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Initial Presentation of G6PD with Hemolysis Associated with Methemoglobinemia: Case Report

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ABSTRACT

Background: Methemoglobinemia results from elevated amounts of oxidized hemoglobin in the blood with an ensuing change in oxygen dissociation curve and lack of oxygen delivery to tissue. **Objective:** This study aimed to accurately how to diagnose a case of methemoglobinemia. **Patients and methods:** A hypoxic state that presents as headache, nausea, weakness, and confusion is a rare symptom of methemoglobinemia. We report on a 5-year-old kid who presented with diarrhea and vomiting for three days, along with a hypoxic episode during which the face mask oxygenation did not increase saturation. **Results:** After additional testing, it was determined that there was acute intravascular hemolysis due to elevated levels of lactate dehydrogenase, unconjugated bilirubin, and reduced hemoglobin levels. Analyzing blood gas confirmed that methemoglobinemia was the diagnosis. After receiving a transfusion of packed red blood cells and careful management, the hypoxia was resolved. **Conclusion:** Hypoxia with a saturation gap greater than 5% that does not improve with additional oxygen therapy should raise concerns about MetHb.

Keywords: Glucose-6-phospate dehydrogenase deficiency, Methemoglobinemia, Acute hemolysis.

INTRODUCTION

The oxidation of divalent ferro-iron of hemoglobin (Hb) to ferri-iron of methemoglobin (MetHb) is associated with a rare disorder called methemoglobinemia. Both hereditary and acquired mechanisms can lead to methemoglobinemia. The majority of cases are acquired, primarily as a result of exposure to chemicals that either directly or indirectly oxidize hemoglobin. The condition known as methemoglobinemia disease is caused by autosomal dominant variants in the globin genes or autosomal recessive variants in the CYB5R3 gene in inherited forms [1]. Few research has documented hemolysis and methemoglobinemia occurring simultaneously following an infection [2-4].

CASE REPORT

Three days ago, a 5-year-old kid with rapid onset pallor associated with vomiting and diarrhea came to the Department of Emergency Medicine. The child's examination revealed that he was pale, unwell-looking, and afebrile. His pulse rate was 141 beats per minute, his blood pressure was 103/62 mmHg, and his saturation on pulse oximetry was 56% on room air, which did not improve with a non-rebreather face mask at 15 L/min. While, the other respiratory results were normal, he had moderate tachypnea. Lung fields were audible during auscultation, and the cardiovascular exam was normal. His pH was 7.41, HCO_3^- was 16.4 mmol/L, PO_2 was 5.1 kPa, pCO_2 was 3.5 kPa, lactate was 3.4 mmol/L, SaO_2 was 72.8 %, hemoglobin was 53 g/L, methemoglobin level was 16.4%, and saturation gap was 72.8-56 = 16.8%, > 5%. These were the results of his initial blood gas study. The patient's cardiac and respiratory causes of hypoxia were ruled out by the unremarkable results of the 12-lead ECG and chest radiograph. His laboratory results included the following: Total serum bilirubin was 50.1 mcmol/L), direct was 11.2 mcmol/L, hemoglobin (Hb) was 55 g/L, white blood cell count was 34.45 10*9/L, neutrophils' count was 78.8%, reticulocytes' count was 8.63%, lactate dehydrogenase (LDH) was 913 U/l, and alanine aminotransferase (ALT) was 12U/l. All of which suggest intravascular hemolysis. A peripheral blood smear revealed that ferritin was 11,127 micg/L, glucose 6-phosphate dehydrogenase was 0.61, and normochromic normocytic anemia. C-reactive protein in serum was 4.97. His hemoglobin climbed to 70 gm/l after receiving a total of three units of packed red blood cells (PRBC) consecutively. A thorough examination of his prescription records revealed no offending drugs as the reason of the hemolysis. Since the child's clinical condition improved after receiving PRBC transfusion, methylene blue was not given. His 94% saturation was an improvement. HB (107 g/l) and Liver function tests (direct bilirubin = 3.6 & total bilirubin = 34.5) were repeated. After 72 hours, the blood culture revealed no growth. On the third day of stay, the patient was released from the hospital after a repeated blood gas measurement, which showed a methemoglobin level of 4.9%. Following a two-month discharge, a follow-up G6PD screen revealed a low level of 0.19, consistent with G6PD insufficiency, which consists with G6PD deficiency.

DISCUSSION

The ferrous (Fe^{2+}) ion is oxidized to its ferric (Fe^{3+}) form in methemoglobin, a modified form of hemoglobin that is unable to bind oxygen and keeps it from reaching the tissues. RBCs employ a variety of procedures to convert MetHb to deoxyhemoglobin in order to maintain the steady-state level of less than 2% of total hemoglobin. Topical anesthetics, antimalarial drugs, meals high in nitrates or nitrites, or hereditary/genetic conditions (deficiency in cytochrome b5 reductase, haemoglobin M & cytochrome b5) can all cause methemoglobinemia [5]. The erythrocyte enzyme systems that catabolize excess methemoglobin generated in the blood are nicotinamide adenine dinucleotide (NADH) -cytochrome b5 reductase (main route) and nicotinamide adenine dinucleotide phosphate (NADPH) methemoglobin reductase (secondary pathway) (Figure 1).

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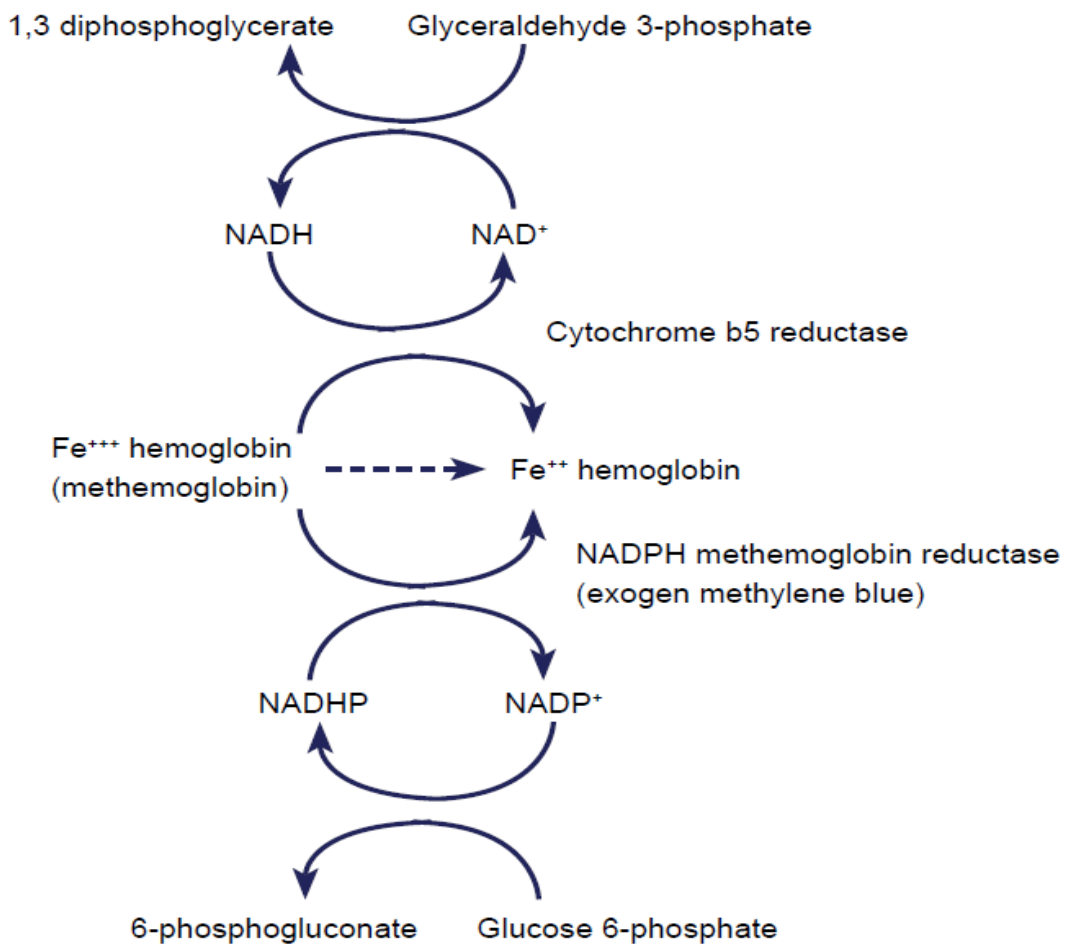

Figure (1): Metabolic pathways for the reduction of methemoglobin.

The range of clinical presentation includes slightly symptomatic to cases with severe symptoms. Depending on the percentage of MetHb, the presentation's severity was shown in table (1) [6].

Table (1): signs, symptoms and severity level of methemoglobinemia

MetHb level	Signs	Symptoms
<10%	Low pulse oximeter readings, alteration of the skin color (pale, gray, blue)	Asymptomatic
10%-30%	Cyanosis Dark brown blood	Asymptomatic/confusion
30%-50%	Dyspnea, dizziness, syncope	Confusion, chest pain, palpitations, headache, fatigue
50%-70%	Tachypnea, metabolic acidosis, dysrhythmias, seizure, delirium, coma	Confusion, chest pain, palpitations, headache, fatigue
>70%	Severe hypoxemia, death	

The gold standard for diagnosing MetHb is co-oximetry [7]. The co-oximeter uses spectrophotometry, which uses a variety of wavelengths, to quantify the concentration of various haemoglobin types in the blood. When arterial blood gases are examined, the pO_2 is normal but the observed oxygen saturation is reduced [8]. The severity and clinical presentation of the patient's acute hemoglobinemia dictate the treatment plan. The therapeutic activity level in asymptomatic individuals is estimated to be 30%. Patients who are symptomatic, meaning they exhibit clinical or test evidence of tissue hypoxia, or who have concomitant illnesses that impact oxygen delivery, such as circulatory failure or anaemia, should get treatment at levels between 10% and 30% [9]. The use of methylene blue is the recommended approach. Administering a 1 to 2 mg/kg (0.1–0.2 mL/kg) intravenously of 1% solution takes three to five minutes. Yet, when giving methylene blue to those who have G6PD impairment, care must be taken. NADPH reduces methylene blue to its active metabolite, leukomethylene blue. Individuals without G6PD are unable to decrease methylene blue due to insufficient NADPH availability. Consequently, it will function as an oxidant, failing to lower methemoglobin levels in individuals with G6PD deficiency and leading to the onset or exacerbation of hemolytic anaemia [10].

If methemoglobinemia poses a life-threatening risk to a G6PD-deficient individual, methylene blue injection has been recommended as the first line of therapy. The dose should be titrated higher to further reduce methemoglobinemia, starting at a lower level of 0.3 to 0.5 mg/kg. Exchange transfusion should be considered, and the methylene blue therapy should be stopped if the hemolysis gets worse [9]. Erythrocyte transfusion is advised as a therapy for both functional and real anaemia in cases of severe (hemolytic) anaemia.

CONCLUSION

Hypoxia with a saturation gap greater than 5% that does not improve with additional oxygen therapy should raise concerns about MetHb. The majority of blood gas analyzers find MetHb. Hemolysis-related symptomatic MetHb necessitates supportive care, including packed red blood cell transfusion, cause identification, and treatment.

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