Acquired Methemoglobinemia - A case report
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Abstract: This is a case report of 4 years old male child who presented with central cyanosis, involuntary movements, weakness of the trunk and respiratory distress. There was a history of accidental ingestion of 3 tablets of dapsone (100 mg each). Oxygen saturation was low in spite of high flow oxygen with blood drawn for investigations showing chocolate brown in color. Clinical diagnosis of methemoglobinemia was made. G6PD levels in blood were checked and child was started on intravenous methylene blue after drawing blood for methemoglobin levels. All his symptoms like cyanosis, involuntary movements, irritability disappeared drastically with two doses of methylene blue. Lab levels of methemoglobin came as 19.6. Child was discharged home on fourth day. Naranjo algorithm score was obtained which denotes a Probable Adverse Drug Reaction.

Keyword: Dapsone Poisoning, Involuntary movements, Methemoglobinemia.

Case Report

Four years old male child was brought to emergency department (ED) of our hospital with complaints of bluish discoloration of lips and tongue for the past two hours. Mother noticed peculiar movements of upper limb and tongue for the past one hour. Child was not able to support himself and did not recognize his mother. Mother also complained of vomiting and difficulty in breathing. On eliciting a detailed history, mother noticed that the child was playing with a strip containing dapsone tablets which she was prescribed for leprosy and she later found 3 tablets (100 mg each) were missing. The child was apparently normal before this episode with no significant past history.

Examination: The child was awake, confused and irritable, did not recognizes his mother. He had central cyanosis and was tachypneic. His pulse rate was 120 per minute, respiratory rate - 40 per minute and blood pressure was 100/70 mm of Hg and temperature was 98.2 degree Fahrenheit. Neurological examination revealed involuntary movements of choreathetoid nature involving both upper limbs and tongue. He had truncal ataxia, nystagmus and hypotonia. Deep tendon reflexes were just elicitable and bilateral plantar reflex was flexor response. Rest of his neurological examination was normal and other system examination were also normal. On applying the Naranjo Algorithm Questionnaire to this child, the score arrived were five. The Naranjo score of 5 – 8 indicates that the event is "Probable" Adverse Drug Reaction (7).

CHOCOLATE COLOUR OF METHEMOGLOBIN

Management: The Child’s oxygen saturation never improved with high flow oxygen and blood drawn for routine investigation was chocolate brown in color. Complete blood count was hemoglobin – 11.2 gm/dL, total count – 6400 cells/cumm, differential count – P64% L34% E2%, platelet – 2-3 lakhs cells/cumm and hematocrit was 33%. Peripheral smear showed normocytic normochromic red blood cells with platelets single and clumps. Blood urea – 26mg/dl, creatinine – 0-6 mg/dl, serum sodium – 136 meq/dL, potassium – 3.6 mEq/dL, bicarbonate – 19 mg/dL. His chest x-ray and ECG was normal. Child was given gastric lavage, kept nil per oral with supplemental oxygen through non rebreathing mask. He was started on maintenance intravenous fluids. With background history of accidental dapsone injection with cyanosis and chocolate brown color of blood, a clinical diagnosis of methemoglobinemia was made and the decision to start the child on Intravenous methylene blue rescue was made. G6PD levels were done which were 17.8 % (normal – 7 – 24 %). Blood samples for methemoglobin level estimation was
taken. The lab report for methemoglobin level was high (19.6%). 30 mg (2mg/kg) of Inj.Methylene blue (1% solution) diluted with 20 ml of normal saline was given intravenously slowly over 10 minutes under vitals monitoring.

Good clinical response was noted in the form of improvement in involuntary movements, irritability, but saturation remained low. As oxygen saturation did not improve with first dose, child was given second dose of intravenous methylene blue. The oxygen saturation improved dramatically after the second dose from 84% to 96% with supplemental oxygen and child passed green colored urine twice.. The child was kept under observation for 3 days which was uneventful.

**Discussion**

Dapsone is 4, 4’ – diamino diphenyl sulphone used as a chemotherapeutic agent for leprosy. It is also used in the treatment of dermatitis herpetiformis, maduromycosis, and pneumocystis carinii pneumonia in HIV infection (5). Methemoglobinemia occurs when red blood cells contain greater than 1% of methemoglobin. Methemoglobin contains iron in ferric state (Fe3+) rather than ferrous state (Fe2+) (6). This structural change decreases the binding capacity of oxygen at alveolar level causing anemic hypoxia. Methemoglobinia is commonly acquired rather than inherited and the causes are Toxin induced – Secondary to ingestion or skin exposure to an oxidizing agent. Common agents are antibiotics (sulphonamides, Dapsone), local anesthetics (benzocaine, lignocaine), aniline, phenazopyridine, napthaline, inorganic and organic nitrates, nitrates, chlorates (3). Acidosis secondary to dehydration/diarrhea. Secondary to ingestion of water containing nitrates can acquire in very young infant in whom toxic ingestions is uncommon. Genetic causes – Cytochrome b5reductase deficiency (3). The clinical manifestations are directly related to methemoglobin levels. Child will not have any symptoms when the levels are less than 10%. Cyanosis appear between 10 and 20%. Signs of anxiety, headache, tachycardia, occurs between 20 and 30%. Fatigue, confusion, dizziness, tachypnoea, tachycardia occurs between 30 and 50%. Coma, seizures, arrhythmias, acidosis occurs above 50% and death occurs above 70%. This child presented with altered consciousness, irritability, disorientation, central cyanosis, tachypnea, tachycardia, with nystagmus hypotonia and involuntary movements (3).

Standard treatment protocol for toxin induced methemoglobinemia is gastric lavage followed fluid resuscitation and intravenous methylene blue. Methylene blue combines with reduced nicotinamide dinucleotide phosphate (NADPH). In the presence of NADPH methemoglobin reductase produce leukomethylene blue, which then reduces methemoglobin to hemoglobin. Methylene blue also acts as cofactor to accelerate the conversion of methemoglobin to hemoglobin (6). Methylene blue is given in intravenous route as 1% solution at 1–2mg/kg diluted in normal saline infused over 3 to 5 minutes. It can be repeated at 1 mg/kg to maximum of 7 mg/kg since methylene blue itself can be toxic and cause chest pain, dyspnea and hemolytic anemia (6). 6GPD levels should be checked before starting methylene blue as it may cause hemolytic anemia in 6GPD deficient individuals. A study was done to compare intermittent Vs Continuous intravenous methylene blue therapy in patients with dapsone induced methemoglobinemia and found that continuous intra venous methylene blue therapy produced significant decline in methylene blue level then intermittent regimen (1).

Exchange transfusion may be considered for patients who are 6GPD deficient and severely symptomatic or for those patients who do not respond to methylene blue.