Acquired Methemoglobinemia – A Case of Aniline Dye Exposure

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Abstract

Normal hemoglobin has HbA, which is seen in 95% of the normal population and that contains iron in reduced form i.e. Fe^{2+}. When this hemoglobin undergoes oxidation, the ferrous form Fe^{2+} is converted to the ferric Fe^{3+} state and methemoglobin is produced. The ferric state in methemoglobin renders it unable to bind to oxygen and results in a leftward shift of the oxygen-hemoglobin dissociation curve. Acquired methemoglobinemia is a rare but potentially fatal disorder. We report a case of acquired methemoglobinemia that was treated as ARDS with steroids and bronchodilator therapy.

Keywords: acquired methemoglobinemia, aniline, cyanosis, dye

Introduction

Methemoglobinemia is a disorder which involves increased levels of methemoglobin in the blood. Its causes could be congenital or acquired. When hemoglobin undergoes oxidation from ferrous to ferric form, the affinity of oxygen is increased but the ability to release oxygen to tissues is decreased. This produces a leftward shift of the oxygen dissociation curve. Clinical features and symptoms are proportional to methemoglobin levels in the blood. Above 20%, the levels produce cardiac and neurologic symptoms and above 70%, it is fatal. The apt diagnosis of methemoglobinemia and timely management reduces the mortality rate. Here we are discussing a case report of acquired methemoglobinemia who was treated with steroid and bronchodilator therapy for ARDS.

Case Report

28-year-old male patient who was referred from a private hospital in an intubated state with i/v/o ARDS and altered sensorium. On arrival at the hospital and after taking detailed history it was revealed that the patient was found in a drowsy state outside the factory while returning home. Then by his co-workers, the patient was taken to a local hospital where i/v/o saturation of 35% patient was intubated and he was put on ventilator support. Along with CBC, liver function test and kidney function test, COVID RT PCR was also sent. The patient was started on hydrocortisone 10mg tds IV, Ceftriaxone 1gm bd and Neb duolin tds. Even after 4 hours, the saturation was 35% so the patient was referred to our centre. On examination, the patient was drowsy and arousable and the repeatedly asking patient was even following commands. His pulse was 74, blood pressure was 110/70, and SpO_2 was 35% at FiO_2 100% with central cyanosis. His respiratory system was clear, air entry was equal on both sides and no added sounds were observed. We immediately got the clue that 'it's not his lungs but it's his blood'. We made a call to the factory owner and got to know that the patient was dealing with aniline dye. His methaemoglobin levels were sent which was 42%, and CBC, liver function test and kidney function tests were normal. Chest X-ray was normal. He was given methylene blue at a dose of 1mg/kg IV over 30 mins and serial monitoring of methaemoglobin levels was done. After 6 hours the patient was fully conscious and oriented. His SpO_2 at FiO_2 60% was 35%. ABG pH was 7.41, pO_2 was 206, pCO_2 was 44, and HCO_3 was 27.3. So the patient was

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extubated and put on nasal O_2 @ 5lph. The patient's saturation took 7 days to return to normal 95% without O_2 and normal methaemoglobin levels. The patient was then discharged.

Discussion

Methemoglobinemia is a disorder which involves increased levels of methemoglobin in the blood. [1, 3, 5] Normal hemoglobin has HbA, which is seen in 95% of the normal population and it contains iron in reduced form i.e. Fe^{2+}. When this hemoglobin undergoes oxidation, the ferrous form Fe^{2+} is converted to the ferric Fe^{3+} state and methemoglobin is produced. The ferric state in methemoglobin renders it unable to bind to oxygen and results in a leftward shift of the oxygen-hemoglobin dissociation curve. Its causes could be congenital or acquired. [2, 4, 5, 6]

Causes of Acquired Methemoglobinemia [4, 7, 8, 10]

Certain chemicals can accelerate the rate of methemoglobin formation and lead to acquired methemoglobinemia.

Table 1: Chemicals Causing Methemoglobinemia [4, 7, 10]

Chemicals Causing Methemoglobinemia
Aniline and its derivatives
Benzocaine
Chlorate
Chloroquine
Dapsone
Lidocaine
Naphthalene
Nitrates and derivatives
Phenacetin
Prilocaine
Pyridium
Sulphonamides

Aniline is a prototypical aromatic amine that is in a pale yellow liquid form with an unpleasant odour of a rotten fish. It is used in the production of dyes, rubber processing chemicals, shoe polish, paint, and varnish. [10, 11] The most common path to occupational exposure is inhalational or absorption of the chemical into the skin.

Clinical Features

Clinical features depend on the level of methemoglobinemia. [1, 3, 4, 7, 8, 9] Central cyanosis is the hallmark sign, where the blood turns brown and is classically described as 'chocolate coloured.' [10, 11, 4]

Table 2: Clinical Features of Methemoglobinemia [1, 4, 8, 9]

Methemoglobin concentration	Clinical features
0-3%	Nil
10-20%	Mild symptoms, Cyanosis chocolate brown
0-50%	Dyspnoea, Decreased exercise tolerance, Dizziness, Tachycardia
>50%	CNS hypoxia, Seizures, Coma, Arrhythmia, Metabolic acidosis, Tachypneo
>70%	Severe hypoxia, Death

Diagnosis [10, 11]

The diagnosis should be suspected in any patient known to develop methemoglobinemia. Characteristically, central cyanosis does not resolve on providng the patient with 100% oxygen therapy. Rule of ABC (Airway, Breathing, Circulation) to be assessed. If clinically suspected, a simple bedside filter paper test can be done. A drop of blood is to be placed on a filter paper, if the cyanosis is due to deoxyhemoglobin- it will redden, and if it is due to methemoglobin- it will not. Then to confirm, multiple wavelength co-oximeter needs to be done.

Following Points to be Considered During Diagnosis:

1. Clinical history of exposure to dye.
2. Investigation:

   ABG: As a Pulse oximeter cannot be accurately used to assess saturation, ABG is recommended

   Filter paper test: Place a drop of blood on the filter paper. Dark blood due to deoxyhemoglobin will redden on exposure to air while methemoglobin will not

   Multiple wavelengths co oximeter needs to be done

   Potassium cyanide test: To differentiate between meth and sulfhemoglobin

Management [5, 7, 10, 11]

The first and most important management strategy is avoidance of exposure by cleaning the exposed areas with water. Gastric lavage with activated charcoal is to be given if consumption is suspected.[5,10] For mild cases usually, no treatment is needed and patients usually recover in 36 to 48 hours. However, for severe cases, medical therapy is to be considered. Methylene blue is the drug of choice to be given at a dose of 1mg/kg

dissolved in D5% over 5 to 30 minutes. [11,12] It should not be dissolved in 0.9% NaCl as chloride reduces the solubility of methylene blue. It greatly accelerates the NADPH-dependent methemoglobin reductase system by acting as a cofactor. The effect of methylene blue is seen within 60 minutes. If no response or less response is observed, repeat of the dose is to be given after 1 hour. The maximum dose should not exceed 7mg/kg. In patients with aniline dye exposure, the maximum dose of methylene blue is two doses, as an excess dose of methylene blue may enhance hemolysis, as both aniline and methylene blue can undergo coupled reactions with oxyhemoglobin to generate free radicals. [12] Side effects include nausea, dizziness, tachycardia, hypertension, and urinary tract infection. Methylene blue can cause skin necrosis. [12]

G6PD testing is to be done. Methylene blue is ineffective in G6PD-deficient individuals. [11] If the patient is found deficient, exchange transfusion or hyperbaric oxygen is to be considered. In patients with HbM, where methylene blue is ineffective, hyperbaric oxygen is to be given.

Conclusion

Methemoglobinemia is a rare diagnosis and is usually missed if the proper history of the inducing agents is not available. However, as it can be found in industrial workers, details of occupational history are very important. Clinical suspicion of cyanosis not responding to 100% oxygen is an important clue. The case highlights the importance of the difference between the SpO_2 probe and ABG. ABG demonstrates normal pO_2 with low SpO_2. This helps in differentiating the causes of central cyanosis. It is also important for hospitals located near industrial areas to keep the availability of methylene blue as it is a life-saving antidote.

Detailed and diligent history-taking is always essential in managing any emergency. Methemoglobinemia is a rare but a commonly found finding in industrial areas.

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