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CASE REPORT

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Acquired methemoglobinemia due to nitrobenzene poisoning: An unusual acquaintance

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Key Clinical Message

Nitrobenzene poisoning is a rare yet life-threatening contention. The ensuing acute methemoglobinemia has a high fatality rate, hence early prompt intervention is required. Methylene blue (intravenous or oral) and ascorbic acid are the cornerstones of management. They must be administered to suspected patients without tardiness.

Abstract

An aromatic organic chemical used in paints and the printing industry is nitrobenzene. Its poisoning causes potentially fatal methemoglobinemia. One aspect of its management involves reducing the iron moiety from its ferric to ferrous form by administering intravenous methylene blue. A 23-year-old man who had deliberately consumed nitrobenzene presented to us with a history of headache and vomiting. He was diagnosed to have methemoglobinemia on the basis of clinical grounds and was managed successfully with intravenous methylene blue and vitamin C.

KEYWORDS

ascorbic acid, methemoglobinemia, methylene blue, nitrobenzene, poisoning

1 | INTRODUCTION

Poisoning constitutes one of the top causes of premature death. Deliberate ingestion contributes to a large proportion of instances, whereas children are frequently inflicted with accidental poisoning. Deliberate or premeditated poisoning is commonly linked to antecedent psychiatric illness, personal, and societal stresses. Timely intensive management is crucial to prevent serious complications and mortality.[1]

An oxidizing nitrite chemical, nitrobenzene (nitrobenzol or oil of mirbane), is frequently found in metal polishes, soaps, shoe polishes, synthetic rubber, paints, dyes, and printing. Inhaling, consuming, or coming into contact with nitrobenzene-containing products can expose members of the public to nitrobenzene.[1–3]

Nitrobenzene is a powerful oxidant of hemoglobin iron moiety, resulting in methemoglobinemia, which impairs hemoglobin capacity to carry oxygen. In acute poisoning, patients may show clear signs of hypoxia, such as palpitations, tightness in the chest, cyanosis, and dyspnea. In instances of severe poisoning, hemolysis, high-grade pyrexia, seizures, and renal and hepatic dysfunction are proposed to occur.[3–5]

Vitamin C and intravenous methylene blue are frequently used to treat severe toxicity.[4–6] Although clinical ground provides the main diagnostic clue, co-oximeter is the supreme standard.[7]

2 | CASE HISTORY AND EXAMINATION

A 23-year-old male presented to our emergency department with a history of headache and nausea after ingestion of about 15 mL of 20% nitrobenzene by mixing with water. He is a painter by occupation, has no known comorbidities, and history regarding drug intake is negative.

On examination, heart rate was 90/min, blood pressure was 125/90 mm Hg, and respiratory rate was 22/min. He was conscious and oriented according to the time, place, and person and had a Glasgow Coma Scale of 15/15. However, he exhibited central and acral cyanosis (Figures 1 and 2) and SpO_2 on room air was 82%. Therefore, a high fixed performance venturi mask was used to provide supplemental oxygen. But it failed to resolve cyanosis and increase SpO_2.

3 | INVESTIGATIONS

Intravenous cannulation was done, and blood samples were collected in vacutainers and sent to the laboratory for complete blood count, renal function test, and liver function test. Similarly, an arterial sample was withdrawn for blood gas analysis, which showed a pH of 7.31, PaO_2 of 195 mm Hg, PCO_2 of 36 mm Hg, SaO_2 of 98%, and HCO_3^- of 22 mEq/L. The collected blood samples appeared dark brown in color (Figure 3), which implied the presence of probable methemoglobinemia. The chest X-ray showed very minimal pleural effusion bilaterally, and electrocardiogram was normal. Reports of investigations sent to the laboratory revealed the following parameters:

Hemoglobin: 13.5 g/dL; total leukocyte count: 12,700/mm^3.
Urea: 45 mg/dL; creatinine: 1.4 mg/dL; sodium: 141 mEq/L; potassium: 4.6 mEq/L.
Total bilirubin: 1.5 mg/dL; AST: 55 IU/L; ALT: 64 IU/L.

4 | MANAGEMENT AND OUTCOME

A nasogastric tube was inserted, and gastric lavage was done with normal saline and activated charcoal. He was shifted to the ICU and managed with intravenous methylene blue (dose of 1 mg/kg, administered over the course of 10 min as a 1% solution in 50 mL of normal saline), intravenous vitamin C (1 g three times a day), and other supportive measures. The patient's condition gradually improved; by Day 2, central and peripheral cyanosis resolved, and oxygen saturation was maintained between 95% and 97% without supplemental oxygen. During ICU stay, the patient was hemodynamically stable,

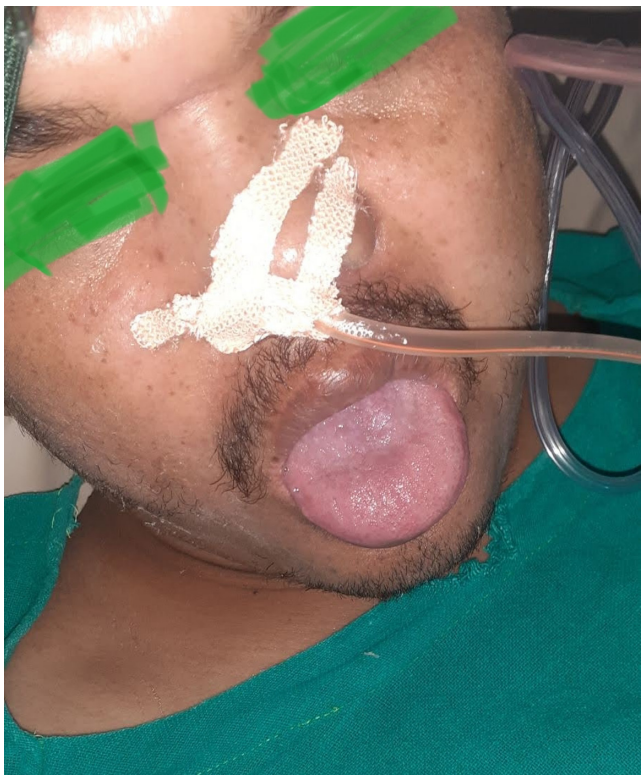

FIGURE 1 Picture showing central cyanosis.

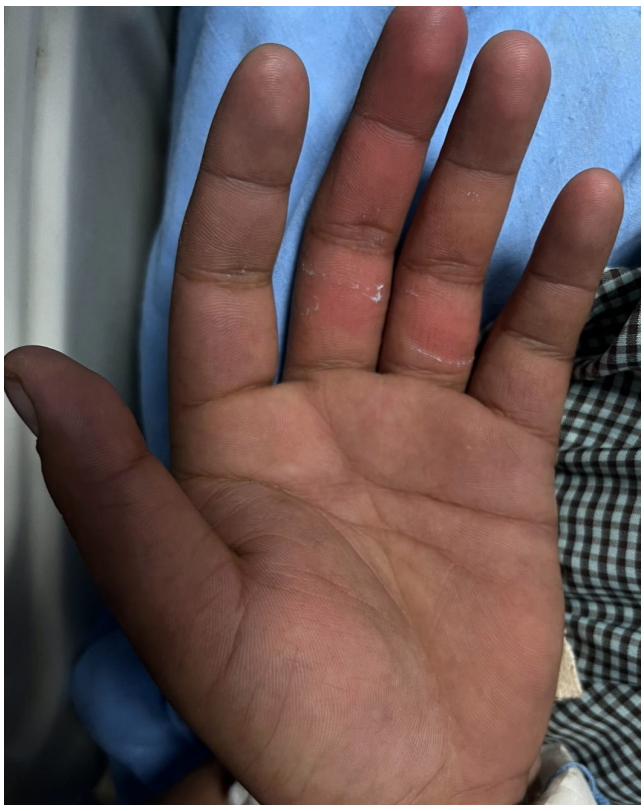

FIGURE 2 Picture showing peripheral cyanosis.

renal perfusion was well maintained with crystalloids (urine output was >0.5 mL/kg/h), and oral feeding was commenced after 18 h of admission. He was shifted to the ward on Day 4 and got discharged on Day 5 of admission.

5 | DISCUSSION

Due to the fact that it is lipophilic, nitrobenzene is readily absorbed by the respiratory system, gastrointestinal tract, and skin upon exposure.[1] It afterward piles up in the stomach, liver, brain, adipose tissue, and blood. Methemoglobin makes up less than 1% of the entire hemoglobin under physiological normal circumstances, with equates exceeding this measurement being referred to as methemoglobinemia.[2,3] Significant methemoglobinemia causes the blood to appear chocolate brown. The hexose monophosphate (HMP) and diaphorase workflows, two reductive engines found in red blood cells, are mainly accountable for maintaining this low level.[1]

The clinical symptoms are rated based on methemoglobin levels, which is depicted by the table presented below.[8,9]

Methemoglobin concentration	Clinical picture
<1.5 g/dL (<10%)	No symptoms
1.5–3.0 g/dL (10%–20%)	Cyanosis
3.0–4.5 g/dL (20%–30%)	Anxiety, lightheadedness, headache, and tachycardia
4.5–7.5 g/dL (30%–50%)	Fatigue, disorientation, tachypnea, increased tachycardia, and increased lactate
7.5–10.5 g/dL (50%–70%)	Seizures, arrhythmias, coma, and lactic acidosis
>10.5 mg/dL (>70%)	Death

Our patient had a history of consumption of about 15 mL of 20% nitrobenzene (3 g) by mixing it with water. On examination, he exhibited central and peripheral cyanosis with no systemic complaints. Therefore, the level of methemoglobin in our patient can be correlated to about 10%–20% from the abovementioned table while taking into account his clinical picture. However, the fatal dose of nitrobenzene reported by the literature ranges from 1 to 10 g.[8]

Methemoglobin levels between 40% and 50% of total hemoglobin induce the central nervous system and cardiovascular system to be profoundly depressed.[4] The transition from aerobic to anaerobic respiration lingers exponentially at this level of methemoglobinemia, which manifests as stupor, arrhythmias, hypotension, respiratory depression, encephalopathy, lactic acidosis, and transaminitis.[5,6]

There is a discrepancy between the oxygen saturation determined by pulse oximetry and the oxygen saturation computed from PaO_2 in methemoglobinemia. PaO_2 is normal in this circumstance. Despite a normal PaO_2, the outcome is hypoxic tissue damage.[3–5]

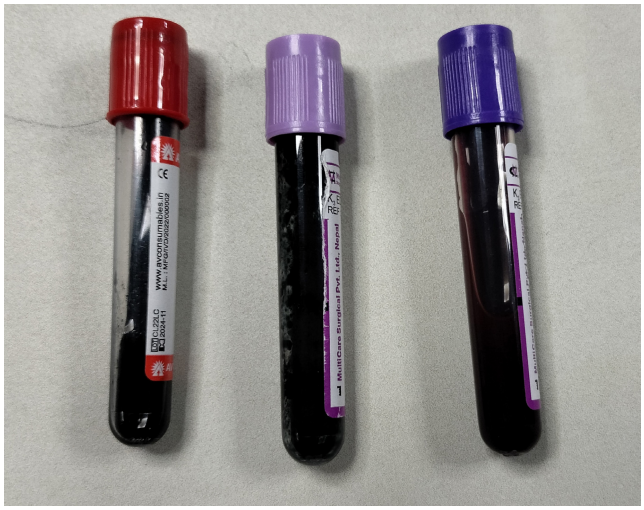

FIGURE 3 Blood sample appearing dark brown in color.

Typical history, cyanosis (central and peripheral) that lacks response to oxygen supplementation, striking oxygen saturation gap (difference between SaO_2 on arterial blood gas analysis and SpO_2 from pulse oximeter) of more than 5% and bitter almond odor provide ample proof of methemogloninemia.[1,2] However, co-oximetry holds the highest norm in determining methemoglobinemia.[7]

In our case, the diagnosis of methemoglobinemia was supported by cyanosis not responding to oxygen, presence of very dark brown blood during sample collection, and a 26% saturation gap between SaO_2 and SpO_2 with a history of nitrobenzene consumption.

Methemoglobinemia may have an acquired or congenital etiology. Local anesthetics (benzocaine, prilocaine), dapsone, and nitrates are examples of oxidizers responsible for drug-induced methemoglobinemia.[1–3]

The two primary protocols for treating nitrobenzene toxicity are supportive therapies and decontamination. The major objective is to achieve a maximum reduction in methemoglobin and eliminate the toxin from the body.[1]

Mainly, the treatment should focus on the correction of physiological derangements. Supportive therapy entails the use of vasopressors for tissue perfusion, mechanical ventilation for oxygenation, and the use of sodium bicarbonate and hemodialysis to mitigate lactic acidosis.[2]

Methemoglobinemia is dealt with oxygen and methylene blue infusion. It is administered intravenously (IV) over 5 min at a dose of 1–2 mg/kg as a 1% solution in normal saline. If necessary, the administration can be repeated an hour afterward.[4,5] Utilizing the HMP shunt pathway's nicotinamide adenine dinucleotide phosphate (NADPH), it transforms into leucomethylene blue, which

acts as an electron donor and converts methemoglobin to hemoglobin. Since glucose is crucial for NADPH synthesis in erythrocyte via the HMP shunt pathway, dextrose can be administered for boosting the therapy's efficacy.[4–6]

There is substantial evidence in the literature to justify the use of intravenous methylene blue; however, when there is concern about the unavailability of intravenous preparation, enteral administration can also be done. This can be inferred from the report published by Shrestha et al. where oral methylene blue was administered to a patient with severe methemoglobinemia (the patient was mechanically ventilated, required vasopressor support, and hemodialysis for refractory metabolic acidosis) due to nitrobenzene poisoning and was able to produce a successful outcome.[9]

In scenarios where methylene blue is contraindicated or ineffective, high doses of vitamin C have great benefit. Vitamin C is a powerful antioxidant and free radical scavenger. It is recommended at doses of 1 g administered IV three times a day. Hyperbaric oxygen therapy, red blood cell exchange transfusions, and *N*-acetyl cysteine are often used as alternatives in refractory cases.[1–3]

Additional treatment modalities such as gastric lavage with activated charcoal, induced vomiting with polyethylene glycol, and forced diuresis may substantially bring down methemoglobinemia.[1]

6 | CONCLUSION

Poisoning with nitrobenzene is an infrequent but potentially fatal condition. Due to the high mortality rate of the accompanying acute methemoglobinemia, early and vigorous care is required. Treatment with oxygen, methylene blue, and vitamin C produces favorable outcomes and rapid recuperation.[1–9]

AUTHOR CONTRIBUTIONS

Sunil Bhatta: Conceptualization; formal analysis; resources; writing – original draft; writing – review and editing. **Pusp Raj Awasthi:** Supervision; writing – review and editing.

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None.

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None.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data described to support the findings are openly accessible in the article.

ETHICS STATEMENT

This is a retrospective case report, and no sampling was used. The ethical approval can be waived.

CONSENT

Written and informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Yogesh S, Seshadri H, Umadevi TB, et al. Acute methemoglobinemia due to crop-flowering stimulant (nitrobenzene) poisoning: a case report. *Cureus*. 2023;15:e47766.
2. Zhao L, Jian T, Shi L, et al. Case report: Methemoglobinemia caused by nitrobenzene poisoning. *Front Med*. 2023;10:1096644.
3. Chongtham DS, Phurailatpam J, Singh MM, Singh TR. Methemoglobinemia in nitrobenzene poisoning-a case report. *J Indian Med Assoc*. 1999;97:469-470.
4. Manolasya V, Soumya M, Harshavardhan RG, Sowjanyalakshmi T, Sreevidya B, Katyarmal DT. Methaemoglobinaemia due to nitrobenzene poisoning. *J Clin Sci Res*. 2019;8:159-161.
5. Padyana M, Shetty AJ, Suresh PK. Nitrobenzene poisoning with methemoglobinemia. *Indian J Case Reports*. 2019;5:59-60.
6. Nitrobenzene poisoning with cyanosis: report of case. *JAMA*. 1920;74:1518-1519.
7. Kumar A, Chawla R, Ahuja S, Girdhar KK, Bhattacharya A. Nitrobenzene poisoning and spurious pulse oximetry. *Anaesthesia*. 1990;45:949-951.
8. Ramtel R, Adhikari B, Shrestha M, Hirachan N, Poddar E, Shrestha S. Diagnosis and management of nitrobenzene poisoning in a low-resource setting: a case report. *Ann Med Surg*. 2022;81:104553.
9. Shrestha N, Karki B, Shrestha PS, Gami R, Acharya SP, Acharya S. Management of nitrobenzene poisoning with oral methylene blue and vitamin C in a resource limited setting: a case report. *Toxicol Rep*. 2020;7:1008-1009.

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