ECTOPIC ADRENOCORTICOTROPIN PRODUCTION IN A PATIENT WITH LUNG CANCER- A CASE REPORT

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Abstract:

Various malignancies have been associated with ectopic adrenocorticotropin hormone production causing paraneoplastic Cushing's syndrome. The most common culprits are small cell lung carcinoma, carcinoid tumors and medullary cancer of the thyroid. Early suspicion and appropriate work up can help diagnose and manage the excessive adrenocorticoid state.

Keywords:

Ectopic, adrenocorticotropic, Cushings, small cell cancer, paraneoplastic, metabolic alkalosis

BACKGROUND:

Ectopic adrenocorticotropin (ACTH) production causing paraneoplastic Cushing's syndrome has been associated with various malignancies such as small cell lung carcinoma, carcinoid tumors and medullary carcinoma of thyroid. [1-4] We present a rare case of a 61year old male with paraneoplastic Cushing's syndrome in association with adenocarcinoma of the lung.

Case Presentation:

A sixty one year old male with past medical history significant for 40 pack per year tobacco abuse and alcoholism presented to our institution after sustaining an accidental fall. He had a previous admission at our institution for shortness of breath 3 months ago and at that time his work up led to a computed tomography (CT) scan of his chest, which revealed a 6.6 x 8.2 cm right lower lobe lung mass. He left the hospital against medical advice. On his present admission his blood pressure was elevated at 160/88 mm of mercury, heart rate 90 per minute, respiratory rate 20 per minute and oral temperature 37.1 degrees Celsius. Physical examination revealed an ill appearing male who appeared older than his stated age, with diminished breath sounds bilaterally and bibasilar crackles on chest auscultation. His heart sounds were regular with no murmurs or rubs heard. His abdomen was distended, non- tender, with positive fluid thrill. His upper extremities were remarkable for clubbing and had pitting edema up to thighs in his lower extremities.

His laboratory studies showed serum sodium 144 meq/L, serum potassium 2.4meq/L, serum chloride 92meq/L, serum bicarbonate >40meq/L, serum blood urea nitrogen 21 mg/dl, serum creatinine 0.67 mg/dl, serum glucose 143 mg/dl, serum calcium 8.3 mg/dl and serum magnesium 1.8 mg/dl. His coagulation profile was within normal limits. His blood work 3 months ago had revealed serum sodium of 136meq/L, serum potassium 4.1meq/L, serum chloride 106meq/L, serum bicarbonate 23meq/L,

serum blood urea nitrogen 8 mg/dl, serum creatinine 0.63 mg/dl and serum glucose 104 mg/dl. His urine was clear with pH 7.0, 3 + glucose and trace protein with random urinary chloride 99meq/L and urine potassium 44.4meq/L. His 24-hour urine free cortisol level was elevated at 8925.6mcg/24 hr (normal-4.0-50.0 mcg/24 hr). His serum hormone analysis showed elevated ACTH level of 731 g/ml (normal reference range: 6 to 50 g/ml).

He had a repeat CT scan of his chest, abdomen and pelvis (Figure 1-2) that showed progression of his lung mass, with multiple enlarged mediastinal lymph nodes with multiple lesions throughout the liver. The largest lesion was in the central aspect of the liver measuring 6.1 x 8.1 cm. Also noted were multiple bony lesions and bilateral adrenal lesions. The biopsy of his liver mass showed metastatic adenocarcinoma (figure 3), consistent with lung primary, positive for CK7 and TTF1 and negative for CK20 and CDX2.

Patient also had magnetic resonance imaging of his brain, which did not reveal any pituitary lesions. His transthoracic echocardiogram showed normal left ventricular systolic function with no significant valvular abnormalities.

The constellation of findings, including blood chemistry with severe hypokalemia and metabolic alkalosis, presence of anasarca, hypertension and hyperglycemia along with elevated serum ACTH and urine free cortisol with a diagnosis of adenocarcinoma of the lung was consistent with ectopic ACTH Cushing's syndrome (5). He was started on Ketoconazole and spironolactone, which led to normalization of his serum potassium and metabolic alkalosis (6). However his general condition continued to deteriorate. Eventually palliative care team was consulted and because of lack of social support with no family, poor functional status, poor prognosis and patient choice, he was transferred to inpatient hospice. He died 2 months later. Although his ectopic Cushing's syndrome was detected promptly and managed appropriately his prognosis was poor because of his metastatic adenocarcinoma of the lung.

Discussion:

Ectopic ACTH production with paraneoplastic Cushing's syndrome associated with adenocarcinoma of the lung is very rare. To the best of our knowledge, we have come across very few cases associated with non-small carcinoma of lung (7-10). The treatment of the ectopic ACTH syndrome is surgical excision of the tumor if feasible, thereby removing the source of ACTH. Unfortunately, most if not all of the metastatic cancers cannot be treated by surgical excision. For these patients, hypercortisolism can be controlled with medications like ketoconazole, metyrapone and etomidate (6, 11). Our patient was treated with ketoconazole. Most patients with overt metastases at the time of presentation die from the cancer within one to years, although patients with indolent tumors may survive for many years.

Persistent hypokalemia and metabolic alkalosis in a patient with Lung cancer should prompt consideration for diagnosis of ectopic ACTH secretion and paraneoplastic Cushing's syndrome. Aldosterone producing adenomas, bilateral idiopathic hyperaldosteronism and ectopic aldosterone-producing tumors could present with similar picture and should be included in the differential diagnosis (12-13). Although most commonly seen with small cell lung carcinoma and other neuroendocrine tumors, clinicians should consider this diagnosis in patients with adenocarcinoma of lung and treat accordingly to improve the outcome of patients.

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Figure 1

Figure 2

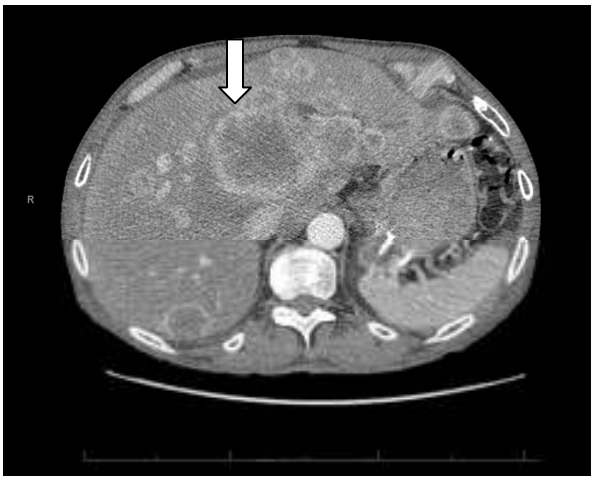

Figure 3

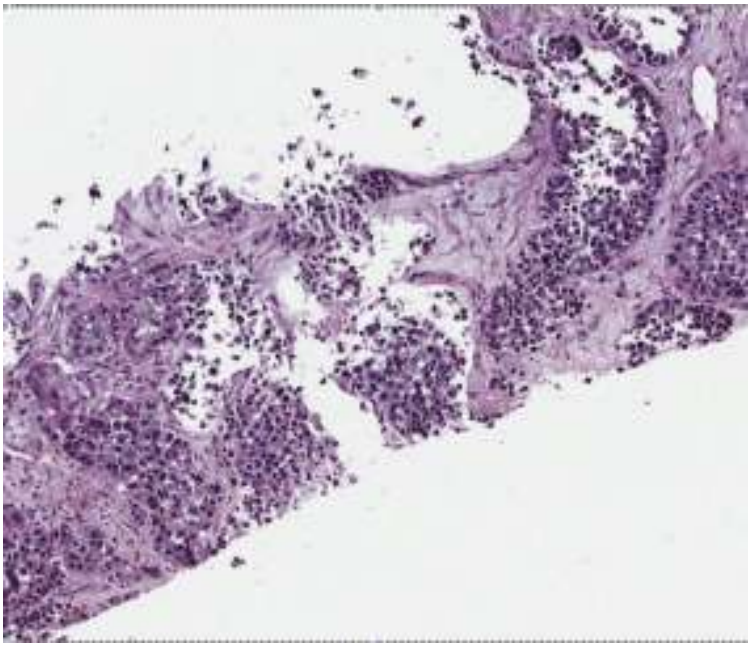
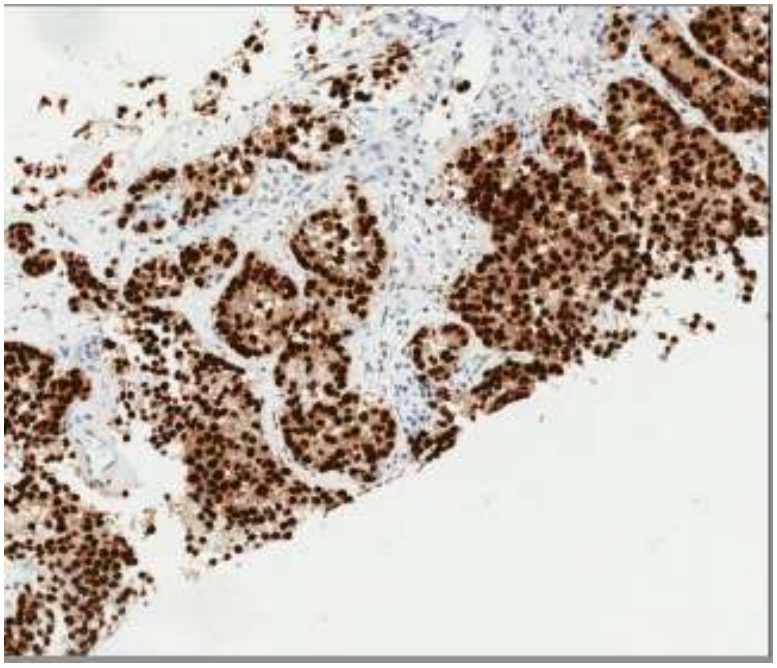
Figure 4