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Case Report Open Access

Methemoglobinemia and Uremia from an Unusual Poison

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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 alkalinization; 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 alkalinisation, 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 hypoxemia 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, SpO_2 85% on room air which improved to 94% on 6 liters of O_2. 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 *103(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), pCO_2 34.8 (38-42 mmhg), pO_2

50.5 (85-95 mmhg), bicarbonate 20.4 (23-28 meq/L) and oxygen saturation (SpO_2) 85% (95-97%) suggesting severe hypoxemia. Chest imaging showed no acute cardiopulmonary process.

Hemolysis worsened with hematocrit dropping to 20.5% (36-50%) and LDH worsened to 2399 U/L. He developed nonoliguric acute kidney injury with creatinine increasing to 4.45 (0.6-1.5) mg/dl. Serum methemoglobin was still high at 4.5%. (Refer table 1 for trend of biochemical markers).

Day of admission	Day 1	Day 3	Day 5	Day 7	Day 9	Day 11
Hemoglobin(g/dl)	8.0	7.2	8.3	8.0	7.3	9.2
Creatinine(mg/dl)	1.45	6.65	9.96	12.27	13.05	7.93
LDH(U/L)	979	2399	1948	880	-	-
Methemoglobin (%)	9.1	4.5	1.9	<1.5		

Table 1: Progression of biochemical markers during admission.

Treatment

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).

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 where as 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, naphthol-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.

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

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

Table 2: Spectrum of naphthalene toxicity.

Methemoglobinemia is caused by the oxidation of ferrous (Fe^{2+}) to ferric (Fe^{3+}) Hb. It renders hemoglobin incapable of carrying oxygen 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].

Treatment is usually supportive. Naphthalene toxicity warrants hospital admission for close monitoring. Hemolysis requires blood transfusions and hemoglobinuria should be managed with urinary alkalinization if necessary. Hemodialysis is primarily for treating kidney injury from hemolysis and there is a report of a case of severe naphthalene poisoning who survived after dialysis [5].

Methylene blue acts as an oxidizing agent and can be used to treat methemoglobinemia [6]. Methylene blue is reduced to leukomethylene blue by accepting electrons from NADPH. Leukomethylene blue donates an electron donor reducing methemoglobin to hemoglobin. G6PD deficiency results in low levels of NADPH which is required for methylene blue to be effective. Hence, its use is not recommended in G6PD deficient individuals [7]. As our patient's MetHb level was less than 30%, he did not receive methylene blue.

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.

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