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CASE REPORT

Surviving Fatal Methemoglobinemia: A Case Report

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Abstract

Background: Methemoglobinemia is one of the rare causes of cyanosis, encountered in the Emergency Department. It can be congenital or acquired, affecting the oxygen binding capacity of hemoglobin, thus shifting the oxyhemoglobin dissociation curve to the left. It is potentially life-threatening, but it responds well to specific therapies, if recognized and intervened early. MetHb levels >70% are often described as incompatible with life.

Case: Here, we describe two cases of near-fatal MH (MetHb levels >70%), one with intentional and the other with accidental ingestion of substance-producing MH, and its management which highlights how timely diagnosis and prompt appropriate treatment in the Emergency Department can be lifesaving. Both cases were at physiological extremes on arrival to the ED. However, the early clinical suspicion and prompt diagnosis of methemoglobinemia, which was confirmed by blood co-oximetry, helped expedite the delivery of specific anti-dote for methemoglobin, i.e., intravenous methylene blue. Both patients responded well to the treatment and were hemodynamically stable within 6 hours

Conclusion: Cyanosis, which does not respond to oxygen, and low saturation levels not responding to oxygen therapy should raise the suspicion of Methemoglobinemia (MH). Early diagnosis and prompt administration of methylene blue are the key factors for survival.

Keywords: Methemoglobinemia, Methylene Blue, Cyanosis, Sodium Nitrite, Oxyhemoglobin Dissociation Curve

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INTRODUCTION

Methemoglobinemia (MH) is not a common entity encountered in the emergency departments (ED). Inadequate data is available to determine the true incidence of methemoglobinemia [1]. Congenital MH is caused by a defect in cytochrome b5 reductase or mutations in the genes that code for globin proteins [2]. Acquired MH occurs due to the administration of drugs like benzocaine, prilocaine, and dapsone or the ingestion of sodium nitrite, dyes, fertilizers, paints, and solvents [1,3-6]. In normal physiological conditions, hemoglobin contains iron in its reduced form or ferrous state (Fe2+), which enables it to bind to oxygen. In MH, iron is present in its oxidized state or ferric state (Fe3+), which precludes its oxygen binding capacity and shifts the oxyhemoglobin dissociation curve to the left, severely affecting oxygen delivery and causing tissue hypoxia [7]. MH is not a very common entity encountered in the ED. Here, we describe two cases of near-fatal acquired MH and its management which highlights how timely diagnosis and prompt appropriate treatment in the ED could be lifesaving.

CASE REPORT

Case -1

A 17-year-old male was brought to our ED, with a history of an unrecorded amount of sodium nitrite ingestion, about 40 minutes ago, with an episode of vomiting and loss of consciousness. He was brought in a gasping state with a palpable central pulse. The patient on arrival had bluish discoloration of the tongue, lips, and fingernails. He had a pulse rate (PR) of 150/min, blood pressure (BP)-88/54mmHg, peripheral oxygen saturation (SpO2)-75%, Glasgow Coma Score (GCS) was E1V1M1. Pupils were bilaterally normal size, reactive to light, and random blood sugar (RBS) was 221mg/dl. Respiratory and cardiac systemic examination was normal. Immediately, bag and mask ventilation and preoxygenation were started, two wide-bore intravenous access (IV) were secured, and 1000mL of intravenous fluid bolus of normal saline (NS) was administered. He was intubated and kept on mechanical ventilator. Despite giving a fraction of inspired oxygen (FiO2) of 100%, SpO2 only increased to a maximum of 85%. Due to inadequate response to fluid bolus vasopressor, support was started with noradrenaline (5mcg/min) titrated to maintain a mean arterial pressure of 65mmHg. He was a known case of major depressive disorder with a history of suicidal thoughts and attempts in the past, currently on therapy. The blood drawn was dark brown **(**Figure – 1a**)**. Arterial blood gas (ABG) analysis showed pH- 7.384, PaCO2- 39.4, PaO2-66, SaO2-39.6%, HCO3- 23, lactate=3.9. Saturation gap (difference between SpO2 and SaO2) was 35%. Co-oximetry revealed methemoglobin levels of 75.1%. Hence, the diagnosis of

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methemoglobinemia was confirmed. On reassessment after the above interventions, the patient was still cyanosed, with BP of 90/60 mmHg and SpO2 of 85%. Point-of-care ultrasound revealed normal lung fields and normal cardiac contractility. The electrocardiogram suggested sinus tachycardia. The urine drug screen panel was negative.

Gastric lavage was done and activated charcoal (1gm/kg) was administered as the time of presentation was less than 1 hour. The patient was given the first dose of methylene blue 1mg/kg(50mg) IV over 5 minutes, and IV ascorbic acid infusion (2gm over 1 hour). The patient was re-evaluated and a repeat dose of IV methylene blue (1mg/kg) was administered after 30 minutes due to no improvement in hemodynamic parameters. Two hours after the first dose of methylene blue, repeat ABG showed improvement in SaO2 levels{pH- 7.398, HCO3- 20, SaO2=99%, lactates- 2.9}. Methemoglobin levels decreased to 13.9 %. PR decreased to 90/min, BP improved to 110/70mmHg without pressure support, SpO2-97% on same ventilator settings, and GCS improved to E4VtM6, the colour of blood turned back to red and urine turned green **(**Figure – 1b and 2**)**. He was shifted to the intensive care unit (ICU) and subsequently extubated on day 1. He was discharged after a neuropsychiatric evaluation with no neurological impairment on day 4.

Case-2

A 45-year-old adult male presented to our ED, with a history of ingestion of an unknown substance, about 6 hours later followed by multiple episodes of vomiting and abdominal pain. On arrival, we noticed bluish discolouration of fingertips, toes, and tongue (figure 3). His peripheries were

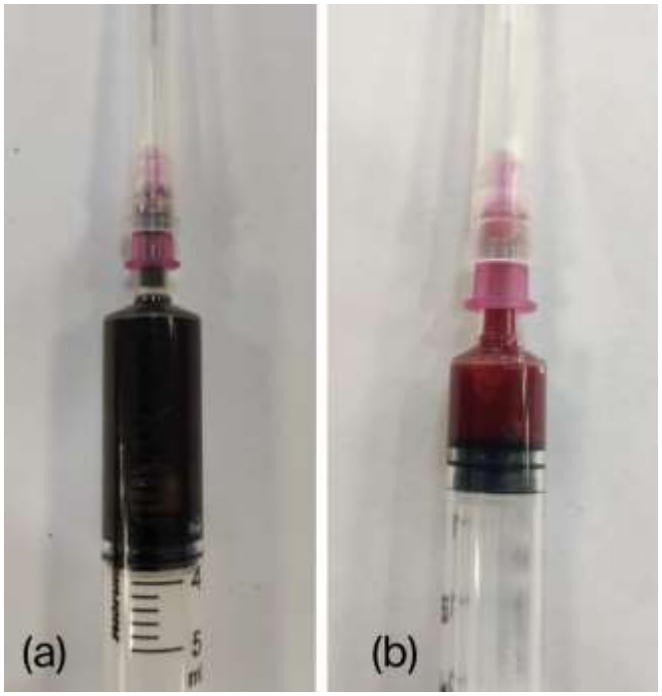

Figure 1a. Chocolate brown color venous blood sample of the patient at presentation. **Figure 1b. Change in color of the blood after methylene blue administration**

Figure 2. Green urine after methylene blue administration

cold with prolonged capillary refill time (> 3 seconds).

He was drowsy with SpO2 of 79% on room air and, a respiratory rate of 18/minute. Breath sounds were bilaterally symmetrical. His BP was 80/60 mmHg with a pulse rate of 79/minute, GCS of E3V5M5, pupils were bilaterally equally reacting to light with no focal neurological deficit. Random blood sugar was found to be 179mg/dl. He was immediately started on high-flow oxygen (15L/min) with a non-re-breathing mask. 1500ml of 0.9% normal saline was given as a bolus, and thereafter commenced on vasopressor support with noradrenaline (5mcg/min) titrated to maintain mean arterial pressure of 65mmHg. However, the oxygen saturation did not improve with high-flow oxygen. Meanwhile, the arterial blood gas analysis showed metabolic acidosis, normal PaO2 levels - lactates were 8.1 {pH- 7.233, pCO2- 20.6, pO2- 344 (on 15 liters of oxygen), SaO2%- 71.9, HCO3- 8.8}. The blood drawn was dark brown. On reassessment, the patient was still cyanosed. Repeat evaluation of the vital parameters showed improvement in BP- 90/60mmHg, but no improvement was observed in SpO2 levels. Point-of-care ultrasound revealed normal lung fields with normal cardiac contractility. Electrocardiogram was normal. Chest X-ray also showed no abnormality. A dark chocolate-coloured blood sample, cyanosis not improving on supplemental oxygen, with normal lungs and cardiac status led us to a working diagnosis of methemoglobinemia (MH).

Blood for co-oximetry was sought, which revealed methemoglobin levels of 76%. Hence, the diagnosis of Methemoglobinemia was confirmed due to some unknown substance ingestion. Intravenous (IV) methylene blue 1 mg/kg (50mg) was given over 2 minutes. The patient was re-evaluated every 20 minutes and two repeat doses of IV methylene blue were administered one hour apart. His cyanosis and hemodynamics improved (shock resolved and vasopressor support was taken off). A repeat ABG also showed improvement in metabolic acidosis {pH- 7.255, HCO3- 14.1, lactates- 2.6.}. Methemoglobin levels also decreased to 25.7%. The patient was discharged the next day from the ED.

Consent Statement: A written informed consent to

Figure 3. Bluish discoloration of fingernails and tongue at presentation, with suspected methemoglobinemia

participate and publish clinical case details of the patient was obtained from the legal guardian (case1) and the patient himself (case2).

DISCUSSION

Early suspicion and diagnosis of methemoglobinemia and antidote administration are of paramount importance as prompt treatment could be life-saving. MH can easily be missed as initial signs and symptoms (hypotension, tachycardia, and cyanosis) are non-specific. The presence of chocolate brown blood on phlebotomy, saturation gap, and persistent cyanosis not responding to oxygen therapy should raise a suspicion of MH. Normal MetHb levels in the blood are 1-3%. Cyanosis and chocolate brown blood are seen at levels above 15%. If the levels are higher than 25%, it can cause clinically significant symptoms like dyspnoea, syncope, headache, and weakness. Levels above 50% may cause profound metabolic acidosis, arrhythmia, and seizures, and >70% are incompatible with life [7-9].

Intravenous methylene blue is the antidote for MH. Methylene blue activates the pathway that reduces methemoglobin to hemoglobin using nicotinamide adenine dinucleotide phosphate (NADPH) generated by glucose-6-phosphate dehydrogenase (G6PD) in the hexose monophosphate shunt [10,11]. Intravenous methylene blue 1-2 mg/kg infused over 5 minutes is advocated for the treatment of methemoglobinemia. It can be repeated after 30-60 minutes in the absence of clinical improvement [10,11]. Underlying conditions like G6PD and NADPH-MetHb reductase deficiency should be considered if the patient shows no improvement with repeated doses of methylene blue [1,11]. Parenteral ascorbic acid (up to 10 gm/dose) has been used as a bridging agent or alternative treatment when parenteral methylene blue was not available [12,13]. Exchange transfusion or blood transfusion and hyperbaric oxygen may be beneficial in extreme cases [11].

CONCLUSION

Two cases of acquired methemoglobinemia are presented here. Clinico-laboratory pearls like cyanosis not resolving with supplemental oxygen, dark chocolate-coloured blood, the requirement of co-oximetry, and intravenous methylene blue administration are important cues for suspicion, early diagnosis, and management of this life-threatening condition.

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