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Latter to Editor

Rare Inhalation Methemoglobinemia

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Sir

Poisoning by ingestion of nitrate compounds has been well documented. We present a case of life threatening methemoglobinemia following accidental inhalation of nitrobenzene, managed successfully with intravenous methylene blue, ascorbic acid and mechanical ventilation.

Acute methemoglobinemia often presents as a medical emergency requiring immediate treatment. Nitrobenzene is an oxidising compound used in the manufacture of aniline, pesticides, rubber chemicals and printing materials.

A 24 year male was received in the emergency department with unconsciousness, frothing from mouth and cyanosis. A brief history revealed that the patient was found lying unconscious at his workplace, a printing industry. On examination GCS was E1V1M1 along with central and peripheral cyanosis. A heart rate of 86/min and a blood pressure of 122/72 mmHg was recorded. Respiratory rate was 5-6/min, gasping in pattern. Since the patient was unconscious and had shallow respiration, he was immediately intubated to secure the airway and 100%O_2 was administered. Suspecting poisoning, gastric lavage with $KMnO_4$ was performed, but clear returning lavage fluid indicated that poisoning was not due to ingestion. Patient was shifted to ICU and after obtaining a sample for blood gas analysis put on mechanical ventilation with a FiO_2 of 100%. Initial SpO_2 was 78%. Blood drawn for Arterial Blood Gas (ABG) analysis was brownish and ABG analysis showed metabolic acidosis with pH=7.06, pCO_2=38.2, pO_2=177.8, HCO_3=10.6, SaO_2=98.5%, Na^+=133.1, K^+=3.8 and Cl^-=97.4. This presentation prompted us towards a provisional diagnosis of methemoglobinemia although there were no signs of ingestion. For confirmation, quantitative determination of blood methemoglobin concentration was done. Laboratory report determined a methemoglobin level of 74%. We administered injection of methylene blue (1%) 2mg/kg IV over 10 minutes and ascorbic acid 200 mg IV. Over the next 4 hours patient's SpO_2 improved to 86%. Over 6 hours central cyanosis gradually disappeared and patient gradually regained consciousness. Over next 2 days, patient's SpO_2 improved slowly up to 94%. Patient could be extubated on the 3rd day. There were no derangements in cardiac, liver or renal functions.

Later, on regaining consciousness, patient gave history that while filling printer cartridges, the dye got accidentally spilled and he inhaled a lot of fumes before falling unconscious. We hereby stress that even inhalation of such fumes can be toxic and one must strongly suspect this in absence of signs of ingestion.

As far as pathophysiology is concerned, in methemoglobinemia iron in hemoglobin is oxidized from ferrous (Fe^{2+}) state to the ferric (Fe^{3+}) state. This oxidized form of hemoglobin i.e. methemoglobin is unable to bind O_2 and imparts a brownish colour to blood. The physiologic homeostasis is maintained by either of two processes i.e. reduction reactions and enzyme aided reactions. The reduction reactions involve glutathione reductase, ascorbic acid and catalase. Among the enzymatic activity, 95% is through NADH dependent methemoglobin reductase and the rest 5% through NADPH reductase. It is worthwhile to note that methylene blue is a cofactor for NADPH reductase.[1]

Normally circulating blood has <1% methemoglobin. The symptoms of methemoglobinemia depend on the blood methemoglobin level and are as follows:

<25% methemoglobin: Central and perioral cyanosis.

35-40% methemoglobin: Dyspnea, dizziness, fatigue and headache.

50-60% methemoglobin: Severe lethargy and stupor.

>70% methemoglobin: Patient becomes comatose and sometimes can be fatal.

Clues to a provisional diagnosis of methemoglobinemia include:

- History of ingestion of nitrate chemicals
- Central cyanosis
- Low SpO^2 despite a normal ABG PaO^2
- Persisting cyanosis despite oxygen therapy
- Brownish discolouration of blood
- Associated acidosis can worsen the symptoms

The definitive diagnosis is made by quantitative estimation of blood methemoglobin levels by a co-oximeter. Oxygen saturation calculated by other methods, although low, underestimates the true degree of methemoglobinemia.[2]

The patient can be managed by administering 100% oxygen, although it does not reduce methemoglobin level, it maximizes tissue oxygen delivery. Patients should be sedated to reduce activity as activity increases oxygen demand.[3] Specific therapy involves administration of 1% methylene blue (methylthionine chloride) in a dose of 2mg/kg IV over 5-10 min and may be repeated after one hour if not resolved.[4] Methylene blue causes reduction of ferric iron of hemoglobin to ferrous form. Maximum dose should not exceed 7mg/kg.[5] Exchange transfusion should be considered in G6PD deficient patients. Toludine blue can be an alternative to methylene blue. Vitamin C (ascorbic acid) is also useful as it helps reduction of methemoglobin.[3]

To conclude, though methemoglobinemia due to nitrobenzene is caused by ingestion, fatal methemoglobinemia can occur following inhalation also, unsuspectingly, and one must always strongly consider possible inhalational toxicity.

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