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Toluene inducing acute respiratory failure in a spray paint sniffer

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Summary

Background: Toluene, formerly known as toluol, is an aromatic hydrocarbon that is widely used as an industrial feedstock and as a solvent. Like other solvents, toluene is sometimes also used as an inhalant drug for its intoxicating properties. It has potential to cause multiple effects in the body including death.

Case Report: I report a case of a 27-year-old male, chronic spray paint sniffer, who presented with severe generalized muscle weakness and developed acute respiratory failure requiring ventilatory support. Toluene toxicity was confirmed with measurement of hippuric acid of 8.0 g/L (normal <5.0 g/L).

Conclusions: Acute respiratory failure is a rare complication of chronic toluene exposure that may be lethal if it is not recognized immediately. To our knowledge, this is the second case of acute respiratory failure due to toluene exposure.

key words: **toluene • hippuric acid • acute respiratory failure • spray paint sniffer**

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Background

Toluene is an aromatic hydrocarbon with widespread industrial use as an organic solvent [1,2]. Acute and chronic exposure is known to cause multiple effects in the body, affecting the central nervous, cardiovascular, renal, and gastrointestinal system. It also produces severe acid-base and electrolyte disturbances [1–4]. I report a rare case of a chronic toluene abuser who presented with generalized muscle weakness and developed acute respiratory failure.

Case Report

A 27-year-old male presented to the Emergency Room with an acute episode of severe generalized weakness. It was associated with 3 episodes of vomiting. There was not reported use of any drug or medication. He admitted having a similar, but less severe episode few weeks before which resolved with no intervention. His medical history was otherwise unremarkable. On initial examination, his vital signs were heart rate of 101 beats per minute, respirations of 22 breaths per minute, temperature of 98.4°F, blood pressure of 130/74 mm Hg, and oxygen saturation of 96% on 2 liters. He was alert and oriented with mild distress due to weakness. Neurological examination demonstrated flaccid extremities with profound motor weakness 1/5 and hyporeflexia. Initial laboratory data revealed potassium of 1.5 mmol/L, CO2 of 14, calcium of 9.2 mg/dL, magnesium of 3.0 mg/dL, alkaline phosphatase 297 IU/L, ALT 70 IU/L, AST 51 IU/L, BUN of 5 mg/dL, creatinine of 1.0 mg/dL, CPK 615 IU/L. Urine pH 5.5, (Table 1). Electrocardiogram showed sinus tachycardia with intra-ventricular conduction delayed, QTc prolongation of 702 ms, and Q waves in inferior leads (Figure 1).

He was initially treated aggressively with intravenous potassium chloride and Lactated Ringers, and then admitted to Intensive Care Unit for close monitoring. Six hours later, he developed severe respiratory distress and hypoxia. His arterial blood gas on FiO2 100% showed pH 7.026, pCO2 60.9 mm Hg, pO2 310.3 mm Hg, and HCO3 15.6 mmol/L. He was intubated and placed on ventilatory support. Potassium was still 1.5 mmol/L, phosphorus 1.2 mg/dL, CO2 15 mmol/L and chloride 119 mmol/L. Aggressive replacement of potassium and phosphorus was continued and due to his severe acidosis bicarbonate drip was started. Additional workup results are showed in Table 1.

A diagnosis of hypokalemic muscular paralysis with acute respiratory failure was made. He had also developed elevation of transaminases, hypophosphatemia, hyperchloremic non-anion gap metabolic acidosis, and acute renal failure. However, the cause was still unclear.

Table 1. Serum and urine chemistry during hospital course and 6 months after discharge.

Laboratory test	Reference range	Admission	After 8 hours	After 24 hours	After 96 hours	After 6 months
Blood						
Sodium (mmol/L)	136–144	139.0	142.0	149.0	141.0	144.0
Potassium (mmol/L)	3.6–5.1	1.5	1.5	2.4	4.0	2.8
Chloride (mmol/L)	103–114	113.0	119.0	126.0	111.0	109.0
CO2 (mmol/L)	21–31	14.0	15.0	14.0	25.0	23.0
Magnesium (mmol/L)	1.8–2.5	3.0	2.9	2.8	2.1	–
Phosphorus (mmol/L)	2.3–7.0	1.2	1.2	1.3	2.5	–
BUN (mg/dL)	7–21	5.0	7.0	8.0	9.0	11.0
Creatinine (mg/dL)	0.6–1.3	1.0	0.8	1.1	0.6	0.7
CPK (IU/L)	24–273	615.0	–	521.0	439.0	–
ALT (IU/L)	8–45	70.0	–	48.0	–	141.0
AST (IU/L)	12–35	51.0	–	33.0	–	70.0
Alk Phos (IU/L)	36–115	297.0	–	238.0	–	207.0
Arterial pH	7.35–7.45	7.03	7.08	7.33	7.32	–
Arterial pCO2 (mmHg)	35.0–45.0	60.9	52.8	33.2	33.1	–
Arterial pO2 (mmHg)	80.0–100.0	310.3	421.3	132.5	85.5	–
FiO2 (%)		100 (NRM)	100 (Vent)	45 (NC)	21 (RA)	
Urine						
pH	5–8	5.5	–	6.0	–	–
Potassium	–	9.7	–	–	–	–

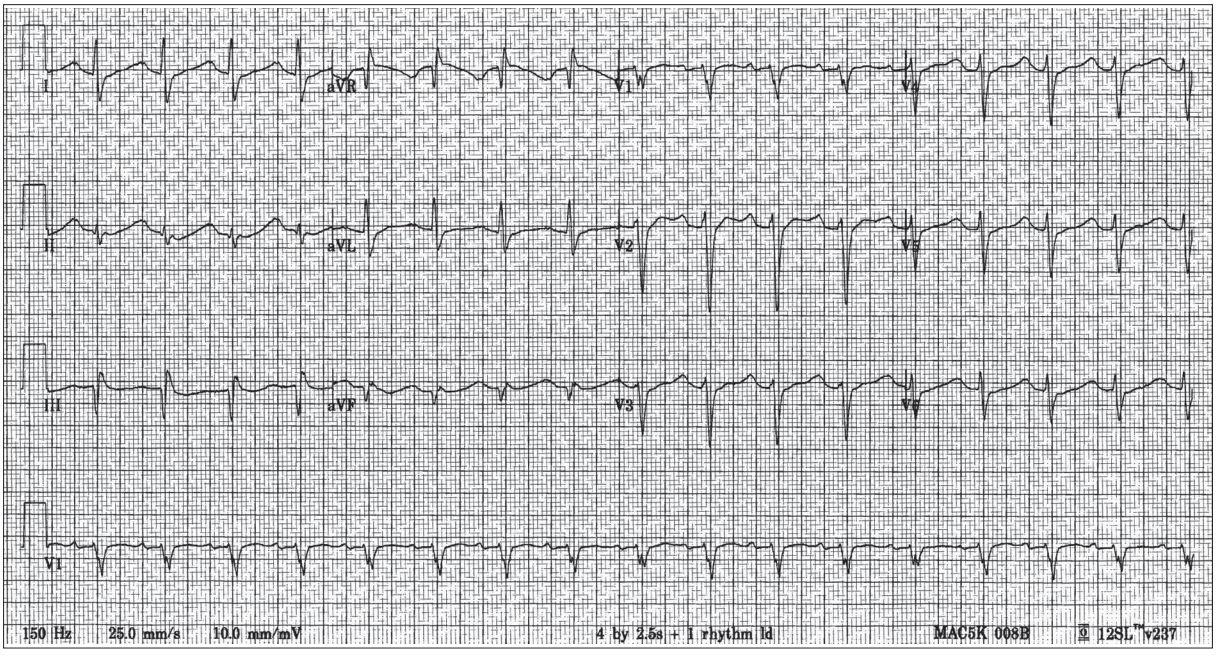

Figure 1. Admission EKG.

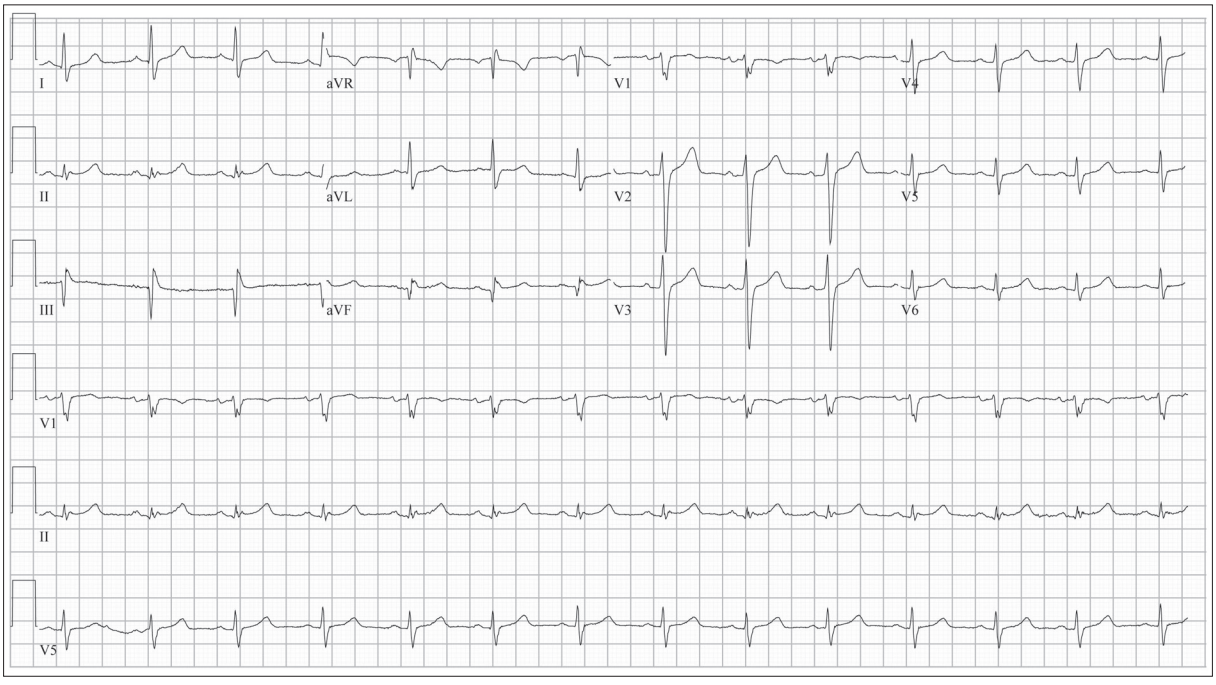

Figure 2. Discharge EKG.

After approximately 16 hours of being intubated, he started recovering his strength. He was able to move all extremities and also remove his endotracheal tube by himself. Fortunately, he did not develop any sign of respiratory distress and remained respiratory and hemodinamically stable. Patient was again interviewed in order to identify any possible cause of his illness. Finally, he confessed being a spray paint sniffer for the last 15 years at least three to four times per week. A spray paint can was obtained showing that one of its components was toluene. Hippuric acid level in urine was ordered to confirm toluene toxicity. The level was 8.0 g/L (normal <5.0 g/L).

He remained in the hospital five days on continuous electrolyte replacement and periodic monitoring. His clinical condition improved rapidly as well as all abnormalities found in the initial workup (Table 1) and electrocardiogram (Figure 2). He was finally discharged with advice to avoid paint spray sniffing and close follow-up with the outpatient clinic. Unfortunately, he never had any follow-up, but he had an Emergency Room visit six months afterwards for an episode of foot cellulitis. During this visit blood work still showed low potassium of 2.8 mmol/L (Table 1).

Discussion

Toluene is an aromatic hydrocarbon and one of the main compounds of glue, gasoline, acrylic paints, varnishes, lacquer, paint thinners, adhesives, and so forth [2,4–7]. Besides industrial exposure, toluene toxicity can occur either from accidental or deliberate inhalation or direct absorption through the skin, but the most frequent and widespread cause of intoxication is sniffing [3,5,6,8,9]. Incidence of solvent abuse is rising and has reached epidemic proportion in some countries, with increased prevalence among children and adolescents, and this fact underlines the importance of recognizing this clinical entity [3,6,8].

Toluene accumulates in adipose tissues when absorbed by skin or ingested due to its hydrophilic properties [4,7]. On the other hand, since it is a volatile compound it is rapidly cleared via the lungs when inhaled [3,10].

Toluene uses the cytochrome P-450 system in the cytoplasm of hepatocytes for its metabolism. It is then metabolized to benzyl alcohol that is more water soluble. An oxygen atom is inserted to it by alcohol dehydrogenase to form benzoic acid. Finally, this acid is conjugated to hippuric acid by adding a glycine group in the hepatocyte mitocondria. Hippuric acid is the byproduct of toluene that may be used as an indirect measure of toluene level [1–5,10].

Multiple effects have been associated with toluene exposure which depends on the concentration and length of exposure. Although the central nervous system appears to be the most sensitive to its effects, the rest of systems might be also affected. There are several reports describing cardiovascular, renal, and gastrointestinal effects as well as acid-base and electrolyte disturbances which have been so severe to produce death [1–6,8,9].

The patient described is a chronic toluene sniffer who presented with severe generalized weakness followed by acute respiratory failure. He also developed elevation of transaminases, non-anion gap metabolic acidosis, and acute renal injury. He was treated with aggressive potassium and phosphorus replacement for hypokalemia and hypophosphatemia respectively, ventilatory support for respiratory failure, bicarbonate infusion for severe acidosis and urine alkalinization, and fluid supplementation for acute kidney injury. Fortunately, his condition improved rapidly within five days and he was able to be discharged.

The effects of toluene toxicity in this patient are clear. He developed many of them such as non-anion gap metabolic acidosis which is the result of overproduction of hippuric acid. This is an indirect way of sodium bicarbonate loss in the urine due to the binding of the conjugate base of hippuric acid and sodium or potassium [17,9,10].

Another toluene effect seen is distal tubular acidosis (RTA) type 1 manifested as potassium wasting in the urine and severe hypokalemia, hypophosphatemia, urine pH greater than 5.5 and positive urine anion gap due to low excretion of $NH4^+$ [1–3,5,8,9]. Potassium wasting might be explained by the same mechanism of potassium binding to bicarbonate and then excrete in the urine [2,10]. However, the urine potassium in this patient was low (9.7 mmol/L) which goes against RTA. In this case, hypokalemia may have been due to chronic low potassium intake or extra renal losses which were not known at the time of presentation. Another point to be considered is that the measurement of potassium was done in a spot urine sample. The best way to quantify it is with 24-hour urine collection which would show the real amount of potassium wasted if any.

His urine anion gap was negative which also goes against RTA [1]. In RTA, there is inability of the kidneys to excrete $NH4^+$, so Cl^- will not be increased in urine and the gap will not be affected, so it will be zero or positive [10]. A postulated explanation is that in chronic metabolic acidosis, as seen in chronic exposure to toluene, the rate of $NH4^+$ urinary excretion is increased due to the main driving force is an increase of NH3 in the medullary interstitium as a result of augmented ammoniagenesis [10]. This is relatively larger than the increment in H^+ secretion [7,9]. Thus, the urine $NH4^+$ excretion rate is increase in conjunction with a higher pH of the urine. There is also an impaired ability to sustain a steep pH gradient in the collecting duct as deducted from the finding of a urine pH greater than 5.5 during metabolic acidosis, inability to increase the pCO2 in highly alkaline urine appropriately and a decrease rate of secretion of H^+ in turtle bladder exposed to toluene [10].

Conclusions

There are multiple systemic effects of chronic toluene exposure that has been reported. Acute respiratory failure is a rare complication that may be lethal if it is not recognized immediately. Thus, I suggest that any patient who presents with unexplained hypokalemic muscular paralysis along with renal tubular acidosis with or without respiratory failure should be questioned about the possibility of toluene abuse.

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