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A Rare Case Of Dapsone Poisoning Presenting With Methemoglobinemia

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Abstract

Methemoglobinemia (MetHb) characterised by functional anaemia and tissue hypoxia, is a rare cause of cyanosis and generally not considered in the initial differentials. MetHb should be considered as a potential diagnosis in cyanosed patients with normal PaO2, and in the absence of cardio-respiratory causes. If left untreated, the disease can be fatal.

Published literature indicates 15% incidence of MetHb secondary to medication use. Among these, dapsone has been noted to be the most common. Methylene blue is the most effective antidote for acquired methemoglobinemia. When methylene blue is not available, alternative treatments such as ascorbic acid and hyperbaric oxygen can be useful.

We hereby describe the initial presentation, diagnosis and treatment of a case of dapsone induced MetHb, in a young female who presented to the emergency department with central cyanosis.

Keywords: Dapsone, Methemoglobinemia, Methylene blue, Cyanosis

Introduction

Methemoglobinemia (MetHb) being a rare cause of cyanosis is generally not considered in its differential diagnosis and is characterized by functional anemia and tissue hypoxia.

It is an abnormal Hb produced physiologically by auto-oxidation. If this process of auto oxidation is impaired either due to genetic defect or due to exogenous drugs/ toxins, its level starts rising.

Once it is >3%, tissue hypoxia ensues.

Methemoglobinemia should be considered in differential diagnoses of cyanosed patient with normal ABGs, PaO2 and cardio- respiratory status. If left untreated, the disease can be fatal.

Methemoglobinemia is a life-threatening condition that can be difficult to diagnose. It is more often an adverse medication effect, most commonly related to dapsone use. Methylene blue is the most effective antidote for acquired methemoglobinemia.

Case Report

A 21 year old female was bought to our hospital emergency room with a 1 day- complaints of vomiting, dizziness, generalised weakness and breathlessness.

Our patient had a notable history of allegedly consumption of 20-25 tablets of Dapsone, after which she had 3 episodes of vomiting.

On arrival to Emergency room, her lips were pale, nail beds were cyanotic. On examination, the patient was alert and appeared comfortable. She was afebrile, but her heart rate was tachycardia at 120 beats/min, her respiratory rate was 28 breaths/min, and her blood pressure was 128/76 mm Hg. She was not in respiratory distress but had marked peripheral and central cyanosis. Digital pulse oximetry showed an oxygen saturation of 72 % on room air. Results of a physical examination of her cardiovascular and respiratory systems were unremarkable. The patient's medical history was significant for Leprosy .

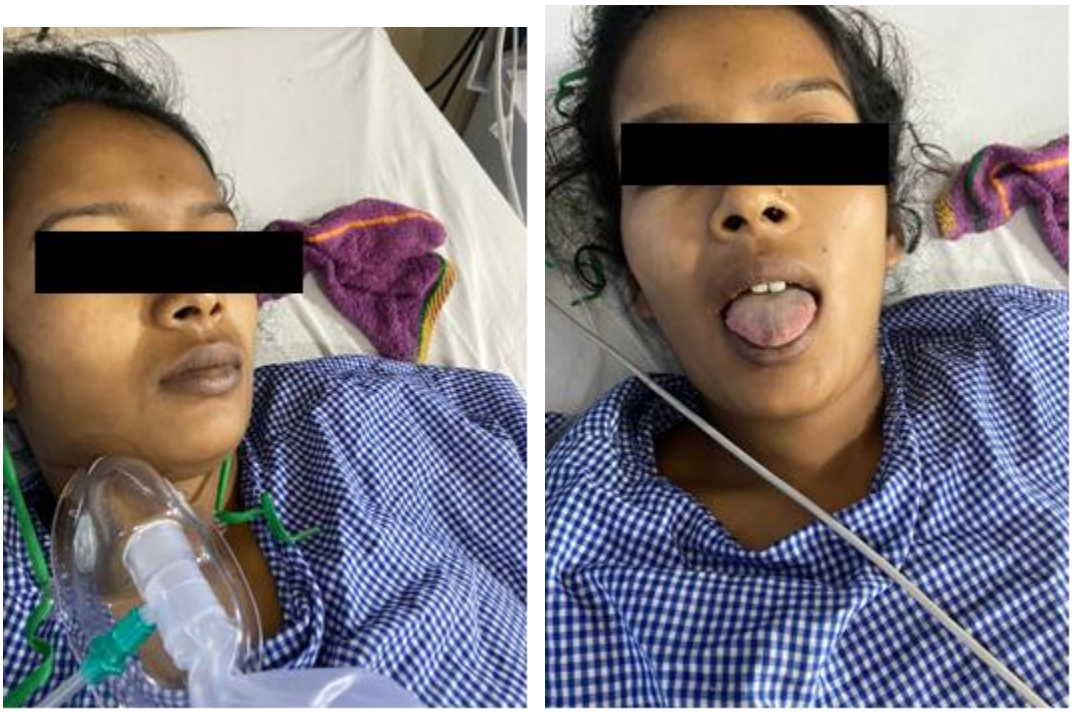
Oxygen (15 L/min by non rebreather mask) was started but her oxygen saturation did not rise above 88 %. ECG and chest X ray were normal.

Two arterial blood samples taken appeared chocolate brown. Analysis of arterial blood gas from both samples revealed a Po2 of 340 mm Hg (on 15 L via NRBM) a Pco2 of 23 mm Hg, a pH of 7.49 , a bicarbonate level of 21.5 mmol/L, and an oxygen saturation of 99%. Methemoglobinemia secondary to dapsone use was suspected and methemoglobin level tests were ordered.

Antidotal therapy with 1% Methylene blue (1mg/kg body weight) was administered intravenously Within 15 minutes of methylene blue therapy, the central and peripheral cyanosis started to resolve. The patient was admitted to our hospital. Her methemoglobin level improved from 8.3% to 1.6% the following day. Two days later, as she was clinically well with an oxygen saturation of 95% measured by pulse oximetry, she was discharged from hospital.

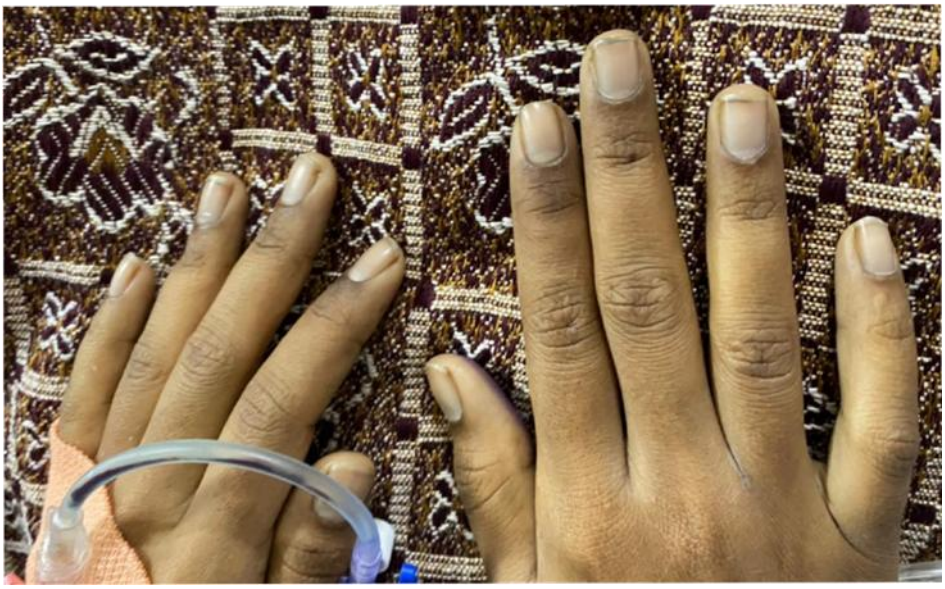
On Arrival To Emergency Room

Cyanosis At Initial Presentation



Chocolate Brown Coloured Blood

Peripheral Cyanosis At Initial Presentation



Abg On Arrival (On Nrbm 15 L)

Instrumentation Laboratory

IENT SAMPLE REPORT

HOSPITAL KAMOTHE

tus: ACCEPTED
10/2021 15:21:22
ple Type:
Arterial
mple No.: 140
erator:
DR NAMAN
tient:
Name:
UNKNOWN
Sex: U
nstrument:
Model: GEM 3000
S/N: 31063

Measured (37.0C)

pH	7.49	
pCO2	23	mmHg
	345	mmHg
	92	mg/dL
ac	1.1	mmol/L
ict	34	%

Derived Parameters

Ca++(7.4)	-----	
HCO3-	17.5	mmol/L
HCO3std	21.5	mmol/L
TCO2	18.2	mmol/L
BEecf	-5.8	mmol/L
BE(B)	-4.5	mmol/L
SO2c	100	%
THbc	10.5	g/dL
?A-aDO2	-----	

Methylene Blue Excreted In Urine

Discussion

Dapsone (4,4′-diaminodiphenyl sulfone) is a sulfone antibiotic and potent anti-inflammatory that inhibits folate synthesis. Dapsone is metabolized in the liver via the cytochrome P450 pathway to potent oxidants that are responsible for its adverse hematologic

effects namely, hemolytic anemia and methemoglobinemia.

What Is Methemoglobinemia?

Methemoglobin is an aberrant form of hemoglobin arising from oxidation of iron in the normal heme molecule from the ferrous form (Fe2+) to the ferric (Fe3+) form. The presence of ferric heme molecules causes a structural change in the hemoglobin molecule, resulting in reduced oxygen-carrying capacity and impaired unloading of oxygen at the tissue This left shift in the oxygen saturation curve results in functional anemia.Typically, red blood cells maintain a steady-state methemoglobin level of less than 1% via 2 main enzymatic pathways. Elevation in methemoglobin levels can be caused by congenital enzyme deficiencies or exposure to exogenous oxidizing agents that disrupt the equilibrium established by these pathways. Several exogenous oxidizing agents are known to cause acquired methemoglobinemia. Dapsone is the medication that most commonly causes methemoglobin, but other offending drugs include the local anesthetics benzocaine and lidocaine.There is a paucity of literature regarding the incidence of dapsone-induced methemoglobinemia.

Signs And Symptoms

Clinical symptoms of methemoglobinemia depend on the serum concentration of methemoglobin. Peripheral and central cyanosis are usually seen at a serum methemoglobin level of 15%.

Methemoglobin levels of 30% to 45% result in headache, fatigue, tachycardia, weakness, and dizziness, while levels above 60% result in cardiac arrhythmia, dyspnea, seizures, and coma. Death typically occurs at methemoglobin levels greater than 70%.

Diagnosis

Diagnosis of methemoglobinemia is normally based on clinical symptoms and an elevated serum methemoglobin level. However, serum methemoglobin levels are not always immediately available. Therefore, the typical oxygen “saturation gap” observed between arterial blood gas analysis and pulse oximetry readings is helpful for making the diagnosis of methemoglobinemia.

The saturation gap arises owing to the limitations of pulse oximetry. Pulse oximetry can only measure 2 hemoglobin species— oxyhemoglobin and reduced hemoglobin. As other hemoglobins such as methemoglobin rise, the oxygen saturation on pulse oximetry falls and plateaus at 85%.This saturation gap, where oxygen saturation levels measured with pulse oximetry are substantially lower than arterial blood gas oxygen saturation levels, should alert the practitioner that an alternative, nonfunctional species of hemoglobin is present. Also, in cases of methemoglobinemia, arterial blood samples will be a characteristic chocolate-brown colour.

Management

Initial management of patients with methemoglobinemia is supportive care with discontinuation of the offending agent. For patients with signs of hypoxia or methemoglobin levels exceeding 30%, administration of intravenous methylene blue at 1 to 2 mg/kg is required. In vivo, methylene blue is reduced by NADPH (reduced form of nicotinamide adenine dinucleotide phosphate)–methemoglobin reductase to leukomethylene blue.

Leukomethylene blue subsequently acts as an artificial electron donor to methemoglobin, thereby enhancing the erythrocyte’s ability to reduce methemoglobin. If symptoms persist after 1 hour, repeat doses are given with caution, as accumulation of the drug can result in increased production of methemoglobin. Studies support the use of activated charcoal to improve clearance rates of methemoglobin at lower concentrations of methylene blue, particularly in cases of accidental or intentional dapsone overdose. If symptoms persist despite the above-outlined therapy, hemodialysis might be required.

Conclusion

The nonspecific presentation of methemoglobinemia can make it difficult to recognize in clinical practice. However, clinical symptoms, the characteristic saturation gap between oxygen saturation on pulse oximetry and on arterial blood gas analysis, and serum methemoglobin levels aid in making the diagnosis.

Favourable outcomes are usually seen with prompt diagnosis and treatment. Physicians and other health care workers should always consider adverse

medication reactions in the differential diagnosis of atypical or unusual clinical presentations.

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