RESEARCH ARTICLE

METHEMOGLOBINEMIA DUE TO BIOLOGICAL POISONING – CASE REPORT

Geethika Sai Nutakki¹, Indraja Siripurapu¹, Ch. Manoj Kumar² and T V D Sasi Sekhar³.

1. Postgraduate, General Medicine, Dr. Pinnamaneni Siddhartha Institute of medical sciences and research foundation, Chinaoutpalli, Krishna district, Andhra Pradesh.
2. Associate Professor, Dept. of General Medicine, Dr. Pinnamaneni Siddhartha Institute of medical sciences and research foundation, Chinaoutpalli, Krishna district, Andhra Pradesh, India.
3. Professor and HOD, Dept. of General Medicine, Dr. Pinnamaneni Siddhartha Institute of medical sciences and research foundation, Chinaoutpalli, Krishna district, Andhra Pradesh, India.

Manuscript Info

Abstract

Acquired methemoglobinemia is a dyshaemoglobinemia which results from exposure to various oxidizing agents, results in impaired oxygen delivery to the tissues and can be potentially fatal if untreated. Deliberate ingestion of certain herbicides, insecticides, and pesticides may produce this condition. We report 2 cases of methemoglobinemia due to intentional ingestion of pesticides which were marketed to be safe and contain only biological extracts and fillers. Methylene blue, ascorbic acid, blood transfusion and exchange transfusion are the various modalities of treatment.

Introduction:

Methemoglobin (MetHb) is a dyshemoglobin, represents the oxidized form of hemoglobin (Hb), the ferrous (Fe²⁺) state of iron is transformed into ferric (Fe³⁺) state, which makes it incapable of binding to oxygen. Acquired methemoglobinemia is more common than inherited and results from exposure to various oxidizing agents such as nitrates, nitrites, aniline, dapsone, local anaesthetics, herbicides and pesticides. We report 2 cases of methemoglobinemia induced by ingestion of pesticides with suicidal intent.

Case presentations:

Case 1:
A 25-year-old woman presented to emergency with alleged history of poisoning with pesticides within 40 minutes after consumption. She was found unresponsive and was intubated and mechanically ventilated. At presentation, she was cyanotic with pulse rate, 90 beats/min; respiratory rate, 28 breaths/min; and blood pressure, 130/80mmHg. Bilateral breath sounds were clear. Bilateral pin point pupils with sluggish reaction to light were noted. Within 3 hours after admission, she became hemodynamically unstable and developed generalized tonic clonic seizures. Oxygen saturation measured by pulse oximetry (SpO₂) was 67% at ambient air and 88% with 100% oxygen. Her blood samples appeared chocolate brown. Arterial blood gas (ABG) analysis with CO-oximetry (SIEMENS Rapid point 500) showed a partial pressure of O₂ (pao₂) 467.5mmHg, arterial O₂ saturation of 99% (SaO₂) and MetHb of 78%. She was treated with 1% methylene blue, ascorbic acid, exchange transfusion, antiepileptics, and inotropic support but despite of treatment, she expired on day 3.

Corresponding Author:-Geethika Sai Nutakki.
Address:-Postgraduate, General Medicine, Dr. Pinnamaneni Siddhartha Institute of medical sciences and research foundation, Chinaoutpalli, Krishna district, Andhra Pradesh.
Case 2:
A 25-year-old man was brought to emergency with alleged history of poisoning with about 100ml of pesticide within 90 minutes of ingestion. At presentation, he was conscious, coherent and cyanotic. His vital signs were as follows: pulse rate, 120/min; blood pressure, 130/80mmHg and respiratory rate, 26 breaths/min. SpO2 was 70% at ambient air and 86% with oxygen supplementation of 6L/min. Bilateral breath sounds were clear. Bilateral pin point pupils with sluggish reaction to light were noted. Within 30min. of hospitalization, he became unconscious for which he was intubated and mechanically ventilated. ABG analysis with CO–oximetry showed paO2, 621mmHg, SaO2, 99% and MetHb, 80%. Patient had troponin I&T positive and urine for myoglobin was positive.

He was administered 1% methylene blue (1mg/kg). CO-oximetry after 1 hour showed MetHb of 50%. A single volume of exchange transfusion was done. He gained consciousness and became oriented. Two doses of 1% methylene blue were repeated with an interval of 12 hours to prevent rebound methemoglobinemia and MetHb was 6.2% after 3rd dose. In addition, he received inj. vitamin C 500mg in 5%dextrose once daily. He was extubated on 4th day and discharged after 7 days of admission, MetHb was 2% at the time of discharge without any neurological deficit.

Discussion:
Methemoglobinemia (MetHb>2%) is an altered state of hemoglobin which results when there is an overwhelming oxidative stress exceeding the normal protective mechanisms. Acquired methemoglobinemia is induced by exposure to various oxidizing agents, most commonly due to nitrates and nitrites (1, 2).

The clinical manifestations (Table I) of methemoglobinemia are due to impaired oxygen delivery to the tissues and hence correlate with severity of methemoglobinemia.

<table>
<thead>
<tr>
<th>Methemoglobin %</th>
<th>Signs and symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 15%</td>
<td>Asymptomatic</td>
</tr>
<tr>
<td>20-30%</td>
<td>Cyanosis, headache, fatigue, mental status changes, syncope, dizziness, and exercise intolerance</td>
</tr>
<tr>
<td>30-50%</td>
<td>Shortness of breath and headache</td>
</tr>
<tr>
<td>50-70%</td>
<td>Lethargy, stupor, dysrhythmias, seizure, coma</td>
</tr>
<tr>
<td>&gt;70%</td>
<td>Death</td>
</tr>
</tbody>
</table>

The onset of signs and symptoms in our cases was 30-60 minutes after pesticide ingestion. We observed bilateral pin point pupils in two cases and positive troponin and myoglobin in one case but this finding was not seen with similar poisoning described by George et al(4).

Common insecticides that induce methemoglobinemia include indoxacarb, aluminium phosphide, and paraquat. The pesticide consumed in our case reports contains biological extracts, stabilizers and fillers which was marketed to be safe and no mention of an antidote. We found only one case report (4) of toxicity with the similar pesticide in the literature. Biological extracts are rich in nitrogenous products and hence can potentially cause methemoglobinemia (4).
Methemoglobinemia should be suspected clinically by the presence of cyanosis in the presence of a normal PaO2 and chocolate-brown colored blood (Figure 1). The presence of methemoglobinemia can be suspected when the SpO2 is significantly different from the SaO2 ("saturation gap"). This saturation gap between SaO2 and SpO2 greater than 5% is a diagnostic clue to the presence of MetHb. To confirm methemoglobinemia, carbon monoxide (CO)-oximetry is required. Even CO-oximeters cannot distinguish between MetHb and sulhemoglobin due to similar absorbance peaks at 630 nm. MetHb was detected by absorption spectrophotometry after addition of sodium cyanide in the clinical biochemistry laboratory.

Management of acute methemoglobinemia begins with discontinuation of the offending agent. Methylene blue (MB) is the first line antidotal therapy which provides an artificial electron transporter for the reduction of MetHb via the NADPH dependent methemoglobinreductase system. Methylene blue is indicated when MetHb exceeds 25-30% in asymptomatic patient or when the patient exhibits symptoms of oxygen deficiency, such as dyspnea and alteration of...
consciousness (7). The recommended dose of 1% methylene blue for adults is 1-2 mg/kg diluted in 100 ml of isotonic saline, infused intravenously over 5 minutes. The response is usually rapid within 30 minutes; the dose may be repeated in one hour if the level of methemoglobin is still high one hour after the initial infusion (8). Dextrose containing fluids should be co-administered in order to increase NADPH formation. Injection ascorbic acid (300 to 1000 mg/day) may be useful which activates alternate minor pathway. Serial measurements of methemoglobin levels should be performed following treatment with MB as rebound methemoglobinemia may occur up to 18 hours after MB administration. The dose can be repeated hourly up to a maximum of 7 mg/kg over 24 hours (9). As observed in one of our patients, symptoms of dyspnea and depressed mental status improved within 30 minutes of MB injection. Caution should be exercised to avoid over dosage (>7 mg/kg) because cumulative doses of MB can cause dyspnea, chest pain, hemolysis and paradoxical methemoglobinemia in some susceptible subjects. Methylene blue should not be administered to patients with known glucose 6-phosphate dehydrogenase (G6PD) deficiency.

Severe methemoglobinemia (MetHb > 70%) is usually fatal, as evidenced in our first case though survival has been reported with a MetHb level of 80% in our case2 and previous reports (4, 10).

In case of unresponsive methemoglobinemia with MB, exchange transfusion or hyperbaric oxygen may be beneficial (5).

Fig 1: ABG suggestive of methemoglobinemia (met Hb :80.17%)
Fig 2: Chocolate brown colored blood due to methemoglobinemia on the left

Conclusion:
We conclude that every physician should be cautious in cases of poisoning with unknown chemical composition which may potentially cause fatal complications like methemoglobinemia. A high index of clinical suspicion of methemoglobinemia is required in all cases of unexplained cyanosis.

Consent:
Written informed consent was obtained from the patient’s guardian/parent for the publication of this report.

Conflicts of interest: None

References:
4. George T, Shaikh AL, Thomas L, Kundavaram AP.
5. Severe methemoglobinemia due to insecticide poisoning. Indian J Crit Care Med 2014; 18:113-4