



A CASE OF DAPSONE INDUCED CYANOSIS IN THE EMERGENCY DEPARTMENT

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Abstract : Acquired Methemoglobinemia is unusual. It should be suspected in an adult presenting with acute or subacute onset of cyanosis when respiratory and cardiovascular reasons are unlikely. Here, the venepuncture reveals dark brown (chocolate) colored blood. In spite of free flow supplement of 100 oxygen, the pulse oximetry shows low oxygen saturation while blood gas analysis shows normal or elevated PaO₂. The measurement of methemoglobin level is diagnostic and history of exposure to the offending agent is contributory. Intravenous Methylene blue is highly effective to tide over the dangerous consequences. Overdose or accidental ingestion of dapsone tablets has been reported to cause symptomatic acquired methemoglobinemia in adults. Due to the long oxidative of the dapsone prolonged management with IV methylene is mandatory as seen in this case.

Keyword : Dapsone, Acquired Methemoglobinemia, Pulse oximetry, Methylene blue

INTRODUCTION: Dapsone is a synthetic sulfone that has been traditionally employed in the treatment of leprosy, acne vulgaris and wide variety of dermatological diseases in tropical world. Because of its use in various conditions its toxicity is commonly seen in adults. However dapsone intoxication in children is usually accidental and invariably fatal. The toxicity is directly proportional to the methemoglobin level in blood. In the light of wide spread use of dapsone the emergency physician may encounter patients who present to the emergency department with symptoms and signs that are caused by the toxic effects of this drug. Timely and accurate diagnosis and management is essential.

CASE PRESENTATION:

A 30 year old female patient was admitted in our IMCU with history of consumption of 51 tablets with which her brother was being treated for leprosy. The nature of the drug was not known on admission. The patient presented 10 hours after consumption with history of recurrent bouts of vomiting. The next day morning she had crampy abdominal pain. She developed bluish discoloration of the lips and finger tips 3 hours after ingestion which gradually increased in intensity. The patient was drowsy, dyspneic on admission. The patient was cyanosed without jaundice or clubbing or pedal edema. The heart rate was 90 per minute. The respiratory rate was 28 per minute. The blood pressure was 110/60 mm Hg.

The pulse oximeter showed oxygen saturation of 84% which improved only marginally with free flowing oxygen supplementation. Examination of the chest, heart, abdomen was normal. The blood collected for the investigation had chocolate brown colour shown in figure no.1. Her Hb -11.6 Gm%, TC- 7000 cells /cumm, DC- P90 L9 M1, Platelet count – 3.62 lakhs. Her blood glucose, renal, liver functions were normal. Urine routine examination revealed no abnormality. Peripheral smear showed microcytic hypochromic anemia with reactive neutrophilia. The met hemoglobin level was 29% (around 3.9 Gm/ dl). The blood gas analysis showed normal oxygen tension with mild compensated metabolic acidosis. ECG, Chest Xray , USG abdomen, Echocardiogram were normal. Gastric lavage was done and activated charcoal was administered. She was treated with IV methylene blue at 2 mg/kg IV infusion. The cyanosis improved dramatically and the oxygen saturation (SpO₂) rose to 94%. Next day SpO₂ fell down to 88% and it improved with second dose of IV methylene blue. She was treated with cimetidine, riboflavin, packed cell transfusion. She was kept in IMCU for 1 week and then discharged home in stable condition.



BLOOD OF THE THE PATIENT (ARROW) WITH NORMAL BLOOD SAMPLE (NO ARROW)

DISCUSSION:

Dapsone was first introduced in 1943 as an effective chemotherapeutic agent for leprosy and still an important drug for the treatment of this disease. The other uses of Dapsone are Dermatitis herpetiformis, Madura mycosis, Panniculitis due to alpha 1 antitrypsin deficiency and *Pneumocystis carinii* pneumonia in HIV patients. Dapsone poisoning results not only in methemoglobinemia but also in hemolytic anemia, hepatitis, coma, seizures and metabolic acidosis.

In both oxygenated and deoxygenated hemoglobin the iron remains in the ferrous (Fe 2+) state. This is essential for its oxygen transport function. The oxidation of the hemoglobin converts iron into ferric (Fe3+) state, yielding methemoglobin. The heme iron in methemoglobin does not bind to oxygen. Hence metHb does not carry oxygen and it is non functional. The ferrous iron of the deoxygenated hemoglobin is slowly oxidized to methemoglobin at a rate of 3 % per day. But the intraerythrocytic methHb reducing systems (NADPH dependent cytochrome B5 reductase, mainly NADPH -Methemoglobin Reductase and NADPH-Glutathione Reductase) help to keep its level below 1%. More than 2% of methemoglobin is abnormal.

Methemoglobinemia of more than 10 % produces clinical cyanosis. Deep cyanosis and irritability are seen when the level is above 20 %. Cardiorespiratory compromise is seen with levels above 40%. At levels beyond 60% it causes severe cardiorespiratory depression, coma and eventually death.

For the diagnosis of methemoglobinemia cardio pulmonary causes of cyanosis must be excluded first. Look for the evidence of any offending agent. The patient blood will be relatively chocolate colour, will not turn to bright red colour when dried up in a filter paper if there is methemoglobinemia. The pulse oximeter oxygen saturation tends to be low inspite of oxygen supplementation while the oxygen tension (SpO2) tends to be normal. Spectrophotometry can estimate the Met-Hb at 632 nm which is abolished by treating the sample with cyanide. The blood gas analyzer if calibrated can be used to estimate the met-Hb levels.

While the cyanosis is a key to diagnosis, confusion often occurs because of the low oxygen saturation seen with pulse oximetry. Standard colorimetric pulse oximeters provide a constant reading in the low 80s in the presence of methHb, thus giving falsely low readings in mild toxicities, and falsely high readings in severe toxicities. On the other hand, most arterial blood gas analyzers calculate the oxygen saturation based on the PaO2 and therefore give false high values. Where available potassium cyanide test can also be tried. This test can distinguish between met-Hb and sulf-Hb, as former reacts with cyanide to form cyan-metHb which has bright red colour. Sulf-Hb does not react with cyanide and therefore does not change colour.



Patient receiving IV methylene blue

CONCLUSION:

1. Methemoglobinemia should be suspected in any patient admitted to emergency department with cyanosis which is not responding to oxygen with difference between the recorded and measured saturation of oxygen.
2. The prolonged oxidative action of the dapsone sustains the production of the met-Hb making it imperative to diagnose toxicity and to monitor treatment over time.
3. The mainstay of therapy is methylene blue, which needs to be given for prolonged period unless the patient is G6 PD deficient.
- 4 Identification and the removal of the offending agent is central to the management.

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