

Case Study

ECTOPIC ADRENOCORTICOTROPIN PRODUCTION IN A PATIENT WITH ADENOCARCINOMA OF THE LUNG - A CASE REPORT

Abstract:

Various malignancies have been associated with ectopic adrenocorticotropin hormone production producing paraneoplastic Cushing's syndrome, most commonly being Small cell cancer of the Lung, Carcinoid tumors and Medullary cancer of the thyroid. Diagnosis is confirmed by elevated serum adrenocorticotropin and free urine cortisol levels. Treatment of choice is surgical excision of the source of excess hormone if feasible. Medical treatment includes use of steroidogenesis inhibitors Metyrapone and ketoconazole. Early suspicion and appropriate work up can help diagnose and manage the excessive adrenocorticoid state.

Keywords:

Ectopic, adrenocorticotropin, Cushing's, small cell cancer, paraneoplastic, metabolic alkalosis, steroidogenesis inhibitors.

BACKGROUND:

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

Case Presentation:

We present the case of a 61 year old male with past medical history significant for 40 pack-year tobacco abuse and alcoholism who 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 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 demonstrated hypokalemia with metabolic alkalosis with serum sodium 144 milli-equivalent per liter, serum potassium 2.4 milli-equivalent per liter , chloride 92 milli-equivalent per liter, Bicarbonate >40 milli-equivalent per liter, BUN 21 milligram per deciliter, serum creatinine 0.67 milligram per deciliter and glucose 143milligram per deciliter. His liver function tests were significant for elevated alkaline phosphatase 132 units per liter, aspartate aminotransferase 64 units per liter and alanine aminotransferase 125 units per liter. His coagulation profile was within normal limits. His blood work 3 months ago did not exhibit metabolic alkalosis, hypokalemia or hyperglycemia as noted now. His urine was clear with pH 7.0, 3 + glucose and trace protein, with random urinary chloride 99 milli-equivalent per liter and urine potassium of 44.4 milli-equivalent per liter. His 24 hour urine free cortisol level was elevated at 8925.6microgram (normal- 4.0-50.0 microgram per 24 hours). His serum hormone analysis showed elevated ACTH level of 731 gram per milliliter(normal reference range 6 to 50 gram per milliliter).

He had a repeat CT scan of his chest, abdomen and pelvis (Figure 1A and B) 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. Biopsy of his liver mass showed metastatic adenocarcinoma (Figure 2A and B), consistent with lung primary, positive for CK7 and TTF1 and negative for CK20 and CDX2.

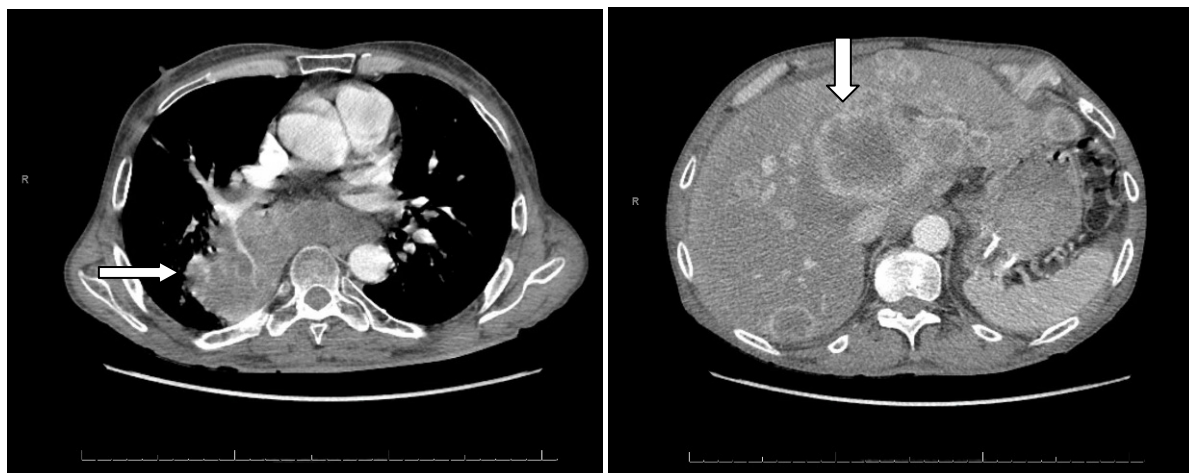


Figure 1A shows CT scan of the chest showing large mass in the right lower lobe, with multiple enlarged mediastinal lymph nodes, largest in the subcarinal region. **Figure 1B** shows CT scan of the abdomen showing significant hepatic metastatic disease with multiple target lesions throughout the liver, largest in the central aspect of the liver, measuring 6.1 x 8.1 cm.

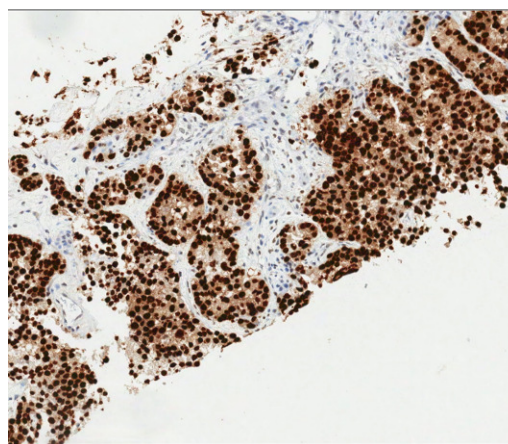
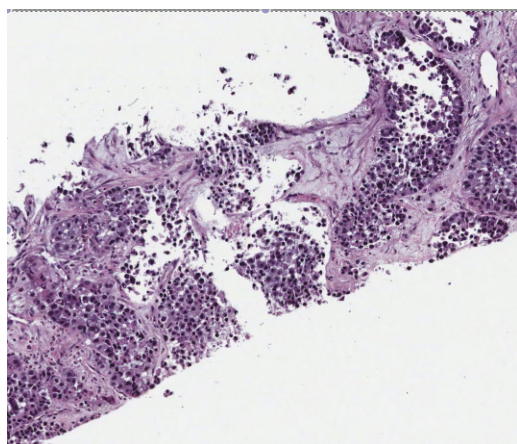


Figure 2A H and E stained tissue of the liver core biopsy shows an infiltrate of malignant cells which occasionally form glands. **Figure 2B** TTF1 shows strong positivity. The immunophenotype profile (CK7+, TTF1+, CK20-, and CDX2-) is consistent with a metastatic adenocarcinoma of lung primary.

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 elevated urine free cortisol in a patient with adenocarcinoma of the lung was consistent with ectopic ACTH Cushing's syndrome (5). Subsequently patient was started on steroidogenesis inhibitor Ketoconazole and aldosterone antagonist 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 steroidogenesis inhibitors such as ketoconazole, metyrapone and etomidate, which inhibit aldosterone production (6, 11). 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. Although most commonly seen with small cell lung cancer 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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