ejpmr, 2025, 12(4), 360-362

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

DAPSONE INDUCED METHEMOGLOBINEMIA: CASE REPORT

Naveen Kumar[1], Aiswarya Wilson[1], Aalia P.S.[1], Dr. Hari Lakshmanan*[2] and Dr. Aneesa Sherif[3]

[1]Department of Pharmacy Practice, St.Joseph's College of Pharmacy, Cherthala.
[2]Senior Consultant, Department of Pulmonary Medicine, VPS Lakeshore Hospital, Maradu, Kochi.
[3]Medical Officer, Department of Pulmonary Medicine, VPS Lakeshore Hospital, Maradu, Kochi.

***Corresponding Author: Dr. Hari Lakshmanan**

Senior Consultant, Department of Pulmonary Medicine, VPS Lakeshore Hospital, Maradu, Kochi.

Article Received on 01/01/2025 **Article Revised on 22/02/2025** **Article Published on 14/03/2025**

ABSTRACT

Dapsone, a sulfone compound widely used for various dermatological and infectious conditions, is associated with adverse effects such as Heinz body hemolytic anemia and methemoglobinemia. Methemoglobinemia is a rare but potentially life-threatening condition where hemoglobin is oxidized to methemoglobin, impairing oxygen delivery and leading to hypoxia. We report two cases of dapsone-induced methemoglobinemia who presented with persistent hypoxia without an alternate etiology. Both patients exhibited a characteristic "saturation gap" (low SpO_2 with normal PaO_2 in arterial blood gas analysis). Given their history of prolonged dapsone use, the drug was discontinued, following which showed significant improvement in oxygen saturation confirming the diagnosis. Dapsone-induced methemoglobinemia should be considered in patients with unexplained hypoxia, especially when a saturation gap is observed. Early identification and discontinuation of dapsone are crucial for preventing severe complications. A high index of suspicion and close monitoring patients on dapsone therapy is key to early diagnosis.

KEYWORDS: Dapsone, Methemoglobinemia, Hypoxia, Saturation gap.

INTRODUCTION

Dapsone is a sulfone compound commonly used for various medical conditions including leprosy. A significant adverse effect associated with Dapsone is the development of Heinz body hemolytic anemia and methemoglobinemia which manifests as hypoxia.

Methemoglobinemia is a rare and potentially life-threatening hematologic disorder of hemoglobin, in which iron contained within the heme moiety becomes oxidized from ferrous iron to ferric iron at a concentration greater than 1% in the blood. Methemoglobin is an aberrant form of hemoglobin and the presence of ferric heme molecules causes a structural change in the hemoglobin molecule, resulting in reduced oxygen-carrying capacity and subsequent hypoxia and hypoxemia.

Here, we present two cases of patients who presented with hypoxia due to dapsone induced methemoglobinemia emphasizing the awareness of this entity and need for monitoring the patients on dapsone especially in cases with asymptomatic dapsone induced Methemoglobinemia.

CASE PRESENTATION

Case 1

A 58 Year old female, presented with complaints of dyspnea for six days, cough for two weeks. Her family members had recent respiratory infection. Her past medical history included bilateral varicose vein with varicose ulcer right medial malleolus and Type II diabetes mellitus (on diet control). She was prescribed on Tab Colchicine 0.5mg, Tab Dapsone 100mg and Tab Folic acid 5mg once daily, Tab Deflazacort 6 mg twice daily from elsewhere which she had been taking for nearly three months.

For her present respiratory infection, she had consulted a nearby hospital (2 days back) from where she was diagnosed with pneumonia and started oral antibiotics (Tab cefixime) and supportive medicines which provided some relief.

However, her dyspnea aggravated since 6.12.24 morning and hence came to the Emergency department. On arrival, she was conscious, oriented, dyspneic, and afebrile, SpO2- 84 % on room air and 92% 4 liter oxygen, and other vitals were stable. Bilateral wheeze on auscultation, ABG showed dark reddish blood (Fig 2) pH-7.50, pCO2- 29, pO2- 146, HCO3- 22.5 (respiratory alkalosis). Chest X-ray (Fig. 1) was non contributory.

For her present lower respiratory tract infection, was treated with oxygen, steroids (Inj Methylprednisolone), antibiotics (Inj Ceftriaxone), bronchodilators, nebulisation and other supportive measures. She also had hyponatremia which was corrected through IV and oral measures. However, despite controlling wheezing and improvement in dyspnea, saturation via pulse oximetry remained low around 80% in room air. CT pulmonary angiogram was taken which showed no evidence of pulmonary thromboembolism. As there was no other causes to explain hypoxia, with significant discorrelation between saturation via. Pulse oxymetry and pO2 in ABG, along with a history of prolonged dapsone intake, possibility of dapsone induced methemoglobinemia was considered. Subsequently, Dapsone was withheld. Methemoglobin quantitative estimation was 0.9 (within normal range) andG6PD quantitative assay was 8.59U/g Hb (within normal range). She was started on Tab Vitamin C as she remained symptomatically stable, and was discharged on Home oxygen support. At discharge, SpO2 was 92% on 6L O2 and 84% in room air. She was reviewed 2 weeks post-discharge when she had no significant symptoms, and SpO2 levels improved to 97% in room air.

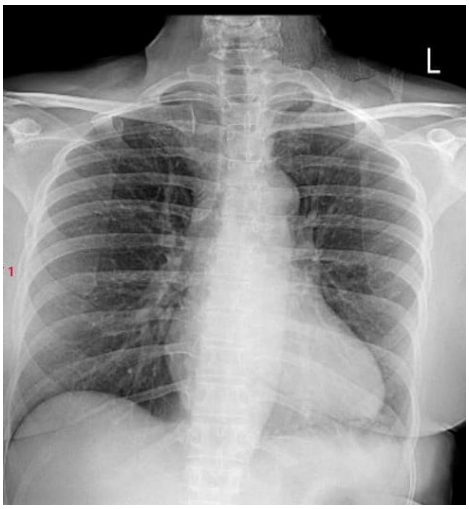

Fig 1: Chest X-Ray.

Fig 2: Dark red arterial blood sample.

Case 2

A 68year old female, presented to the emergency department with complaints of cough, scanty mucoid expectoration since one month. She reported no fever, sore throat or dyspnea. Her past medical history included bilateral varicose vein with varicose ulcer over right lateral malleolus, Skin ichthyosis, carcinoma ovary in 1996(status post-surgery and chemotherapy), uncontrolled type 2 diabetes mellitus, hypothyroidism, and osteoarthritis knee. Her regular medications for last 2 weeks (to be confirmed) included Tab Dapsone 100mg once daily, Tab Colchicine 0.5mg and other medications for comorbidities.

At presentation, she was conscious, oriented, and not dyspneic she had bilateral wheeze on auscultation. SpO2 86 % on room air and 92 % on 4liter oxygen, and other vitals were within the normal range. Chest x-ray (Fig 3) was non contributory. Arterial Blood Gas (ABG) analysis showed - pH -7.43, pCO2 -36.4 mmHg, pO2 -88 mmHg, HCO3 -24.4 mEq/L. She was diagnosed with Asthma flare up, treated with controller inhaler (Formetrol + budesonide 400mcg MDI 1-0-1), oxygen support @ 4liter per minute, oral bronchodilators and other supportive measures. Sputum culture was sterile. ECHO showed normal left ventricular systolic function, and ejection fraction of 62%. CT pulmonary angiogram showed no pulmonary thromboembolism or significant lung parenchymal changes. Mild diffuse long segment thickening of esophagus, Soft tissue mass (11.2mm) in the left breast lower medial quadrant, Small axillary lymph nodes bilaterally. USG abdomen showed grade 1 fatty liver, bilateral kidneys with mild cortical echogenicity and preserved cortico medullary differentiation. Her SpO2 was low at 85% on room air despite controlling dyspnea. There is no alternate causes to explain hypoxia, significant discorrelation between saturation by pulse oximetry and po2 by ABG, along with a history of prolonged dapsone intake, diagnosis of dapsone induced methemoglobninemia was considered. Subsequently, Tab Dapsone was discontinued. Following this, her SpO2 gradually improved to 94% on room air and was discharged on regular controller inhaler and other regular medications for comorbidities.

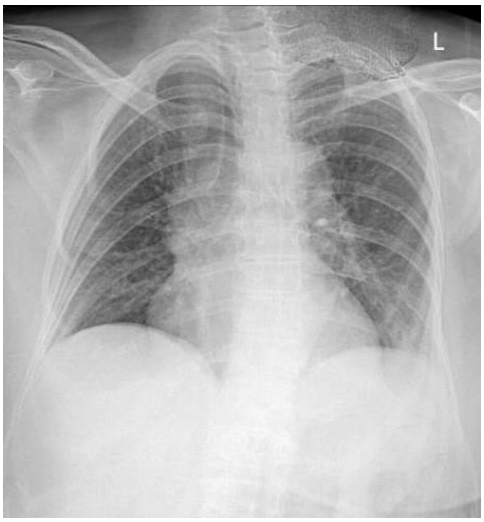

Fig. 3: Chest X-Ray.

CASE DISCUSSION

Dapsone (4, 4′-diaminodiphenylsulfone), an aniline derivative belonging to the group of synthetic sulfones has anti-inflammatory, antibacterial, and immunosuppressive properties. It is used in a wide variety of medical conditions, such as leprosy, dermatitis herpetiformis, autoimmune bullous dermatoses, malaria, and Pneumocystis jirovecii infections. The hydroxylamine derivatives present in dapsone induce severe oxidative stress to the hemoglobin inside the erythrocytes.

Dapsone undergoes hepatic acetylation to monoacetyl-dapsone (MADDS), which is hydroxylated by cytochrome P-450 to dapsone hydroxylamine (DDS-NOH), a key mediator of both its efficacy and adverse effects like methemoglobinemia and hemolysis. Dapsone is among the offending drugs that cause acquired methemoglobinemia alongside nitrite and nitrate derivatives, sulfonamides, phenazopyridine, and some anesthetics and antimalarials.

The characteristic finding of methemoglobinemia is low SpO2 but with normal levels of PaO2 on ABG analysis because methemoglobin does not affect oxygen delivery to the blood plasma in the alveoli, thus PaO2 remains unaffected. It was evident in both our cases

Initial management for methemoglobinemia is the discontinuation of the offending agent. For patients, with methemoglobin levels exceeding 30% or signs of hypoxia, administration of methylene blue intravenously at 1 to 2 mg/kg is often required. Treatment with methylene blue is contraindicated in conditions like G6PD deficiency and in individuals taking serotonergic agents due to the risk of serotonin syndrome. Methylene blue has been shown to be a potent monoamine oxidase inhibitor. Alternative treatments include hyperbaric oxygen, exchange transfusions, activated charcoal, or high-dose vitamin C. As intravenous methylene blue was not available, the first patient was treated with Vitamin C while stopping dapsone and the second patient was monitored after stopping dapsone. Hypoxia improved in both the cases subsequently. Dapsone must be used with caution in the following conditions: a) Glucose-6-phosphate dehydrogenase deficiency. b)Met-Hb-reductase deficiency c)Severe hepatopathy d)Cardiac insufficiency/heart failure e)Pulmonary diseases f)Co-medication with met-Hb-inducing drugs or compounds, respectively.

Our case also highlights the fact that dapsone can induce methemoglobinemia even when methemoglobin levels are within the normal range as evidenced in case No.1

CONCLUSION

Methemoglobinemia is a cause of hypoxia and cyanosis. It can be a potentially fatal condition if not addressed in a timely manner or left untreated. Our cases emphasize the importance of detailed history taking, including medication chart review and a high index of suspicion.

ACKNOWLEDGEMENT

The authors would like to thank the management of St. Joseph's college of pharmacy cherthala and VPS Lakeshore Hospital, Maradu.

REFERENCE

1. Barclay JA, Ziemba SE, Ibrahim RB. Dapsone-induced methemoglobinemia: a primer for clinicians. Ann Pharmacother, 2011; 45(9): 1103-1115. doi:10.1345/aph.1Q192.
2. Burke P, Jahangir K, Kolber MR. Dapsone-induced methemoglobinemia: case of the blue lady. Canadian Family Physician, Sep. 1, 2013; 59(9): 958-61.
3. Lovell KK, Momin RI, Sangha HS, Feldman SR, Pichardo RO. Dapsone Use in Dermatology. Am J Clin Dermatol, Sep. 2024; 25(5): 811-822. doi: 10.1007/s40257-024-00879-8. Epub 2024 Jul 30. PMID: 39078587; PMCID: PMC11358223.
4. Lathrop G, Fullmer R. A Case Report of Acute-on-Chronic Methemoglobinemia. Clin Pract Cases Emerg Med., Jan. 2025; 9(1): 86-89. doi: 10.5811/cpcem.31025. PMID: 39903620
5. Shenouda M, Padilla M, Silva J, Castillo H, Austin A. Dapsone-Induced Methemoglobinemia: A Case Report. Cureus, Feb. 21, 2022; 14(2): e22466. doi: 10.7759/cureus.22466. PMID: 35371634; PMCID: PMC8942638.
6. Wozel G, Blasum C. Dapsone in dermatology and beyond. Arch Dermatol Res., Mar. 2014; 306(2): 103-24. doi: 10.1007/s00403-013-1409-7. Epub 2013 Dec 6. PMID: 24310318; PMCID: PMC3927068.
7. Singh S, Sethi N, Pandith S, Ramesh GS.Dapsone-induced methemoglobinemia: "Saturation gap"-The key to diagnosis. J Anaesthesiol clin pharmacol, Jan. 2014; 30(1): 86-8. doi:10.4103/0970-9185.125710.PMID:24574600; PMCID: PMC3927300