

Naphthalene-Induced Methemoglobinemia and Hemolysis in a G6PD-Deficient Child: A Rare Case Report

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ABSTRACT

Background: Naphthalene ingestion poses a substantial risk of oxidative hemolysis and methemoglobinemia in glucose-6-phosphate dehydrogenase (G6PD)-deficient children, particularly in regions where household mothball use is common.

Case Summary: A 2-year-old girl with known G6PD deficiency initially presented asymptomatic after ingesting a naphthalene ball, with normal oxygen saturation and no significant laboratory abnormalities. Within hours, she developed progressive irritability and unexplained hypoxia that showed no improvement with supplemental oxygen and occurred without respiratory distress. Severe hemolysis and methemoglobinemia were subsequently confirmed. She demonstrated rapid clinical and biochemical improvement following packed red blood cell (PRBC) transfusion, while methylene blue was avoided due to her G6PD deficiency and toxicology guidance.

Conclusion: Close monitoring and early transfusion-based management are crucial in G6PD-deficient children with naphthalene ingestion to prevent neurological complications and ensure a good clinical outcome.

Keywords: G6PD Deficiency, Naphthalene Poisoning, Methemoglobinemia, Oxidative Hemolysis, Blood Transfusion

Introduction

Naphthalene is an aromatic hydrocarbon widely used in mothballs, especially within households in the Middle East. It undergoes hepatic metabolism to oxidative compounds that can lead to red blood cell damage and methemoglobinemia in susceptible individuals (Pannu and Singla, 2020; Eskandarani and Alghamdi, 2020). G6PD deficiency is highly prevalent in the region (ranging from 10–30% in parts of Saudi Arabia and the Gulf), predisposing affected children to severe hemolytic crises following exposure to oxidizing agents (Roghani *et al.*, 2024; Dela Cruz *et al.*, 2019).

Hypoxia unresponsive to supplemental oxygen is a hallmark of methemoglobinemia, making timely recognition critical for pediatric emergency and intensive care providers (Kaminecki and Huang, 2021). This case highlights the importance of early transfusion-based management when methylene blue is contraindicated (Ahmad *et al.*, 2020; Nongrum *et al.*, 2021).

Case Presentation

Presentation

A previously healthy 2-year-old girl with confirmed G6PD deficiency accidentally ingested one mothball. She was alert and initially asymptomatic with oxygen saturation (SpO₂) 100% on room air and normal vital signs. Initial laboratory tests showed hemoglobin (Hb) 8.5 g/dL, methemoglobin (MetHb) 1.6%, and normal bilirubin.

Clinical Course

Three hours after admission, she acutely deteriorated with SpO₂ falling to 80% despite supplemental oxygen and without any clinical signs of respiratory distress. She developed marked irritability and dark brown urine, although urinalysis demonstrated no microscopic hematuria. Despite administration of IV midazolam (0.1 mg/kg) and oral chloral hydrate (30 mg/kg), irritability persisted, indicating neurological distress from tissue hypoxia.

Investigations

Repeat laboratory testing demonstrated a significant drop in Hb to 6.5 g/dL and a rise in MetHb to 16%. Bilirubin was mildly elevated (40 µmol/L), consistent with intravascular hemolysis. Arterial oxygen tension (PaO₂) and lactate remained normal. Reticulocyte count was 3.6%, indicating appropriate marrow response. Peripheral smear showed bite cells, blister cells, and schistocytes, confirming oxidative hemolysis.

Interventions

High-flow nasal cannula (HFNC; 10–12 L/min, FiO₂ 50–60%) provided minimal improvement in oxygen saturation. Based on toxicology guidance from the American Academy of Pediatrics, UpToDate, and consultation with Poison Control Centre Abu Dhabi, methylene blue was avoided due to risk of worsening oxidative hemolysis in G6PD-deficient children.

A PRBC transfusion was initiated, leading to a rapid clinical response: SpO₂ normalized (98–100%) and MetHb fell to 10% within 15 minutes, with complete resolution of irritability.

On Day 3, Hb again declined to 7.9 g/dL with a mild transient rebound in MetHb to 3.6% and tachycardia, although oxygen saturations were maintained. Given the continued oxidative stress vulnerability, a second PRBC transfusion was administered.

Outcome

By Day 5, Hb was 9.0 g/dL and MetHb < 1%. Bilirubin levels normalized, and the child was discharged home without neurological sequelae. Full recovery was confirmed on follow-up at Day 7.

Table 1: Hematologic Trends During Hospitalization.

Day	Hb (g/dL)	MetHb (%)	Clinical Notes
Day 1-During Admission	8.5	1.6	Stable
Day 1-At 3 hours	6.5	16	Hypoxia, irritability
After 1st PRBC Transfusion	7.5	10	Rapid improvement
Day 2	8.5	2.6	Recovery phase
Day 3	7.9	3.6	Rebound; PRBC transfused
Day 5 Discharge	9	< 1	Full recovery

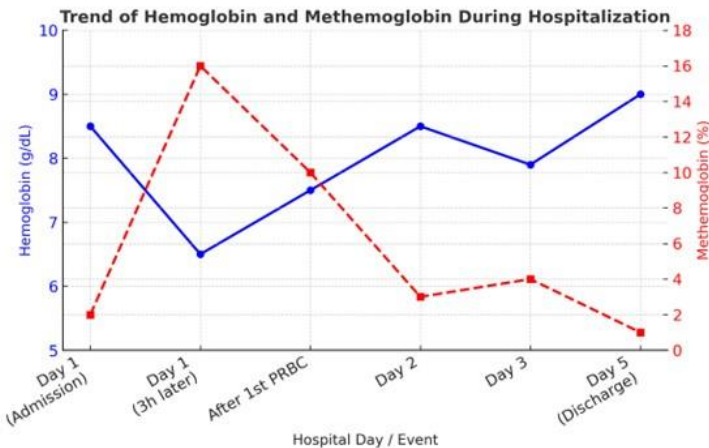


Figure 1: Trend of Hemoglobin and Methemoglobin During Hospitalization.

Discussion

Naphthalene exposure produces a dual hematologic insult in susceptible hosts: (i) methemoglobinemia, which creates a functional anemia with tissue hypoxia unresponsive to supplemental oxygen, and (ii) oxidative hemolysis, which acutely reduces oxygen-carrying capacity (Pannu and Singla, 2020; Roghani et al., 2024). This dual mechanism has been consistently described in earlier pediatric

reports (Ahmad *et al.*, 2020; Dela Cruz *et al.*, 2019). In our patient, the coexistence of persistent hypoxia despite normal PaO₂, marked irritability, and rapid neurological recovery following PRBC transfusion supports impaired oxygen delivery as the proximate cause of neurologic symptoms rather than direct neurotoxicity.

Pathophysiology and Diagnostic Pearls

Naphthalene undergoes hepatic oxidation to naphthoquinones, generating reactive oxygen species that convert ferrous (Fe²⁺) hemoglobin to ferric (Fe³⁺) methemoglobin and destabilize erythrocyte membranes (Trevisan *et al.*, 2001; Pannu and Singla, 2020).

G6PD-deficient cells lack sufficient NADPH to maintain reduced glutathione, rendering them highly vulnerable to oxidative injury. Both Kapoor, *et al.* (2014) and Roghani, *et al.* (2024) emphasized that G6PD-deficient individuals develop more severe and prolonged hemolysis after oxidant stress. Peripheral smear findings of bite and blister cells, as seen in our case, are pathognomonic and align with those described by Eskandarani and Alghamdi (2020) and Nongrum, *et al.* (2021).

Differential Diagnosis

The differential for acute methemoglobinemia includes nitrite/nitrate ingestion, topical anesthetic exposure (benzocaine, prilocaine), dapsone toxicity, and rare congenital cytochrome-b₅ reductase deficiency (Kaminecki and Huang, 2021). Ahmad, *et al.* (2020) described a similar presentation following mothball ingestion but without early neurologic irritability. The combination of a known ingestion, absence of exogenous drugs, and smear-confirmed oxidative changes in our case strengthened the attribution to naphthalene.

Therapeutic Strategy and Guideline Alignment

According to the American Academy of Pediatrics and UpToDate guidance (Kaminecki and Huang, 2021; Methemoglobinemia, 2025), methylene blue should be avoided in G6PD-deficient patients due to the paradoxical risk of worsening hemolysis. Both sources recommend supportive care and PRBC transfusion to restore oxygen-carrying capacity when methemoglobinemia coexists with anemia.

Roghani, *et al.* (2024) and Nongrum, *et al.* (2021) reported adjunctive use of antioxidants such as N-acetylcysteine and ascorbic acid, though with variable success. In contrast, our case demonstrated complete reversal with transfusion alone-without the need for adjuncts or exchange transfusion-

highlighting that timely blood replacement can be curative when methylene blue is contraindicated.

Comparison with Previous Reports

Prior pediatric case reports have documented naphthalene-induced hemolysis (Eskandarani and Alghamdi, 2020; Dela Cruz *et al.*, 2019; Roghani *et al.*, 2024), yet few explicitly linked early neurological irritability to hypoxic stress before overt anemia or cyanosis. Our report is distinctive in demonstrating early irritability as a sentinel sign of tissue hypoxia and a complete response to PRBC transfusion alone in a Middle Eastern child, where G6PD deficiency prevalence exceeds 10% in some communities (Pannu and Singla, 2020).

Regional Implications and Prevention

In the Middle East and South Asia, widespread household use of naphthalene balls persists despite known toxicity (Pannu and Singla, 2020; Roghani *et al.*, 2024). Public education and hospital protocols should emphasize early co-oximetry, avoidance of methylene blue, expedited transfusion when indicated, and Poison Control consultation (Methemoglobinemia, 2025).

Limitations

We did not quantify a complete MetHb decay curve or confirm enzyme subtype through molecular testing; however, the consistent exposure history, biochemical pattern, and response to therapy support the diagnosis (Ahmad *et al.*, 2020).

Clinical Take-Home

In children with hypoxia unresponsive to oxygen and suspected oxidant exposure, early co-oximetry and transfusion are vital (Kaminecki and Huang, 2021). Methylene blue should be avoided in G6PD deficiency; timely PRBC transfusion ensures neurologic recovery (Nongrum *et al.*, 2021; Roghani *et al.*, 2024).

Conclusion

In G6PD-deficient children, naphthalene poisoning can rapidly progress to life-threatening hemolysis and methemoglobinemia. Early recognition, transfusion-focused management, and avoidance of methylene blue are essential to prevent neurological complications.

Ethics and Consent: Written informed consent was obtained from the patient's guardians

Conflict of Interest: None declared.

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Author Contributions: R. Mallavarapu – Patient care, data collection, literature review manuscript writing. Co-authors – Assisted in patient care and critical manuscript review.

References

- Ahmad R, Amir SH, Khan SA. Naphthalene Mothballs Poisoning Leading to Intravascular Hemolysis: A Case Report. *J Emerg Med* 2020; 58: e1-e3.
- Dela Cruz M, Khalid MM, Mostafa A, Ershad M, Vearrier D, McKeever R. Hemolytic Crisis following Naphthalene Mothball Ingestion in a 21-Month-Old Patient with Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency. *Case Rep Pediatr* 2019; 2019: 1092575.
- Eskandarani RM, Alghamdi FS. Naphthalene Toxicity in a Three-Year-Old Child Complicated by Severe Hemolytic Anemia and Mild Methemoglobinemia: A Case Report. *J Emerg Med* 2020; 59: e113-e117.
- Kaminecki I, Huang D. Methemoglobinemia. *Pediatr Rev* 2021; 42: 164-166.
- Kapoor R, Suresh P, Barki S, Mishra M, Garg MK. Acute intravascular hemolysis and methemoglobinemia following naphthalene ball poisoning. *Indian J Hematol Blood Transfus* 2014; 30: 317-319.
- Methemoglobinemia. UpToDate. Last accessed October 2025. Available from: <https://www.uptodate.com>
- Nongrum SM, Chandel AB, Varma R, Jategaonkar S, Jain M. Hemolytic Anemia and Hypoxic Brain Injury following Mothball Ingestion in a G6PD Nondeficient Infant: A Case Report. *Journal of Child Science* 2021; 11: e296-e298.
- Pannu AK, Singla V. Naphthalene Toxicity in Clinical Practice. *Curr Drug Metab* 2020; 21: 63-66.
- Roghani SH, Arif MA, Niazi R, Mansoor S. Naphthalene or Mothball Poisoning Manifesting as Acute Intravascular Haemolysis and Acquired Methemoglobinemia. *Cureus* 2024; 16: e64325.
- Trevisan A, Rossi di Schio M, Pieno M. Haemolytic anaemia after oral self-giving of naphthalene-containing oil. *J Appl Toxicol* 2001; 21: 393-396.