Hypertensive Emergency in a Patient with Metastatic Small Cell Lung Cancer
Authors: Michael Loudin, MD†, Joel Papak, MD‡
†Department of Medicine, Oregon Health & Science University, Portland, OR ‡Division of Hospital Medicine, Veterans Affairs Hospital, Portland, OR

Presentation:
A 72-year-old man presented to the hospital with several days of abdominal pain with bloating, progressive dyspnea, lower extremity edema, and was found to have hypertensive emergency. His blood pressure on admission was 210/90, an EKG showed new T wave inversions and ST depressions in V3-V6 and his troponin was elevated at 0.06 ng/mL (normal < 0.04). His initial potassium was low at 1.8 mmol/L; magnesium was normal at 2.2 mg/dL, and he exhibited a metabolic alkalosis with a bicarbonate of 43 mmol/L and a chloride of 87 mmol/L. Physical exam was significant for tender hepatomegaly and lower extremity pitting edema.

Hospital Course:
With aggressive blood pressure control and electrolyte repletion both his EKG and potassium normalized and troponin levels down-trended. The patient was also found to have newly diagnosed hyperglycemia with blood glucose levels in the low 300 mg/dL range. A CT abdomen/pelvis was significant for widespread masses in the liver, bones and adrenals (figure 1a). Given the patient’s elevated blood pressure and low potassium with adrenal masses there was concern for hyperaldosteronism. Plasma renin activity and serum aldosterone concentrations were low at 1.52 ng/mL/h and 4 ng/dL respectively, consistent with hypercortisolism. A follow up chest CT was obtained which showed a right upper lobe mass with characteristics of primary lung cancer (figure 1b). A percutaneous biopsy of one of the liver masses was performed and pathology was consistent with metastatic small cell lung carcinoma (SCLC). A dexamethasone suppression test was significant for a cortisol that remained elevated at 21.6 mcg/dL and a midnight salivary cortisol was high at 0.54 mcg/dL, consistent with hypercortisolism, likely from an extra-pituitary source. Spironolactone was added to the patient’s anti-hypertensive regimen with good effect.

Diagnosis of Ectopic ACTH Syndrome
• Three main steps: confirmation of hypercortisolism, differentiation of adrenocorticotropic (ACTH) independent and ACTH dependent causes, and differentiation between pituitary and ectopic sources of ACTH.
• Definitive diagnosis requires reversal of clinical picture after tumor resection or demonstration of immunohistochemical staining in tumor tissue.
• Bilateral inferior petrosal sampling (BIPSS) is gold standard for differentiation of pituitary and ectopic sources of ACTH.

TABLE 2: Presentation of Ectopic ACTH Syndrome Secondary to SCLC vs Other Malignancies

<table>
<thead>
<tr>
<th>Other Malignancy</th>
<th>SCLC</th>
<th>Other Malignancy</th>
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</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>Skin Hyperpigmentation</td>
<td>Weight Loss</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Metabolic Alkalosis</td>
<td>Absence of Moon Faces</td>
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<tr>
<td>Cushingoid Features</td>
<td>Hypokalemia</td>
<td>Cerebellar degeneration &lt; 1%</td>
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Treatment of Ectopic ACTH Syndrome
• Optimal management is surgical resection (only possible in 40% of cases) and associated with complete remission in 80% of cases.
• Ketoconazole and metyrapone are preferred due to their efficacy and safety, metyrapone has a more rapid onset.
• Hypokalemia may be treated with oral supplementation and spironolactone.
• Though it is generally thought that reduction of tumor burden results in a decrease in plasma ACTH level, chemotherapy instituted in patients with ectopic ACTH syndrome can result in an acute increase of plasma ACTH and an exacerbation of hypercortisolism.

Figure 1: Adrenal Metastases

Figure 2: Lung Mass

Discussion:
• Association of Cushing’s syndrome with SCLC first described in 1928
• Because presenting symptoms can be mistakenly interpreted as progression of underlying malignancy, and all symptoms of ACTH production do not necessarily present simultaneously, delay in diagnosis may occur, which carries additional morbidity.
• SCLC associated with EAS is more resistant to chemotherapy and is responsible for a high rate of life threatening complications such as severe infections, and gastrointestinal bleeding or ulcerations.
• Patients with EAS at presentation have significantly shorter survival (mean 4 months) compared to those with EAS diagnosed later in the course of their SCLC (median survival 11 months).
• Achieving control of hypercortisolism before administering chemotherapy may ameliorate the prognosis of these patients.

References