

CASE REPORT

# Food protein-induced enterocolitis syndrome in an infant presenting with methemoglobinemia: a case report

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## ABSTRACT

**Background:** Methemoglobinemia is a condition in which the iron in hemoglobin is oxidized from the ferrous to ferric state, resulting in oxygen desaturation and cyanosis. It can be congenital or acquired, with acquired causes including the ingestion of certain medications or chemical products or infections such as sepsis or gastroenteritis.

**Case Presentation:** Herein, we report the case of a young infant who presented with diarrhea and cyanosis and was found to have significant methemoglobinemia which most likely was secondary to severe diarrhea. It was managed successfully with methylene blue, he was diagnosed later as case of food protein-induced enterocolitis syndrome.

**Conclusion:** Clinicians should consider profound diarrhea as a potential cause of methemoglobinemia to enhance early intervention.

## Introduction

Methemoglobinemia is a condition in which the iron in hemoglobin is oxidized from the ferrous to the ferric state, rendering it unable to bind oxygen. This results in oxygen desaturation and a bluish discoloration of the skin, known as cyanosis. Methemoglobinemia can be hereditary or acquired and is caused by various factors, including exposure to certain drugs, chemicals, or toxins [1]. Congenital causes are attributed either to a defect in the enzyme cytochrome b5 reductase or mutations in the globin genes that produce hemoglobin M [2]. Acquired causes of methemoglobinemia include the ingestion of certain medications or chemical products such as benzocaine, phenazopyridine, dapsone, and nitrates/nitrites [3,4]. Other factors such as gastroenteritis and sepsis can also lead to methemoglobinemia [5].

Young infants are more vulnerable to methemoglobinemia owing to various factors. One reason for this is the low level of nicotinamide adenine dinucleotide + hydrogen reductase in infants aged <4 months [6]. Additionally, fetal hemoglobin is more prone to oxidation than is adult hemoglobin [7,8].

Herein, we report an unusual case of a young infant presenting with cyanosis who was found to have a high methemoglobin level, which was most likely secondary to diarrhea. To the best of our knowledge, no similar cases have been reported in Saudi Arabia.

## Case Presentation

A male infant was born full-term via normal spontaneous vaginal delivery. The mother had gestational diabetes mellitus but managed it with diet. She also had human papilloma virus warts during her pregnancy. The delivery was uneventful, and the infant, which weighed 3.3 kg at birth, did not require admission to the neonatal intensive care unit and was discharged with his mother in stable condition. However, at 20 d of age, the mother stopped breastfeeding and introduced formula feeding, as she felt that she was not producing enough milk. The infant started to have watery yellowish diarrhea, which persisted even after multiple visits to primary health care centers and changing the milk formula four times. The last formula was partially hydrolyzed, and the mother noticed some improvement as the incidents of diarrhea decreased from approximately 11 to 8 times per day for 1 week; however, the diarrhea worsened again 10 d prior to presentation

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to our emergency department. After the infant received the 2-month vaccine, the mother noticed a decrease in activity and bluish discoloration of the lips for 3 d. The infant was brought to the emergency department and was found to have desaturation, bluish discoloration of the lips, and dusky appearance of the skin. Oxygen therapy was initiated through a face mask, which resulted in a mild improvement in oxygen saturation.

The parents neither reported any history of similar presentations or conditions in the family nor any history of congenital heart diseases, hematological diseases, or the use of medication or herbs. Notably, the parents are second cousins and have three other healthy children.

Upon examination, the vital signs of the infant were within normal limits, except for an oxygen saturation of 88% in room air, which increased to 92% with the administration of oxygen via a face mask.

Physical examination revealed a conscious, alert, and irritable infant with a dusky, bluish appearance of the lips and skin. Respiratory, cardiac, and abdominal examinations were unremarkable.

Bedside echocardiography was performed to check for congenital cyanotic heart disease; however, the results were unremarkable. A point-of-care venous blood gas test was also conducted, which indicated metabolic acidosis (pH = 7.19, HCO<sub>3</sub> = 11) and a high methemoglobin level (21.7). As a result, the toxicologist on-call advised treatment with 2 mg/kg intravenous methylene blue; once administered, the oxygen saturation began to improve, and the cyanotic appearance of the infant turned normal.

After approximately 1 hour, repeated blood gas tests showed an improvement in his methemoglobin level from 21.7 to 2.4. All other laboratory examinations, including blood count, renal function, hepatic function, and stool analysis, were unremarkable.

Subsequently, the infant was admitted to the ward for further observation and evaluation. We identified that the diarrhea was caused by a cow milk protein allergy. Hence, the infant was started on a hydrolyzed formula, which led to improvement. Further follow-up appointments with a pediatrician and geneticist revealed no concerns, and no genetic testing was deemed necessary, as methemoglobinemia was most likely caused by diarrhea.

A recent follow-up at the age of 6 months with a pediatrician revealed that the infant had been experiencing vomiting and diarrhea after being introduced to solid foods, such as rice and cereal, leading to a diagnosis of food protein-induced enterocolitis syndrome.

## Discussion

Methemoglobinemia can lead to tissue hypoxia and significant morbidity; thus, being well-informed about its grave nature is imperative. Methylene blue is the standard treatment for this condition [8,9]. Notably, infants <2 months old are at the highest risk of developing methemoglobinemia [8,9,10], with one of the leading causes in this age group being acute diarrhea. Diarrhea may cause methemoglobinemia due to intestinal inflammation, which can lead to a decrease

in catalase activity and an increase in nitrate levels [11]. Therefore, young infants presenting with diarrhea should be screened for methemoglobinemia as a proactive measure [12]. Over the years, the correlation between diarrhea and methemoglobinemia has been increasingly recognized, with numerous case reports surfacing. For instance, a case of food protein-induced enterocolitis syndrome was reported in which the patient suffered from severe methemoglobinemia (66 %) and required intubation and resuscitation with fluid and a total of 3 mg/kg of methylene blue divided into two doses 3 hour apart for the methemoglobin level to drop to 3% after the second dose; subsequently, the child improved clinically and was discharged in good condition after starting on hydrolyzed formula [13]. Similarly, in another case of food protein-induced enterocolitis syndrome, a young infant presented with diarrhea, profound metabolic acidosis, and methemoglobinemia (>25 %), which was successfully treated with methylene blue [14].

## Conclusion

Considering methemoglobinemia as a potential differential diagnosis in infants presenting with profound diarrhea and cyanosis is crucial. Increasing the awareness of such presentations may help prevent further complications and enhance early intervention.

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## Conflict of interest

All authors have no conflict of interest to disclose.

## Authors' contribution

Abdulaziz Alareefy: Primary author, Writing the manuscript, reviewing the literature and reviewing the case scenario.  
Hessah Hushan: Co-author, Writing the case presentation.  
Adel Alsaedi: Co-author, Reviewing the whole manuscript.

## Ethical consideration

Written informed consent was obtained from the parents of our indexed case consenting for sharing their child's case for scientific contribution and publication.

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