Accidental toluene overdose in a patient with altered level of consciousness and a raised anion gap acidosis of unknown cause

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Introduction

Toluene is an aromatic hydrocarbon commonly used as a key ingredient in paints, glues, resins and rubber (Camara-Lemarroy et al, 2015). Overdose with toluene can go unrecognised (Omar et al, 2011). This case report describes a patient who presented with an altered level

Case report

A 29-year-old white female presented to the emergency department with a 1-day history of lethargy and confusion. She had a medical history of Raynaud's syndrome, alcohol excess (reported as abstinent for months) and pancreatitis.

The patient was unable to provide a full history at presentation. Collateral history indicated that she had been out with friends the previous evening. No alcohol or illicit substance intake was reported. The patient reported progressive symptoms of headache, nausea, vomiting and lethargy for several days. Confusion resulted in emergency department presentation. The patient denied any alcohol drug or toxin ingestion.

Admission observations were sinus tachycardia (125 beats/minute), blood pressure 145/55 mmHg and tachypnoea (34 breaths/minute) with normal oxygen saturations. The patient appeared hypovolaemic with cool peripheries and prolonged capillary refill time.

Her Glasgow Coma Score was 12/15 (E3V4M6), and the patient was not orientated and had slurred speech. No focal neurological deficit, meningism or other gross abnormalities were found on physical examination.

Venous blood gas demonstrated an anion gap metabolic acidosis: pH 6.87, pO2 5.5 kPa, pCO2 3.2 kPa, HCO3- 6.4 mmol/litre, base excess -29 mmol/litre, lactate 0.2 mmol/litre, glucose 4.6 mmol/litre, Na 147 mmol/litre, K + 4.6 mmol/litre, Cl- 119 mmol/litre, carboxyhaemoglobin 1.4% (albumin corrected anion gap 18.6 mmol/litre and delta ratio 0.5). Urinary ketones were 4+, beta human chorionic gonadotrophin was negative. Blood alcohol, paracetamol and salicylate levels were undetectable, and a urine toxicology screen was negative. Mild hepatorenal injury was evident on biochemistry (Table 1).

Intravenous antibiotics with CNS penetrance were prescribed and stopped after one dose since CNS infection was thought to be of low likelihood. Computed tomography head/venogram revealed no acute intracranial pathology. The patient was admitted to the critical care unit where intravenous bicarbonate therapy started.

Electrolyte management was challenging. The patient developed hypokalaemia; the serum potassium nadir value was 2.9 mmol/litre on admission. Hypernatraemia (159 mmol/litre) and hypophosphataemia (<0.2 mmol/litre) developed, requiring management. The patient had not experienced any cardiac arrhythmias. Renal replacement therapy was considered, but not required.

Collateral history was taken from the patient's mother. It was revealed that as part of her alcohol rehabilitation, the patient had been making jewellery for 2 months, using epoxy glue, in a small unventilated room at her home. Epoxy glue contains toluene which was considered as a possible toxic exposure. The case was discussed with the local clinical pharmacology team and the national poison information service who confirmed that the presentation was in keeping with toluene poisoning.

After 24 hours, the patient's neurological status recovered and she was able to confirm the collateral history. Her pH normalised and the sodium bicarbonate infusion was stopped. Her urine output improved, and her biochemistry returned to baseline. The patient was discharged home after a 5-day admission.

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Table 1. Admission laboratory values

Measurement (SI unit)	Value (laboratory normal range)	Measurement (SI unit)	Value (laboratory normal range)
Haemoglobin (g/litre)	150 (120–160)	Chloride (mmol/litre)	118 (95–108)
Mean cell volume (fl)	107.8 (80–97)	Albumin (g/litre)	52 (35–50)
White cell count (10^9/litre)	23 (4–11)	Phosphate (mmol/litre)	0.58 (0.8–1.5)
Neutrophils (10^9/litre)	19.24 (2–7.5)	Calcium (corrected) (mmol/litre)	2.23 (2.2–2.6)
Lymphocytes (10^9/litre)	1.66 (1.5–4.5)	Magnesium (mmol/litre)	0.8 (0.7–1)
Glucose (mmol/litre)	4.1 (4.1–11)	Alanine transaminase (U/litre)	194 (10–50)
Platelets (10^9/litre)	328 (150–400)	Alkaline phosphatase (U/litre)	248 (30–130)
Sodium (mmol/litre)	143 (133–146)	Bilirubin (µmol/litre)	15 (0–21)
Potassium (mmol/litre)	4.6 (3.5–5.3)	Amylase (U/litre)	42 (28–100)
Urea (mmol/litre)	4.4 (2.5–7.8)	C-reactive protein (mg/litre)	5.1 (<5)
Creatinine (µmol/litre)	80 (59–104)	International normalised ratio	1.1 (≤1.1)
Estimated glomerular filtration rate (ml/min/1.73m^2)	77 (>90)	Prothrombin time	12.2 (10–13)
Urine osmolality (mOsmol/kg)	426 (50–1200)		

of consciousness and a profound acidaemia of uncertain aetiology. This demonstrates the need to keep an open mind when working through the causes of a raised anion gap metabolic acidosis.

Discussion

This patient presented with a common combination of issues: confusion with profound acidaemia. The initial anion gap was 18 mEq/litre. This did not immediately correct with intravenous bicarbonate but required days of careful electrolyte titration.

The differential diagnosis included alcohol excess, diabetic or alcoholic ketoacidosis and/or ingestion of other toxin or poison. The presence of ketones in the urine raised the possibility of ketoacidosis as the aetiology, but normal blood glucose levels, no history of diabetes and rapid correction with oral nutrition made this diagnosis unlikely as the underlying cause. The elevated levels of urinary ketones were felt to be primary, resulting from a history of poor oral intake in the context of recent alcoholism and several days of minimal oral intake secondary to nausea and vomiting.

The mechanism of this potassium wasting is a type 1 distal renal tubular acidosis that leads to a pronounced increase in secretion of potassium. This is thought to be because the distal tubule is unable to excrete hydrogen ions as ammonium. This potassium wasting is accompanied by an acidosis provoked by the conversion of toluene to hippuric acid by benzoic acid. The accumulation of hippuric acid results in a raised urinary anion gap acidosis (Camara-Lemarroy et al, 2015). Unfortunately, it was not possible to measure toluene levels or hippuric acid urinary levels at the authors' hospital, so the diagnosis is a purely clinical one based on the presenting history. Other case reports have demonstrated the ability to test for these, but it often takes too long to obtain a result to be of clinical benefit. Most patients with toluene toxicity do not present with an anion gap, but early in presentation a gap may form. This patient had a raised anion gap on presentation with a delta ratio of 0.5, which represents a mixed anion/non-anion gap, whereas ketoacidosis would be expected to produce a delta ratio closer to 1.0 (Dickson and Luks, 2009). In this case the diagnosis was made by re-examining the available evidence and paying close attention to the collateral history highlighting the patient's use of epoxy resin in a small, poorly ventilated room.

Learning points

- The differential diagnosis of raised anion gap acidosis of unknown cause should include drug or toxin exposure.
- A thorough history of all possible drug and environmental exposures should form part of the assessment of any patient who presents with reduced level of consciousness and metabolic disturbance
- Toluene is a chemical that is present in many commercial and industrial products and is commonly used as a drug of abuse.
- This case report describes accidental environmental exposure to toluene and adds to the literature consisting of case reports and case series through description of a relatively unusual presentation of toluene overdose.

Toluene is an aromatic hydrocarbon, often found as an ingredient in paints, paint thinners, glues and disinfectants. It is the intoxicating element of many inhaled substances of abuse. Its effects last for days because its hydrophobic nature results in accumulation in the body (Hobara et al, 2000; Guo, 2015).

The wide range of morbidity that can be caused by toluene overdose includes sudden cardiac death, hypokalaemic paralysis, hepatotoxicity, renal failure and rhabdomyolysis (Dickson and Luks, 2009; Camara-Lemarroy et al, 2015). Prolonged QTc has been reported in people with chronic toluene exposure, and the majority of arrhythmias reported are thought to be the result of significant hypokalaemia (Camara-Lemarroy et al, 2015). Life-threatening arrhythmias may be exacerbated by the profound metabolic acidosis observed.

Hepatotoxicity related to toluene has been reported previously (Camara-Lemarroy et al, 2015) and appeared to be characteristically present in this patient, with no evidence of raised bilirubin levels or hepatic insufficiency, but a raised alkaline phosphatase level which persisted for several days before returning to a normal range at the end of the hospital admission. Subacute toluene exposure results in abnormalities in liver function test results through a variety of mechanisms, including increased oxidative stress and CYP2E1-dependent chlorzoxazone hydroxylation.

Toluene overdose is sparingly reported, primarily as individual case reports. One case series (Camara-Lemarroy et al, 2015) reported 20 admissions with toluene overdose in 5 years. This article found that altered mental state on admission, female gender, renal failure and severe acidaemia were associated with a worse outcome, including death, and that intensive care should be considered for management. There is no antidote and treatment is primarily supportive.

This case underlines the need for careful collateral history in cases where the underlying aetiology of reduced level of consciousness and metabolic derangement is unclear.

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References

Camara-Lemarroy CR, Rodríguez-Gutiérrez R, Monreal-Robles R et al. Acute toluene intoxication – clinical presentation, management and prognosis: a prospective observational study. BMC Emerg Med. 2015;15(1):19. https://doi.org/10.1186/s12873-015-0039-0

Dickson R, Luks A. Toluene toxicity as a cause of elevated anion gap metabolic acidosis. Respir Care. 2009;54(8):1115–1117

Guo T. A rare but serious case of toluene-induced sudden sniffing death. J Acute Med. 2015;5(4):109–111. https://doi.org/10.1016/j.jacme.2015.09.006

Hobara T, Okuda M, Gotoh M et al. Estimation of the lethal toluene concentration from the accidental death of painting workers. Ind Health. 2000;38(2):228–231. https://doi.org/10.2486/indhealth.38.228

Omar A, Rahman M, Abuhasna S. Reported survival with severe mixed acidosis and hyperlactatemia after toluene poisoning. Saudi J Anaes. 2011;5(1):73–75. https://doi.org/10.4103/1658-354X.76474