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Case Report

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A CASE REPORT ON METHEMAGLOBINEMIA ACQUIRED DUE TO PESTICIDE POISONING

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ABSTRACT

Methemoglobinemia is a rare but life-threatening clinical condition that requires rapid diagnosis and treatment to achieve a favorable outcome. While there are multiple known causes of acquired methemoglobinemia**,** pesticide exposure is a rare and less frequently reported etiology. We present a case report of methemoglobinemia caused by pesticide ingestion, highlighting varying responses to different treatment modalities. This report discusses treatment options ranging from conventional methylene blue therapy to more advanced approaches, such as exchange transfusion and hyperbaric oxygen therapy**.** Our findings indicate that monitoring methemoglobin levels over an extended period may be necessary due to the risk of relapse. For refractory cases that do not improve with methylene blue, exchange transfusion proves to be an effective alternative treatment.

KEYWORDS: Acquired, Methemoglobinemia, Methemoglobin, Exchange transfusion, Hyperbaric oxygen therapy, Methylene blue.

INTRODUCTION

Methemoglobinemia is a condition with life-threatening potential in which diminution of the oxygen-carrying capacity of circulating hemoglobin occurs due to the conversion of some or all of the four iron species from the reduced ferrous (Fe2+) state to the oxidized ferric (Fe3+) state. Ferric iron is unable to bind and transport oxygen. Methemoglobinemia (MetHb) is a severe condition precipitated by oxidant stressors in the body. It occurs due to the oxidation of the ferrous ion (Fe^{2+}) in the heme molecule of hemoglobin, resulting in the formation of the ferric ion (Fe^{3+}). This dyshemoglobin has a reduced ability to bind oxygen, thereby decreasing the blood's oxygen-carrying capacity. Additionally, it impairs the release of oxygen to tissues, leading to tissue hypoxia. Methemoglobinemia can be classified as either congenital or acquired. Drug-induced MetHb is commonly associated with agents such as dapsone, local anesthetics (e.g., benzocaine, lidocaine), and antimalarials (e.g., primaquine).

In this report, we discuss three cases of acquired MetHb caused by a rare etiology - pesticide consumption. These cases highlight varied clinical presentations, severities, and treatment responses (refer to Table 1).

Table 1: Patient characteristics and outcome.

Patient parameters	ICU Course	ICU Outcoms
34- year-old female 1:2 compound	Ventilated Methylene blue 7 mg/kg HBOT one session Three cycles of exchange transfusion (350 mL + 1 + 1L)	Discharged alive on day 12

CASE REPORT

A 34-year-old female with no known comorbidities presented with a reported history of consuming approximately 100 mL of a pesticide (1:2 compound containing bioemulsifier 6%, oligosaccharide 8%, and fillers/carriers 86%). At the local hospital, she received a gastric lavage and activated charcoal. She was noted to have central cyanosis involving the lips and tongue. She was suspected of having methemoglobinemia (MetHb) and was administered three doses of intravenous

methylene blue, 100 mg each, over a span of 24 hours. Due to a lack of improvement, she was referred to our hospital for further management. On admission to the ICU, her Glasgow Coma Scale (GCS) score was 15/15, oxygen saturation (SpO_2) was 80% on 10 L of oxygen, and she was hemodynamically stable. Co-oximetry revealed MetHb levels of 30%. She was administered 50 mg of intravenous methylene blue, and her glucose-6-phosphate dehydrogenase (G6PD) levels were found to be normal. A repeat co-oximetry showed a MetHb level of 9.9%, but it rose again within 12 hours to 24.5%. Consequently, an exchange transfusion was planned. Only 350 mL venesection was done, as blood pressure dropped drastically. It was managed with colloids, 1 unit of packed RBC, and fresh frozen plasma was transfused. Repeat MetHb was 36%, and the patient was becoming drowsy. Hence, another dose of IV methylene blue of 100 mg was given. Subsequently, MetHb decreased to 14.2. Though there was a response to methylene blue, the effect was not sustained and was reaching the toxic dose. A single session of HBOT at 2.2 two atmospheres absolute for 90 minutes was done. Post-HBOT, MetHb paradoxically increased to 21.1 and then 33.8%. So, IV methylene blue 50 mg was again given. Repeat MetHb was 10.2 and then 14.1%. High volume exchange transfusion was planned, 1 L venesection done, with two units packed RBC replacement, noradrenaline, and colloid cover. MetHb levels dropped to 13% but then increased again to 19%. Therefore, another session of exchange transfusion with 1L venesection was performed the next day, and subsequently, MetHb dropped to 12.7% and remained low. In total, IV methylene blue was used six times (7 mg/kg), exchange transfusion was performed three times, and one session of HBOT was administered. Finally, the MetHb level was 8.5%, stopped increasing, and the patient was shifted to the ward on day 7. In the subsequent days, methemoglobin levels dropped to 0.3%. The patient was weaned off oxygen support and discharged on day 12 of the hospital stay, with normal SpO2 and remained stable on follow-up after 1 week.

DISCUSSION

Methemoglobinemia (MetHb**)** is a condition characterized by methemoglobin levels in the blood exceeding the normal threshold of 2%. It may arise from congenital causes**,** such as a deficiency in the nicotinamide adenine dinucleotide (NADH)-dependent enzyme, cytochrome B5 reductase**,** which is inherited as an autosomal recessive disorder. The NADH-dependent reduction system is primarily responsible for reducing 99% of the endogenous methemoglobin produced in the body.[2] Methemoglobinemia (MetHb) is a condition characterized by methemoglobin levels in the blood exceeding the normal threshold of 2%. It may arise from congenital causes**,** such as a deficiency in the nicotinamide adenine dinucleotide (NADH)-dependent enzyme, cytochrome B5 reductase, which is inherited as an autosomal recessive disorder. The NADH-dependent reduction system is primarily responsible for reducing 99% of the endogenous methemoglobin produced in the body.[2]

Acquired causes of methemoglobinemia include exposure to various drugs and chemicals, sepsis, severe gastroenteritis with dehydration in infants, and sickle cell crisis. Pesticides as a cause of acquired MetHb are less well-known, with the incidence not clearly established, but it is an important consideration in countries where pesticides are extensively used in agriculture. Indoxacarb**,** aluminium phosphide**,** and paraquat are the insecticides most commonly implicated in MetHb. Other agrochemicals containing biological extracts, stabilizers, and fillers - such as the compound used in our patients - are also known to cause MetHb. Biological extracts are rich in nitrogenous products, which can potentially induce MetHb.[3]

Clinically, this results in low SpO2 on pulse oximetry, development of cyanosis, and a chocolate-brown color of blood, with normal partial pressure of oxygen and calculated SpO2 on arterial blood gas analysis. Acute MetHb should be suspected in patients with central cyanosis and low peripheral SpO2 that does not respond to high-flow oxygen therapy. To determine the SpO2, the oximeter calculates the ratio of absorbance at two wavelengths. MetHb absorbs light equally at both 940 nm and 660 nm. In the presence of 100% MetHb, the ratio of absorbance of light at 660 nm to 940 nm is about 1.0. Therefore, at higher MetHb levels, SaO2 tends toward 85% regardless of the true percentage of oxyhemoglobin.[4]

A difference of >5% between the SpO_2 by pulse oximetry and blood gas analysis is abnormal. Patients with clinically significant MetHb usually have a saturation gap greater than 10%. Co-oximetry measures SpO_2 using different wavelengths of light to distinguish between fractions of oxyhemoglobin, deoxyhemoglobin, and methemoglobin, but it is not widely available.

Methylene blue is the antidote of choice for MetHb. This is an oxidant dye that channels the NADPH-reductase pathway, which is an alternate pathway in the metabolism of endogenous methemoglobin. Methylene blue acts as a co-factor for this enzyme and is reduced to methylene leucoblue, which then acts as an electron donor for methemoglobin. Symptomatic MetHb or levels above 20% are treated with 1–2 mg/kg IV bolus over 5–10 minutes. This will bring down the methemoglobin levels in 30–60 minutes. Additional doses of 1 mg/kg bolus can be given after rechecking levels. The total dose should not exceed 7 mg/kg as this can lead to chest pain, dyspnea, hypotension, and hemolysis with Heinz bodies.[5] Still, this total cumulative dose is not clear as to the time span in which this dose is acceptable. The first case that we described, though, responded to methylene blue treatment alone; the response varied from our previous experiences by requiring repeated doses 3 times.[5]

For refractory cases, such as our second and third cases, not improving with methylene blue, the next option is to consider either HBOT, plasmapheresis, or exchange transfusion.[6] There are multiple case reports published on the use of HBOT, but there is no clear recommendation for its use. HBOT is not commonly available in all the centers, and the dose and treatment protocol are not clearly defined. The efficacy of hyperbaric oxygen is also not proven. In one of our patients described with refractory MetHb, we tried one session of HBOT, and it did not even have a temporary response.[7]

In a systematic review, therapeutic whole blood exchange (TWBE) led to a survival rate of 81.6% in patients refractory to methylene blue.[8] Although TWBE has good efficacy, it still has setbacks, such as the availability of adequate blood bank support and the difficulty of the technique when special exchange equipment is not available. The exact volume to be exchanged and the number of sessions required are also not validated. Complications during the procedure, such as hypotension, necessitate close monitoring in the ICU. We encountered this issue in our last patient during the first session, where we reduced the volume exchanged, but it did not have the desired effect. The subsequent sessions were performed using a dialysis line dedicated to the exchange, and the patient was simultaneously volume-resuscitated with colloids. In both refractory patients in whom we attempted exchange transfusion, two well-performed sessions of 1L exchange on subsequent days were found to be efficacious with minimal complications. Plasmapheresis was attempted in one of the refractory patients but was not beneficial. Methylene blue use is contraindicated in G6PD-deficient patients, making it mandatory to consider exchange transfusion as the option for higher levels of symptomatic MetHb.[9]

CONCLUSION

Pesticide poisoning is a rarely reported cause of acquired methemoglobinemia (MetHb)**.** A high index of suspicion in these cases is crucial for early diagnosis and appropriate management. Methylene blue is the treatment of choice for symptomatic patients or when methemoglobin levels exceed 20%. Continuous monitoring of methemoglobin levels may be necessary over an extended period due to the potential for relapse. In refractory cases that do not respond to methylene blue, exchange transfusion serves as an effective alternative treatment modality.

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