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Rapid-onset methemoglobinemia from traditional-medicine-induced potassium nitrate poisoning: successful treatment with methylene blue—a case report

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Abstract

Background Potassium nitrate poisoning is a rare but potentially serious condition that can result in methemoglobinemia and subsequent cyanosis. This case report presents a unique instance of rapid-onset methemoglobinemia resulting from the ingestion of a traditional medicine preparation containing potassium nitrate, known as "kalmi shora."

Case presentation A 14-year-old Pakistani boy reported to the emergency department with a history of sudden-onset headache, drowsiness agitation, irritability, and generalized cyanosis. Pulse oximetry showed a concerning oxygen saturation level of 58%, whereas arterial blood gas analysis revealed a normal partial pressure of oxygen (90 mmHg). The profile of abrupt onset of symptoms, generalized cyanosis, and the discrepancy between the partial pressure of oxygen and oxygen saturation readings necessitated a comprehensive assessment including inquiries into potential toxins. The peculiar appearance of the blood, resembling chocolate in color, further indicated the possibility of methemoglobinemia. The patient was successfully treated with methylene blue, leading to a prompt resolution of symptoms.

Conclusion This case highlights the significance of considering toxin exposures, such as traditional-medicine-induced poisoning, in emergency settings. The report contributes to the medical literature by highlighting the potential risks associated with traditional remedies and emphasizes the critical role of prompt diagnosis and intervention in optimizing patient outcomes. Recognition of the specific etiology of methemoglobinemia, in this case, traditional medicine ingestion, is essential for effective management in emergency medicine.

Keywords Methemoglobinemia, Kalmi shora, Potassium nitrate poisoning, Methylene blue

Background

Methemoglobinemia, a rare disorder, involves the oxidization of divalent ferrous iron in hemoglobin to ferric iron, causing allosteric changes and irreversible oxygen binding that result in "functional anemia" characterized by impaired oxygen release without a decrease in hemoglobin levels [1]. Clinical manifestations depend upon the percentage of methemoglobin present in the blood.

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Mild cases (1–15%) manifest with subtle symptoms such as fatigue and headache, while moderate (15–30%) cases present with clinically evident cyanosis. Severe methemoglobinemia (30–50%) manifests as pronounced cyanosis, dyspnea, and confusion. In cases when the percentage of methemoglobinemia exceeds 50%, life-threatening consequences might develop [2]. Congenital forms of methemoglobinemia result from inherent enzyme deficiencies, whereas acquired methemoglobinemia is often associated with exposure to certain medications (for example, dapsone, lidocaine, and benzocaine) and compounds containing nitrate, chlorate, and aniline groups [3]. One intriguing subset of acquired methemoglobinemia arises from the ingestion of traditional medicines, with potassium nitrate-containing remedies.

Potassium nitrate, frequently referred to as saltpeter, is a useful chemical molecule used in fertilizers, food preservation, and pharmaceutical uses [4]. The inadvertent ingestion of this compound can result in methemoglobinemia, disrupting normal oxygen transport and manifesting as cyanosis and other clinical symptoms. We present a distinctive case of rapid-onset methemoglobinemia resulting from the ingestion of a traditional medicine preparation, "kalmi shora," containing potassium nitrate. The utilization of methylene blue as a successful treatment modality and the subsequent resolution of symptoms further emphasize the significance of accurate diagnosis and management. This compound's unique ability to restore functional hemoglobin from methemoglobin offers a therapeutic pathway to counter the adverse effects of potassium nitrate poisoning. This case exemplifies the significance of broadening diagnostic horizons in emergency settings. While immediate cardiac and respiratory concerns are paramount, neglecting potential toxic exposures can lead to diagnostic delays. Swift identification of the underlying causative factor, such as toxin-induced methemoglobinemia, ensures timely intervention, ultimately optimizing patient outcomes. This case contributes to the scientific literature by highlighting the potential risks associated with traditional remedies and emphasizes the importance of prompt diagnosis and intervention in such cases. Our case report also underscores the vital importance of considering poisoning as a potential diagnosis in emergency presentations, particularly when symptoms mimic other medical conditions.

Case description

A 14-year-old Pakistani boy presented to the emergency department of a tertiary care hospital with a history of sudden onset of severe generalized headache, shortness of breath, and bluish discoloration of the nose, lips, cheeks, skin of back of trunk, limbs, and nail beds. These symptoms had been present for approximately 1.5 hours prior to presentation. Additionally, the patient's family reported increasing agitation, drowsiness, and a reduced ability to respond to commands effectively. The patient's medical history included left-sided loin pain and burning micturition suggestive of a potential urinary tract infection. However, there was no history of congenital heart disease or respiratory tract infections that could contribute to the symptoms observed. There was no history of any relevant genetic or hereditary conditions. On further inquiry on drugs and substance abuse, the family only reported the use traditional medication (kalmi shora) in powder form, one tablespoon for renal lithiasis 2 hours before his presentation to the emergency room (Fig. 1). On physical examination at the time of presentation, the patient appeared acutely unwell with a pulse rate of 113 beats per minute, blood pressure of 100/60 mmHg, and respiratory rate of 30 breaths per minute. Additionally, the patient was hypothermic (temperature 34.5 °C). Oxygen saturation (SpO2) was critically low at 58%. Pronounced cyanosis was observed on the trunk, chin, lips, oral mucosa, and nail beds, signifying compromised oxygenation. The patient was delirious with an altered state of consciousness and showed extreme restlessness and a Glasgow Coma Scale score of 12, alongside normal pupillary responses. Cardiovascular auscultation revealed no murmurs, while respiratory assessment showed an increased respiratory rate without any notable adventitious sounds, wheezing, or crepitation. All routine baseline investigations, including electroencephalography (EEG), cardiac enzyme test, and chest X-ray, were unremarkable. A dark-brown blood color was noticed while obtaining an arterial blood sample (Fig. 2). Arterial blood gas analysis revealed significant acidemia with a pH of 7.02, normal partial pressure of oxygen (pO_2 90 mmHg), decreased oxygen saturation (SpO_2 85%), reduced partial pressure of carbon dioxide (pCO_2 23 mmHg), excess bases (−24.0 mmol/L), and noticeably elevated lactate (20 mmol/L). Urine toxicology was unremarkable for any toxin. The diagnostic challenge in this case stemmed from the patient's tachypnea and abrupt drop in oxygen saturation, which typically evoke concerns about cardiac and respiratory etiologies. However, the absence of suggestive ischemic heart disease history, the patient's young age, the absence of cardiac murmurs on auscultation, the normal electrocardiogram (ECG), and the cardiac enzyme levels ruled out cardiac causes. Similarly, the lack of fever and cough, the normal respiratory examination, and the unremarkable chest X-ray also excluded respiratory illness as a cause. A lack of substance abuse history and normal urine toxicology excluded common culprit drugs. Notably, the chocolate-colored blood upon sampling, the incongruity between oxygen saturation and

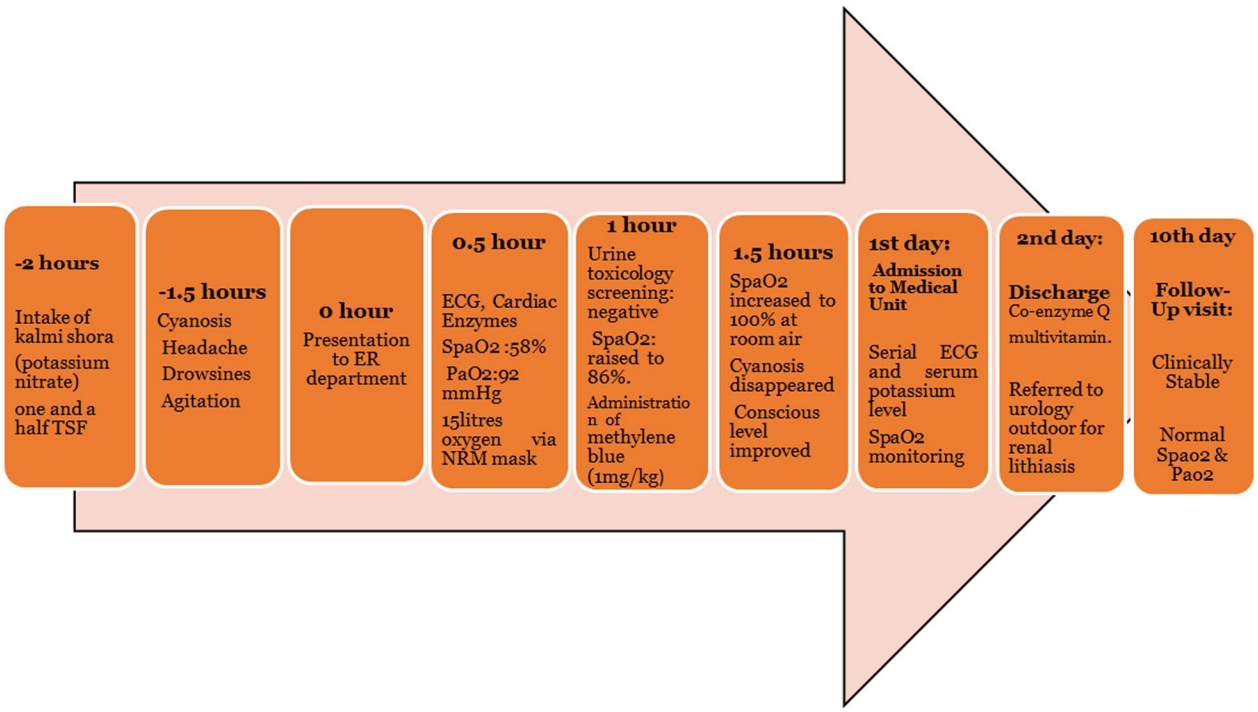

Fig. 1 Timeline of events: from presentation to follow-up and outcome. *TSF* tablespoon, *ER* emergency room, *ECG* electrocardiogram, *SpaO2* peripheral oxygen saturation, *PaO2* partial pressure of oxygen in arterial blood, *NRM* non-rebreather mask

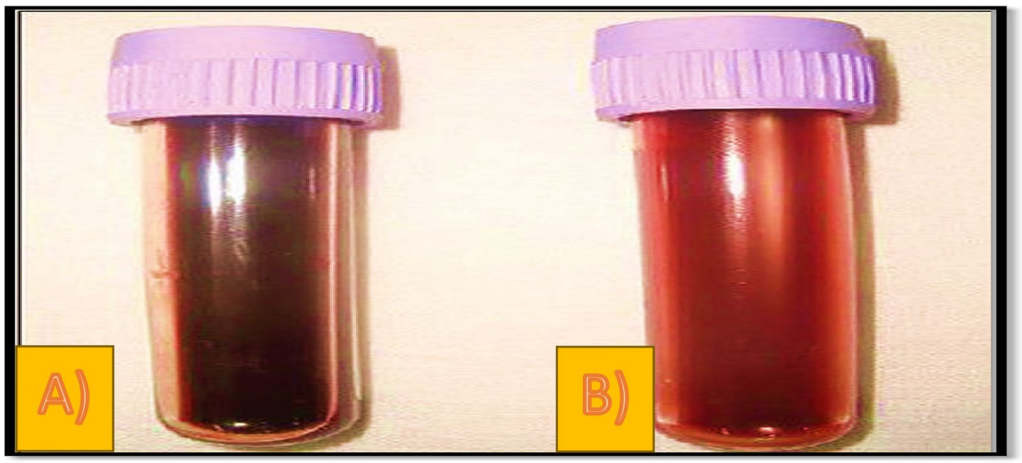

Fig. 2 **A** Chocolate-colored blood at presentation. **B** Post-methylene blue treatment showing restored normal blood color

pO_2 levels, and the sudden-onset cyanosis point toward nitrate methemoglobinemia. Upon further inquiry, the family revealed that the patient had received a traditional medication called "kalmi shora" from a traditional healer. Subsequent search of the medication confirmed its potassium nitrate content, leading to the diagnosis of potassium nitrate-induced methemoglobinemia. However, the serum methemoglobin level was not assessed due to cost constraints and limited availability of the test. Following his initial presentation, the patient received immediate interventions in response to his condition. Initially, 15 l of oxygen supplementation was administered through a non-rebreather mask, resulting in improved oxygen saturation to 86%, although cyanosis persisted. Given the consideration of respiratory and cardiac arrhythmic causes, the patient was administered a single intravenous dose of 100 mg hydrocortisone and a single infusion of 10% calcium gluconate in 100 ml normal saline over 10 minutes,

respectively. Subsequently, a bolus of methylene blue (1 mg/kg over 10 minutes) and 20 ml/kg of colloid were administered. Within 10 minutes, the patient's oxygen saturation reached 100% on room air, accompanied by restored consciousness and a significant reduction in cyanosis. Following transfer to the medical ward, the bluish discoloration completely resolved within 30 minutes. During his 2-day hospitalization, the patient remained vitally stable and received oral multivitamins, received co-enzymes (100 mg once daily), and was closely monitored for arrhythmia throughout his stay. After a comprehensive 2-day medical stay, the patient showed significant improvement in his clinical condition. He was discharged with a prescription for multivitamin supplementation and co-enzyme Q, which he was advised to continue for a month. Additionally, the patient was recommended to visit the urology ward for further evaluation and management of his renal lithiasis. During subsequent outpatient visits, the patient's progress was closely monitored. It was emphasized that he should refrain from using the traditional medication "kalmi shora" to prevent a recurrence of such adverse effects.

Discussion

Methemoglobinemia, resulting from the oxidation of ferrous iron to its ferric state in deoxyhemoglobin, hinders the efficient binding of oxygen, leading to compromised oxygen transport [5, 6]. This condition is driven by an excessive influx of oxidants, which can originate from various sources, including certain medications, chemicals, and, in this case, traditional remedies like "kalmi shora." The natural reduction of methemoglobin to hemoglobin is facilitated by NADH cytochrome-β5-reductase (NCR) enzymes, maintaining a balance between the two forms. Adults, who possess lower NCR activity, are at a higher risk of methemoglobinemia due to their diminished capacity to convert methemoglobin back to hemoglobin [7]. Elevated methemoglobin levels beyond 1–2% are considered abnormal, warranting clinical attention. Pediatric patients, as in our case, are particularly vulnerable due to their inherent NCR enzyme limitations. Manifestations of methemoglobinemia manifest when methemoglobin levels exceed 15%, encompassing symptoms such as headache, lethargy, tachycardia, hypotension, and cyanosis. Notably, methemoglobin levels exceeding 50% are frequently fatal, underscoring the gravity of this condition. A distinctive hallmark of methemoglobinemia is the paradoxical presentation of profound cyanosis accompanied by a surprisingly alert and composed state—a phenomenon colloquially referred to as the "living dead" [8]. This striking contrast between the cyanosis appearance and the absence of expected cardiovascular or respiratory distress serves as a diagnostic clue, distinguishing methemoglobinemia from other conditions presenting with cyanosis. Our case report highlights a rare instance of rapid-onset methemoglobinemia resulting from the ingestion of a traditional medicine preparation containing potassium nitrate, commonly known as "kalmi shora." The presentation of cyanosis, drowsiness, and other systemic symptoms in a young patient, as described in this case, posed a diagnostic challenge initially suspected to be of cardiac or respiratory origin. However, meticulous clinical evaluation and investigation played a pivotal role in establishing the diagnosis and initiating prompt treatment. Nitrates are metabolized in the liver to glycerol dinitrate, glycerol mononitrate, and inorganic nitrite, which oxidizes hemoglobin to MetHb [9]. A review of pertinent literature underscores the significance of our case. Cases of methemoglobinemia stemming from potassium nitrate exposure have been documented [10]. No case of traditional-medicine-induced methemoglobinemia has been reported yet. Cases like this one also accentuate the importance of prompt recognition and intervention to mitigate potentially severe consequences. Methylene blue's role in reverting methemoglobin to hemoglobin, demonstrated in our case, is well documented in the literature as an effective therapeutic approach [11]. The cyanosis and hypoxia observed in this patient were consistent with the compromised oxygen transport resulting from elevated methemoglobin levels. Notably, the atypical blood coloration resembling chocolate further hinted at the possibility of methemoglobinemia.

In resource-constrained settings, the availability of diagnostic tests can be limited. In this case, the lack of access to methemoglobin level testing due to cost constraints underscores the challenges faced in confirming the diagnosis definitively. The decision to proceed with empirical treatment, including methylene blue administration, was driven by the clinical presentation and the rapid improvement observed, reinforcing its therapeutic importance in methemoglobinemia management. The significance of considering traditional remedies as potential sources of toxicity cannot be understated. The ingestion of "kalmi shora" in this case exemplifies the potential dangers associated with the unregulated use of herbal and traditional medications. The case underscores the importance of educating patients about potential risks and seeking medical advice before utilizing such treatments. Furthermore, this case emphasizes the essential role of thorough history-taking and systematic clinical assessment. In this instance, the patient's history of "kalmi shora" use and the subsequent inquiry into its composition proved pivotal in establishing the diagnosis. Timely diagnosis, initiation of specific treatment with methylene blue, and avoidance of the triggering agent led

to the prompt resolution of symptoms, highlighting the critical role of accurate diagnosis in optimizing patient outcomes.

In conclusion, this case report underscores the clinical and diagnostic challenges associated with traditional-medicine-induced methemoglobinemia. It highlights the importance of considering toxic etiologies and broadening diagnostic horizons, particularly in emergency settings. While traditional medicines may offer therapeutic benefits, their potential risks should be acknowledged and patients educated accordingly. This case contributes to the growing body of literature emphasizing the importance of vigilance and timely intervention in managing methemoglobinemia induced by traditional remedies.

Conclusion

Potassium nitrate poisoning resulting in methemoglobinemia can lead to rapid-onset cyanosis and tissue hypoxia. Timely administration of methylene blue is crucial for the successful treatment of methemoglobinemia in such cases. This case emphasizes the importance of recognizing and managing this rare but potentially life-threatening complication associated with potassium nitrate ingestion, particularly when prescribed by traditional healers.

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Author contributions
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Availability of data and materials
All necessary data and materials supporting the findings of this study are provided within the manuscript. Requests for additional information can be directed to the corresponding author.

Declarations

Ethics approval and consent to participate
This study, involving human participants and data, adheres to ethical standards. Ethical approval was granted by the Ethics Review Committee of King Edward Medical University and Mayo Hospital Lahore, with reference number 317/01/2024. Informed consent was obtained from the participant.

Consent for publication
Written informed consent was obtained from the patient's legal guardian for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests
The authors declare no conflicts of interest; the report is unbiased and without financial support or incentives.

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