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A PATIENT WITH ALCOHOLIC KETOACIDOSIS AND PROFOUND LACTEMIA

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☐ **Abstract—Background: Alcoholic ketoacidosis (AKA) is a complex syndrome that results from disrupted metabolism in the setting of excessive alcohol use and poor oral intake. Dehydration, glycogen depletion, high redox state, and release of stress hormones are the primary factors producing the characteristic anion gap metabolic acidosis with an elevated ß-hydroxybutyrate (ß-OH) and lactate. Case Report: We present the case of a 47-year-old man who presented to the emergency department with metabolic acidosis and profoundly elevated lactate levels who had AKA. He recovered completely with intravenous fluids and parenteral glucose administration. Why Should an Emergency Physician Be Aware of This?: Emergency physicians should always consider the immediately life-threatening causes of a severe anion gap metabolic acidosis and treat aggressively based on the situation. This case highlights the fact that AKA can present with an impressively elevated lactate levels. Emergency physicians should keep AKA in the differential diagnosis of patients who present with a similar clinical picture.**

☐ **Keywords—acidosis; alcohol; ketones; lactate**

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INTRODUCTION

Alcoholic ketoacidosis (AKA), first described in 1940, is a metabolic process that occurs in chronic alcoholics after a period of binge drinking and cessation of food and water consumption (1). In the absence of normal caloric intake, hepatic glycogen stores in the liver are consumed, insulin levels decline, and a starvation response ensues. The starvation response includes the release of glucagon, cortisol, growth hormone, and catecholamines, which in turn mobilize other metabolic substrates (e.g., fatty acids and amino acids) as alternatives to glucose.

The pathophysiology of AKA differs from starvation ketoacidosis because of the consumption of ethanol. The concurrent metabolism of ethanol alters the typical starvation metabolic profile in a number of ways. First, ethanol is metabolized to acetate. The excess acetate accrued readily combines with the acetyl coenzyme A formed in response to fatty acid oxidation, creating acetoacetate. Second, ethanol metabolism produces an excess of reducing potential via the formation of nicotinamide adenine dinucleotide hydride. This excess reducing potential has two effects: first, it favors the conversion of pyruvate to lactate, and second, it favors the conversion of acetoacetate to β-hydroxybutyrate (β-OH). In patients with starvation ketosis, acetoacetate is readily converted to acetone, but in patients with

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AKA, little acetone is formed because β-OH production is favored. Therefore, in contrast to patients with diabetic ketoacidosis, patients with AKA have higher β-OH to acetoacetate and lactate to pyruvate ratios (2). In addition, in the setting of normal caloric intake, ethanol intoxication alone favors conversion of pyruvate to lactate but rarely results in a severe lactate-associated acidosis (3). The unique pathophysiology of AKA requires ethanol intoxication in conjunction with decreased caloric intake.

The differential diagnosis of a lactate-associated anion gap metabolic acidosis is broad and contains many serious or life-threatening conditions, including many toxicologic causes. The diagnosis is therefore based on careful history and physical and laboratory evaluations. In this case report, one of the highest serum lactate levels measured in a living patient with AKA is discussed.

CASE REPORT

A 47-year-old man with a history of alcohol dependence and depression who was prescribed citalopram, mirtazipine, trazodone, and venlafaxine was transported to the emergency department (ED) for evaluation of altered mental status. The patient had reportedly been drinking alcohol continuously for 3 days and was found sedated on the floor of his hotel room. The prehospital evaluation included a capillary glucose of 53 mg/dL and 25 g of intravenous dextrose was administered without clinical improvement.

In the ED, the patient was somnolent but arousable and answered questions appropriately. Initial vital signs included: a temperature of 36.8°C, a heart rate of 130 beats/min, a respiratory rate of 18 breaths/min, blood pressure 129/86 mm Hg, and room air oxygen saturation 97%. He adamantly denied the use or intake of other substances or medications, denied visual hallucinations, and admitted to not eating any food for the several days while binge drinking.

The serum laboratory analysis revealed the following: sodium 137 mEq/L (reference range 136–146 mEq/L), potassium 6.1 mEq/L (3.5–5.0 mEq/L), chloride 96 mEq/L (98–107 mEq/L), bicarbonate <5 mEq/L (21–31 mEq/L), blood urea nitrogen 41 mg/dL (8–26 mg/dL), creatinine 2.9 mg/dL (0.5–1.4 mg/dL), glucose 98 mg/dL (70–99 mg/dL), and creatinine phosphokinase 960 IU/L (0–200 IU/L). Serum lactate was measured at 22 mmol/L (0.5–1.6 mmol/L). His arterial blood gas measured pH 7.07, $PaCO_2$ 18 mm Hg, PaO_2 149 mm Hg, and base deficit 24 mEq/L. Urinalysis detected small ketones without crystals, and the urine did not fluoresce with a Wood's lamp. Measured serum osmolality and ethanol were 363 mOsm/kg (273–295 mOsm/kg) and 178 mg/dL, respectively. The calculated osmolal gap was 31 mOsm/kg (0–10 mOsm/kg). Serum salicylate and acetaminophen levels were undetectable. A qualitative urine drugs of abuse immunoassay detected no substances.

Because of the severe anion gap acidosis and osmolal gap, the patient was initially presumed to have ingested a toxic alcohol. The patient was administered intravenous (IV) fomepizole (1500 mg), sodium bicarbonate (300 mEq IV), thiamine (100 mg IV), folinic acid (50 mg IV), and pyridoxine (50 mg IV). A 5% dextrose in 0.9% normal saline solution bolus of 1000 mL was given and he was subsequently started on an infusion at 150 mL/hr. In addition, the patient was persistently hypotensive despite fluid resuscitation (blood pressure ranges from 76–98/38–55 mm Hg); therefore, a norepinepherine infusion was initiated. A medical toxicology consultation was obtained. He was then admitted to the intensive care unit and, over the next 11 hours, the severe metabolic derangements normalized and norepinephrine was discontinued. Serum methanol, ethylene glycol, and isopropanol levels were undetectable. Initial serum acetoacetate and β-OH levels, which were not immediately available, measured 130 mcg/L (normal <30 mcg/L) and >2 mmol/L (normal <0.27 mmol/L), respectively. He was discharged uneventfully on hospital day 10 and never had alcohol withdrawal.

DISCUSSION

This case presentation describes one of the highest serum lactate concentrations in a patient with AKA published in the English literature. Measured lactate concentrations in the setting of AKA are usually <10 mmol/L; however, similarly high lactate concentrations are uncommonly reported (3–6). Shull and Rapoport reported a serum lactate of 23.8 mmol/L in 2010 and Ishii et al reported a lactate of 32 mmol/L in 1996 (7,8). Both of these patients improved with supportive care alone.

Although mortality is rare, the management of AKA requires meticulous supportive care with the goal of reversing the perturbed metabolic pathways (9,10). Treatment focuses upon the administration of crystalloids, dextrose, and thiamine. Potassium, magnesium, and other vitamins should also be replaced on an individual basis. Most importantly, administration of dextrose and thiamine is paramount. Five percent dextrose–containing solutions have been shown to decrease the concentration of β-OH faster than normal saline alone and are essential for stimulating insulin release, decreasing glucagon secretion, arresting ketogenesis, and restoring appropriate nicotinamide adenine dinucleotide hydride/nicotinamide adenine dinucleotide ratios (11,12). Thiamine supplementation is also of utmost importance. Thiamine facilitates entry of pyruvate into the Krebs cycle and restoring normal adenosine triphosphate production. Because thiamine is often deficient in chronic alcoholics, patients suffering from AKA should routinely receive parenteral thiamine supplementation (13–15).

The differential diagnosis of patients with a profound anion gap metabolic acidosis includes clinical conditions, such as toxic alcohol poisoning, electron transport chain poisoning (e.g., cyanide), biguanide toxicity, seizure, acute renal failure, and shock. The case presented here was concerning for a toxic alcohol ingestion, which prompted the empiric administration of fomepizole, folate, bicarbonate, and pyridoxine. Many toxic ingestions in the setting of profound acidemia require emergent hemodialysis. However, with the lack of an identifiable toxic ingestion, in conjunction with the appropriate history and clinical findings, the diagnosis of AKA was made. The patient's rapid improvement with proper supportive measures, coupled with the presence of a markedly elevated serum β-OH concentration and negative additional testing, confirmed the diagnosis of AKA. This clinical approach prevented more aggressive interventions, such as hemodialysis.

WHY SHOULD AN EMERGENCY PHYSICIAN BE AWARE OF THIS?

The patient described here presented with a severe anion gap metabolic acidosis and elevated lactate and β-OH levels. In conjunction with targeted care, he improved rapidly. Emergency physicians should always consider the immediately life-threatening causes of a severe anion gap acidosis and treat aggressively based on the situation. This case highlights the fact that AKA can present with an impressively elevated lactate level and a profound metabolic acidosis. The emergency physician should keep AKA in the differential diagnosis of those who present with this clinical picture. However, prompt consultation with a medical toxicologist or regional poison center is always prudent to assist in diagnosis and management, because toxicologic causes predominate this differential diagnosis.

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