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Case Report
Methemoglobinemia

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A Rare Case Of Benzocaine-Induced Methemoglobinemia

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Methemoglobinemia is an uncommon haemoglobinopathy but potentially fatal if unrecognized or untreated at the earliest. It can either be congenital or acquired. Acquired can be after using topical anaesthetics such as nitrates, benzocaine, and lidocaine. The present study reports a rare case of benzocaine to induce Methaemoglobinemia. A 20-day-old male baby presented to the emergency room with complaints of seizure-like activity in the past hour, bluish discolouration of the skin for the past 1 day and loose watery stools for 3 days. The baby was irritable, crying with central cyanosis, and had 2 episodes of seizures upon arrival. He was tachypnoeic with saturations were 85% on room air along with tachycardia. Perianal rash with excoriation of overlying skin was present. The rest of the examination was unremarkable. He was managed with supplemental oxygen, IV antiepileptic and supportive treatment. His septic screen was normal; the Chest x-ray was unremarkable, and the 2D Echo showed a structurally normal heart with normal biventricular function. His percutaneous oxygen saturation remained 85-88% despite the administration of 100% oxygen. His arterial blood sample had a dark chocolate colour appearance, with normal PaO2 levels on blood gases. His methaemoglobin levels were 21.7%. After two doses of methylene blue (1 mg/kg/dose) were administered, his cyanosis abated and oxygenation improved. Repeat methaemoglobin levels were 1.3%. A relook into the history revealed the use of Mucopaine gel for a perianal rash which contains Benzocaine confirming it as Benzocaine-induced Methaemoglobinemia.

Keywords: Methaemoglobinemia, Benzocaine, Cyanosis

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Introduction

Methaemoglobinemia is an uncommon but potentially fatal haemoglobinopathy. It leads to rapid oxygen saturation and therefore requires prompt recognition and treatment [1,2]. It can be induced by congenital mutations or it can be acquired. One of the ways to acquire it is by using topical anaesthetics such as nitrates, benzocaine, and lidocaine [3]. The first case of benzocaine-induced Methaemoglobinemia was reported in 1977 [4]. It occurs in approximately 3.5 out of 10,000 cases of reported Methaemoglobinemia[5,6]. Those who are unknowingly susceptible to developing Methaemoglobinemia and receive anaesthetics during hospital procedures are at risk of serious adverse effects and clinical deterioration if not treated correctly.[5]

Case Report

A 20-day-old male baby weighing 1.7 kgs born out of a non-consanguineous relationship to a primi mother was brought to the emergency room with complaints of seizure-like activity in the past 1 hour, bluish discolouration of the skin for the past 1 day and loose watery stools since 3 days. He was delivered by LSCS at 34 weeks (Indication: Premature rupture of membranes) with a birth weight of 1.6 kgs and required positive pressure ventilation for 30 seconds to initiate breathing at the referral hospital. After a NICU stay for 1 week, the baby was discharged with a weight of 1.57 kg. No other significant history was noted.

Within a few minutes of arrival, the baby had 2 episodes of seizures in the form of cyclical movements involving all 4 limbs, each episode lasting for 2-3 minutes. On examination, the baby was irritable, crying with central cyanosis. He was tachypnoeic (RR: 70/min), with bilateral equal air entry on auscultation. Saturations were 85% in all 4 limbs on room air. He had tachycardia (HR: 180/min), no audible murmur, with bilaterally well-felt femoral pulses and no radio femoral delay.

Central cyanosis was present, with cool peripheries and mottled skin. Capillary filling time was prolonged (> 3 seconds). Blood pressures in all 4 limbs were within the normal range. Perianal rash with excoriation of overlying skin was present. The rest of the systemic and general examination was unremarkable.

Figure 1: Note the central cyanosis over the lips, and tongue along with the mottled skin.

He was managed as per the unit protocol with supplemental oxygen and other supportive treatment. Considering sepsis, he was initiated on IV antibiotics. IV antiepileptics were administered to control the seizures. Sepsisscreen was normal. Chest x-ray was unremarkable with normal lung fields and no cardiomegaly. However, his percutaneous oxygen saturation remained at 85-88% despite the administration of 100% oxygen. Hence 2D Echo was done which showed a structurally normal heart with normal biventricular function. Once cardiopulmonary causes of cyanosis were ruled out, other causes were considered. His arterial blood sample had a dark chocolate colour appearance, with normal PaO2 levels on blood gases and no improvement in supplemental oxygen.

Table1: Arterial Blood Gas at Admission

Arterial Blood Gas at Admission		Arterial Blood Gas with Supplemental Oxygen
pH	7.49	7.39
pO2	120 mmHg	158 mmHg
pCO2	27 mmHg	30 mmHg
Bicarbonate	23.7	20.5
Base excess	-1.6	-5.8
Lactate	47 mg/dl	45 mg/dl.

The table compares the Arterial blood gas of the baby done at admission and after providing supplemental oxygen. There was no improvement in pO2 values.

With the above picture in mind, his methaemoglobin levels were sent which were 21.7%, which is considered lethal. Immediately, two doses of methylene blue (1 mg/kg/dose) were administered following which his cyanosis

Abated and oxygenation improved. Repeatmethaemoglobin levels were 1.3%. As Methaemoglobinemia was confirmed, a relook into the history for any drug exposure revealed that the parents were using Mucopaine gel for a perianal rash which contains Benzocaine confirming it as Benzocaine induced Methaemoglobinemia.

Discussion

Methemoglobinemia is a form of haemoglobin that has been oxidized, changing its heme iron configuration from Fe2+ to Fe3+ (ferric state) [3]. Congenital causes of Methaemoglobinemia include being deficit in the enzyme cytochrome b5 reductase (Cyb5R) [7].

Mechanism of Methaemoglobinemia

Drugs like benzocaine cause an oxidative stress converting Fe2+ to Fe3+ increasing the levels of methaemoglobin. Absence of or low levels of Cyb5R lead to congenital Methaemoglobinemia.

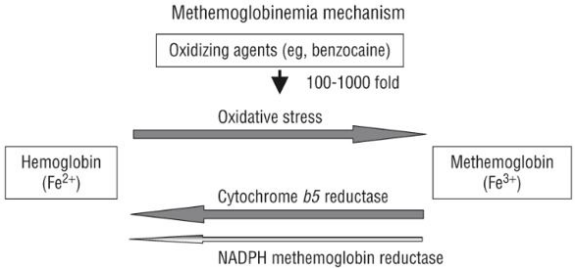

Figure 2: Mechanism ofMethaemoglobinemia

Patients with Methaemoglobinemia can be asymptomatic.[3] Once, levels exceed 20%, they can develop hypoxia, cyanosis, shock, seizures and altered mental status such as in this patient. Levels>70% are typically fatal.[7]

Methaemoglobinemia can be treated with methylene blue or ascorbic acid [3].).Methylene blue is a reducing agent through the nicotinamide adenine dinucleotide phosphate (NADPH) methaemoglobin reductase pathway and in low concentrations, it is reduced to leucomethylene blue, which reacts with methemoglobin in the blood, reducing to haemoglobin [3]. A low dose of methylene blue is given, 1-2 mg/kg of 1% solution IV over five minutes, and the dose can be repeated within one hour if hypoxia symptoms aren't resolved [7]. This patient was given 1 mg/kg of 1% methylene blue, which resolved his symptoms and normalized his methemoglobin levels to 1.1%.

Conclusion

In conclusion, Methaemoglobinemia is typically diagnosed through clinical findings. When a patient is diagnosed with Methaemoglobinemia, treatment should be focused on providing supplemental oxygen therapy and giving the patient methylene blue as quickly as possible. Therefore, in inpatients with cyanosis and without cardiac or pulmonary symptoms, Methaemoglobinemia should be suspected. The diagnosis is made clinically with chocolate-coloured blood and unresponsiveness to oxygen therapy. Low-dose methylene blue should be easily available, especially when topical anaesthetics are used. It is also important to be aware that over-the-counter products such as Mucopaine gel can precipitate Methaemoglobinemia in susceptible individuals.

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