Acute Fatal Arsenic Intoxication: A Case Report and Review of the Literature

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Abstract

A 45 year-old man was brought to the emergency department having ingested an unknown quantity of a green substance that was subsequently found to be a termite killer containing arsenic trioxide. Despite aggressive resuscitation, chelation therapy and gastrectomy, he died within 24 hours of presentation. We present the clinical course, pathological findings and a literature review of this rare and often fatal condition.

Keywords: Arsenic trioxide; Chelation therapy; Gastrectomy; Suicide; Resuscitation; Toxicology; Pesticides

Case Report

A 45-year-old man was found by his wife having attempted suicide by ingesting an unknown green substance. This was subsequently indentified as a termite poison brought from China some years earlier. It had a thick paint-like consistency with no discernable odour and no identifiable markings on the packaging (Figure 1). The patient had a history of depression and had recently been admitted to a psychiatric unit following a previous suicide attempt. He was treated with escitalopram but he had recently been non-compliant with this. The exact time of ingestion was unclear but estimated at 10 hours prior to presentation. On arrival at the Emergency Department, he had a temperature of 36.2°C, GCS of 15, a sinus tachycardia with a heart rate of 120, blood pressure of 120/70, oxygen saturations of 98% on room air and a blood sugar level of 5.2 mmol/l. He was vomiting profuse amounts of green liquid and continually passing green watery diarrhea (Figure 2) but there was no haematemesis or PR blood loss. His examination findings were otherwise unremarkable; notably his pupils were 3 mm and reactive, there was no hyper-salivation or lacrimation, his chest was clear and abdomen was soft. He had normal muscle tone and reflexes.

His ECG showed a sinus tachycardia with normal QRS width and QT interval and chest X-ray revealed a radio-opaque mass in the stomach (Figure 3). Initial blood tests demonstrated normal urea, creatinine and electrolytes, a normal full blood count and a normal acid base status. Serum paracetamol, salicylate and alcohol levels were all undetectable. He significantly deteriorated over the following hours with ongoing green vomitus and diarrhoea. He became hypotensive despite aggressive fluid resuscitation and developed profound circulatory insufficiency with lactic acidosis. Repeat blood sampling 5 hours post presentation revealed a potassium of 2.8 mmol/l (3.5-5.0), creatinine of 134 μmol/l (64-104). Arterial blood gas showed pH of 7.24 (7.35- 7.45), PaO$_2$ 93 mmHg (83-108), PaCO$_2$ 28 mmHg (35-48), HCO$_3$ 11 mmol/l (24-32) lactate 10.2 mmol/l (0.5-1.6). His ECG at 6 hours post presentation showed sinus tachycardia at a rate of 150 with deep widespread ST depression. A Transthoracic Echocardiogram revealed an Inferior Vena Caval diameter of 0.8 cm with complete inspiratory collapse and an empty left ventricle with normal systolic function, both findings consistent with profound hypovolaemia. During these first 6 hours, the patient had received 8 litres of crystalloid and was requiring rapidly increasing amount of noradrenaline to maintain his

Figure 1: Photograph of the thick green paint like pesticide in the unlabelled packaging.

Figure 2: From Left to right, samples of the termite poison, urine, vomit and faeces.

Figure 3: Chest Radiograph showing radio-opaque material in the stomach.

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Received November 07, 2015; Accepted January 03, 2016; Published January 10, 2016


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blood pressure. The ingredients of the termiticide had not, at this stage been identified but in the context of the worsening clinical situation, it was decided, after further discussion with the National Poisons Information Services, to commence chelation therapy based on clinical and radiological suspicion of acute arsenic poisoning. Dimercaprol was administered at a dose of 225 mg (3 mg/kg) by intra-muscular injection.

Urgent gastroscopy was performed which demonstrated large volumes of the green material adherent to the gastric mucosa. Attempts to remove this endoscopically proved unsuccessful although large ulcerated areas were visualized beneath some sections. Of note the oesophagus and duodenum appeared normal. At 10 hours post presentation his clinical status had continued to worsen despite a total of over 20 litres fluid resuscitation and high dose inotropic support with noradrenaline and vasopressin. He remained profoundly acidic with a pH of 6.94 and HCO3 of 12 mmol/l and a urea of 4.7 mmol/l. He also developed disseminated intravascular coagulation as manifested by an INR of 2.91, APTT 73.2 secs (26-36), D-Dimer 3.69 μg/ml (<1.00) and fibrinogen 0.60 g/l (2.00-4.00). His platelets had fallen to 62 but haemoglobin remained stable at 136. In consultation with the general surgical team, it was decided to perform an emergent gastrectomy as the last possible life-saving option in order to remove the arsenic load. Intra-operatively, however, he became haemodynamically unsustainable and resuscitation was ceased. The urine arsenic eventually was reported at 2.5 mmol/l. He developed frank pulmonary oedema and became haemodynamically unstable and was unresponsive to noradrenaline and vasopressin. He remained profoundly acidotic with a pH of 6.94 and HCO3 of 12 mmol/l BE -17.9 and lactate 10.4 mmol/l. His potassium, despite aggressive intra-venous replacement, had fallen to 2.5 mmol/l. He developed frank pulmonary oedema and became anuric with a creatinine of 171 mmol/l and a urea of 4.7 mmol/l. He also developed disseminated intravascular coagulation as manifested by an INR of 2.91, APTT 73.2 secs (26-36), D-Dimer 3.69 μg/ml (<1.00) and fibrinogen 0.60 g/l (2.00-4.00). His platelets had fallen to 62 but haemoglobin remained normal at 136.

Figure 4 shows the macroscopic appearance of the stomach. Microscopically, sections demonstrated extensive oedema of the glands and submucosal layers. Erosion of the innermost component, the foveolae, was also present. Overlying the gastric mucosa was a fibrinous exudate entrapping red blood cells and crystalline material, the latter being consistent with the consumption of an arsenic compound.

Pathological Findings

Figure 4 shows the macroscopic appearance of the stomach. Microscopically, sections demonstrated extensive oedema of the glands and submucosal layers. Erosion of the innermost component, the foveolae, was also present. Overlying the gastric mucosa was a fibrinous exudate entrapping red blood cells and crystalline material, the latter being consistent with the consumption of an arsenic compound.

Discussion

Arsenic is an abundant semi-metal with widespread use in industry, agriculture and medicine. Historically it was famously used in homicide as the similarity of its severe gastrointestinal toxicity to infections like cholera [2] made it difficult to be traced. Unfortunately today, chronic arsenic poisoning due to exposure to agricultural agents remains a significant cause of morbidity and mortality, particularly in the developing world [3]. Inorganic salts of arsenic are the most toxic, in particular trivalent arsenic (III) such as arsenic trioxide, and pentavalent arsenic (V) (such as sodium or copper arsenate) which is approximately 60 times less toxic [4]. Arsenic (III) has many toxic effects relating to enzyme inhibition and ionic mimicry, but in particular it inhibits pyruvate dehydrogenase and thus interferes with the Kreb’s cycle [5]. Arsenic (V) directly poisons ATP synthesis by displacing inorganic phosphate [6]. Other features may result from binding sulfhydryl groups of surface proteins and oxidative stress from glutathione depletion [4]. The lethal oral dose in humans is variously reported as 120-200 mg [4], 100-300 mg (6) or 200-300 mg [7,8]. There have however been cases of survival following ingestion of massive doses of arsenic trioxide with one report of survival after ingestion of 54 g [9]. Clinical manifestations of acute toxicity classically include severe gastrointestinal upset associated with gastritis and usually an oesophagitis, due to adherent arsenic compound. This may be of such severity as to necessitate surgical intervention, particularly where decontamination fails because of adherence of the material to injured epithelium [9,10]. Haemodynamic collapse as a result of hypovolaemia and peripheral vasodilatation has been previously described along with cardiac dysfunction, including tordes de pointes [11]. Acidosis occurs as a result of the fluid loss and pre-renal renal failure, along with lactate produced due to tissue hypoperfusion and the inhibition of ATP synthesis. Acute arsenic poisoning also affects the haematological system causing haemolysis and coagulopathy, it causes acute renal and hepatic failure, and an acute neurological insult with delirium and seizures. Polyneuropathy may occur in chronic toxicity or in survivors of acute overdose, [9,10,12].

Early diagnosis is difficult in cases where there is not a clear history of deliberate or accidental ingestion, or clues such as occupational exposure to arsenic. The clinical features above may suggest the diagnosis, but in an undifferentiated poisoning, estimations of urine arsenic may be helpful. Spot urinary arsenic levels higher than 0.67 to 1.33 μmol/L [13] are suggestive of arsenic toxicity, and calculation of arsenic to creatinine ratio may help, as levels above 100 microg/g-creatinine are toxic. Blood levels may also be high (more than 0.067 μmol/L), and abdominal radiographs may demonstrate radio-opaque material within the gastrointestinal tract [14]. Termite poisons are known to contain multiple agents with documented human toxicity [8,9]. These include organophosphates (e.g. chlorpyrifos) [15], phenylpyrazoles (e.g. fipronil) [16], chloronicotinyls (e.g. imidacloprid) [17,18] pyroles (e.g. chlorfenapyr) [19] and pyrethroids (e.g. bifenthrin) [20]. Benzoylureas (e.g. hexaflumuron) are also used widely, but there are no documented cases of human poisoning. There are also a large number of termiticides used to treat wood that contain toxic metal salts, including chromated copper arsenate and other arsenic (III) and (V) compounds.

The principle of management in acute arsenic poisoning are:

1. Supportive therapy with meticulous attention to haemodynamic support and maintenance of circulating blood volume.
2. Decontamination. Gastrointestinal decontamination may reduce the absorbed dose however arsenic is poorly adsorbed onto charcoal [13] and whole bowel irrigation has been reported to have little effect [21]. Gastrointestinal injury maybe so severe that surgical intervention is necessitated [9,10].
3. Enlarge elimination. This is performed with chelation therapy [13] with agents including British anti-Lewisite (BAL) and dimercaprol. The rationale for chelation is based largely on case series and case control data and observations that delayed chelation is associated with poor outcome [22]. Other agents such as oral 2,3-dimercaptosuccinic acid.
acid (DMSA) or 2,3-dimercaptopropane-1-sulfonate (DMPS) are less toxic and water soluble and DMPS can be given intravenously [13]. There are some reports of D-penicillamine being effective [23].

Other potential treatments based on individual case reports or series include haemodialysis [24], although its effect may be limited [25], plasma and/or red cell exchange transfusion has been described for arsenic gas toxicity) [26,27], and experimentally, immunotherapy [28].

Conclusion

Arsenic and its compounds are uncommon but potentially lethal toxins, sometimes seen in acute massive poisoning. We present a case of acute poisoning presenting with signs of severe toxic effect and organ dysfunction, where the diagnosis was uncertain on history. The patient rapidly deteriorated and despite chelation therapy died of multi-organ failure. Arsenic and related compounds should be considered in the differential diagnosis of any acute ingestion or poisoning, particularly where there are prominent gastrointestinal symptoms. Urinary arsenic levels may help where there is diagnostic uncertainty. Early decontamination, chelation therapy and intensive supportive care should be initiated in symptomatic massive poisoning as multi-organ failure. Arsenic and related compounds should be considered in the differential diagnosis of any acute ingestion or poisoning, particularly where there are prominent gastrointestinal symptoms. Urinary arsenic levels may help where there is diagnostic uncertainty. Early decontamination, chelation therapy and intensive supportive care should be initiated in symptomatic massive poisoning as multi-organ failure can be rapidly progressive and severe.

References


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