Respiratory Medicine Case Reports 25 (2018) 177–180

Contents lists available at ScienceDirect

Respiratory Medicine Case Reports

journal homepage: www.elsevier.com/locate/rmcr

Case report

# Severe metabolic alkalosis–a diagnostic dilemma

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A B S T R A C T

*Background:* Cushing's syndrome due to ectopic ACTH secretion has been associated with many cancers; most commonly small cell carcinoma of the lung and bronchial carcinoid tumors. Usually, patients who confer this diagnosis have poor prognosis.

*Case presentation:* A 66-year-old female presented with worsening shortness of breath and weakness over three days. Initial laboratory derangements included severe hypokalemia and metabolic alkalosis. Treatment included high amounts of potassium chloride and acetazolamide. Imaging studies revealed anterior medial right upper lobe lung mass as well as suspicion for many liver metastases. Liver biopsy was sought and was positive for small cell carcinoma.

*Conclusion:* We describe a case of severe metabolic alkalosis and hypokalemia in a patient with Cushing's syndrome due to ectopic ACTH secretion from small cell lung cancer. To our knowledge, this is the first case identified which exhibited such significant metabolic derangements in the form of serum and arterial blood bicarbonate. As prognosis is quite poor, we recommend swift diagnosis and management.

## 1. Introduction

Cushing's syndrome is a clinical condition caused by an excess of glucocorticoids [1]. The syndrome is characterized by the development of a “Cushingoid” appearance (truncal obesity, moon facies due to facial fat deposition, abdominal striae, hirsutism), arterial hypertension, proximal myopathy, thin skin, easy bruising, diabetes mellitus, apparent mineralocorticoid excess and neuropsychiatric disorders [2]. It is most commonly caused by steroid administration leading to exogenous hypercortisolism [2]. It may also be due to endogenous steroid production, either secondary to adrenocorticotropic hormone (ACTH) overproduction from a pituitary adenoma (Cushing's disease) or ectopic ACTH secretion (EAS), or from glucocorticoid overproduction from an ACTH-independent adrenal tumor [3]. Cushing's syndrome due to EAS has been associated with many cancers although it most commonly arises from small cell carcinoma of the lung (SCLC) and bronchial carcinoid tumors [4]. Metabolic derangements due to the apparent mineralocorticoid excess may be the presenting features in Cushing's syndrome secondary to EAS. Here we describe a case of severe metabolic alkalosis and hypokalemia in a patient with Cushing's syndrome due to EAS from a SCLC.

## 2. Case Presentation

A 66-year-old woman presented with a three day history of progressively worsening shortness of breath associated with weakness. She had a past medical history significant for COPD on 5 L/min home oxygen, diabetes mellitus type 2, congestive heart failure, hypothyroidism and coronary artery disease. Her home medications included aspirin, furosemide, atorvastatin, amlodipine, clopidogrel, metoprolol, diazepam, metformin, nitroglycerin, potassium chloride, and trazodone. She was an active two pack-per-day smoker with a 100-pack-year smoking history. She had a heart rate of 96 bpm, blood pressure of 150/64 mmHg, respiratory rate of 28, and 94% saturation by pulse oximetry on 15L oxygen via non-rebreather mask. Physical exam was significant for cushingoid features, bilateral crackles of the posterior lung fields, and bilateral lower extremity edema.

Admission laboratory data revealed a sodium 149 mmol/L (136–145 mmol/L), potassium 1.5 mmol/L (3.5–5.1 mmol/L), chloride 87 mmol/L (98–107 mmol/L), CO2 67 mmol/L (21–32 mmol/L), and glucose 227 mg/dL (70–110 mg/dL). Arterial blood gas analysis revealed a pH of 7.65, PaCO2 83 mmHg, bicarbonate 91.4 mmol/L, PaO2 49 mmHg on 60% FiO2. Urine chemical analysis revealed chloride 92

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https://doi.org/10.1016/j.rmcr.2018.08.019
Received 8 February 2018; Received in revised form 23 August 2018; Accepted 23 August 2018

**Abbreviation list**

| | |
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| ACTH | adrenocorticotropic hormone |
| EAS | ectopic ACTH secretion |
| SCLC | small cell carcinoma of the lung |
| COPD | Chronic Obstructive Pulmonary Disease |
| L | liter |
| dL | deciliter |
| FiO2 | Fraction of inspired oxygen |
| Mmol | millimole |
| Ng | nanogram |

mmol/L, sodium 19 mmol/L, creatinine 51 mg/dL, potassium 37 mmol/L, and urea nitrogen 455 mg/dL. Electrocardiogram was remarkable for ectopic atrial tachycardia, moderate ST depression, and non-specific ST elevation in V1-V2 and aVL. Chest x-ray (Fig. 1) showed a widened mediastinum. Computed tomography of the chest (Figs. 2a and b, 3) revealed a 3 × 1.5 cm mass in the right upper lobe suspicious for malignancy, extensive metastatic mediastinal and hilar lymphadenopathy resulting in narrowing of the superior vena cava, and innumerable hepatic metastases. Cushing's syndrome secondary to ectopic ACTH secretion was suspected and further workup revealed renin 3.2 ng/mL/hr (0.5–4.0 ng/mL/hr), aldosterone 6.3 ng/dL (4–31 ng/dL), ACTH 235 pg/mL (6–58 pg/mL), and 24-h free urine cortisol 1440 mg/dL (< 45 mg/dL). Liver biopsy (Fig. 4a/b/c) was performed and revealed metastatic small cell carcinoma.

She was treated with amiloride, potassium repletion and supplemental oxygen which led to resolution of her hypokalemia and near normalization of her serum bicarbonate. Serum potassium levels were monitored closely as there was a concern for development of abrupt hyperkalemia with correction of the patient's alkalosis. Acetazolamide was administered to aid in correction of the patient's severe alkalosis. Amiloride administered to reduce the excretion of potassium as repletion of the patient's serum potassium was difficult to manage. Given the patient's significant comorbid conditions and poor prognosis, end of life care was approached per patient wishes and the patient died on hospital day 12.

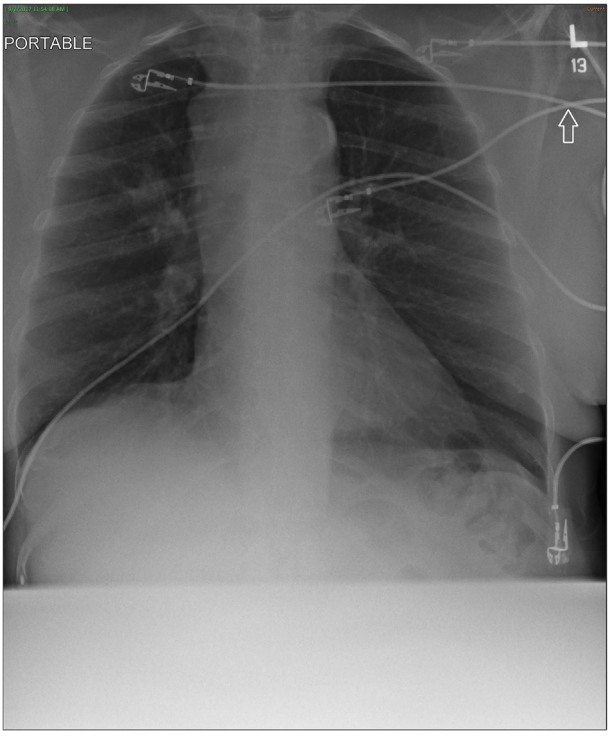


**Fig. 1.** Portable Chest X-ray on presentation.

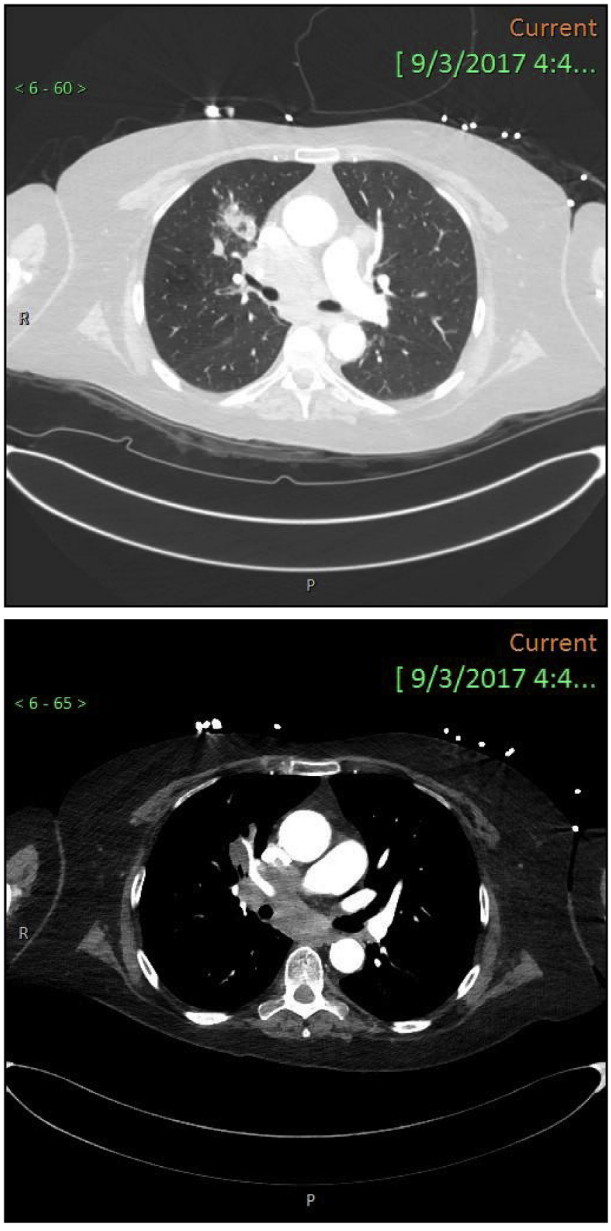


**Fig. 2.** (a): Chest CT angiogram demonstrating a 3.0 × 1.5 cm mass in the anterior medial right upper lobe of the lung. (b): Chest CT angiogram demonstrating mediastinal and right hilar lymphadenopathy.

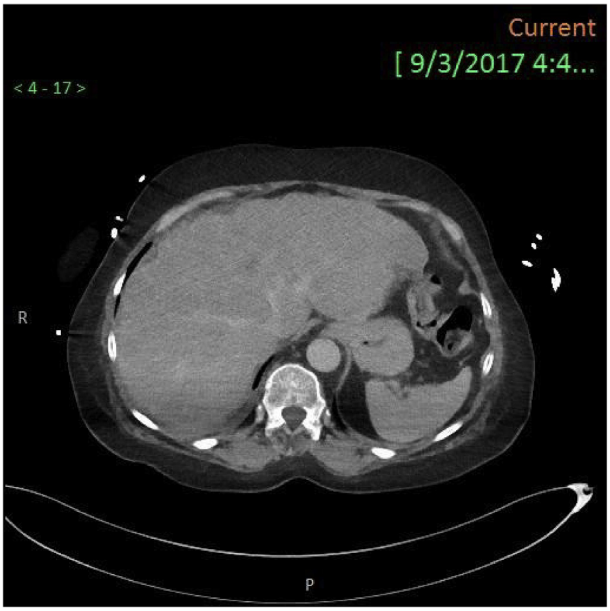


**Fig. 3.** CT abdomen demonstrating innumerable hepatic metastases.

## 3. Discussion

Ectopic ACTH-producing SCLC is seen in approximately 1–5% of cases of SCLC [5,6]. Our patient initially presented with dyspnea and weakness and was found to have a lung mass on chest radiograph. The severe hypokalemia and metabolic alkalosis led us to suspect Cushing's syndrome secondary to a presumed lung cancer. Normal renin and aldosterone levels along with elevated ACTH and 24-h free urine cortisol confirmed the diagnosis of Cushing's syndrome. Inferior petrosal sinus sampling was bypassed given the high clinical suspicion for EAS secondary to lung malignancy, and a liver biopsy confirmed the diagnosis of metastatic small cell carcinoma.

Our case is unique in that this profound metabolic alkalosis with bicarbonate level has not been reported previously in our research of primary literature. Late presentation due to metabolic derangements caused by apparent mineralocorticoid excess is commonly seen in EAS secondary to malignancy—the underlying cancers tend to be aggressive and thus the Cushingoid features do not have time to develop. Additionally, the highly catabolic state induced by malignancy may obscure the antianabolic effects of the high cortisol levels seen in Cushing's syndrome. Amiloride was carefully given as there was a concern for Liddle's syndrome. It has been reported that providing amiloride would cause profound hypotension if in fact our patient had Liddle's syndrome. Other diagnoses such as Barrter and Gitelman syndromes were considered and ruled out secondary to the above laboratory data and clinical presentation.

It is important to consider EAS in individuals with severe metabolic derangements otherwise not explained by common etiologies, especially in those patients presenting with a lung mass and the triad of hypertension, hypokalemia, and metabolic alkalosis.

## Conflicts of interest

None of the authors that contributed to this manuscript have any conflicts of interest.

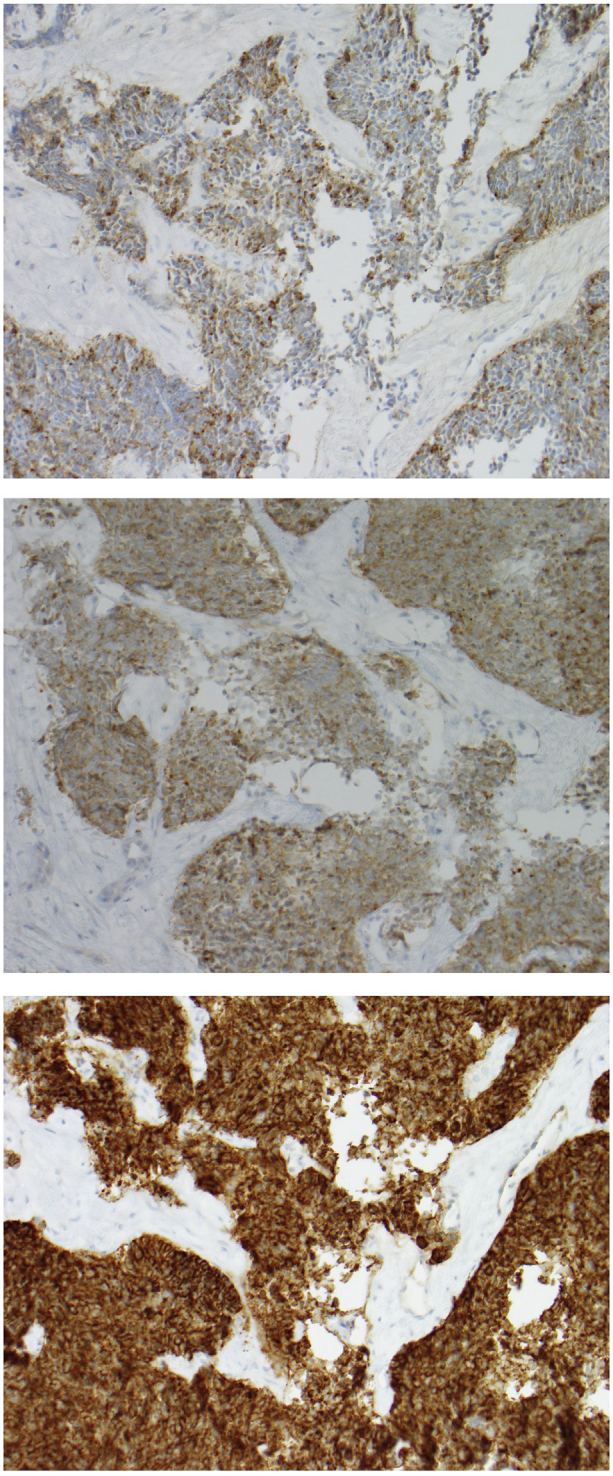

**Fig. 4.** (a): Chromogranin A (liver biopsy) immunostain is focally and weakly positive in the cytoplasm (brown color). Chromogranin A can stain weaker in SCLC than in typical carcinoid tumors [7]. (b): Synaptophysin (liver biopsy) immunostain is diffusely and moderately positive in the cytoplasm (brown color). Synaptophysin can stain weaker in SCLC than in typical carcinoid tumors [7]. (c): CD56 (liver biopsy) immunostain is diffusely and strongly positive in the cytoplasm (brown color). CD56 is the most sensitive for SCLC and the least specific marker for other tumor sites [7]. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

## Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.rmcr.2018.08.019.

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