Acute hemolytic anemia with rare etiology

Saumya Gupta[1], Eram Nahid[2], L P Meena[3]

From [1]Assistant Professor, [2]Junior Resident, [3]Associate Professor, Department of General Medicine, Institute of Medical Sciences-Banaras Hindu University Campus, Varanasi, Uttar Pradesh, India.

Correspondence to: Dr. Saumya Gupta, Department of General Medicine, Institute of Medical Sciences-Banaras Hindu University Campus, Varanasi - 221005, Uttar Pradesh, India. E-mail: g_saumya@yahoo.com

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ABSTRACT

Naphthalene is a widely used industrial and household chemical in the form of mothballs. But it has rarely been used as an agent of poisoning worldwide. Here, we describe the case of acute hemolytic anemia with methemoglobinemia following ingestion of naphthalene mothballs. A 26-year-old female ingested 6 mothballs and presented three days later with hemolysis and methemoglobinaemia. She was given intravenous methylene blue, N-acetylcysteine and ascorbic acid, besides supportive treatment. Renal replacement therapy in the form of hemodialysis was done on an alternate day basis. She was discharged after ten days on outpatient follow-up.

Keywords: *Methemoglobinemia, Methylene blue, N-Acetylcysteine, Renal replacement therapy.*

Naphthalene is commonly found in moth repellent products such as mothballs. It is well absorbed from oral, dermal and inhalational exposure. Accidental ingestion has resulted in toxicities and even death [1]. They are commonly used in households. It has rarely been an agent of poisoning worldwide [1].

Here we present the case of a 26-year-old female ingested 6 mothballs, presented three days later with hemolysis and methemoglobinaemia and managed by giving intravenous methylene blue, N-acetylcysteine and ascorbic acid besides supportive care.

CASE REPORT

A 26-year-old female patient presented to the emergency 72 hours after oral ingestion of 6 naphthalene balls with suicidal intent. She did not have any significant past medical history. She complained of vomiting and pain abdomen a few hours after the ingestion and decreased urine output a day later. She consulted some local practitioner and presented to us on the third day.

On presentation, she was drowsy, afebrile, had a pulse rate of 120/minute, BP 110/70 mm Hg, respiratory rate 30/minute, SpO_2 75% on oxygen at 6 l/min via simple face mask. She was pale and jaundiced and had rapid shallow breathing. On chest auscultation, bilateral crepitations were present. Cardiovascular and abdominal examinations were within normal limit. On neurological examination, there was no focal neurological deficit, pupils were bilaterally normal size reacting to light.

Initial investigations revealed severe anemia with hemoglobin of 4.3g/dL and hematocrit of 9.1%. There was leukocytosis with marked neutrophilia (Total Leukocyte Count of 36,000/µL with 80% neutrophils), platelet count of 304,000/mm [3] and deranged coagulation profile with International normalized ratio (INR) of 2.28. Presence of clinical jaundice and total bilirubin measuring 7.30mg/dL with indirect hyperbilirubinemia and urine positive for hemoglobin suggested intravascular hemolysis. Methaemoglobin was 7.1%. Liver function tests (LFT) were deranged with elevated liver enzymes (aspartate transaminases of 420). Renal functions were deranged with Blood Urea Nitrogen (BUN) of 90mg/dL and serum creatinine of 5.2mg/dL.

Electrocardiogram was done and suggestive of sinus tachycardia. Arterial Blood Gas (ABG) was suggestive of severe metabolic acidosis with a pH of 7.01, HCO3 of 4.3 and a Base Excess (BE) of 25.1mmol/L. The patient was catheterized which revealed the presence of dark (cola) colored urine. Gastric lavage was not done with activated charcoal in view of late presentation. Repeat ABG showed severe metabolic acidosis with a pH of 6.917, HCO_3 of 7.7, BE of 24.7mmol/L, pO_2 of 114.8 mm Hg, lactates of 7.7 with methemoglobin of 7.1%.

Hemodialysis was done in view of severe metabolic acidosis and acute renal failure. Subsequently, after hemodialysis her acidosis improved with post-dialysis ABG suggestive of pH of 7.340, pO_2 of 63.3 mm Hg, HCO_3 of 21.3 and BE of 0.7mmol/L. Her methemoglobin levels decreased, with first day reading of 7.1% to 2.2% on the second day. Her hemoglobin increased to 11.5g/dL after 5 units packed red cell transfusion. Glucose 6 Phosphate Dehydrogenase (G6PD) levels were done and IV methylene blue 75mg (1.5 mg/kg) was prescribed on day 2 and N-Acetylcysteine (NAC) 1.2 gm daily was started. Vasopressor support in the form of norepinephrine infusion was started in view of hemodynamic instability.

On Day 3 of admission, the hemoglobin was 10.8g/dL, and there was some improvement of methemoglobin which decreased

to 1.7%. Her urine output was low and hemodialysis was given on alternate day basis. From Day 4, she started improving. Her hemoglobin was stable at 9.0g/dL and no further transfusion was required. Her total bilirubin dropped to 1.20mg/dL with improving liver function test. Her renal functions were improving, SpO_2 was consistently more than 95% and ionotropic support was tapered off. Her hemoglobin improved to 10.0g/dL. BUN decreased to 23mg/dL with serum creatinine of 1.5mg/dL. Her LFTs returned to normal. Subsequently, she was discharged on day 10. On follow-up of the patient after 1 month, both the renal and liver functions of the patient were normal.

DISCUSSION

Naphthalene mothballs are commonly used in households. It has rarely been an agent of poisoning worldwide [1]. Severe hemolysis from naphthalene poisoning is rare and can be a challenge to clinicians.Naphthalene is a bicyclic aromatic hydrocarbon with a molecular weight of 128 (C10H8) [2]. The clinical features of naphthalene ingestion includes gastrointestinal effects such as nausea, vomiting, abdominal pain, diarrhea etc.; renal effects like increased creatinine level, increased serum urea nitrogen level, hematuria, renal tubular acidosis; respiratory effects such as congestion, acute respiratory distress syndrome (noted at 2ppm); hepatic effects like jaundice, hepatomegaly, elevated liver enzyme levels (noted at 0.02mg/kg per day)and neurologic effects like confusion, lethargy, vertigo, fasciculations, convulsions, anesthesia, cerebral oedema, coma (coma is noted at 0.05mg/kg body weight per day) [3]. Studies have demonstrated that toxic manifestations of naphthalene may be due to enhanced production of free oxygen radicals, resulting in lipid peroxidation and deoxyribonucleic acid damage [4]. Ascorbic acid acts as a free radical scavenger [5].

Hemolysis occurs particularly in patients with G6PD deficiency, who have a low tolerance to oxidative stress. Renal failure as a complication of naphthalene-induced hemolysis and hemoglobinuria has been reported [6]. Methaemoglobinaemia commonly occurs in naphthalene poisoning. Methemoglobin is abnormal hemoglobin in which the iron moiety of unoxygenated hemoglobin is in the ferric (Fe^{+3}) state rather than the ferrous state (Fe^{+2}). Thus, methemoglobin is the oxidized form of hemoglobin, which does not bind oxygen and increases the affinity of oxygen for the partially oxidized portion of haemoglobin [7].

Pulse oximetry is unreliable in the setting of methaemoglobinaemia. A high concentration of methemoglobin causes the saturation to approximate 85%. When the patient is hypoxic (saturation 40-50%), the methemoglobin artifactually increases the pulse oximeter reading to 85%. Conversely, if the oxygen saturation is 100%, the methemoglobin spuriously decreases the pulse oximeter reading to around 85% [8]. Co-oximetry is the gold standard in these patients [7]. When the concentration of methemoglobin in the blood is above 1.5%, the patient develops cyanosis [7].

The treatment of hemolytic anemia with methemoglobinemia includes specific as well as supportive treatment [7]. Specific treatment includes the use of methylene blue and exchange transfusion [9]. Exchange transfusion is the treatment of choice in patients with G6PD deficiency as methylene blue itself may induce hemolysis and cause paradoxical methemoglobinaemia in these patient [10]. NAC may be used in the treatment of methemoglobinaemia as a reducing agent especially in patients with G6PD deficiency [10]. Supportive treatment includes various measures to maintain the airway, breathing and circulation (which may include endotracheal intubation, mechanical ventilation and use of inotropes).

CONCLUSION

In summary,acute hemolytic crisis and methemoglobinemia can be a manifestation of naphthalene mothball ingestion.Naphthalene poisoning is uncommon but can prove fatal, especially in patients who are G6PD deficient. But if managed properly, the patient can have a good outcome.

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