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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.

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

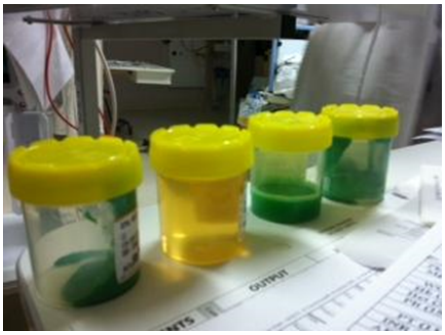

Figure 2: From Left to right, samples of the termite poison, urine, vomit and faeces.

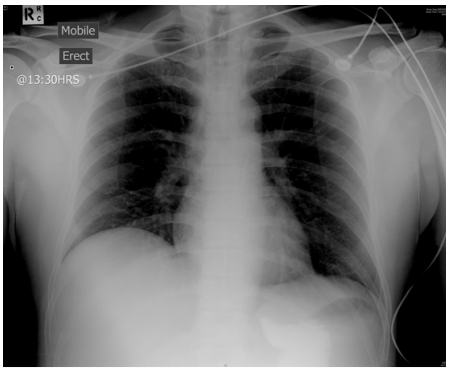

Figure 3: Chest Radiograph showing radio-opaque material in the stomach.

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

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Figure 4: Appearance of the stomach at post mortem.

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 oesphagus 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 acidotic with a pH of 6.94 and HCO_3 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 mmo/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 unsupportable and resuscitation was ceased. The urine arsenic eventually was reported at 160 µmol/l (<0.4 µmol/l) and serum arsenic at 10.5 µmol/l (<1 µmol/l) with urinary levels of over 13.5 µmol/l being confirmatory of acute arsenic ingestion [1].

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 form 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 maybe 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 vasodilation has been previously described along with cardiac dysfunction, including torsades 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] pyrroles (e.g. chlorfenapyr) [19] and pyrethroids (e.g. bifenthrin) [20]. Benzoylureas (e.g. hexaflumaron) 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. Enhance elimination. This is performed with chelation therapy [13] with agents including British anti-Lewisite (BAL) and dimecaprol. 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-dimercaptosucinic

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 arsine 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 can be rapidly progressive and severe.

References

1. Murray, Daly, Little, Cadogen (2011) Toxicology Handbook, (2ndedn.) Churchill Livingston.
2. Shetty P (2005) The verdant assassin. The Lancet 365: 746.
3. Argos M, Kalra T, Rathouz PJ, Chen Y, Pierce B, et al. (2010) Arsenic exposure from drinking water, and all-cause and chronic-disease mortalities in Bangladesh (HEALS): a prospective cohort study. Lancet 376: 252-258.
4. Ratnaike RN (2003) Acute and chronic arsenic toxicity. Postgrad Med J 79: 391-396.
5. Jomova K, Jenisova Z, Feszterova M, Baros S, Liska J, et al. (2011) Arsenic: toxicity, oxidative stress and human disease. J Appl Toxicol 31: 95-107.
6. Goldfrank LR, Flomenbaum N (2006) Biochemical and metabolic principles. In: Goldfrank's toxicologic emergencies. McGraw-Hill Professional 208.
7. Schoolmeester WL, White DR (1980) Arsenic poisoning. South Med J 73: 198-208.
8. Jolliffe DM, Budd AJ, Gwilt DJ (1991) Massive acute arsenic poisoning. Anaesthesia 46: 288-290.
9. Dueñas-Laita A, Pérez-Miranda M, González-López MA, Martín-Escudero JC, Ruiz-Mambrilla M, et al. (2005) Acute arsenic poisoning. Lancet 365: 1982.
10. Kim LH, Abel SJ (2009) Survival after a massive overdose of arsenic trioxide. Crit Care Resusc 11: 42-45.
11. Ortega Carnicer J, Ruiz Lorenzo F, Mañas García D, Ceres Alabau F (2006) [Early onset of torsades de Pointes and elevated levels of serum troponin I due to acute arsenic poisoning]. Med Intensiva 30: 77-80.
12. Vantroyen B, Heilier JF, Meulemans A, Michels A, Buchet JP, et al. (2004) Survival after a lethal dose of arsenic trioxide. J Toxicol Clin Toxicol 42: 889-895.
13. Graeme KA, Pollack CV Jr (1998) Heavy metal toxicity, Part I: arsenic and mercury. J Emerg Med 16: 45-56.
14. Hilfer RJ, Mandel A (1962) Acute arsenic intoxication diagnosed by roentgenograms. Report of a case with survival. N Engl J Med 266: 663-664.
15. Kingston RL, Chen WL, Borron SW, Sioris LJ, Harris CR, et al. (1999) Chlorpyrifos: a ten-year US poison center exposure experience. Vet Hum Toxicol 41: 87-92.
16. Lee SJ, Mulay P, Diebolt-Brown B, Lackovic MJ, Mehler LN, et al. (2010) Acute illnesses associated with exposure to fipronil--surveillance data from 11 states in the United States, 2001-2007. Clin Toxicol (Phila) 48: 737-744.
17. Iyyadurai R, George IA, Peter JV (2010) Imidacloprid poisoning--newer insecticide and fatal toxicity. J Med Toxicol 6: 77-78.
18. Yeh IJ, Lin TJ, Hwang DY (2010) Acute multiple organ failure with imidacloprid and alcohol ingestion. Am J Emerg Med 28: 255.
19. Choi UT, Kang GH, Jang YS, Ahn HC, Seo JY, et al. (2010) Fatality from acute chlorfenapyr poisoning. Clin Toxicol (Phila) 48: 458-459.
20. Ray DE, Forshaw PJ (2000) Pyrethroid insecticides: poisoning syndromes, synergies, and therapy. J Toxicol Clin Toxicol 38: 95-101.
21. Isbister GK, Dawson AH, Whyte IM (2004) Arsenic trioxide poisoning: a description of two acute overdoses. Hum Exp Toxicol 23: 359-364.
22. Kosnett MJ (2010) Chelation for heavy metals (arsenic, lead, and mercury): protective or perilous? Clin Pharmacol Ther 88: 412-415.
23. Peterson RG, Rumack BH (1977) D-penicillamine therapy of acute arsenic poisoning. J Pediatr 91: 661-666.
24. Vaziri ND, Upham T, Barton CH (1980) Hemodialysis clearance of arsenic. Clin Toxicol 17: 451-456.
25. Blythe D, Joyce DA (2001) Clearance of arsenic by haemodialysis after acute poisoning with arsenic trioxide. Intensive Care Med 27: 334.
26. Danielson C, Houseworth J, Skipworth E, Smith D, McCarthy L, et al. (2006) Arsine toxicity treated with red blood cell and plasma exchanges. Transfusion 46: 1576-1579.
27. Song Y, Wang D, Li H, Hao F, Ma J, et al. (2007) Severe acute arsine poisoning treated by plasma exchange. Clin Toxicol (Phila) 45: 721-727.
28. Leikin JB, Goldman-Leikin RE, Evans MA, Wiener S, Hryhorczuk DO (1991) Immunotherapy in acute arsenic poisoning. J Toxicol Clin Toxicol 29: 59-70.