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Case Report

Methemoglobinemia Induced by Dermal Exposure to Aniline Dye

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Abstract

We report a case of severe methemoglobinemia induced by dermally absorbed aniline dye in a young adult.The purpose of this case report is to increase awareness among healthcare providers about the occurrence of such cases in the industrial beltin the Delhi NCR region which has textile units using aniline compounds as fabric dyes.

Keywords - Methemoglobinemia, Aniline dyes, Methylene Blue

Introduction

Methemoglobin (MetHb) is a modified form of normal haemoglobin where ferrous iron (Fe2+) is oxidized to ferric iron (Fe3+). MetHb cannot bind oxygen, and hence it cannot carry oxygen to tissues. The human body can tolerate a very small amount (less than 1%) of methemoglobinemia, but a higher level is likely to cause tissue hypoxia.[1-4] This occurs in the presence of 1.5 g/dL (10%) of methaemoglobin (as compared with 5 g/dL of deoxygenated haemoglobin). Methemoglobinemia can be both congenital and acquired.It is commonly caused by exposure to certain drugs, like benzocaine and dapsone, chemicals such as nitrobenzene and aniline compounds, exhaust fumes from internal combustion engines, herbicides and pesticides that oxidize haemoglobin to MetHb,[5-11]

The most common routes of occupational exposure to nitrobenzene are inhalation and absorption through the skin.[12].Nitrobenzene and Aniline are typical aromatic nitro and amino compounds that cause methemoglobinemia.The reduction of nitrobenzene to aniline, which is used in the production of dyes, rubber processing chemicals, and antioxidants occurs once nitrobenzene is metabolized within the body, and this process oxidizes the haemoglobin in the blood into MetHb, resulting in methemoglobinemia. [1,13]

Case Report

A 19-year-old male was brought to the Emergency room of our hospital, a tertiary care centre situated in the sub-urban industrial belt of the Delhi NCR region.He worked in atextile unit. The patient was carrying a canisterof ananiline dye on his motorbike, which got spilled onto his clothes over the abdominalarea.Half an hour after that, the patient felt dizzy and went to sleep without changing his clothes. The patient woke up after 2 hours with shortness ofbreath,nausea, vomiting and bluish discolouration of his skin. He was immediately rushed to the Emergency Room of GS Medical College & Hospital Hapur,Uttar Pradesh.

At the time of presentation, thepatient was conscious but confused, his blood pressure was 130/ 90 mmHg, his pulse rate was 102 beats per minute, Spo2 was 80 % on room air, his respiratory rate was 32 /min, his body temperature was 36.8°C. Central cyanosis was noticed on lips, tongue, and extremities (Fig 1)The patient was in respiratory distress using accessory muscles of respiration.The rest of the general physical examination & systemic examination was unremarkable.The blood sample withdrawn for routine lab workup appeared chocolate brown in colour which raised the suspicion of methemoglobinemia. His MetHb was 46.8 %. He was given oxygen therapy at 5l/min with a face mask. His soiled clothes were removed and the involved area of skin was washed with soap and water.7 ml of 2% methylene blue diluted in 100 ml of saline solution and 2 gm Ascorbic acid were given via intravenous infusion. Following this patient started showing improvement in cyanosis, respiratory distress and sensorium within 2 hours. The methemoglobin levels measured again after 2 hours of starting the treatment with oxygen and methylene blue and ascorbic acid normalized had normalized to 0.8%. Other laboratory investigations conducted are given in Table 1.

Figure 1 A

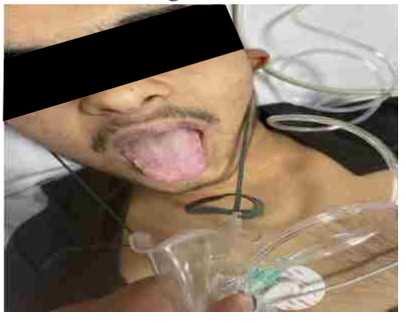

Figure 1 B

Fig.1 - Clinical photograph of the patient priorto starting treatment(fig.1A) and 2 hours after treatment (fig.1B) showing remarkable improvement in the cyanosis

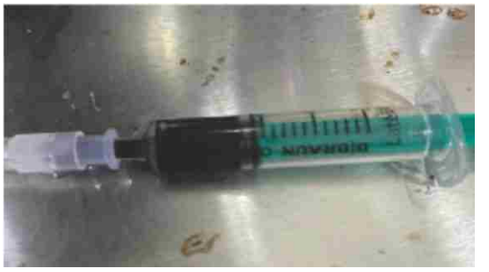

Figure 2 A

Figure 2 B

Fig.2 - Color of the venous blood at the time of presentation(fig.2A) and 2 hours after treatment(fig.2B)

Table 1: Laboratory Investigations

Parameters	**Initial**	**After 2 hour**
PH	7.40	7.40
PCO_2 (mmHg)	37.4	41.3
PO_2 (mmHg)	185	221
HCO_3 − (mmol/L)	23.0	23.5
O_2 saturation (%)	98.3	98.5
Methemoglobin (%)	46.8	0.8
	At time of admiision	**At time of discharge**
HB	13.50 Gm/Dl	13.30 Gm/Dl
TLC	10,460	10,100
Platelet	2.60	2.58
S. Creatinine	0.70	0.60
Blood Urea	40	39
T. Bilirubin	1.00	0.90
SGOT	50	46
SGPT	45	42

DISCUSSION

Based on the history of the patient's exposure to aniline dye,clinical features of central cyanosis and hypoxia (Spo2 80 % on ambient air) within few hours of dermal exposure and measurements of serum methemoglobin levels,the diagnosis of methemoglobinemia was confirmed. His MetHb was 46.8 3% on presentation and 0.8 %2hours after the treatment. His symptoms and signs of methemoglobinemia gradually alleviated, and he was discharged from the hospital onthe third day of hospitalization.

Symptoms of methemoglobinemia are proportional to the methaemoglobin levelsand roughly follow the following pattern.

- < 10% - None (patients with underlying diseases may have more symptoms at the lower level)
- 10-20% - Slight discolouration (e.g., pale, grey, blue) of the skin
- 20-30% - Anxiety, headache, tachycardia, light-headedness
- 30-50% - Dyspnoea, weakness, confusion, chest pain
- 50-70% - Arrhythmias; altered mental status, delirium, seizures, coma; profound acidosis
- > 70% - Usually, death[14]

In congenital methemoglobinemia, asymptomatic and characteristic diffuse persistent slate-grey cyanosis is present from birth. In acquired acute methemoglobinemia, a history of exposure to methemoglobinemia-inducing substances is usually present. The history of glucose-6-phosphate dehydrogenase (G6PD) deficiency should be ascertained before starting treatment with methylene blue in the acute setting.

Physical findings may include discolouration of the skin and blood. Cyanosis occurs in the presence of 1.5 g/dl of methaemoglobin as compared with 5 g/dl of deoxygenated haemoglobin. Seizures, coma, dysrhythmiasboth bradyarrhythmias and tachyarrhythmias, lactic acidosis, and cardiac or neurologicischemic manifestations may occur. The pallor of the skin or conjunctiva or icterus wassuggestive of haemolytic anaemiadue to haemolysis that may occur in cases of G6PD deficiency after methylene blue infusion.

For bedside diagnosis of methemoglobinemia - examination of blood colour on white filter paper after exposure to room air or after aerating a tube of blood with 100% oxygen is very helpfulin the diagnosis of methemoglobinemia. If the blood remains dark with these manoeuvres, then methemoglobinemia is likely. Measurement of methaemoglobin levels with C0-Oximetry or with modernBlood Gas Analysers confirms the diagnosis. Pulse oximetry is less accurate than CO-oximetry in the setting of methemoglobinemia, except for newer multiwavelength pulse oximeters. Complete blood count (CBC), reticulocyte counts, lactate dehydrogenase (LDH), indirect bilirubin, and haptoglobin may be useful to rule out haemolysis. Lab tests such asliver function tests, electrolyte concentrations, blood lactate levels, blood urea nitrogen (BUN), and creatinine are helpful for the identification of organ failure and general end-organ dysfunction.

Haemoglobin electrophoresis to identify haemoglobin M. DNA sequencing of the globin chain gene or mass spectrometry may be required for diagnosisin some difficult cases. Specific enzyme assays for causative deficiencies in inherited methemoglobinemia are needed.

For the management of methemoglobinemia, early clinical recognition is essential. Treatment is determined by the symptoms. Severe methemoglobinemia can be life-threatening and necessitate emergency therapy.Chronic mild methemoglobinemia may be completely asymptomatic and necessitate no specific therapy.No specific therapy is available forthe pharmacologic treatment of hereditary forms of methemoglobinemia except for the long-term use of general antioxidants likeAscorbic acid andRiboflavin to reduce cyanosis in cases of inherited methemoglobinemia.

Initial therapeutic measures include administration of supplemental oxygen, skin decontamination in case of dermal exposure and determination of the underlying aetiology (e.g., toxin or drug) or identification of the offending oxidizing substance. Some of the commonly used

drugs in a clinical setting are benzocaine, lidocaine, chloroquine, primaquine, clofazimine, dapsone, amylnitrate, isobutylnitrate, silvernitrate,metoclopramide,nitric oxide, nitroglycerin,nitroprusside, sodium valproate, sulphonamides,nitrofurane and p-aminosalicylic acid.Treatment is advisable for patients who have suffered acute exposure to an oxidizing agent and have methaemoglobin levels of 20% or higher, as well as for those with lower methaemoglobin levels but who have a significant cardiac, pulmonary, or hematologic disease. Treatment modalities include methylene blue – the primary emergency treatment for documented symptomatic methemoglobinemia. However, it is contraindicated in G6PD deficiency and is ineffective with haemoglobin M.

Exchange transfusion can be considered for patients who do not respond to methylene blue orG6PD-deficient individuals who are severely symptomatic. Hyperbaric oxygen treatment when methylene blue therapy is not feasible, ineffective or contraindicated. IV hydration and bicarbonate can be used for metabolic acidosis. Other medications include ascorbic acid, riboflavin, cimetidine, and N-acetylcysteine.

This case highlights the fact that all industrial workers who handle methemoglobinemia - causing substances should be provided with personal protection kits. Medical institutions in the vicinity of industrial belts using the aniline dye should ensure readily available stocks of 2% methylene blue. In addition to textile industries, methemoglobinemia-causing substances, such as nitrobenzene and aniline, can be absorbed by workers at petrochemical plants in various ways, and symptoms may not appear for a few hours after exposure. Industrial units that handle such substances must have a strict maintenance system in place, as well as a protection system for workers, including regular exposure check-ups and an emergency patient management system to ensure that all workers have access to timely diagnosis and treatment at appropriately equipped medical facilities.

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