Clinical Article

Unexplained Cyanosis and Irritability in a 20-month-old Child

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Abstract

We report a child with sudden onset of cyanosis, persistent crying and irritability following the accidental ingestion of mothballs. Based on the clinical picture, the low pulse oximetry, color of the blood, and the composition of mothballs, methemoglobinemia was diagnosed and the child was promptly treated with methylene blue. *Int Pediatr. 2004;19(2):106-108.*

Key words: Methemoglobinemia, cyanosis, mothballs

Introduction

A 20-month-old boy previously well was brought to our emergency department for generalized bluish discoloration and irritability that had occurred two days earlier. There was no fever, cough or shortness of breath, and the past medical history was negative regarding cardiovascular diseases. The mother did not witness any abnormal movements or loss of consciousness, however, reported worsening irritability, persistent crying and refusal to feed on the day of admission. She recalled seeing her child playing with mothballs with some pieces in his mouth on the day she was moving the carpets to the family store room only few hours prior to the illness. There are no drugs or other chemicals at home. The child vomited once and passed a foul, greenish watery bowel movement when he was first noted to becoming bluish.

On physical examination, the child was cyanotic and irritable. Cyanosis was not relieved by oxygen, face mask 6 L/min. Temperature: 37.2°C (rectally), respiration: 30/min, pulse: 132/min, BP: 85/58, pulse oximetry: 75%. Lips, tongue and mucous membranes were blue. Breathing was normal and heart rate and rhythm were regular. Pulses were equal and strong in all extremities.

CBC: hemoglobin12.5 g/dL, white blood count 12,300/mm3, normal differential and platelet count. Blood glucose normal, blood urea nitrogen (BUN), creatinine, and electrolytes were normal. Arterial blood gas pH, 7.42; PO2, 295 mm Hg; PCO2 33 mm Hg; oxygen saturation 99%. Methemoglobin level, 27% (normal, 0.4-1.5).

Discussion

The diagnosis of methemoglobinemia was suspected in view of the sudden onset of cyanosis that was unresponsive to oxygen administration (in a previously healthy child), and the disparity between bed side pulse oximetry reading (75%), and the high PO2 (295 mm Hg) by arterial blood gases. While collecting the blood for arterial gases, it was noted it had a chocolate brownish color, consistent with methemoglobin. The diagnosis was subsequently confirmed by measuring methemoglobin level (27%). As soon as methemoglobinemia was suspected, methylene blue 1 mg/kg intravenously was administered over 10 minutes. After 15 minutes, oximetry increased to 90%, and after 45 minutes cyanosis resolved, while oximetry became 96%.

Although methemoglobinemia is not a common hematological disorder, it continued to be reported from all countries due to the exposure of different environmental (such as Naphthalene, Table 1), and pharmaceutical agents (including local anesthetics such as EMLA cream, Table 2).

Methemoglobin is a hemoglobin that contains iron in the ferric state (Fe^{+3}), instead of ferrous (Fe^{+2}), and is incapable of binding oxygen, thus reduces the oxygen-carrying capacity. In addition, methemoglobinemia shifts the oxygen dissociation curve to the left. Ferric heme groups impair the release of oxygen to the tissues. Organs with high oxygen demands (CNS, cardiovascular) are the first to manifest

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Table 1 - Environmental agents that cause methemoglobinemia

Aniline dyes	Naphthalene
Aromatic amines	Nitrobenzene
Arsine	Nitrofurans
Butyl nitrite	Nitrophenol
Chlorates	Nitrozobenzene
Chlorobenzene	Resorcinol
Chromates	Silver nitrate
Dimethyltoluidine	Trinitrotoluene
Foods containing nitrates/nitrites in well water	

Table 2 - Pharmaceutical agents that cause methemoglobinemia

Local anesthetic (prilocaine, EMLA)	Nitrates/Nitrites
Sulfonamides	Phenazopyridine
Primaquine	Quinones
Phenacetin	
Nitroprusside	
Dapsone	
Nitroglycerine	

toxicity. Oxygenated blood is red, deoxygenated is blue, and blood-containing methemoglobin is chocolate-brown color. Methemoglobin is formed continuously under normal conditions, but its concentration is maintained at low levels (below 1.5%) by two RBC enzyme systems, NADH and NADPH-dependent methemoglobin reductase both reduce methemoglobin to hemoglobin.[1]

Children are particularly susceptible to methemoglobinemia as the erythrocyte protective mechanism has not fully matured, and the NADH methemoglobin reductase concentration is low. Significant signs and symptoms of methemoglobinemia become apparent as the methemoglobin fractions exceed 25%. This includes headache, dyspnea, lethargy, drowsiness. At fractions above 50-70% seizures, altered level of consciousness, dysrhythmias are common. Levels above 70% are usually lethal. Patients with levels below 20% are often asymptomatic except for the generalized cyanosis. The diagnosis is confirmed by direct measurement of methemoglobin fractions by a multiple wavelength co-oximeter. Arterial blood gas measures the actual oxygen saturation (also referred to as co-oximetry).[2] Analysis of blood gas measures the partial pressure of oxygen (PO2) and calculates the oxygen saturation by the oxy-hemoglobin dissociation curve. In patients with methemoglobinemia, pulse oximetry is useless, displaying levels below 90% regardless of the true oxygen saturation. Methemoglobin absorbs light at wavelengths that also absorb deoxyhemoglobin and oxyhemoglobin. Thus, methemoglobin interferes with the colorimetric testing that is used to obtain the percentage of oxyhemoglobin and deoxyhemoglobin.

Methemoglobinemia could also result from a rare hereditary disorder of hemoglobin M, most are autosomal recessive. Several types are described, ranging from deficiency of cytochrome b5 reductase in RBC, to the generalized reductase deficiency affecting all tissues (thus accompanied by neurological abnormalities that occur at an early age).[3]

Mothballs and flakes are widely available moth repellent agents, commonly sprinkled on carpets prior to their removal and storage at the end of the winter season. The active ingredients of mothballs are: Naphthalene and Pardichlorobenzene. Both substances are reported to cause methemoglobinemia, in addition to hemolytic anemia in sickle cell and G6PD deficient patients. Immediate management after ingestion of mothballs includes induced emesis because of the large size of these balls. Gastric lavage might be useful for ingestion of flakes, but its effectiveness may be limited by naphthalene's poor water solubility. Information on activated charcoal is scant, but adsorption is thought to occur. Syrup of Ipecac may be indicated in the pre-hospital setting if given within 30 minutes after ingestion, contraindicated in the presence of depressed consciousness or loss of protective reflexes. Urine alkalinization is useful if hemolysis occurs.[4]

The first line antidote for methemoglobinemia is methylene blue. It uses the NADPH-reducing system to convert iron from the ferric to the ferrous state. The dose is 1-2 mg/kg intravenously, with the positive effect seen within 30-60 minutes. A second dose may be given if no response is seen with in an hour. Caution should be exerted in patients who have G6PD deficiency, as treatment with methylene blue could be ineffective or could cause hemolysis.[5] Patients with hereditary methemoglobinemia have been successfully treated with daily doses of vitamin C.

Conclusion

The clinician should suspect methemoglobinemia in a child who develops unexplained cyanosis, unrelieved by oxygen therapy, and whose pulse oximeter shows low readings despite a high PO_2 on arterial blood gas. A chocolate-brownish blood color is very suggestive. A history of exposure should be sought in order to determine a causative agent. The treatment of choice for symptomatic cyanotic patients is intravenous methylene blue.

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