

Case Report

Accidental Dapsone Induced Methemoglobinemia in a Young Child

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ABSTRACT

Acquired Methemoglobinemia is unusual. It should be suspected in a child 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 children and adults. This appears to be the first case reported in a young child from the Middle East Gulf region.

KEYWORDS: cyanosis, dapsone, methemoglobinemia, methylene blue

INTRODUCTION

In both the oxygenated and deoxygenated hemoglobin, the iron remains in the ferrous (Fe⁺⁺) state and this is essential for its oxygen transport function. Oxidation of hemoglobin iron to the ferric (Fe⁺⁺⁺) state yields methemoglobin. The ferric iron in methemoglobin does not bind oxygen. Hence, methemoglobin does not carry oxygen and is non-functional. The ferrous iron of deoxygenated hemoglobin is slowly oxidized to methemoglobin at a rate of about 3% per day, but the intrerythrocytic methemoglobin reducing enzyme systems (NADH-dependant Cytochrome P5 Reductase, mainly NADPH - Methemoglobin Reductase and NADPH-Glutathione Reductase) help to keep its level below 1%. More than 2% of methemoglobin^[1] is abnormal. Hereditary methemoglobinemias are either due to enzymopenia^[2], or structurally abnormal hemoglobin variants where iron is stabilized in the ferric state (thus becoming non-functional). The agents implicated in acquired methemoglobinemias are nitrites and nitrates^[3], nitric oxide, sulphones (e.g. dapsone), local anesthetics (e.g. benzocaine), and other agents like aniline dyes, chlorates, pyridium, phenacetin, sulphonamides, etc. Young infants are more susceptible to oxidant drugs due to their low levels of red cell NADH- Cytochrome P5 reductase activity.

CASE REPORT

We report a case of acquired methemoglobinemia due to accidental dapsone poisoning in a child aged 19 months. He presented to us six hours after accidental ingestion of an unknown number of dapsone tablets used by his mother. He developed bluish discoloration of lips and fingertips three hours after ingestion gradually increasing in intensity. The child was fully conscious but irritable. He was deeply cyanosed, but there was no respiratory distress when he arrived. The heart rate was 128/m and the respiratory rate was 36/m. The blood pressure was 100/55 mmHg. Examination of the chest, heart and abdomen was normal. Pulse oximetry showed an oxygen saturation of 85% which improved only marginally with free flowing oxygen supplementation. The blood collected for investigations had chocolate brown color and a drop of blood on a filter-paper did not become red as compared to control (Filter-Paper Test for Methemoglobinemia). The Blood Gas Analysis showed normal oxygen tension with mild compensated metabolic acidosis. His hemoglobin was 94 g/L, reticulocyte count 1%, WBC 16,400/cmm and platelets 407,000/cmm. Blood glucose, renal and liver functions were normal. The methemoglobin level was 28.1%. Gastric lavage was done and activated charcoal and sorbitol were administered. His G6-PD level was normal. Intravenous methylene blue (1%) 1 mg/kg diluted in distilled water was administered slowly over ten

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minutes. The cyanosis improved dramatically and the oxygen saturation rose to 97%. He became less irritable. About ten hours after admission, he developed mild cyanosis and irritability again. The methemoglobin level was 21%. This improved with a second dose of IV methylene blue. Oral ascorbic acid (vitamin C) 500 mg/day was given for three days. The methemoglobin level was insignificant on the next two days and he was discharged home.

DISCUSSION

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 cardio-respiratory depression, drowsiness, coma and eventually death.

Dapsone (DDS-diamino diphenyl sulphone) can induce methemoglobinemia in chronic overdosage or acute intoxication. At times, it can precipitate acute hemolytic anemia^[4]. Dapsone is used in leprosy, dermatoses, as well as in pneumocystis carini pneumonia prophylaxis (in combination with trimethoprim) in HIV patients. It is implicated in many case reports^[5-12] in children and adults as a cause of symptomatic methemoglobinemia of varying severity, either by overdosing or accidental ingestion. This case appears to be the first reported in a young child from the Middle East Gulf region.

For the diagnosis of methemoglobinemia, cardiac and pulmonary diseases as a cause of cyanosis must be excluded first. Look for evidence of any offending agent. The patient's blood will be relatively chocolate brown colored and will not turn to bright red color when dried on a filter paper, if there is at least 25% methemoglobinemia. The pulse oximetry oxygen saturation tends to be lower in spite of oxygen supplement while the oxygen tension (PaO₂) tends to be normal. Spectrophotometry can estimate the methemoglobin band at 632 nm (which is abolished by treating the sample with cyanide). The Blood Gas Analyzer, if calibrated can be used to estimate the methemoglobin concentration.

Asymptomatic drug induced acquired methemoglobinemia usually disappears after discontinuation of the drug and does not require any further specific treatment. Elimination of toxic agents by gastric lavage and catharsis are important in acute severe overdosage. In a symptomatic patient, the methemoglobin level has to be monitored. IV methylene blue (tetramethylthionine chloride) 1% at a dose 0.1 - 0.2 ml/kg (1 - 2 mg/kg) is usually

sufficient to reduce methemoglobin. The dose may be repeated after one hour in cases of persistence or recurrence of symptoms. Ascorbic acid may be used as an alternative or adjuvant treatment. Both methylene blue and ascorbic acid reduce methemoglobin in presence of NADPH dependant methemoglobin reductase enzyme. They are effective both in drug or toxin induced methemoglobinemia and hereditary methemoglobinemia due to NADH-cytochrome P5 reductase deficiency, but not effective in those due to structural abnormalities of hemoglobin. As the efficiency of methylene blue depends on adequate amounts of NADPH, care should be taken to exclude G6-PD deficiency. In a G6-PD deficient patients, methylene blue may aggravate methemoglobinemia. Cumulative doses of methylene blue exceeding 7 mg/kg may cause distressing symptoms like hemolytic anemia^[11], dyspnea, chest pain, and tremor etc. In severe resistant cases, exchange transfusion^[12] may be necessary.

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