Methemoglobinemia and Uremia from an Unusual Poison

Arjun Sekar, Subhash Paudel, Siva P Sivakumar and Ashish Verma
St. Vincent Hospital, Worcester, Massachusetts, USA

*Corresponding author: Arjun Sekar, MD, Internal Medicine Resident, St. Vincent Hospital Medicine, 123 Summer Street, Worcester, Massachusetts 01608, USA, Tel: 7742321971; E-mail: arjun_sekar@hotmail.com

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Abstract

Introduction: Naphthalene toxicity is an unusual form of poisoning and poses a diagnostic and therapeutic challenge due to its rare occurrence and complicated clinical course.

Case Report: We report a case of naphthalene toxicity from non-accidental, non-suicidal ingestion of mothballs in a 56 year old male who presented with methemoglobinemia, hemolytic anemia and respiratory failure. He was treated with supportive management with blood transfusions, urinary alkalization; hemodialysis for acute kidney injury and he also required noninvasive ventilation for hypoxemic respiratory failure.

Discussion: The crucial aspect in the acute management of any poisoning is knowledge about its toxic manifestations, lethal dose and options for treatment including available antidotes. Mothball poisoning is rarely encountered in North America and awareness of its toxicity and treatment is crucial as the history may not be forthcoming in many instances. In many parts of the world naphthalene containing mothballs are still available commercially. We discuss the method for determining the more toxic form of mothball poisoning and the spectrum of its toxicity. We review the multidisciplinary approach to manage its complicated clinical course including possible antidotes.

Introduction

Naphthalene toxicity is a rare form of poisoning and poses a diagnostic and therapeutic challenge due to its complicated clinical course.

We report a case of naphthalene toxicity from non-accidental, non-suicidal ingestion of mothballs in a 56 year old male who developed methemoglobinemia, hemolytic anemia and respiratory failure. He received blood transfusions, urinary alkalisation, and hemodialysis for acute kidney injury and high flow oxygen for hypoxemic respiratory failure.

We discuss the bedside method for determining the more toxic form of mothball poisoning and the spectrum of its toxicity. We also describe the steps in managing hemolysis and hypoxia caused by naphthalene toxicity including the therapeutic utility of methylene blue.

The crucial aspect in the acute management of any poisoning is knowledge about its toxic manifestations, lethal dose and options for treatment including. This is crucial as history may not be forthcoming in many instances.

Case Presentation

A 56 year African American male presented to the hospital with shortness of breath and jaundice. Symptoms began after he started chewing and sniffing a total of 4 mothballs a few days earlier with a perception that it would improve his halitosis as suggested by his friend. Dyspnea progressively worsened and he also noticed yellowish discoloration of his eyes, fatigue and dark red colored urine. Past medical history was pertinent only for hypertension for which he was advised lifestyle measures.

Initial vital signs revealed; BP-160/85 mmhg, pulse rate 80 beats per minute, respiratory rate 24 per minute, SpO2 85% on room air which improved to 94% on 6 liters of O2. Positive physical findings included scleral icterus, mild cyanosis, tachypnea with clear lungs and no respiratory distress.

Investigations

Initial biochemical markers showed total white count 21.4*10^3 (3.9-11/microL), anemia with hemoglobin (Hb) 8.0 (12.5-17.0 g/dl), hematocrit (Hct) 25.4% (36-50%), BUN 35 (5-26 mg/dl), creatinine 1.45 (0.6-1.5 mg/dl), total bilirubin 16.1 (0.01-1.2 mg/dl), direct bilirubin 0.8 (0.0-0.4 mg/dl) and methemoglobin (Methb) level 9.1% (Normal <1.5%).

Positive hemolytic markers included a reticulocyte count 5.7% (0.6-2.6%), absolute reticulocyte count 146.7 (35-101), lactate dehydrogenase (LDH) 979 (Normal<226 U/L), low haptoglobin and some schistocytes and bite cells in the peripheral smear. Urine analysis showed grossly red urine, few WBC’s and no RBC’s or casts, suggesting hemoglobinuria. Initial arterial blood gas was normal.

G6PD levels tested initially were normal 200 U (Normal: 146-376 U) and toxicology screen for salicylates, acetaminophen and other addictive substances negative. Hepatitis panel, chest imaging and renal ultrasound were normal.

However, few hours later his respiratory status worsened and he became more hypoxic requiring 100% supplemental oxygen. Arterial blood gas showed pH 7.37 (7.38-7.42), pCO2 34.8 (38-42 mmhg), pO2...
Methemoglobin was still high at 4.5%. (Refer table 1 for trend of both. This simple test helped us identify the more severe form of saturation (SpO\(_2\)). Mothballs are used to protect clothing and fabrics from moths by acting as insecticides. PDCB containing mothballs are also floats in salt solution whereas a paradichlorbenzene mothball sinks in water and can be fatal. Differentiation from PDCB is crucial. One simple way to differentiate between the two is to test the ability to float in water and shifts the oxyhemoglobin curve to the left. Pulse oximetry may become unreliable in the setting of methemoglobinemia, registering a false high in patients with severe methemoglobinemia and a false low in patients with mild methemoglobinemia [4].

Clinically, naphthalene has a wide spectrum of toxicity (table 2). There have been deaths associated with naphthalene toxicity [3].

Table 1: Progression of biochemical markers during admission.

<table>
<thead>
<tr>
<th>Day of admission</th>
<th>Day 1</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 7</th>
<th>Day 9</th>
<th>Day 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>8.0</td>
<td>7.2</td>
<td>8.3</td>
<td>8.0</td>
<td>7.3</td>
<td>9.2</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>1.45</td>
<td>0.65</td>
<td>9.95</td>
<td>12.25</td>
<td>13.05</td>
<td>7.93</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>979</td>
<td>2399</td>
<td>1948</td>
<td>880</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Methemoglobin (%)</td>
<td>9.1</td>
<td>4.5</td>
<td>1.9</td>
<td>&lt;1.5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2: Spectrum of naphthalene toxicity.

<table>
<thead>
<tr>
<th>System</th>
<th>Clinical Features</th>
<th>Mechanism</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>Hypoxia</td>
<td>Methemoglobinemia (in susceptible individuals)</td>
</tr>
<tr>
<td>Renal</td>
<td>Dark urine, acute kidney injury</td>
<td>Hemoglobinuria, hemolysis</td>
</tr>
<tr>
<td>Hematological</td>
<td>Jaundice, anemia</td>
<td>Hemolysis (especially in G6PD deficient individuals)</td>
</tr>
<tr>
<td>CNS</td>
<td>Confusion, seizures</td>
<td>Leukoencephalopathy (rare)</td>
</tr>
<tr>
<td>Skin</td>
<td>Dermatitis</td>
<td>Hypersensitivity</td>
</tr>
</tbody>
</table>

Discussion

Mothballs may contain naphthalene or paradichlorbenzene (PDCB). Mothballs are used to protect clothing and fabrics from moths by acting as insecticides. PDCB containing mothballs are also sold as air fresheners. As the toxicity from naphthalene is severe and can be fatal, differentiation from PDCB is crucial. One simple way to differentiate between the two is to test the ability to float in water and saturated salt solution [1]. Naphthalene mothball sinks in water and floats in salt solution whereas a paradichlorbenzene mothball sinks in both. This simple test helped us identify the more severe form of poisoning in our patient.

Naphthalene is readily absorbed in the systemic circulation by the skin or inhalation and is initially metabolized into a number of reactive metabolites by cytochrome P450 oxidation and then excreted in the urine. Following liver metabolism, naphthal-alpha, the most potent derivative of naphthalene, causes hemolysis with severe anemia and Heinz bodies’ formation [2]. Patients with low tolerance to oxidative stress like those with G6PD deficiency are particularly at higher risk for hemolysis. In our patient, G6PD testing done during active hemolysis was normal, but low weeks after the acute hemolysis had resolved. During active hemolysis measuring G6PD levels is unreliable as it can be falsely normal.

Initial treatment was mainly supportive with blood transfusions, oxygen and close monitoring of biochemical parameters.

He was on a nonrebreather mask for hypoxia where repeat blood gas revealed; pH 7.35 (7.38-7.42), pCO\(_2\) 36.3 (38-42) mmhg, pO\(_2\) 70 (85-95) mmhg, bicarbonate 20 meq/L (23-28), SpO\(_2\) 93% showing some improvement in hypoxia.

Isotonic bicarbonate infusion was administered to alkalinize urine and for metabolic acidosis. He required a single session of hemodialysis for persistent uremia. Thereafter, his kidney function improved gradually without need for further dialysis. Methylene blue was held as methemoglobin levels trended down.

Outcome and Follow up

After treatment, hypoxia, uremia and anemia improved. Methemoglobin levels trended down to undetectable levels. On discharge, hypoxia had resolved, creatinine improved to 6.7 mg/dl and hemoglobin 8.8 g/dl. The initial leukocytosis resolved spontaneously after a few days. A few weeks later CBC was normal but G6PD levels were low at 62 U (Normal: 146-376 U) confirming G6PD deficiency. A year later, he has chronic kidney disease with creatinine of 1.8 mg/dl (0.6-1.5).

To conclude, intentional naphthalene toxicity is unusual in the US and can present with hemolysis and methemoglobinemia. Naphthalene mothballs have been banned in many European countries and in the US its packaging and processing is strictly monitored. In cases of unknown poisoning or acute cases of hemolysis, naphthalene toxicity must be considered as part of the differential diagnosis.

References


