The Journal of Emergency Medicine, Vol. 46, No. 3, pp. e69–e74, 2014

0736-4679/$ - see front matter

ELSEVIER

http://dx.doi.org/10.1016/j.jemermed.2013.08.068

Selected Topics: Toxicology

MASSIVE ETHYLENE GLYCOL POISONING TRIGGERS OSMOTIC DEMYELINATION SYNDROME

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□ **Abstract—Background: Ethylene glycol is a toxic organic solvent implicated in thousands of accidental and intentional poisonings each year. Osmotic demyelination syndrome (ODS) is traditionally known as a complication of the rapid correction of hyponatremia. Objective: Our aim was to describe how patients with ethylene glycol toxicity may be at risk for developing ODS in the absence of hyponatremia. Case Report: A 64-year old female patient was comatose upon presentation and laboratory results revealed an anion gap of 39, a plasma sodium of 150 mEq/L, a plasma potassium of 3.5 mEq/L, an osmolal gap of 218, an arterial blood gas pH of 7.02, whole blood lactate of 32 mEq/L, no measurable blood ethanol, and a plasma ethylene glycol concentration of 1055.5 mg/dL. The patient was treated for ethylene glycol poisoning with fomepizole and hemodialysis. Despite having elevated serum sodium levels, the patient's hospital course was complicated by ODS. Conclusions: Rapid changes in serum osmolality from ethylene glycol toxicity or its subsequent treatment can cause ODS independent of serum sodium levels.** © **2014 Elsevier Inc.**

□ **Keywords—ethylene glycol; fomepizole; renal dialysis; acidosis; lactic; calcium oxalate; osmotic demyelination syndrome; extra pontine myelinolysis**

INTRODUCTION

Ethylene glycol is a toxic organic solvent commonly found in automobile antifreeze. In 2010, 5725 single-exposure ethylene glycol events were reported by the American Association of Poison Control Centers, with 528 exposures in patients 5 years of age or younger, 145 exposures in patient ages 6−12, and 5027 exposures in patients older than 12 years of age (1). Much of the danger of ethylene glycol ingestion results from metabolism to toxic compounds. Ethylene glycol is metabolized by a series of steps to glycolic acid and oxalic acid, the latter of which has the potential to cause severe renal injury by crystallization of oxalate. Ethylene glycol ingestion can also cause increased blood lactate concentration secondary to conversion of nicotinamide adenine dinucleotide (NAD^+) to NADH during the enzymatic steps involved in ethylene glycol metabolism. The increased NADH/NAD^+ ratio promotes pyruvate conversion to lactate resulting in lactic acidosis (2−5).

After ethylene glycol ingestion, patients often present with an altered mental state that is difficult to distinguish from other toxic ingestions or a variety of other medical conditions. Clinicians must rely on laboratory data to make a diagnosis of ethylene glycol poisoning and to determine a treatment plan that will prevent end organ damage. With aggressive treatment, patient survival has been reported for ingestions of up to 3 L of ethylene glycol (6). If diagnosed early enough, ethylene glycol poisoning can usually be treated effectively by administration of either ethanol or fomepizole, both of which inhibit the rate-limiting first step in the metabolism of

RECEIVED: 27 February 2013; FINAL SUBMISSION RECEIVED: 2 June 2013;
ACCEPTED: 15 August 2013

ethylene glycol and prevent the formation of toxic metabolites. Massive ethylene glycol ingestions or ingestions that present late (with conversion to metabolites already assumed to have occurred) generally require hemodialysis to clear ethylene glycol and the toxic metabolites.

Osmotic demyelination syndrome (ODS) was first described as central pontine myelinolysis (CPM) by Adams in 1959, as his initial paper demonstrated four patients with characteristic myelin loss specifically confined to the central pons (7). He noted this phenomenon in patients with chronic alcohol abuse and malnutrition and, by the mid 1970s, several papers associated CPM with rapid correction of hyponatremia (8,9). Recently, the term *ODS* was introduced as an umbrella term to describe both extra pontine and central pontine myelinolysis, as the literature is now describing demyelination outside of the pons associated with a wide variety of medical conditions.

In this case report, we describe a massive ethylene glycol poisoning that was recognized and treated appropriately with fomepizole and hemodialysis, but the patient's subsequent clinical recovery was complicated by ODS.

CASE REPORT

A 64-year old female with medical history including hypertension and hypothyroidism was transported to the emergency department (ED) after her daughter found her prone in the bathroom incontinent of stool, having difficulty speaking, and with altered mental status. At the scene, paramedics found her responsive only to pain, with mumbling speech and no purposeful movements. There was no evidence of external trauma and no open bottles or pill containers were noted. Finger-stick glucose did not demonstrate hypoglycemia and naloxone given per protocol did not change her clinical status.

On presentation to the hospital, her vital signs were temperature 36.1°C, blood pressure 101/50 mm Hg, heart rate 81 beats/min, respiratory rate 20 breaths/min, O_2 saturation 96% on 15 L via face mask, and Glascow Coma Scale score of 7. An endotracheal intubation was performed. Her screening physical examination before intubation showed no major abnormalities aside from her depressed neurological status.

An electrocardiogram showed a sinus rhythm with a rate of 71, a PR interval of 140 ms (120−200 ms), normal QRS width, and a QTc of 499 ms with nonspecific ST-T wave abnormalities in the inferior and lateral leads. A chest x-ray showed the endotracheal tube to be in the proper position without evidence of pneumothorax, infiltrates, or abnormal pulmonary vasculature. A computed tomography of the head was negative for intracranial hemorrhage. An arterial blood gas revealed: pH of 7.02 (reference range 7.35–7.45), a pCO_2 of 30 mm Hg (reference range 35−45 mm Hg), a pO_2 of 317 mm Hg (reference range 80−90 mm Hg), a base excess of −23 mEq/L (reference range −2 to 2 mEq/L), and a bicarbonate of 7 mEq/L (reference range 22−26 mEq/L) on 100% FiO_2. The basic electrolyte panel revealed: sodium 150 mEq/L (reference range 135−145 mEq/L), potassium 3.5 mEq/L (reference range 3.5–5.0 mEq/L), chloride 107 mEq/L (reference range 95−107 mEq/L), bicarbonate 5 mEq/L (reference range 24−32 mEq/L), blood urea nitrogen 27 mg/dL (reference range 10−20 mg/dL), creatinine 2.3 mg/dL (reference range 0.6–1.2 mg/dL), and glucose 120 mg/dL (reference range, 70−140 mg/dL for random level). The anion gap was 39 (reference range < 17), whole blood lactate concentration was 32.0 mEq/L (reference range 0.5–2.2 mEq/L), blood ethanol level was <10 mg/dL, and plasma osmolality was elevated at 536 mOsm/kg (reference range 275−295 mOsm/kg), with an osmolal gap of 218 mOsm/kg (reference range < 16 mOsm/kg). A urine drug screen was negative, salicylate levels were < 2.5 mg/dL, and acetaminophen levels were < 1.1 μg/mL. Urine microscopy showed no evidence of infection or abnormal casts.

Based on the patient's neurological status, significantly elevated lactate levels, a marked osmolal gap, and a negative ethanol test result, an ingestion of a toxic alcohol (e.g., methanol, ethylene glycol, isopropyl alcohol) was suspected. A toxic alcohols panel was ordered and empiric fomepizole therapy was initiated.

The patient was then transferred to the medical intensive care unit (MICU) in critical condition and a nephrologist was consulted. Plasma ethylene glycol concentration was determined to be 1055.5 mg/dL using the gold standard method of gas chromatography with flame ionization detection, using a method described previously (10). Gas chromatography analysis did not reveal the presence of acetone, ethanol, isopropanol, methanol, or propylene glycol (lower limit of detection for all five analytes of 10 mg/dL). The patient received fomepizole 750 mg i.v. every 12 h with the intermittent hemodialysis, as well as thiamine 100 mg i.v. every 6 h for cofactor therapy (11). Table 1 outlines the overall course of treatment and the ethylene glycol levels after each dialysis run.

The patient's mental status marginally improved despite normalization of the acidosis and osmolal gap, and removal of the ethylene glycol (Table 2). She was extubated on hospital day 3, but demonstrated periods of alternating agitation and somnolence. She demonstrated hyper-reflexia with diffuse bilateral weakness. On hospital day 6, the patient underwent an electroencephalogram (EEG) and magnetic resonance imaging (MRI). The EEG was normal, however, the MRI (Figure 1A−C) demonstrated multiple areas of abnormal T2 prolongation involving the thalami, posterior hippocampi bilaterally, and central pons, without association of restricted diffusion abnormality. These findings were consistent with