SUCCESSFUL TREATMENT OF POTENTIALLY FATAL HEAVY METAL POISONINGS

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Abstract—Pure inorganic heavy metal ingestions for suicidal intent are a rare occurrence. Most case reports on this subject focus on the serious neurological, hepatic, or renal side effects. We describe two cases of significant heavy metal poisonings (arsenic trioxide and mercuric chloride) that were successfully managed with aggressive decontamination and combined chelation therapy. Both chemicals were obtained in pure powder form through the Internet. © 2007 Elsevier Inc.

Keywords—heavy metal; arsenic; mercury

INTRODUCTION

Pure inorganic heavy metal ingestions for suicidal intent are a rare occurrence. Most case reports on this subject focus on the serious neurological, hepatic, or renal side effects. We describe two cases of significant heavy metal poisonings (arsenic trioxide and mercuric chloride) that were successfully managed by combined chelation therapy. Both chemicals were obtained in pure powder form through the Internet.

CASE REPORTS

Case 1

A 30-year-old man with history of four prior medicinal suicide attempts presented to the Emergency Department with a chief complaint of premeditated arsenic trioxide ingestion 14 h before presentation. He bought 1000 mg of the white powder from an Internet auction site for $20. It came in an unmarked clear plastic Ziploc bag. He subsequently mixed the powder with water and ingested the solution.

Three hours after ingestion, the patient developed headache, nausea, and dizziness, followed by more than 10 episodes of repetitive vomiting. He denied hematemesis, diarrhea, abdominal pain, chest pain, or shortness of breath. He notified his mother the morning of presentation of his symptoms and she drove him to the Emergency Department for evaluation. He denied tobacco, alcohol, or other illicit drug use.

The patient had a history of depression and had four prior suicide attempts. He had undergone inpatient psychiatric treatment, including electroconvulsive therapy. He expressed confusion as to why he was still alive after taking such a large dose.

His medications included olanzapine 10 mg per day and venlafaxine HCL 375 mg per day for 5 weeks.

His review of systems was otherwise negative for sleep disturbance, anxiety, syncope, seizures, numbness or tingling of the hands and feet, involuntary movements, tremor, weakness, balance or gait disturbance.

The physical examination on initial presentation included the following vital signs: temperature of 37.1°C (98.8°F) (oral), pulse 112 beats/min, respiratory rate 20 breaths/min, blood pressure 133/98 mm Hg, pulse oximetry 100% on room air, and weight 200 lbs (90.9 kg). His...
general appearance was healthy and he appeared in no acute distress. HEENT (head, eye, ear, nose, and throat) and lung examinations were normal. Cardiac examination was significant for tachycardia with a regular rhythm and no murmur. Abdomen was soft, non-tender, non-distended, and demonstrated normoactive bowel sounds. Neurologic examination demonstrated no signs of central nervous system (CNS) depression. Psychiatric examination demonstrated a flat affect and depressed mood, but no delirium or psychosis.

Electrocardiogram demonstrated sinus tachycardia with a corrected QT interval of 441 ms. Chest X-ray study was unremarkable. Complete blood count, electrolytes, BUN (blood urea nitrogen), creatinine, and aminotransferases were normal. Urine toxicology screen was positive for benzodiazepines. Serum alcohol, acetaminophen, and salicylate levels were negative. His KUB (kidney, ureter, and bladder X-ray) study demonstrated a high-density material within the distal stomach without evidence of obstruction or dilated bowel loops (Figure 1).

Whole bowel irrigation with polyethylene glycol electrolyte solution was initiated in the Emergency Department. This was continued at a rate of 1.5–2 L/h for approximately 12 h after admission. Antidotal treatment for arsenic poisoning was initiated with British Anti-Lewisite (BAL) 5 mg/kg deep intramuscular injections every 6 h for 48 h. After the first dose of BAL (5 mg/kg) the patient began to complain of burning sensation in the lips, throat, and mouth, lacrimation, rhinorrhea, sweating, and nausea. We subsequently decreased the dose to 3 mg/kg every 6 h for 24 h and then 3 mg/kg every 12 h to complete a 10-day course. The patient experienced no further adverse effects of the BAL after the dose adjustment.

He was admitted to the Intensive Care Unit for close monitoring. Twenty-four-hour urine collection was initiated to monitor urine arsenic levels. Blood and stool arsenic levels were also sent. He developed transient transaminase elevation, which normalized over the course of the hospitalization. His neurologic status remained normal.

Serial KUB studies performed over the next 5 days demonstrated stubborn transit beyond the proximal colon (Figure 2). On hospital day 5, the patient underwent colonoscopy with colonic irrigation to remove the radiopaque densities that remained within the cecum and portion of the transverse colon (Figure 3). Post-colonoscopy KUB study demonstrated removal of the agent (Figure 4).

Daily 24-h urine and blood samples were taken and sent to the toxicology laboratory at Mayo Medical Laboratories (Rochester, MN) to be measured for arsenic...
levels. Concentrations were measured by inductively coupled plasma mass spectrometry (ICP-MS). The arsenic was fractionated into organic and inorganic levels. Our patient had significantly elevated levels of both inorganic and organic arsenic. Fecal and hair samples were taken and tested positive for arsenic as well. Results of all other heavy metals including mercury, thallium, and lead were negative.

Serum arsenic levels were low (<0.05 µg/mL) whereas urinary excretion was high (>10,000 µg/gram creatinine) (Tables 1, 2 and Figure 5).

After 10 days of BAL we switched to oral chelation therapy with succimer at a dose of 10 mg/kg twice daily for 14 days.

After he was discharged to the psychiatric unit, we continued to follow the patient’s serum and urinary arsenic levels for several days. His course after discharge was uneventful, and he remained asymptomatic at the 5-month post-ingestion clinic visit.

**Case 2**

A previously healthy 22-year-old man with a history of depression presented to the Emergency Department...
within 1 h after ingesting mercuric chloride. He obtained 250 g (purity 99.9%) directly from a chemical company (Bioworld; Dublin, OH) through the Internet. He mixed 37 g of the powder with water and drank the solution. Within minutes of ingestion, he spontaneously developed streaks of hematemesis and metallic taste. He denied any other symptoms.

His physical examination was unremarkable except for tachycardia. His abdominal X-ray study was unremarkable. Laboratory values were negative except for a random urine mercury of 1290 μg/gram creatinine (normal <4 μg/gram creatinine). A corresponding blood mercury level of 152 μg/L of mercury (normal <10 μg/L mercury) is shown in Table 3. Heavy metal analysis (blood and urine) for arsenic, lead, and thallium were negative.

Within 2 h of ingestion, BAL 3 mg/kg was administered every 4 h intramuscularly. He subsequently developed a rash due to the BAL on day 5 that was secondary to a suspected peanut allergy. The rash resolved with 60 mg of oral prednisone daily for 5 days. At this point, he was started on succimer (10 mg/kg three times daily for 5 days then twice daily for an additional 2 weeks).

Ten days after ingestion, the blood and 24-h urine mercury levels were 26 μg/L and 160 μg/gram creatinine, respectively. Twelve days post-ingestion, his mercury level was 19 μg/L (Table 3).

Subsequent esophagogastroduodenoscopy demonstrated only mild fundal gastric erythema. He was noted to have a mild eosinophilia (absolute eosinophil count of 0.7 to 0.8 thou/cu mm) that required no treatment and resolved.

His hair mercury level 3 weeks post-ingestion was <1 μg/g. His post-treatment recovery was uneventful.

**DISCUSSION**

Case 1 demonstrates several new aspects in the treatment of acute inorganic heavy metal ingestion. First, it seems that gastrointestinal absorption can be delayed for several hours, as demonstrated by the low serum arsenic levels obtained on admission and the first patient’s lack of systemic complaints other than local gastrointestinal complaints. Certainly, the anticholinergic effects of olanzapine can contribute to the delayed absorption. Although pyloric dysfunction has not specifically been associated with arsenic ingestion, it has been described in acid ingestions along with recurrent vomiting (which occurred in this patient) and may contribute in delayed absorption of arsenic (1–3). Furthermore, the low water solubility of arsenic trioxide makes gastrointestinal absorption less efficient than dissolved arsenic (4).

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**Table 1. Arsenic Levels in Patient with BAL**

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 6</th>
<th>Day 7</th>
<th>Day 8</th>
<th>Day 9</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urine*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inorganic</td>
<td>10,276†</td>
<td>3906‡</td>
<td>1284‡</td>
<td>795‡</td>
<td>817‡</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Organic</td>
<td>&lt;15</td>
<td>272‡</td>
<td>187‡</td>
<td>204‡</td>
<td>314‡</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Serum‡</td>
<td>&lt;0.05</td>
<td>0.11</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Stool§</td>
<td></td>
<td>166</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Urinary arsenic range inorganic <25 μg/gram creatinine.
† Random sample.
‡ 24-h urine collection.
§ Serum arsenic reference range normal <0.07 μg/mL.
|| Stool arsenic reference range <20 μg/L.

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**Table 2. Arsenic Levels with Oral Succimer**

<table>
<thead>
<tr>
<th></th>
<th>Day 26</th>
<th>Day 33</th>
<th>Day 128</th>
</tr>
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<tbody>
<tr>
<td>Urine*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inorganic</td>
<td>129</td>
<td>127</td>
<td>16</td>
</tr>
<tr>
<td>Organic</td>
<td>71</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Serum‡</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Hair§</td>
<td>6.0</td>
<td>3.3</td>
<td></td>
</tr>
</tbody>
</table>

* Urinary arsenic range inorganic <25 μg/gram creatinine.
† Random sample.
‡ Serum arsenic reference range normal <0.07 μg/mL.
§ Hair arsenic reference range <1 μg/gram.

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**Figure 5. Arsenic levels with whole bowel irrigation, BAL, and oral succimer therapy.**
This case seems to be the longest reported delay in presentation to treatment of arsenic ingestion without any long-term sequelae. This delay of absorption of >12 h has significant implications in the initial management of these patients. Gastrointestinal decontamination techniques, particularly whole bowel irrigation, can be considered as a viable option in these individuals presenting several hours post-ingestion (5–8). Total decontamination may take days to achieve. Continuous gastric alkaline irrigation for 6 days with repetitive endoscopy was required for gastrointestinal removal of 5 g of trivalent arsenic powder after an intentional ingestion (6). To date, there has never been a controlled study demonstrating the efficacy of this technique in poisoned patients. As with our case, serial plain abdominal radiographs can be used to determine the effectiveness of decontamination.

Second, as demonstrated radiographically in this patient, colonic irrigation is a viable option for late removal of arsenic located in the large intestine. To our knowledge, this is the first use of colonic irrigation for gastrointestinal decontamination. Because whole bowel irrigation only partially removed the arsenic compound, the presence of this metal represented a risk to the mucosal integrity of the colon. Thus, the purpose of this technique was not to prevent absorption of arsenic into the bloodstream, but to prevent caustic injury to the colonic mucosa. The lack of lower gastrointestinal bleeding or symptomatology demonstrates that this local complication did not occur.

Use of BAL is associated with clinical side-effects (9). The mucosal burning sensations the first patient developed soon after 5 mg/kg deep intramuscular BAL administration are well-known dose-effect adverse reactions that are transient and reversible. At this dosage, about 50% of patients exhibit these side-effects. They typically last 45 min to 2 h (9). As a solvent for lipid-soluble compounds, peanut oil, rather than sesame oil, is utilized for dissolution of BAL. The erythematous rash that the second patient developed is characteristic for a peanut allergy cross-reaction and responded appropriately to steroids, however, this etiology was not fully explored. Patients in whom BAL treatment is contemplated should be questioned about a history of peanut allergy.

The clinical effectiveness of chelation therapy is evident in both cases. A dose of 1 mg/kg of arsenic trioxide is considered to be a fatal dose (6). Our patient ingested 1000 mg or 11 mg/kg, 11 times the accepted fatal dose. Other than localized gastrointestinal effects, mild tachycardia, and transient rise in hepatic transaminases, there did not seem to be any sequelae to the ingestion. The clinical systemic effects of acute arsenic toxicity including pancytopenia, diarrhea, electrolyte disturbance, hypovolemic shock, hemolysis, Torsades de Pointes, and acute tubular necrosis were not demonstrated. No complaints of peripheral neuropathy were ever articulated. The fact that his hair arsenic level was only minimally elevated, along with the low serum arsenic levels and elevated urinary arsenic levels, all point to low tissue levels of arsenic due to the effectiveness of combined (parenteral followed by oral) chelation therapy and aggressive decontamination.

Recently published cases describe survival after ingestion of 5 and 9 grams of arsenic trioxide (6,10). Both of these cases had aggressive decontamination and combined BAL and succimer chelation therapy. The latter case developed axonal polyneuropathy, which continued 1 year post-ingestion. A third case from Japan described a fatal ingestion of 20 grams of arsenic trioxide with secondary contamination symptoms of irritation described in 22 clinicians exposed through inhalation of the patient’s gastric contents (11).

Similar to arsenic, inorganic mercury exposure results in corrosive properties with the target organs being the gastrointestinal tract and the kidneys. The average lethal dose of mercuric chloride is about 1 g, and the half-life of inorganic mercury is about 15–28 days (12,13). Other than mild gastric erosions, the patient described in Case 2 demonstrated no renal sequelae despite a reported 37-gram ingestion. As with the patient in Case 1, this patient’s hair mercury level was very low, which is indicative of low tissue levels of this element. Other cases of significant ingestion of mercury (ranging from 100 grams to 3 kg) have similarly been successfully treated with aggressive decontamination and chelation (14,15). Chelation therapy for inorganic mercury toxicity parallels that of inorganic arsenic and lead (5–10 days of parenteral chelation followed by 14–19 days of oral succimer) (16).

### Table 3. Mercury Levels with BAL and Oral Succimer Therapy

<table>
<thead>
<tr>
<th>Mercury Level</th>
<th>Day 0</th>
<th>Day 10</th>
<th>Day 12</th>
<th>Day 14</th>
<th>Day 15</th>
<th>Day 16</th>
<th>Day 19</th>
<th>Day 24</th>
<th>Day 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum*</td>
<td>152</td>
<td>26</td>
<td>19</td>
<td>12</td>
<td>11</td>
<td>6</td>
<td>6</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Urine†</td>
<td>1290</td>
<td>160</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9.4</td>
</tr>
</tbody>
</table>

* µg/L (normal <10 µg/L).
† µg/gram creatinine (normal <4 µg/gram creatinine), all 24-h urine collections.
The increasing availability of toxic substances over the Internet increases the likelihood of exposure to non-medical pure chemical agents and thus it is helpful if emergency physicians are familiar with the immediate management of these exposures (17,18). In fact, in a recent study of 121 products surveyed over a 10-month period on eBay, 25 products were deemed “super toxic” and eight of these products contained arsenic trioxide (17). Both of these cases demonstrate that heavy metals are easily and cheaply (each agent in these cases cost less than $40) obtained through the Internet. Aggressive decontamination techniques, along with prompt use of chelators for severe exposures, can result in successful treatment of massive exposures to heavy metals even if the patient’s presentation is delayed by several hours.

REFERENCES