion

The causes of endogenous ACTH-dependent Cushing's syndrome are Cushing's disease (pituitary adenoma) in about 80% to 85% of cases and the remaining 15% to 20% are due to ectopic secretion by nonpituitary tumors.^[3,4] Hypokalemia is much more prevalent in Cushing's syndrome due to ectopic ACTH secretion than other causes of Cushing's syndrome. However, hypertension is similar between the 2 subgroups.^[5]

Typically, patients with ectopic ACTH tumors have high ACTH levels and cortisol levels fail to suppression with high doses of dexamethasone. However, 20% to 40% of patients with ectopic ACTH demonstrates cortisol suppression on high-dose dexamethasone.^[6] So after normal result of pituitary MRI, we evaluate the patient for ectopic source of ACTH. Axial imaging with thin-cut multislice CT of chest and abdomen or MRI of the

thorax has the highest detection rate for ectopic ACTH syndrome.^[3]

The most common causes of ectopic ACTH are small-cell carcinoma of the lung and bronchial carcinoid tumors.^[3] Bronchopulmonary carcinoid tumors are subclassified by the World Health Organization into typical and atypical carcinoids, according to histopathologic criteria: Typical carcinoids with slow growth that include 90% of lung carcinoids and atypical types grow a little faster with more likely spread to other organs and commonly located in periphery.^[7]

Small peripheral bronchial carcinoids can be missed easily on chest CT scans due to poor inspiratory effort, abdominal fat, and basal atelectasis.^[8] So using a modern multidetector high-resolution CT with 2.5 mm slices from lung apex to iliac crests is recommended.^[9]

With advances in medical and surgical treatments, survival rates for patients with ectopic ACTH have increased. Prognosis depends on the primary tumor histology. Patients with bronchial carcinoids have the best prognosis and considered as a low to moderate grade malignancy.^[9]

In conclusion, the differential diagnosis of ACTH-dependent Cushing's syndrome often presents challenging in endocrinology and requires careful clinical, biochemical, radiological, and pathological investigations. Carcinoid tumors as a treatable cause of hypokalemia and ectopic ACTH syndrome presented as a small peripheral solitary pulmonary nodule should not be missed in clinical practice.

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