CASE REPORT

Expanding the differential: toluene-induced toxicity

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SUMMARY

A 31-year-old woman presented to the hospital with generalised weakness and lower back and abdominal pain. The only significant finding on physical examination was the weakness of the legs. Laboratory analysis in the emergency department revealed that she was hypokalaemic with metabolic acidosis. She was treated with oral and intravenous potassium, which resolved her weakness. During the search for an explanation for her renal tubular acidosis, she said she was exposed to paint exposure while working on a friend's house. She was discharged on correction of her hypokalaemia, and a subsequent test revealed elevated blood toluene level.

BACKGROUND

A national survey conducted in 2012 showed that 9.2% of the US population use illicit drugs. Among this group, half a million people abuse inhalants.¹ Inhalants include a variety of substances such as gasoline, spray paint, solvents, glue, nail polish remover, rubber cement, permanent markers and cleaning fluids.^{2,3} These compounds are abused for their euphoric effects mediated via various neurotransmitter and receptor systems in the brain.⁴ Toluene, a compound found in many of these products, can cause profound effects in the human body, including neurological, gastrointestinal and renal impairment. This case highlights the importance of considering complications of inhalant use in our daily practice.

CASE PRESENTATION

A 31-year-old Hispanic woman with a medical history of depression and anxiety presented to our hospital with acute onset of generalised weakness and lower back and abdominal pain. When the symptoms began, she stated that she was having difficulty moving her arms and legs. Her symptoms progressively worsened over the next 6 days, with numbness and cramps in her hands. She denied any fever, nausea or vomiting, diarrhoea or illicit drug use. She did not take any medications at home except for ibuprofen, which provided no relief of symptoms. On arrival in the emergency department, she was afebrile, with a blood pressure of 128/86 mm Hg, a pulse of 86/min, and a respiratory rate of 18/min. Physical exam revealed 3/5 strength in the arms and legs. Initial laboratory workup showed the following serum concentrations: sodium 142 mEq/L; potassium 2.2 mEq/L; chloride 114 mEq/L; bicarbonate 13 mEq/L; blood urea nitrogen 7 mg/dL; creatinine 0.7 mg/dL; magnesium 3.6 mg/dL and phosphorus 1.4 mg/dL.

A venous blood gas sample revealed a pH of 7.23, with a pCO₂ of 34 mm Hg, pO₂ of 70 mm Hg, and bicarbonate of 14.3 mm Hg. Random blood glucose was elevated at 191 mg/dL on admission, but morning blood glucose was 101 mg/dL and 110 mg/dL on two consecutive days.

Urinalysis showed a urine pH of 6 and 1+ protein. Blood creatine kinase was elevated at 811 U/L (reference range, 30–200 U/L). Salicylate, acetaminophen and ethylene glycol levels were normal, and the urine toxicology screen was negative.

The patient was admitted to the internal medicine service for further management of the hypokalaemia, and metabolic acidosis. In the initial workup of her metabolic acidosis, the anion gap was normal at 17 mEq/L, calculated using the formula (Na+K) – (Cl+HCO₃). The urine pH of 6 was inappropriately high in the setting of metabolic acidosis and indicated renal tubular acidosis. She was started on intravenous and oral potassium and sodium citrate–citric acid. The anion gap subsequently closed, and the bicarbonate level normalised. However, she continued to be hypokalaemic.

We revisited the history in search for a unifying diagnosis to explain the non-anion gap metabolic acidosis and hypokalaemia. The absence of hypertension in conjunction with the acuity of symptoms and metabolic acidosis rendered unlikely certain causes of aldosterone – mediated renal potassium wasting such as primary aldosteronism, hypercortisolism or Liddle's syndrome.⁵ Non-aldosterone-mediated causes of renal potassium wasting, such as diuretic abuse, Bartter's syndrome and Gitelman syndrome were considered less likely based on the absence of metabolic alkalosis, the presence of metabolic acidosis, age at presentation, and prior normal potassium and bicarbonate levels.⁵ Therefore, causes of distal renal tubular acidosis appeared likely in this case. Sjogren's disease, systemic lupus erythematosus and exposure to lithium were ruled out as potential causes of distal tubular acidosis based on the clinical presentation.⁶ We had previously treated a case of toluene toxicity secondary to paint 'huffing' in the same hospital, with a similar presentation of muscle weakness, profound hypokalaemia and non-anion gap acidosis. Our patient denied paint or glue sniffing but she said that she had been exposed to paint while she was working on a friend's house. We thus deduced that toluene exposure was the likely offender in this case.

OUTCOME AND FOLLOW-UP

After potassium correction with a total of 250 mEq over 2 days in the hospital, her weakness resolved, and she could walk in the hallway without difficulty.

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The hypokalaemia and hypophosphataemia resolved, and potassium and alkali supplements were discontinued. She required an appointment with outpatient psychiatry for her depression but failed to follow-up. A few weeks after the patient was discharged, the toluene test sent to an external laboratory came back positive, with a blood level of 4.12 mg/L.

DISCUSSION

This patient presented with common generalised complaints seen in the hospital—weakness and abdominal pain. However, the root cause was one not commonly included in the differential diagnosis of these clinical symptoms. In a large case series of 25 patients with toluene toxicity, the presenting complaint was muscle weakness in 9 (36%), neuropsychiatric symptoms in 10 (40%) and gastrointestinal complaints in 6 patients (24%).⁷

In terms of renal effects, one study observed metabolic acidosis in 59 of 68 episodes of toluene abuse. In 49 of these patients (83%), the acidosis was associated with a normal anion gap as in our patient; in 13 (22%), with an increased anion gap; and in a few patients, with a mixed type of metabolic acidosis.⁸ Though most patients with toluene toxicity do not present with an anion gap, a gap can form initially from the metabolism of toluene into benzoic and hippuric acids, which generate additional hydrogen ions for the body to excrete.^{4,8} If renal elimination of hippuric acid is impaired, the acid can accumulate in the blood to cause an anion gap.⁹ The ensuing distal renal tubular acidosis is theorised to be caused by toluene's impairment of the distal nephron's ability to secrete ammonium ions, the main carrier for excess hydrogen ions.^{8,9} However, decreased urinary ammonium excretion wasn't seen in all toluene patients and further research is needed to explore the toluene effect on the renal tubules.⁸ The excretion of hippurate mandates the excretion of cations, which may be ammonium, sodium or potassium. Because the excretion of ammonium can be initially limited, losses of sodium or potassium may be substantial.⁸ The increased level of mineralocorticoids secondary to volume depletion also contributes to kaliuresis.⁸ Thus, studies have shown that one-fourth of toluene-abusing patients present with profound hypokalaemia, as did our patient.⁸ The distal renal tubular acidosis observed with toluene exposure has been observed to be reversible.¹⁰

This patient's weakness was likely secondary to her profound hypokalaemia, consistent with the clinical improvement observed on potassium replenishment. Toluene intoxication has also been hypothesised to have a direct toxic effect on muscle membranes, leading to rhabdomyolysis. Rhabdomyolysis can also be caused by severe hypokalaemia and hypophosphataemia. We do not suspect this occurred in our case, as the elevated creatine kinase, the hypokalaemia and hypophosphataemia were not at severe enough level to cause rhabdomyolysis.⁷

Metabolic acidosis, hypokalaemia, renal tubular acidosis and muscle weakness have been reported in chronic solvent abusers and not in occupational exposure in painters as was claimed by the patient in this case.¹¹

The treatment of toluene intoxication requires correction of metabolic abnormalities and monitoring of renal function.⁷ Resolution of symptoms is often rapid. Nevertheless, toluene abuse is neither harmless nor an insignificant consideration—mortality of 15% was reported in a recent study.¹² Toluene abuse is an important, yet often missed, differential diagnosis for the patient with weakness, abdominal complaints and metabolic abnormalities.

Learning points

- ▶ In the patient with clinical symptoms of weakness and abdominal pain in conjunction with metabolic acidosis and hypokalaemia, consider toluene abuse—ask about glue, paint, or marker inhalation.
- ▶ Toluene exposure can cause a non anion gap acidosis, anion gap, or mixed metabolic acidosis.
- ▶ Treatment of toluene exposure largely hinges on correcting metabolic abnormalities and counselling the patient about inhalant abuse.

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