CASE REPORT

NAPHTHALENE INDUCED HEMOLYSIS WITH ACUTE KIDNEY INJURY IN A G6PD DEFICIENT BOY

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Abstract

Naphthalene is a chemical substance which is widely used as moth repellent, insecticide and deodorizer. Naphthalene mothballs are potent hemolytic agents specially for pediatric group and Glucose 6 phosphate dehydrogenase (G6PD) deficient individuals. Our patient, a 14-year-old boy got admitted in our institution with progressive pallor, jaundice, hematuria and oliguria. He used to chew naphthalene mixed flavored raw rice for the last six months. On investigation he was found to have features of intravascular hemolysis and AKI necessitating hemodialysis with blood transfusion. His G6PD activity was below normal. After seven sessions of Hemodialysis (HD) his renal function recovered and discharged accordingly. One month post discharge follow up was normal.

Key words: Naphthalene. Mothball. Poisoning. Hemolysis. G6PD. AKI

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Introduction

Naphthalene mothballs are widely available throughout the world. In Bangladesh it is also a very popular and mostly used moth repellent product, as it is cheap and easily available. But it has rarely been an agent of poisoning.[1] It can be accidentally ingested, mostly by infants; dermal and inhalational exposure may also occur; but rare cases of mothball abuse by inhalation have been reported in some case reports.[2,3] The most characteristic sign of naphthalene exposure is headache, vomiting, diarrhea, abdominal pain, fever, altered mental status and consequences of acute intravascular hemolysis leading to anemia, leukocytosis, hematuria, jaundice and kidney dysfunction.[4,5] The fatal dose of naphthalene for human is still unknown, but as little as a single mothball can cause fatal hemolysis in children and in G6PD deficient individuals.[6,7] We are presenting a 14- year- old boy who presented with AKI and features of hemolysis following chronic misuse of Naphthalene.

Our Case

A 14- year- old 9th grade student was admitted to our institution with the complaints of jaundice and passage of blood in urine for 4

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days and scanty micturition for last 1 day. He did not have any past history of similar symptoms or family history or drug history of note. He was the only issue of his non-consanguineous parents. In search of drug induced hemolysis, his parents stated that, he used to chew naphthalene mixed flavored raw rice for 5-6 months. They discovered these in his school bag, pocket and many other places. He was treated in primary health care settings with intravenous infusion and intravenous antibiotic without improvement before referral.

On admission, he was looking ill, conscious and cooperative, with marked pallor and mild jaundice but no cyanosis. His blood pressure was 100/70 mmHg on lying (no postural drop), pulse rate was 100 beats/minute, temperature was 98°F and respiratory rate was 20 breaths/minute. In bed side urine examination: urine was reddish, volume was: 300ml in last 24 hours, dipstick was negative for protein and sugar but positive for blood. His heart sounds were normal and lungs were clear. The abdomen was soft and non-tender. No organomegaly was noted. There was no focal neurological deficit and no KF ring. On the basis of history and clinical findings our provisional diagnosis was AKI due to intravascular hemolysis secondary to chronic naphthalene toxicity.

Initial investigations revealed Hemoglobin (Hb) 5.3 g/dl, Hematocrit 16%, MCV 89 fl, MCH 30 pg, white blood cell count (WBC) 14 x 10y / l, platelet count 300 x 10y / l and ESR 05 mm in 1st hour. Peripheral blood film showed a dimorphic picture with anisocytosis and poikilocytosis. Serum total bilirubin was 5.0 mg/dl with indirect fraction predominance and urine showed no RBC. His serum creatinine was progressively rising; during admission it was 3.4 mg/ dl and after 5 days it became 15.33 mg/dl.

Further investigations proved hemolysis by a raised Reticulocyte count of 4.03% and Haptoglobin level of 10 mg/l. Hemoglobinuria was confirmed with positive urine for Hemoglobin. Serum LDH (1672 U/l) and SGPT (89 U/l) were also raised. Viral screening for hepatitis and Coomb's test were negative. Serum Electrolytes, RBS, TSH, Serum Iron profile, vitamin B 12 and Folate level, ANA, C3, C4 and CPK were within normal limits. Coagulation profile was normal. Hemoglobin electrophoresis was normal. But his G6PD level was below the normal range 5.0 U/ g Hb (where the normal reference range was 6.97-20.5). Flow cytometry for PNH evaluation was not consistent with Paroxysmal nocturnal hemoglobinuria.

Patient was treated with 4 units of blood transfusion and Hemodialysis was given for total seven sessions. His urine gradually became clear, urine volume increased and he became sound clinically. On the 9th day of admission his Hemoglobin improved to 10.7 gm/dl, serum bilirubin level also came down to 2.1 mg/dl on day 5. Serum Creatinine reduced to 1.9 mg/dl from 15.33 mg/dl on 20$^{th.}$ Day. He was discharged after 20 days without any clinical sequelae. During discharge he was advised to avoid some foods and medications and genetic counselling was done regarding G6PD deficiency state. He was referred for psychiatric evaluation.

After one month follow up, his Hemoglobin was 11.5 g/dl and serum creatinine 1.3mg/dl. He never took Naphthalene again. He went to psychiatrist and was diagnosed as having depressive disorder and anti-depressant was prescribed along with counselling.

Table I

Laboratory parameters of the Patient

Laboratory parameters	Hospital stays			
	On Admission	End of 1st week	End of 2nd week	End of 3rd week
Hb% (gm/dl)	5.3	9.7	10.3	11.2
S. Bilirubin (mg/dl)	5.0	2.1	—	—
S. Creatinine (mg/dl)	3.4	11.2	5.3	1.9

Discussion

Naphthalene is a Bicyclic Aromatic Hydrocarbon with a molecular weight of 128 (C10H8).[4,5] Naphthalene is the major ingredient of mothballs which are commonly used in households to protect clothes from moths [6]. One mothball can contain between 0.5 – 5 g of naphthalene depending on the size.[8]

After exposure, Naphthalene is readily absorbed in systemic circulation. Toxic effects had been reported through various modes of exposure, including inhalation, external skin contact and ingestion. Initially it is metabolized into a number of reactive epoxide and quinone metabolites by Cytochrome P450 oxidation. Then excreted in the urine as mercapturic acids, Methylthio-derivatives and glucuronide conjugates.[5]

Following liver metabolism, naphthol-alpha, the most potent derivative of naphthalene, causes hemolysis with severe anemia and Heinz bodies formationt. There is often a concurrent leukocytosis and hemolysis which is more severe in patients with G6PD deficiency.[5] Haemolysis can be slowly progressive and even delayed.[6]

Toxic manifestations occur by enhanced production of free oxygen radicals, resulting in lipid peroxidation and deoxyribonucleic acid damage. G6PD deficient patients have low tolerance to oxidative stress, so hemolysis occurs easilyy.[9.10]

The clinical consequences of Naphthalene exposure may include headache, vomiting, diarrhea, abdominal pain, fever and altered mental status, hepatic and renal impairment.[5] It can also cause perinatal toxicity.[11,12] Due to its potent oxidizing property, Naphthalene converts hemoglobin to methemoglobin, leading to methemoglobinemia; therefore, the presence of cyanosis with normal oxygen saturation in arterial blood gas should raise the suspicion of methemoglobinemia.[13]

The possible mechanism behind renal injury may be the mechanical trauma to Erythrocytes which liberates Hemoglobin to plasma, which is filtered in the glomerulus, then it is incorporated into proximal tubules through the megalincubulin receptor system (present on the apical surface of these cells); intracellular hemoglobin then dissociates into heme and globin. This heme is cytotoxic and can cause AKI by three possible mechanisms: decreased renal perfusion, direct cytotoxicity and intratubular cast formationv .

In this case the boy had G6PD deficiency, fortunately he had never developed features of hemolysis but the continuous exposure to Naphthalene may had induced this hemolytic episode. This is the first reported case of hemolytic anemia occurring after chronic misuse of naphthalene from Bangladesh.

Management is mainly supportive with intravenous hydration, respiratory and blood pressure support and possibly renal replacement therapy. Specific treatment options include: Methylene blue (1-2 mg/kg IV slow infusion) which convert methemoglobin to hemoglobin, Exchange transfusion, NAC and ascorbic acid (300mg daily) as free radical scavenger. Elimination of toxin by any enhanced techniques like continuous renal replacement therapy (CRRT) could be considered, but is still inconclusive.[14, 15]

Conclusion

The aim of this case report is not only to present an unusual case of AKI but also to draw attention of the clinicians and regulatory authorities about the toxic effects of this common household product specially in G6PD deficient individual. The value of careful history elicitation is also highlighted here. Naphthalene toxicity requires a high level of suspicion if exposure is unknown. It should be suspected in patients with acute onset dark brown urine, nausea, vomiting and diarrhea combined with acute hemolytic anemia, methemoglobinemia and acute kidney injury. Management should be individualized. Proper packaging, awareness and regulation act is necessary to control its use.

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