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A CASE OF PRIMAQUINE-INDUCED METHEMOGLOBINEMIA IN A 24-YEAR-OLD FEMALE

General Medicine

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ABSTRACT

Primaquine is an antimalarial medication commonly used for the treatment and prevention of malaria, particularly for eradicating liver stages of Plasmodium vivax and Plasmodium ovale. While effective, primaquine can induce methemoglobinemia, a rare but serious condition characterized by the presence of an abnormal amount of methemoglobin in the blood, impairing the oxygen-carrying capacity of haemoglobin. We report a case of a 24-year-old female diagnosed with methemoglobinemia after mistakenly taking an excessive dose of primaquine for Plasmodium vivax malaria. The patient presented with severe headache, dizziness, and hypoxemia. Laboratory investigations confirmed a methemoglobin level of 19.2%. She was successfully treated with supportive measures, including discontinuation of primaquine and administration of oxygen therapy, leading to significant improvement. This case highlights the importance of recognizing drug-induced methemoglobinemia, particularly in patients with G6PD deficiency, and underscores the need for appropriate therapeutic regimens to ensure favourable outcomes. Despite being a recognized adverse effect, the coexistence of malaria treatment and methemoglobinemia presents a unique clinical challenge that requires prompt diagnosis and management.

KEYWORDS

Primaquine, Methemoglobinemia, Antimalarial, G6PD Deficiency, Reactive Oxygen Species, Haemoglobin, Hypoxemia.

INTRODUCTION :

Methemoglobinemia is a condition where haemoglobin is oxidized from its normal ferrous (Fe2+) state to the ferric (Fe3+) state, forming methemoglobin. This altered form of haemoglobin has a reduced affinity for oxygen and does not release oxygen effectively to tissues, leading to hypoxia. Methemoglobinemia can be caused by exposure to certain drugs, chemicals, or oxidative stress that overwhelm the body's enzymatic reduction pathways. Under normal circumstances, methemoglobin levels are kept below 1% of total haemoglobin through the action of NADH-dependent cytochrome b5 reductase (1).

Primaquine, an antimalarial medication, is known to induce methemoglobinemia. It undergoes hepatic metabolism primarily via the cytochrome P450 enzyme system, producing reactive oxygen species (ROS) that oxidize haemoglobin, thus increasing methemoglobin levels. This risk is particularly significant in individuals with Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency. G6PD is an enzyme crucial for maintaining the redox balance within erythrocytes by producing NADPH, which in turn keeps glutathione in its reduced form to neutralize ROS. Without sufficient G6PD, individuals cannot effectively combat oxidative stress, making them more susceptible to hemolysis and methemoglobinemia when exposed to oxidative agents like primaquine (2, 3).

The clinical presentation of methemoglobinemia can range from mild symptoms such as headache and dizziness to severe manifestations including cyanosis, fatigue, dyspnea, and hypoxemia. Prompt recognition and management are crucial to prevent serious complications. Treatment typically involves discontinuing the offending drug and administering supportive care, including oxygen therapy. In severe cases, pharmacological interventions like methylene blue, which reduces methemoglobin back to haemoglobin, can be used. However, methylene blue must be used cautiously in G6PD-deficient patients due to the risk of inducing hemolysis (4,5).

Understanding the mechanisms and risk factors of drug-induced methemoglobinemia is essential for healthcare providers to ensure timely and effective management, particularly in populations at higher risk, such as those with G6PD deficiency. This knowledge helps in mitigating adverse effects and improving clinical outcomes for affected patients.

Patient Profile :

Age/Gender: 24-year-old female

Initial Presentation: Severe holocranial headache, dizziness, and a sense of impending doom for 2-3 days. No chest pain, breathlessness, abdominal pain, loss of consciousness, or seizures.

Medical History :

Recently treated for Plasmodium vivax malaria with Dengue NS1 positivity. Discharged with a prescription of Primaquine 15 mg once daily. Patient mistakenly took Primaquine 15 mg twice daily.

Clinical Findings On Admission :

Vitals: Temperature: Normal, Pulse: 68/min, Respiratory Rate: 18-22/min, Blood Pressure: 116/72 mmHg, SpO2: 86% on room air (suggestive of hypoxemia).

Physical Examination: Bilateral lung air entry present, clear. Normal heart sounds (S1S2+). No focal neurological deficit.

Syringe showing chocolate brown colour blood in patient with methemoglobinemia

Laboratory Investigation :

	19/08/2023	22/08/2023	26/08/2023
HB (g/dl)	12.1	11.7	11.8
WBC((x10^3/µL)	1.61	5.05	7.62
PLT(x10^3/µL)	124	201	326
MCV(FL) /RDW(%)	87.2/13.4	89.6/13.6	86.7/13.6
HCT (%)	36.5	35	35.9
ESR (mm/hr)	2		
CRP	9.51		
UREA (mmol/L)	11.9		
CREAT (mmol/L)	0.62		
SODIUM (NA+)	137		
POTASSIUM(K+)	4.95		
ALT (IU/L)	96	90	
AST (IU/L)	104	102	
Dengue NS1	POSITIVE		
G6PD Test	NEGATIVE		
MP PC	POSITIVE		
Fraction of Meth HB	19.2% (0-1.5%)		
ABGA on RA	pH: 7.48, pCO2: 25.8		

	mmHg, pO2: 118 mmHg, HCO3-: 18.9 mmol/L, SaO2: 99%		

Radiological Investigation :
Chest X-Ray (CXR) PA View: No abnormality detected.
High-Resolution CT (HRCT) Thorax: No abnormality detected.

Treatment And Outcome :
After discontinuing primaquine,
Patient was treated with oxygen therapy,Ascorbic acid,N-acetyl cysteine.We noted significant clinical improvements in a few days and the patient was discharged with stable condition.

Comparison And Significance :
Comparative Analysis of Case Reports on Primaquine-Induced Methemoglobinemia:

1. Case Report 1:
Patient: 21-year-old male with a history of malaria.
Presentation: Asymptomatic with methemoglobin level of 20.7%.
Treatment: Discontinued primaquine, treated with N-acetylcysteine.
Outcome: Normalized methemoglobin levels without symptoms.(6)

2. Case Report 2:
Patient: 32-year-old male with G6PD deficiency.
Presentation: Symptoms included jaundice, dark urine, fatigue, methemoglobin level of 14%.
Treatment: Stopped primaquine, supportive care, methylene blue.
Outcome: Improved condition with blood transfusion due to severe anemia.(7,8)

3. Case Report 3:
Patient: 24-year-old female without G6PD deficiency.
Presentation: Cyanosis, dyspnea, headache, methemoglobin level of 22%.
Treatment: Oxygen therapy, ascorbic acid, N-acetylcysteine.
Outcome: Complete recovery with normalization of methemoglobin levels.(9)

Significance :
Symptoms: Common symptoms across cases include cyanosis, dyspnea, and headache.

Methemoglobin Levels: Ranged from 14% to 22%, indicating varying severity.

G6PD Status: Both deficient and non-deficient patients experienced methemoglobinemia.

Treatment: Methylene blue is effective but risky in G6PD deficiency; ascorbic acid and N-acetylcysteine are safer alternatives.

Outcome: All cases achieved favourable outcomes with appropriate treatment.

CONCLUSION :
Primaquine-induced methemoglobinemia requires prompt recognition and intervention. Treatment strategies should consider the patient's G6PD status to mitigate risks associated with methylene blue use. Ascorbic acid and N-acetylcysteine are effective alternatives, ensuring safe management and favourable outcomes in both G6PD-deficient and non-deficient individuals.

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