

Fatal Refractory Hypokalemic Paralysis Secondary to Occupational Toluene Exposure: A Case Report

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Abstract

Toluene is an aromatic hydrocarbon widely encountered in occupational settings, particularly in carpentry, painting, and furniture manufacturing. Chronic inhalational exposure can cause acquired distal renal tubular acidosis (dRTA), leading to severe hypokalemia and potentially fatal hypokalemic paralysis. We report the case of a 42-year-old male carpenter with a ten-year history of unprotected daily exposure to organic solvents, who presented with acute flaccid quadriplegia and severe hypokalemia (1.0 mmol/L) in the context of hyperchloremic metabolic acidosis with normal anion gap and renal potassium wasting, consistent with dRTA. Alternative etiologies were systematically excluded. Despite intensive intravenous potassium and magnesium replacement, hypokalemia remained refractory, necessitating mechanical ventilation on day 3 for progressive respiratory failure. Sustained ventricular tachycardia on day 4 was treated with intravenous amiodarone. In the early hours of day 5, the patient suffered a cardiac arrest refractory to advanced cardiopulmonary resuscitation, and no return of spontaneous circulation was achieved. This case illustrates the potentially fatal course of toluene-associated hypokalemic paralysis and underscores the critical importance of occupational history in the diagnostic evaluation of unexplained hypokalemia and acute flaccid paralysis.

Keywords: Toluene; Distal Renal Tubular Acidosis; Hypokalemic Paralysis; Occupational Exposure; Ventricular Arrhythmia

INTRODUCTION

Toluene, an aromatic hydrocarbon widely used in industrial solvents, adhesives, and paints, is a well-documented cause of acquired distal renal tubular acidosis (dRTA). Exposure may occur in recreational settings through deliberate inhalation or in occupational environments, particularly in poorly ventilated workplaces. (1–3)

Chronic toluene exposure is associated with hyperchloremic metabolic acidosis, renal potassium wasting, and severe hypokalemia, which may precipitate acute flaccid paralysis. (4–6)

The underlying mechanism involves hepatic biotransformation of toluene into benzoic acid and subsequently hippuric acid, which impairs distal tubular hydrogen ion secretion by the H⁺-ATPase pump, resulting in urinary acidification failure and renal potassium depletion. (7,8)

Although most reported cases are reversible with appropriate electrolyte replacement, severe and potentially fatal cardiac complications have been described. (9)

We report a fatal case of refractory hypokalemic paralysis possibly related to chronic occupational toluene exposure, illustrating the diagnostic challenges and the life-threatening risk of

malignant ventricular arrhythmias in this condition.

CASE PRESENTATION

A 42-year-old male presented to the emergency department with a five-day history of progressive generalized weakness, preceded by several weeks of fatigue, muscle cramps, and increasing difficulty in ambulation. A detailed occupational history revealed that the patient had worked as a carpenter for approximately ten years, with chronic exposure to industrial solvents. He denied any history of medication use, toxic ingestion, or known past medical conditions. On physical examination, the patient was alert and oriented, with stable vital signs. Neurological assessment revealed severe flaccid quadriparesis with generalized areflexia, without sensory deficits, cranial nerve involvement, or sphincter dysfunction. Initial laboratory investigations demonstrated severe hypokalemia (1.0 mmol/L), hyperchloremic metabolic acidosis with a normal anion gap (9 mEq/L), preserved renal function, and hypomagnesemia. Urinalysis showed inappropriate renal potassium wasting (urine potassium: 17 mmol/L) with a urine pH of 5.5 (Table 1). Electrocardiography demonstrated classical hypokalemic changes, including flattened T waves, ST-segment depression, and prominent U waves (Figure 1). Cerebrospinal fluid analysis was normal, and electromyography showed no evidence of demyelinating or axonal neuropathy.

The metabolic profile, in the context of chronic occupational exposure to industrial solvents, strongly suggested toluene-induced distal renal tubular acidosis (dRTA). Urinary hippuric acid measurement was not performed due to assay unavailability.

The patient was transferred to the intensive care unit for continuous cardiac monitoring and correction of severe electrolyte disturbances. Intravenous potassium chloride was administered via a central venous catheter at 10–15 mmol/h, in combination with magnesium

sulfate infusion (1g/h). Despite ongoing replacement therapy, severe hypokalemia persisted, with serum potassium remaining below 1.5 mmol/L. On day 3, progressive respiratory muscle weakness led to acute ventilatory failure requiring endotracheal intubation and invasive mechanical ventilation. On day 4, the patient developed ventricular tachycardia, managed with intravenous amiodarone (300 mg over 30-60 minutes), followed by continuous infusion (900 mg over 24 hours). In the early hours of day 5, he suffered a cardiac arrest. Advanced life support was immediately initiated, including external chest compressions and repeated intravenous epinephrine (1 mg every 3-5 minutes). Despite 40 min of resuscitative efforts, return of spontaneous circulation was not achieved, and the patient was pronounced deceased.

Table 1. Patients' Laboratory findings on admission

Parameter	Value	Reference Range
Plasma		
Sodium (mmol/L)	139	136–145
Potassium (mmol/L)	1.0	3.5–5.0
Magnesium (mmol/L)	0.5	0.8–1.1
Chloride (mmol/L)	109	98–107
Bicarbonate (mmol/L)	12	22–29
Glucose (mmol/L)	5.6	3.9–6.1
Urea (mmol/L)	0.5	2.5–7.1
Creatinine (μmol/L)	84	62–115
Anion Gap (mEq/L)	9	8–12
Arterial pH	7.31	7.35–7.45
Urine		
Sodium (mmol/L)	15	—
Potassium (mmol/L)	17	—
pH	5.5	—

DISCUSSION

Toluene is a widely used aromatic hydrocarbon encountered in numerous industrial products. (1). Chronic inhalational exposure, particularly in poorly ventilated workplaces, may remain

unrecognized for prolonged periods before presenting with severe metabolic complications.(1–3)



Figure 1. Electrocardiogram showing hypokalemic changes (flattened T waves, ST-segment depression, and prominent U waves).

The renal toxicity of toluene is primarily mediated through its hepatic metabolism. Following absorption, toluene is oxidized to benzyl alcohol and subsequently converted to benzoic acid, which is conjugated to hippuric acid. The accumulation of hippurate anions impairs distal tubular hydrogen ion secretion, resulting in distal renal tubular acidosis. (7,8)

This disorder is characterized by hyperchloremic metabolic acidosis with a normal anion gap, impaired urinary acidification, and renal potassium wasting.(8)

Potassium depletion in this setting is multifactorial. Increased distal delivery of non-reabsorbable anions promotes renal potassium secretion, while secondary hyperaldosteronism further enhances urinary potassium losses. Concomitant hypomagnesemia, as observed in our patient, may aggravate potassium depletion and contribute to refractory hypokalemia by increasing renal potassium wasting.(10,11)

The resulting severe hypokalemia causes skeletal muscle membrane hyperpolarization, reducing neuromuscular excitability and leading to acute flaccid paralysis.(11)

In the present case, the patient's occupation as a carpenter with likely chronic inhalational exposure to toluene-containing solvents, combined with severe hypokalemia,

hyperchloremic normal anion gap metabolic acidosis, preserved renal function, and urinary potassium wasting, strongly supported the diagnosis of toluene-induced distal renal tubular acidosis (dRTA). However, because urinary hippuric acid measurement was unavailable, the diagnosis remained presumptive and alternative etiologies were carefully considered.

Acquired distal renal tubular acidosis may occur in association with autoimmune disorders, hypergammaglobulinemic states, and nephrotoxic drugs (1,7). In parallel, the differential diagnosis of hypokalemic paralysis is broad, including thyrotoxic periodic paralysis, gastrointestinal potassium losses, primary hyperaldosteronism, Bartter syndrome, and Gitelman syndrome (10,11). A systematic clinical and biochemical evaluation, encompassing acid–base status, urinary electrolytes, and renal function, is essential to narrow the diagnostic spectrum (10).

In this case, the absence of autoimmune features, endocrine abnormalities, renal dysfunction, metabolic alkalosis, and gastrointestinal potassium losses further supported toluene toxicity as the most likely diagnosis.

The acute flaccid quadriplegia with generalized areflexia initially raised concern for Guillain–Barré syndrome. However, normal cerebrospinal fluid analysis and the absence of demyelinating or axonal abnormalities on electroneuromyography effectively excluded this diagnosis. Similar presentations have been reported in several cases of toluene-induced hypokalemic paralysis (9,12,13).

According to international society guidelines, the management of severe and refractory hypokalemia is based on prompt and controlled potassium replacement, usually through continuous intravenous infusion under close ECG monitoring, together with magnesium supplementation to facilitate potassium correction and reduce the risk of arrhythmias (14).

In our case, this approach was applied using continuous intravenous potassium chloride (10–15 mmol/h via a central venous catheter) and intravenous magnesium sulfate, under continuous electrocardiographic monitoring.

Although aggressive electrolyte replacement and isotonic saline administration may theoretically influence hydro-electrolyte and acid–base balance, the severe hypokalemia, characteristic electrocardiographic abnormalities, and hyperchloremic metabolic acidosis were already present on admission, prior to any significant therapeutic intervention.

Therefore, the fatal outcome is more attributable to the severity of the underlying disease process rather than to iatrogenic factors.

Despite intensive treatment, serum potassium concentrations remained profoundly low, reflecting ongoing renal potassium losses secondary to persistent tubular dysfunction. The patient subsequently developed progressive respiratory muscle weakness requiring mechanical ventilation. Cardiac arrest occurred on day 5 and was managed immediately according to Advanced Life Support guidelines. (15) However, resuscitative efforts were unsuccessful, and the patient died. Similar fatal outcomes have been reported in the literature in severe cases of toluene intoxication. (5,6)

A major limitation of this report is the absence of direct toxicological confirmation. Urinary hippuric acid measurement, the standard biomarker of toluene exposure, was unavailable in our institution. Furthermore, no post-mortem toxicological investigation was performed. In resource-limited settings, diagnosis may therefore rely on the integration of occupational history, clinical presentation, and characteristic biochemical findings, an approach that has been accepted in comparable published reports. (6,9,13).

CONCLUSION

Toluene-induced distal renal tubular acidosis is a rare but potentially fatal . This case highlights

the diagnostic importance of systematically considering occupational toxic exposures in patients presenting with acute flaccid paralysis, hyperchloremic metabolic acidosis, and renal potassium wasting.

The diagnosis was established by clinical and biochemical exclusion of alternative etiologies, in the absence of direct toxicological confirmation. Clinicians should remain vigilant for the risk of malignant ventricular arrhythmias in severe refractory hypokalemia, and should consider the potential contribution of iatrogenic factors in the context of aggressive fluid and electrolyte therapy. Beyond individual patient management, such cases underscore the obligation to consider occupational disease declaration and workplace investigation to protect potentially co-exposed workers.

Conflict of interest: The authors declare that they have no conflict of interest.

Informed consent: Informed consent was not obtained due to the patient's death. Patient anonymity has been strictly preserved, and no identifying information is included in this report.

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