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Case Presentations of the Harvard Affiliated Emergency Medicine Residencies

ACUTE INTOXICATION

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Dr. Kelsy Greenwald: This is a case of a 27-year-old male who was brought to our emergency department (ED) by security after he was found unresponsive in the lobby of the hospital. Almost immediately upon arrival to the ED, clinicians were called to his bedside for somnolence with shallow breathing. His pupils were 3 mm bilaterally. An i.v. line was inserted and he was given 0.4 mg naloxone i.v. for a suspected narcotic overdose, after which he awoke. He then stated that he was in the hospital because he has a seizure disorder and had not been taking his medication. He was placed on a monitor and his initial vitals were otherwise unremarkable. He was afebrile, with a heart rate of 60 beats/min, blood pressure 137/90 mm Hg, respiratory rate 14 breaths/min, and oxygen saturation 99% on room air. However, during further questioning, he would have intermittent episodes of unresponsiveness, lasting 30 s to 1 min, with staring and drooling. These would resolve spontaneously, and he was breathing spontaneously throughout.

Dr. David Peak: What was your initial differential diagnosis?

Dr. Kelsy Greenwald: A young patient presenting with undifferentiated altered mental status is concerning for toxic ingestion or primary neurologic disorder, such as being postictal, with his reported history of seizures. Given his vital signs, infection was considered less likely. The patient did not have any known thyroid, liver, or kidney disease, no recent neurosurgery, and no other specific risk factors for hyponatremia, hypernatremia, uremia, elevated ammonia, or thyroid dysfunction.

Dr. David Peak: Was the patient able to provide any other history?

Dr. Kelsy Greenwald: The patient was unable to provide further history and insisted that his primary problem was related to seizures. He had been prescribed levetiracetam, but he stated he had not taken his medication for 2 weeks. Of note, the patient also had a history of suicidal ideation. Upon review of his chart, he had presented to another local ED 3 days prior for reported ethylene glycol poisoning; however, at that time, his laboratory test results were reassuring, other than an elevated lactate that improved with fluids. He left against medical advice (AMA). He then presented to our ED 2 days prior to this current presentation, endorsing bilateral flank pain, again stating that he accidentally ingested ethylene glycol the day before. He stated that he had unintentionally poured ethylene glycol instead of soup broth into his meal. Based on the prior record, he reported he consumed approximately 10 spoonfuls of soup before realizing he was drinking antifreeze. He called the area poison control center and was instructed to seek emergency evaluation. In our ED 2 days ago, he appeared clinically well with reassuring laboratory values. He denied a suicide attempt, and he had again left AMA.

Dr. Susan Wilcox: He had left AMA twice. Why did he return the third time?

Dr. Kelsy Greenwald: Once asked specifically about his prior presentations and ethylene glycol ingestion, he repeated his story regarding the mistaken ingestion in his soup. He denied any further ingestion. He stated he

had returned for the persistent 2 days of bilateral flank pain, nausea, one episode of vomiting, and some blurred vision. Review of systems was otherwise negative.

Dr. David Peak: How was the remainder of the physical examination?

Dr. Kelsy Greenwald: As mentioned, the patient had repeated brief episodes of unresponsiveness with staring and drooling, resolving spontaneously. He had right-sided costovertebral angle tenderness and refused to read an eye chart to evaluate his blurred vision. His examination was otherwise unremarkable, with clear lungs, normal heart sounds, no abdominal tenderness, and no other focal neurologic deficits. He had full strength in his bilateral upper and lower extremities and no facial droop. Gait, sensation, pronator drift, and dysdiadochokinesia could not be assessed, given his altered mental status.

Dr. Kathleen Wittels: What were your next steps in management?

Dr. Kelsy Greenwald: Lorazepam and levetiracetam were ordered based on the history of seizure activity. Laboratory tests were ordered and were notable for an initial pH of 7.15, anion gap of 30 mmol/L, osmolar gap 22 mOsm/kg, bicarbonate of 8 mmol/L, and lactate of 9 mmol/L. His initial creatinine was 1.37 mg/dL with potassium of 5.1 mmol/L. His serum toxicology screen, including acetaminophen, salicylates, ethanol, and tricyclics, was negative. We were unable to obtain a urine toxicology screen until the next day. His electrocardiogram was normal sinus rhythm with normal intervals.

Dr. Kelli O'Laughlin: How did you interpret his laboratory data?

Dr. Kelsy Greenwald: Given the large anion gap and osmolar gap, ethylene glycol toxicity was high on the differential, as was methanol. However, we also considered seizures and subsequent lactic acidosis as a contributor to his acidosis. Uremia, diabetic ketoacidosis, alcoholic ketoacidosis, and salicylates were considered unlikely, based on the laboratory data. Iron and isoniazid toxicity were considered unlikely, given the history.

Dr. Susan Wilcox: What further therapy did you initiate?

Dr. Kelsy Greenwald: He received 2 L sodium chloride 0.9%. We also ordered fomepizole 870 mg i.v. and a total of 100 mEq sodium bicarbonate 8.4%. However, there was some delay in giving treatment, as the patient was initially declining any medication. He also produced a written letter with his signature stating he refuses dialysis. He was unable to further describe why he was rejecting the recommended therapies or the consequences of denying treatment. He also could not explain why he carried a letter mentioning dialysis, given he did not have any history of renal problems. The emergency physicians determined he did not have capacity to refuse lifesaving intervention, based on his inability to communicate his decision and demonstrate understanding of the risks and benefits of this decision. Although the patient adamantly denied suicidal ideation, he was placed on an involuntary psychiatric hold because we suspected he had ingested more ethylene glycol in an attempt to hurt himself or end his life. In the Commonwealth of Massachusetts, licensed physicians, qualified psychiatric nurse mental health clinical specialists, qualified psychologists, and licensed independent clinical social workers may hold or restrain a patient against their will when there is reason to believe that failure to hold the patient would create a likelihood of serious harm related to mental illness (1). After learning of the involuntary hold and the plan to continue treatment, the patient became more agitated. He required a total of 3 mg lorazepam and 5 mg haloperidol lactate intravenously, as well as temporary four-point restraints for patient and staff safety.

Dr. Susan Wilcox: Did you reassess how the therapy was working?

Dr. Kelsy Greenwald: After he was given sedating medication, he became calm and the fomepizole and the bicarbonate were given. Repeat laboratory tests drawn 5 h after the original were notable for potassium of 6.3 mmol/L and creatinine of 1.94 mg/dL. Lactate continued to rise to 9.5 mmol/L, bicarbonate continued to be low at 7 mmol/L, though his anion gap had improved slightly to 26 mmol/L with a pH of 7.28. Vital signs at this time were notable for tachycardia of 108 beat/min, blood pressure of 146/103 mm Hg, and respiratory rate of 30 breaths/min, though he continued to have normal oxygen saturation on room air. Based on his high potassium, an electrocardiogram was repeated, which showed peaked T waves. He was given calcium gluconate 1 g i.v., 10 U insulin regular i.v., and 25 g dextrose 50% i.v.

Dr. Kelli O'Laughlin: Were any consulting services involved in this case?

Dr. Kelsy Greenwald: Poison control was contacted and noted that because his laboratory tests 2 days ago were reassuring, he likely had a more recent ingestion, as gross laboratory abnormalities would present over the first 24 h. Nephrology was consulted, given his elevated potassium and low pH. They recommended starting dialysis. Psychiatry was consulted after he had refused treatment, and they agreed he did not have the capacity to make medical decisions.

Dr. David Peak: What was the disposition from the ED?

Dr. Kelsy Greenwald: He was admitted to the medical intensive care unit (ICU) for emergent dialysis.

Dr. Kathleen Wittels: This case became more straightforward once the chart was reviewed for previous visits with ethylene glycol poisoning. Was his presentation otherwise consistent with ethylene glycol poisoning?

Dr. Kelsy Greenwald: Ethylene glycol causes dozens of fatal intoxications in the United States annually; ingestion of 1 g/kg is considered lethal, with much smaller levels still associated with severe toxicity (2). Ethylene glycol has three classic phases: 1) the neurologic phase, with slurred speech, ataxia, somnolence for the first 12 h; 2) the cardiopulmonary phase, with tachycardia, hypertension followed by hypotension, tachypnea, congestive heart failure, pulmonary edema over the next 12–36 h; and 3) the renal phase, with progressive renal injury for the next 24–36 h (3).

However, some patients, as with this case, can have multiple ingestions of ethylene glycol at different times, and many of the stages of presentation can overlap. The gold standard of gas chromatography to measure serum levels of ethylene glycol has limited availability and an extended turnaround time (3). Furthermore, there is little correlation between severity of disease and the level of ethylene glycol. It is important to be suspicious of ethylene glycol intoxication when a patient has a profoundly high anion gap metabolic acidosis, elevated lactate, and high plasma osmolality gap. Patients may also have hematuria and oxaluria (4).

Dr. Eric Nadel: How does ethylene glycol cause these effects?

Dr. Kelsy Greenwald: The liver metabolizes ethylene glycol to glycolaldehyde, using alcohol dehydrogenase, and then to glycolic acid, glyoxylic acid, and oxalic acid. These metabolic byproducts of ethylene glycol result in metabolic acidosis. This process also depletes nicotinamide adenine dinucleotide, and leads to a buildup of lactate (5). The buildup of acids leads to cerebral edema and a reduction in cardiac contractility. Direct toxicity can also lead to acute respiratory distress syndrome. Oxalic acid also precipitates as oxylate crystals leading to blockage of renal tubules (3).

Dr. Eric Nadel: How is ethylene glycol toxicity typically treated?

Dr. Kelsy Greenwald: Rapid treatment with fomepizole and dialysis, if necessary, can be lifesaving. Fomepizole is a competitive inhibitor of alcohol dehydrogenase and prevents further formation of the toxic metabolites of ethylene glycol. Therefore, the effect of fomepizole is dependent on the timing of initiating therapy and the amount of toxic metabolites that have already accumulated. Fomepizole is often initiated as soon as toxic alcohol ingestion is suspected, as side effects are rare (6). It is typically given intravenously with a loading dose of 15 mg/kg, with a maintenance dose of 10 mg/kg every 12 h for the next 48 h, followed by 15 mg/kg every 12 h (5). In addition, ethylene glycol penetrates end-organ tissues more easily in an acidotic environment, and treatment with sodium bicarbonate can be beneficial, with a goal of maintaining pH > 7.0 (2). Dialysis is recommended in addition to fomepizole if there is a high anion gap metabolic acidosis or evidence of end organ damage, regardless of the drug level (7). Fomepizole is dialyzable and dosing should be increased to every 4 h during hemodialysis.

Dr. David Brown: How did the patient do?

Dr. Kelsy Greenwald: The patient was transferred from the ICU to the floor on hospital day 3. His course was notable for a peak ethylene glycol level of 133 mg/L. He received one run of hemodialysis, after which the ethylene glycol level was undetectable on three repeat checks. He sustained a significant acute kidney injury (creatinine peaked at a level of 11.70 mg/dL). He was transferred on hospital day 10 to inpatient psychiatry, where he stayed for an additional 7 days. He was not discharged on any psychiatric medications. Since discharge, he has presented to our ED 5 times over the past year: three times for unwitnessed seizure activity; once for psychiatric evaluation after a bystander called emergency medical services, as he was seen standing on a three-story ledge; and once for nausea, vomiting, and ataxia.

Dr. David Brown: Any final learning points?

Dr. Kelsy Greenwald: Ethylene glycol poisoning should be in the differential diagnosis of a patient with acutely altered mental status. Ethylene glycol should be considered even more likely in a patient with metabolic acidosis or high osmolar gap, and treatment will often have to be started before laboratory confirmation can be obtained. Patients without capacity cannot refuse evaluation or therapy.

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