

## Case Report

# Drug induced methemoglobinemia: a case report

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## ABSTRACT

Methemoglobinemia (MetHb) is an uncommon cause of central cyanosis and hence, not frequently considered in the differential diagnosis. Methemoglobin is an abnormal form of hemoglobin which is produced physiologically due to autooxidation. If this process of autooxidation is disturbed, either due to genetic or due to exogenous drugs/toxins, its level rises in blood leading to tissue hypoxia. It causes central cyanosis when its level exceeds 3%. We present the case of a 19-year-old male patient who was diagnosed with methemoglobinemia due to the use of dapsone for acne vulgaris. Our case emphasizes the significance of detailed history taking, knowledge and high index of suspicion for drug-induced methemoglobinemia.

**Keywords:** Dapsone, Methemoglobin, Central cyanosis

## INTRODUCTION

Methaemoglobin is a form of haemoglobin where the iron molecule is in the ferric state instead of the normal ferrous state. It is incapable of carrying oxygen, causing functional anemia and cellular hypoxia.<sup>1</sup> The purpose of presenting this case is to emphasize the importance of considering rare causes of cyanosis even in the presence of normal cardio-respiratory function, and also the possibility of methemoglobinemia even at low doses of dapsone.

## CASE REPORT

A 19-year-old male presented to the emergency department with a complaint of intermittent chest pain on inspiration for a day. The pain was bilateral, non-radiating, and not accompanied by perspiration, cough, nausea or jaw pain. He denied any complaints of dyspnea, fever, chills, headache, or nausea. Cyanosis was not evident clinically. Upon review of his home medications, it was found that he was taking dapsone 25 mg orally once a day for refractory acne vulgaris.

On examination, his lungs were clear bilaterally, normal S1-S2 without murmurs. There was no visible cyanosis, clubbing or lower limb edema. His oxygen saturation was 90% on room air, 92% on 3 L/min NC O<sub>2</sub> and other vitals were stable.

ECG was normal, chest X-ray was clear bilaterally and CT angio-chest was negative for any pulmonary artery embolism or infiltrates. Pulmonary vascularity was normal. ABG from right radial artery showed a pH of 7.49, O<sub>2</sub> level of 156, HCO<sub>3</sub> of 29.7, base excess of 5.9 and TCO<sub>2</sub> of 30.9. He tested negative for SARS-COV2, influenzae A and B and RSV.

A methemoglobin level of 10.2 was noted confirming the diagnosis of methemoglobinemia which was suspected due to persistent low O<sub>2</sub> saturation by pulse-oximeter but normal PAO<sub>2</sub> and O<sub>2</sub> saturation on ABG. After ruling out other exposures, dapsone induced methemoglobinemia was suspected.

Dapsone was discontinued, and his oxygen levels gradually improved to 94% on room air. The next day, his methemoglobin level decreased to 4.2, partially

confirming the suspicion of Dapsone causing methemoglobinemia.

## DISCUSSION

Methemoglobin forms due to the conversion of iron from the reduced ferrous ( $\text{Fe}^{2+}$ ) state to the oxidized ferric ( $\text{Fe}^{3+}$ ) state. The  $\text{Fe}^{3+}$  does not bind oxygen, and its presence shifts the oxygen dissociation curve to the left. This shift prevents  $\text{Fe}^{3+}$  to release oxygen to the tissues.<sup>2</sup> Physiologically, a miniscule amount of iron oxidizes into the ferric state during the natural delivery of oxygen to the tissues. Our bodies can maintain reduced methemoglobin levels through the activity of cytochrome b5 reductase, which utilizes nicotinamide adenine dinucleotide hydrogen to reduce methemoglobin back to the state of hemoglobin.

Dapsone has anti-inflammatory, antibacterial, and immunosuppressive properties and is used in a varied range of medical conditions, such as leprosy, dermatitis herpetiformis, autoimmune bullous dermatoses, malaria, and *Pneumocystis jirovecii* infections. It has hydroxylamine derivatives that induce critical oxidative stress to the hemoglobin inside the erythrocytes. The characteristic finding of cyanosis with low  $\text{SpO}_2$  but with normal levels of  $\text{PaO}_2$  on ABG analysis is seen. As methemoglobin does not affect oxygen delivery to the blood plasma in the alveoli,  $\text{PaO}_2$  levels remains unaffected.

The first step in the treatment of patients with methemoglobinemia is the discontinuation of the causative agent. For patients with methemoglobin levels >30% or those with signs of hypoxia, administration of methylene blue intravenously at 1 to 2 mg/kg is required.<sup>4</sup> Alternative treatments include, hyperbaric oxygen, exchange transfusions, activated charcoal, or high-dose vitamin C.<sup>4,5</sup>

## CONCLUSION

The use of dapsone for the treatment of acne vulgaris is not common. Dapsone as a causative agent of methemoglobinemia is known, but at lower oral doses is uncommon. Our case highlights the fact that oral dapsone at lower doses can potentially lead to methemoglobinemia and symptoms pertaining to it and hence, clinical vigilance is necessary for the prompt diagnosis and early treatment of the condition. Methemoglobinemia should be considered in the differential diagnosis of central cyanosis and hypoxemia.

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