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Case Report

Methemoglobinemia with hemolytic anaemia as a result of acute dapsone intoxication

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ABSTRACT

We describe a case of methemoglobinemia byacute dapsone intoxication in a 24-year-old female who ingested 20 tablets of Dapsone 100mg. The patient was admitted to the Medicine Emergency and Trauma Centre (METC) at King George's Medical University, Lucknow. On presentation, she exhibited respiratory distress, restlessness, altered behavior, and cyanosis of the lips and fingertips. Arterial blood gas analysis revealed dark brown colored blood with abnormal parameters, including a pH of 7.481, methemoglobin level of 26.6%, and a low oxygen saturation level. Gastric lavage was performed in the casualty department, and the patient was subsequently transferred to the Intensive Care Unit. Treatment involved administration of Methylene Blue and supportive care with supplemental oxygen and ascorbic acid and Vitamin E supplementation. The patient's methemoglobin levels gradually decreased, indicating a response to treatment. Laboratory investigations also revealed evidence of concurrent haemolytic anemia. Patient demonstrated improved respiratory distress and behavior by the treatment.

1. Introduction

Dapsone, a medicine frequently used for a number of infectious and dermatological disorders, is known to cause rare but potentially serious side effects, such as methemoglobinemia and hemolytic anaemia.[1] Methemoglobinemia is the accumulation of methemoglobin, which impairs the ability of red blood cells to carry oxygen,[2] while hemolytic anaemia is the rapid degeneration of erythrocytes.[3] Even though they don't happen often, these issues need to be managed right away to avoid potentially fatal consequences. We describe a case of methemoglobinemia and hemolytic anaemia caused by dapsone in a 24-year-old female here, highlighting the significance of being vigilant for such adverse responses in clinical practice.

2. Case Presentation

A 24-year-old female patient who had ingested 20 Dapsone 100mg tablets was taken to the Medicine Emergency and Trauma Centre (METC) at King George's Medical University due to acute dapsone intoxication. The patient's husband was on tablet dapsone as treatment for leprosy. Upon arrival, the patient exhibited respiratory distress, agitation, and altered behavior. Clinical examination revealed cyanosis of the lips, tongue and fingertips, blood pressure of 140/80 mmHg, heart rate of 110 beats per minute, oxygen saturation (SPO_2) of 80%on 6 liters of oxygen, Glasgow Coma Scale score of E4V5M6, and respiratory rate of 24 breaths per minute. In the emergency room gastric lavage was performed. The arterial blood collected for arterial blood gas (ABG) analysis had a dark brown color. The ABG results were as follows: pH 7.481, oxygen saturation (SO_2) 97.3%, partial pressures of carbon dioxide (19.3 mmHg) and oxygen (PaO_2 149 mmHg),

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Table 1: Methemoglobin and other parameters

	Methemoglobin	SPO_2	Blood Pressure	Heart Rate
Day1	26.6%	80%	140/80 mmHg	110/min
Day2	16.4%	86%	108/72 mmHg	90/min
Day3	9.9%	90%	116/80 mmHg	86/min

bicarbonate (HCO_3^-) 17.9 mmol/L, methemoglobin level of 26.6%, and serum lactate of 1.4. The patient was transferred to the intensive care unit and14 L/min of oxygen was started. Treatment with methylene blue began with a loading dose of 50 mg in 100 ml of normal saline over ten minutes. Following the loading dose, the patient's oxygen saturation increased to 86%, pulse rate to 90 beats per minute, and blood pressure to 108/72 mmHg; however, cyanosis of the lips persisted. A second loading dose of methylene blue 50 mg over 1 hour was administered. After the second dose, the patient's oxygen saturation on room air was 86%, heart rate was 118 beats per minute, and blood pressure was 118/72 mmHg. Subsequently, a continuous infusion of methylene blue was initiated 0.1mg/kg/hr. Eight hours after admission, the patient's methemoglobin level decreased to 16.4%. Additionally, intravenous ascorbic acid and vitamin E supplements were administered. Laboratory investigation reports revealed: Hemoglobin - 10.7 g/dl, total leukocyte count - 16900/cmm, platelet count - 2.20 lac/cu.mm, serum urea - 22.0 g/dl, and serum creatinine - 0.67 g/dl. On the second day after admission, methemoglobin decreased to 12.3%. The patient continued to experience cyanosis of the lips, with an oxygen saturation of 90% without oxygen treatment, but her respiratory distress, agitation, and abnormal behavior improved. On the third day of admission, the methemoglobin level was found to be 9.9%, with a hemoglobin level of 9.9 g/dl, total leukocyte count of 14000/cm, and a peripheral smear showing fragmented red blood cells (RBCs) with Heinz bodies suggestive of hemolytic anemia.(Table 1)

3. Discussion

Methemoglobinemia is serious an adverse effect of dapsone. The signs and symptoms include headache, cyanosis, dizziness, tachypnea and low oxygen saturation, which worsens with higher concentration of methemoglobin in blood.[4] Because dapsone is highly absorbed from the gastrointestinal tract, widely distributed in bodily fluids (volume distribution of 1.5 L/kg), and predominantly protein bound (73%), the clinical manifestations of dapsone toxicity are directly proportional to the amount of dapsone consumed. It is metabolized in the liver by two pathways; (A) acetylation to monoacetyl-dapsone (MADDS) and (B) hydroxylation to N-hydroxy-dapsone (NOH-dapsone). No difference has been found in dapsone serum or plasma concentrations nor any pharmacokinetic parameters of dapsone or MADDS between slow and rapid acetylators. At the same time, the pathway of dapsone metabolism by hydroxylation is less extensively studied.There are no conclusive studies about the elimination half life of the drug in acute intoxication. The hematologic symptoms of an overdose may be caused by NOH-dapsone.[5]

The use of repeated oral activated charcoal to enhance the elimination of both dapsone and MADDS was mentioned in prior papers on instances of acute dapsone poisoning in both adults and children. To impede the enterohepatic circulation of dapsone, repeated charcoal is advised.[6] The rate of elimination of both dapsone and MADDS was three to five times higher in the previous studies done on patients with dapsone intoxication when 80 grams per day of activated charcoal was used for two days.[7] In our patient after gastric lavage activated charcoalwas given,followed by intravenous bolus doses of methylene blue and later continuous infusion of methylene blue.

Methylene blue is indicated in individuals with severe hypoxia and blood methemoglobin levels more than 20%, is the most effective antidote for dapsone overdose.[8] In less than an hour of administration, methylene blue ought to have a substantial effect on the methemoglobin rate.[9] In our case, the blood methemoglobin level significantly fell after starting therapy with methylene blue, falling from 26% on day 1 to 16.4% on day 2, and then falling further to 9.9% on day 3. Due to its oxidant action, which must be monitored, methylene blue still has a small possibility of causing rebound methemoglobinemia 4 to 12 hours following therapy.[9,10]

Hemolytic anemia may follow drug-induced methemoglobinemia, especially following large doses of dapsone. The anemia is characterized by Heinz bodies (precipitated hemoglobin or globin subunits due to denaturation of hemoglobin in erythrocytes) and fragmented red blood cells. Occasionally acute intravascular hemolysis can lead to renal failure.[11] This explains diagnosis of hemolytic anemia observed in our study on day 3 of dapsone poisoning.

Because the toxic agent was consumed at a high dose and was circulated through the enterohepatic system, gastric lavage and subsequent administration of methylene blue infusions was adequate to treat the condition.

4. Conclusion

Methemoglobin, a haemoglobin molecule that contains an oxidised form of iron that cannot bind oxygen and results in an insufficient supply of oxygen to

Table 2: Drugs and substances that can result in the development of methemoglobinemia [12]

Drug group	Drug group Representatives
Local anesthetics	Benzocaine (often used in endoscopic procedures) Prilocaine, tetracaine, lidocaine
Nitrates	Nitroglycerin, Inhaled nitric oxide, Nitroprusside, Oral nitrates, Amyl-nitrate
Antibiotics	Dapsone, Rifampicin, Sulfonamides, Antimalarials
Other drugs	Rasburicase (especially in G6PD deficiency), Cyclophosphamide, Metoclopramide
Environmental causes	Fertilizers, Herbicides, Paints and Rubber

tissues. Methemoglobinemia has two types: genetic methemoglobinemia and acquired methemoglobinemia. Genetic methemoglobinemia is a chronic condition that causes a wide range of morbidities. Patients are typically identified by cyanosis without any other accompanying symptoms. On the other hand, acquired methemoglobinemia is a serious disorder that can be fatal and frequently results due to various medications or substance poisoning. The degree to which symptoms manifest clinically varies from anxiety, dizziness, cyanosis, unconsciousness, epileptic seizures, arrhythmia, and coma, depending on the amount of methemoglobin in the blood. Methemoglobinemia may be suspected if there are unexplained symptoms of refractory hypoxia, cyanosis-saturation gap, and dark brown colored blood; however, the accurate diagnosis is made utilising co-oximetry and measuring methemoglobin levels in the blood. Supportive care and stopping the insulting medicine or substance that caused the methemoglobinemia are the mainstays of treatment for this illness. Despite being a rare ailment, acquired methemoglobinemia can be fatal, hence emergency services should be equipped with methylene blue and vitamin C as countermeasures.

This case report highlights the wide range of clinical manifestations and therapeutic outcomes and contributes to knowledge on dapsone-induced methemoglobinemia and hemolytic anemia. It emphasizes the significance of early detection, immediate methylene blue treatment, and close patient monitoring to guarantee the best management outcomes. To create standardized guidelines for the therapy of this uncommon but potentially fatal adverse medication reaction, additional research and clinical trials are required.

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6. Conflict of Interest

None.

References

1. Zhu YI, Stiller MJ. Dapsone and sulfones in dermatology: overview and update. *J Am Acad Dermatol*. 2001;45(3):420–34.
2. Ludlow JT, Wilkerson RG, and TMN. Methemoglobinemia. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023.
3. Alaarg A, Schiffelers RM, van Solinge W, Wijk R. Red blood cell vesiculation in hereditary hemolytic anemia. *Front Physiol*. 2013;4:365. doi:10.3389/fphys.2013.00365.
4. Iolascon A, Bianchi P, Andolfo I, Russo R, Barcellini W, Fermo E, et al. Recommendations for diagnosis and treatment of methemoglobinemia. *Am J Hematol*. 2021;96(12):1666–78.
5. Zuidema J, Hilbers-Modderman ES, Merkus FW. Clinical pharmacokinetics of dapsone. *Clin Pharmacokinet*. 1986;11(4):299–315.
6. Burke P, Jahangir K, Kolber MR. Dapsone-induced methemoglobinemia: case of the blue lady. *Can Fam Physician*. 2013;59(9):958–61.
7. Hansen DG, Challoner KR, Smith DE. Dapsone intoxication: two case reports. *J Emerg Med*. 1994;12(3):347–51.
8. So TY, Farrington E. Topical benzocaine-induced methemoglobinemia in the pediatric population. *J Pediatr Health Care*. 2008;22(6):335–9.
9. McPherson R, Pincus MR. Henry's clinical diagnosis and management by laboratory methods. 22nd ed. Elsevier; 2011.
10. Toker I, Yesilaras M, Tur FC, Toktas R. Methemoglobinemia caused by dapsone overdose: Which treatment is best? *Turk J Emerg Med*. 2015;15(4):182–4.
11. Rehman HU. Methemoglobinemia. *West J Med*. 2001;175(3):193–6.
12. Ivek I, Knotek T, Ivičić T, Rubinić B, Bajlo P, Hamzić J, et al. Methemoglobinemia - A case report and literature review. *Acta Clin Croat*. 2022;61(1):93–8.

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