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Two Cases of Methemoglobinemia Caused by Prilocaine, A Local Anesthetic

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Abstract

In situations of methemoglobinemia, elevated amounts of methemoglobin decrease hemoglobin's ability to bind oxygen. Cases of methemoglobinemia may appear with a mild or severe presentation at emergency departments. This disorder can be inherited or acquired. In the initial phase of treatment, intravenous administration of methylene blue is preferable. This methemoglobinemia may be caused by prilocaine, one of the local anesthetics used for surgical procedures. This paper attempts to describe the examination, diagnostic, and treatment processes of two patients who presented to the emergency room with cyanosis and shortness of breath following the administration of local anesthetic. We aimed to contribute to the literature by explaining the importance of differential diagnosis, clinical findings, and treatment in methemoglobinemia.

Keywords: Methemoglobinemia; Prilocaine; Local Anesthesia; Methylene Blue

Introduction

Methemoglobinemia is a rare condition characterized by hypoxia referred to as "functional anemia" in the absence of hemoglobin reduction **[1]**. Methemoglobinemia can develop for both genetic and acquired factors **[2]**. Various substances and medications, including nitrites, nitrates, chlorates, quinines, aminobenzenes, nitrobenzenes, nitrotoluenes, phenacetin, chloroquine, dapsone, phenytoin, sulfonamides, and local anesthetics, can cause acquired methemoglobinemia. Mild cases may be asymptomatic, but severe cases may result in cyanosis, tachypnea, tachycardia, hypotension, disorientation, and even death. Variable degrees of cyanosis related with blood methemoglobin levels can be seen in cases of methemoglobinemia **[3]**. Methemoglobinemia caused by the local anesthetic dosage of prilocaine is uncommon. In this series, we aimed to discuss two patients who presented to the emergency room with hypoxia due to methemoglobinemia after administering a local anesthetic (Prilocaine).

Case Presentation

Case-1

A 47-year-old male with no history of chronic diseases was admitted to a private general surgery clinic for abscess draining with laser and local anesthesia due to swelling and pain in the perianal region. Due to shortness of breath and

headache, the patient was brought to the emergency department of our institution, which is a tertiary education and research hospital. It was discovered that shortness of breath began 40 minutes after the injection of a local anesthetic. At the time of his arrival at the emergency room, the patient's vital signs were as follows: blood pressure 112/70 mmHg, saturation 81%, respiration rate 38/min, and heart rate 137/min. The patient was anxious and agitated. He had mildly cyanotic lips. During the patient's examination, bilateral lung sounds were comparable, there was no difference in leg circumference, and bilateral pulses were perceptible. With a reservoir oxygen mask, 15 liters of oxygen per minute were administered to the patient. Sinus tachycardia was found to be present on the electrocardiogram. While pulmonary embolism was being considered as a differential diagnosis for a patient with normal lung sounds, the following arterial blood gas parameters were detected: pH:7.61, pCO2:20 mmol/L, pO2:189 mmol/L (15 lt/minute oxygen treatment with a reservoir oxygen mask), SpO2: 88%, and methemoglobin: 23%. Both d-dimer and troponin were negative in additional blood testing. Methemoglobin value was discovered to be high in the patient, and methemoglobinemia due to the administration of local anesthetics was diagnosed. We contacted the clinic and learnt that a local anesthetic consisting of lidocaine hydrochloride (2 ml ampoule, 20 mg/cc) 8 cc and prilocaine 17 cc (2%, roughly 340 mg) was provided. The patient was administered 1 mg/kg of methylene blue intravenously after a diagnosis of methemoglobinemia. He was transferred to the intensive care unit for treatment and strict monitoring. Four hours after 15 l/min O2 supplementation with a mask and intravenous methylene blue treatment, peripheral cyanosis and respiratory distress completely disappeared in the critical care follow-up. After 24 hours, all complaints were resolved, and arterial blood parameters were pO2:138, pCO2:20, methemoglobin level 2.1%, and SpO2: 96%. The patient was discharged three days after his hospitalization, when his methemoglobin level had decreased to 1.2% and all of his symptoms had subsided.

Case-2

A local anesthetic drug (Prilocain) was delivered for perianal abscess drainage in a medical center to a 45-year-old male patient without a history of chronic illness. The patient's shortness of breath began roughly 45 minutes later. The patient was transported by ambulance to the emergency department of our hospital so because finger-measured SpO2 was 85%. At admission, the patient's vital signs were blood pressure 130/90 mmHg, respiration rate 22/min, SpO2: 89%, and heart rate 120 beats per minute. The only symptoms exhibited by the patient were shortness of breath and a minor headache. Physical examination revealed no evidence of pathology. With a reservoir oxygen mask, high-flow oxygen therapy (15 l/min) was initiated. The arterial blood gas measurements of the patient were pH: 7.44, pCO2:38 mmol/L, pO2:149 SO2: 86, and methemoglobin: 15.1%. The patient's other hematological parameters were confirmed to be normal. According to the information obtained, the patient was administered 15 cc of prilocaine (2%, approximately 300 mg) in a medical center. When methemoglobinemia was diagnosed, 1 mg/kg of methylene blue was administered intravenously. The patient was transferred to our hospital's intensive care unit for close monitoring and treatment. Within hours, the patient's symptoms diminished. The patient, whose methemoglobin level was determined to be 1.8% the next day, was discharged from the hospital after two days of treatment.

Discussion

Methemoglobinemia is a genetic or acquired disorder characterized by the oxidation of divalent ferro-iron of hemoglobin to ferri-iron of methemoglobin **[4]**. The presence of iron in the ferric [Fe3+] state induces allosteric modifications that enable the irreversible binding of oxygen. Ferro-globins in the tetramer change the oxygen-dissociation curve of hemoglobin to the left. This change increases the affinity of ferrous iron for oxygen, resulting in a decrease in tissue oxygenation. As a result, hypoxia and lactic acidosis occur **[5]**.

The most prevalent manifestation of cyanosis is peripheral cyanosis, which occurs when the quantity of methemoglobin in the blood surpasses 10%. When it exceeds 35%, systemic signs such as fatigue, tachycardia, tachypnea, nausea, and vomiting are observed; when it surpasses 55%, arrhythmia, acidosis, lethargy, stupor, and syncope are observed. If it is greater than 70%, it is lethal **[6]**. Due to hypoxia, both patients

presented to us exhibited tachypnea and headache. However, no metabolic acidosis was present.

Congenital methemoglobinemia is caused by a lack of the enzyme cytochrome b5 reductase, which converts methemoglobin to hemoglobin and maintains a steady-state methemoglobin level below 1%. Methemoglobinemia is the result of drug ingestion or toxic exposure that accelerates the transition from the ferrous to ferric state of hemoglobin. Numerous medicines, including sulfonamides, benzocaine, prilocain, lidocaine and various aniline derivatives, and nitrites, can cause methemoglobinemia **[7]**. We learnt that Prilocaine, a local anesthetic, was supplied to our patients prior to the surgical procedure in the medical center.

Prilocaine is an injectable local anesthetic drug that has lately been employed in topical creams. Methemoglobinemia occurs 20-60 minutes after drug administration. The half-life of prilocaine is around 50-60 minutes **[8]**. Its metabolite, o-toluidine, is responsible for methemoglobinemia production **[9]**. Our patients' symptoms appeared within an hour.

Methemoglobinemia is mostly treated by discontinuing exposure to the triggering substance. The treatment approaches include Methylene blue (1-2 mg/kg IV infusion over 3-5 minutes), ascorbic acid (100-300 mg/day), hyperbaric oxygen therapy, and exchange transfusion. Typically, the first-line treatment for moderate to severe cases is methylene blue. It should be administered intravenously to asymptomatic patients with methemoglobin levels above 30% and to symptomatic patients with methemoglobin levels above 15-20%. High dosages (>7 mg/kg) of methylene blue may paradoxically stimulate the formation of methemoglobin **[10]**. The symptoms of the patients whose differential diagnosis we studied and who were identified with methemoglobinemia in blood gas retreated after treatment with methylene blue, and they were discharged the following days in good health.

Conclusion

Initial symptoms for patients with an elevated methemoglobin concentration could include dyspnea, headache, lethargy, and fatigue. There are numerous disorders in the differential diagnosis that can produce similar symptoms. In patients who present to the emergency department with shortness of breath, tachycardia, cyanosis of the lips and extremities, and nausea, the last two days' medications and, if applicable, surgical history should be questioned in terms of the possibility of methemoglobinemia. Low SpO2 despite oxygen therapy, incompatibility between SpO2 and SaO2, cyanotic lips and end organs, chocolate-colored blood, acidosis, and tachycardia should also be evaluated in these patients.

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