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Clinical Communications: Adult

AN UNLIKELY CAUSE OF HYPOKALEMIA

Jason Hine, MD, Ari Schwell, MD, and Norah Kairys, MD

Temple University Hospital, Philadelphia, Pennsylvania
Reprint Address: Jason Hine, MD, E1 Clairmont Court, Portland, ME 04103

□ **Abstract—Background: Hypokalemia is a common clinical disorder caused by a variety of different mechanisms. Although the most common causes are diuretic use and gastrointestinal losses, elevated cortisol levels can also cause hypokalemia through its effects on the renin–angiotensin–aldosterone system. Cushing's syndrome refers to this general state of hypercortisolemia, which often manifests with symptoms of generalized weakness, high blood pressure, diabetes mellitus, menstrual disorders, and psychiatric changes. This syndrome is most commonly caused by exogenous steroid use, but other etiologies have also been reported in the literature. Ectopic adrenocorticotropic hormone production by small-cell lung cancer is one rare cause of Cushing's syndrome, and may be associated with significant hypokalemia. Case Report: We describe the case of a 62-year-old man who presented to the emergency department with weakness and hypokalemia. The patient was initially misdiagnosed with furosemide toxicity. Despite having a 30-pack-year smoking history, this patient's lack of respiratory complaints allowed him to present for medical attention twice before being diagnosed with lung cancer. It was later determined that this patient's hypokalemia was due to Cushing's syndrome caused by ectopic adrenocorticotropic hormone production from small-cell lung cancer. Why Should an Emergency Physician Be Aware of This?: This case reminds emergency physicians to consider a broad differential when treating patients with hypokalemia. More importantly, it prompts emergency physicians to recognize comorbid conditions and secondary, less common etiologies in patients with repeated visits for the same complaint.**

□ **Keywords—hypokalemia; paraneoplastic syndrome; small cell lung cancer; ectopic ACTH; Cushing's syndrome**

INTRODUCTION

Hypokalemia is a frequent clinical entity, estimated to occur in about 3.5% of hospitalized patients (1). The most common causes of hypokalemia are diuretic use and gastrointestinal losses (2). However, numerous less common etiologies can also result in hypokalemia, including renal tubular acidosis, diabetic ketoacidosis, insulin excess, primary hyperaldosteronism, and ectopic adrenocorticotropic hormone (ACTH) production (Table 1) (2–6,8,9,11–13). It is reported that 3.5% of patients on furosemide develop hypokalemia (1). In 2010, approximately 130 million people in the United States reported taking diuretics, contributing to the large prevalence of diuretic-induced hypokalemia (10). Comparatively, there are approximately 430,000 Americans living with lung cancer, of which 15% have small-cell lung cancer (7). Furthermore, only a small subset of these patients with small-cell lung cancer also have ectopic ACTH production (14). Therefore, it is statistically far more common to present with hypokalemia caused by a diuretic than from ectopic hormone secretion from a lung mass.

Informed consent was obtained and is available from the authors upon request.

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Table 1. Common Causes of Hypokalemia, Structurally Divided into Cellular Shifts vs. Whole Body Imbalances

Whole Body Depletion	Cellular Shifts
Diarrhea (3)	Alkalemia (4)
Diuretic use (5)	Hypothermia (6)
Vomiting (7)	Insulin overdose/excess (1)
Poor oral intake	High catecholamine states (2)
Mineralocorticoid excess (8,9)	β-adrenergic use
Excessive sweating/severe burns (10)	Hypokalemic periodic paralysis
Renal tubular acidosis	
Hypomagnesium (11)	
Diabetic ketoacidosis	
Nondiuretic drugs (amphotericin B, ithium, theophylline, quietapine) (3)	

CASE REPORT

A 62-year-old male with a medical history of diabetes mellitus, hypertension, and non-ST segment elevation myocardial infarction (NSTEMI) treated with coronary artery stenting presented with a chief complaint of worsening weakness. This weakness was more pronounced in the morning with associated lightheadedness; there were no complaints of cough or shortness of breath. The patient had a 30-pack-year smoking history and had quit 9 months prior. This was his second presentation to an emergency department with complaints of weakness. Two weeks earlier, the patient had presented to another medical facility and was found to have a low serum potassium level of 1.6 mEq/L. At the time, this was presumed to be secondary to the furosemide he was taking for his hypertension. The patient was discharged home with prescriptions for oral potassium supplementation and spironolactone. The patient did not receive any parenteral potassium or magnesium repletion during the initial visit.

During his second emergency department visit, the patient continued to report weakness but also noted mild sub-sternal chest pain, which had occurred at rest and lasted for 5 minutes. His physical examination was notable for a heart rate of 106 beats/min, blood pressure of 143/89 mm Hg, upper extremity weakness with 4/5 grip strength bilaterally, and symmetric pitting edema to his knees. Additionally, he was found to have serum glucose of 407 mmol/L, a white blood cell count of 16,800/μL with 90% neutrophils, and a serum potassium of 3.0 mEq/L. The patient reported full compliance with his new medications.

Because the patient had complained of mild chest pain, had a history of smoking, and a previous NSTEMI, chest x-ray study, electrocardiogram, and troponin I were obtained. The patient's chest x-ray study (Figure 1) revealed a new perihilar lung mass, further delineated on computed tomography (Figure 2). Inpatient laboratory results revealed a morning serum cortisol level of 57.1 μg/dL (reference 6–22 μg/dL) and an ACTH level of 175.2 pg/mL (reference 6–50 pg/mL). In the context of a new lung mass and elevated cortisol and ACTH levels associated with persistent hypokalemia, it was presumed that the patient likely had an ACTH-dependent Cushing's syndrome related to this lung mass. Biopsy subsequently confirmed the mass to be small-cell lung cancer with ectopic ACTH production, and the patient has since been treated with radiation and chemotherapy.

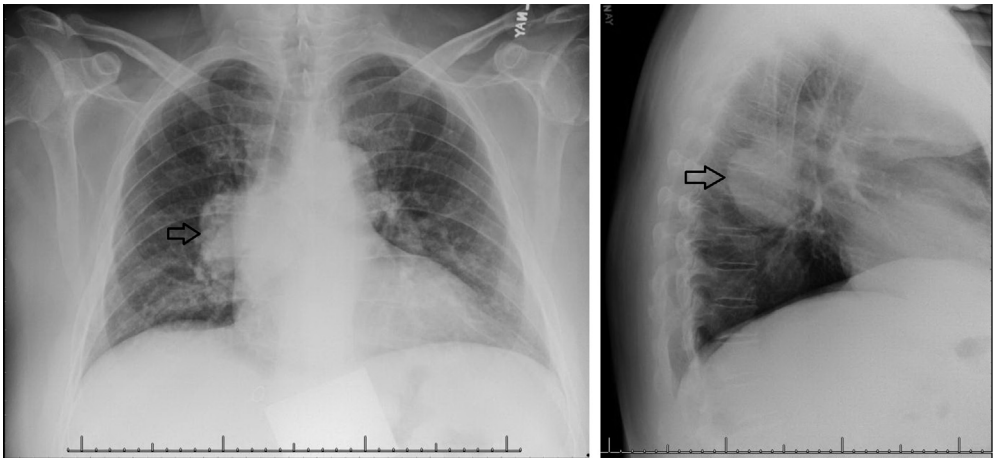

Figure 1. Chest x-ray study (posteroanterior and lateral view). A 7.9-cm mass is seen in the superior segment of the right lower lobe. The mass is more clearly distinguished from hilar anatomy on the lateral view. Arrows represent lung mass.