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Methemoglobinemia after local anesthesia with prilocaine in adults: four case reports

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ABSTRACT

Methemoglobinemia is a serious hematological disease characterized by the incapability of sufficient oxygen delivery to tissues and cyanosis when iron within hemoglobin in ferrous form (Fe+2) is oxidized to ferric form (Fe+3). Methemoglobinemia may be congenital or acquired. While prilocaine-induced methemoglobinemia can be seen in newborns and early pediatric ages, it is a rare condition in adults. We aimed to investigate prilocaine-induced adult methemoglobinemia with four cases.

Keywords: Adult, methemoglobinemia, prilocaine, cyanosis

Hemoglobin (Hb) is a molecule that carries oxygen from respiratory organs to the rest of the body. Hb binds to iron in a ferrous (Fe2+) oxidation state under normal conditions. However, the existence of oxidative stress is known to transform iron into ferric iron (Fe3+). Upon oxidation, hemoglobin or methemoglobin (MetHb) cannot bind to oxygen molecules. In methemoglobinemia, the Hb is unable to release oxygen effectively to body tissues [1].

There are three common causes of methemoglobinemia, including hemoglobinopathies, hereditary enzyme deficiencies (NADH MetHb reductase), and exposure to drugs. Interestingly, hemoglobinopathies and hereditary enzyme deficiencies (NADH MetHb reductase) are the least common causes, whereas exposure to drugs is the most common [2].

Nitrite, nitrate, aniline, and benzene compounds and drugs such as sulfonamides, dapsone, phenacetin, primaquine, and benzocaine are important drugs that cause methemoglobinemia. Prilocaine, an amide compound frequently used as a local anesthetic, may also cause methemoglobinemia [2].

Gray-blue central cyanosis unresponsive to oxygen therapy is a valuable clinical finding. Peripheral cyanosis becomes prominent when blood methemoglobin levels exceed 10%, and tissue hypoxia and diffuse cyanosis are seen in cases with methemoglobin levels ≥35%. When methemoglobin levels approach 70%, the patient falls into a coma and may be mortal if left untreated [3].

We aimed to investigate prilocaine-induced adult methemoglobinemia with four cases.

CASE PRESENTATIONS

CASE 1

A 71-year-old male patient with a body weight of 78 kg and a nephrostomy diagnosed with metastatic bladder cancer was admitted to the urology clinic for bi-

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lateral nephrostomy revision. We consulted the patient who developed local anesthesia with 80 mg of prilocaine and developed low saturation and cyanosis during the procedure. SpO_2 was 75% in room air and 78% with oxygen support, heart rate was 85 beats/min rhythmic, respiratory rate was 17/minute, and arterial blood pressure was measured as 130/75 mmHg. In the physical examination of the patient, his lips and fingertips were slightly cyanotic, and he did not have any respiratory complaints. In the respiratory examination, bilateral breath sounds were heard as decreased at the base of the lung. Electrocardiogram (ECG) was normal sinus rhythm.

In laboratory tests; hemoglobin 8.6 g/dL, hematocrit 26%, MCV 85.0 fL, leukocytes 3200/µL, platelets 261000/µL, pH 7.46, PaO_2 133 mmHg, FO_2Hb 77%, pCO_2 35.7 mmHg, HCO_3act 25.2 mmol/L, MetHb: 20.7% in the blood gas taken by nasal cannula with 5 L/min oxygen support. Similar to the previous ones, bilateral costophrenic sinuses were observed to be closed in the chest X-ray, and there was no other pathology. Thereupon, the patient was evaluated as methemoglobinemia due to local anesthesia. It was detected that methemoglobinemia developed for the first time in a patient who had previously undergone interventional procedures under local anesthesia.

The patient, whose vital signs were stable and asymptomatic, was monitored and followed up with nasal oxygen support. MetHb 11.7%, FO_2Hb 77% in blood gas taken 6 hours later; MetHb %3.0, FO_2Hb 93% in blood gas taken at 12th hour; MetHb was 0.9% and FO_2Hb was 95.8% in the blood gas taken at the 24th hour. In the patient who did not develop any complications during the follow-up, his treatment and follow-up were terminated with only oxygen support, without the need for methylene blue.

CASE 2

A 54-year-old male patient with a body weight of 65 kg, hospitalized in the general surgery ward, was consulted with cyanosis and low saturation unresponsive to oxygen. In the patient with rectal carcinoma and nephrolithiasis, it was learned that cyanosis developed during nephrostomy insertion with 60 mg prilocaine under local anesthesia. In the first physical evaluation of the patient; the general condition was good, he was conscious, oriented, and cooperative, arterial blood pressure was 140/80 mmHg, heart rate was 89 beats/minute rhythmic, and respiratory rate was 18/minute. In the patient whose SpO_2 was 75% measured by pulse oximetry in room air; There was cyanosis in the lips and fingers, both hemithorax were equally involved in breathing, and heart sounds were normal. The patient had no active respiratory complaints. With 4 L/min oxygen support with a nasal cannula, the SpO_2 was 80%. Other system examinations were normal and the patient's ECG was sinus rhythm.

In laboratory tests; hemoglobin 9.42 g/dL, hematocrit 29.2%, MCV 81.0 fL, leukocytes 15880/µL, platelets 506000/µL. Blood gas taken with a nasal cannula with 4 L/min oxygen support revealed pH 7.39, PaO_2 115, FO_2Hb 78%, pCO_2 21 mmHg, HCO_3act 16 mmol/L, MetHb 25.8%. No pathology was detected in the chest X-ray.

Since the general condition was good and he had no symptoms, the patient was monitored and followed up with oxygen support via nasal cannula. After 1 hour, his cyanosis was resolved and he was followed up with oxygen support. MetHb was 8% and FO_2Hb was 88% in the blood gas taken 6 hours later. At the 24th hour after diagnosis, MetHb was 0.2% and FO_2Hb was 96.4% in blood gas. In the patient who did not develop any complications during the follow-up, his treatment and follow-up were terminated with only oxygen support, without the need for methylene blue.

CASE 3

An 81-year-old male patient with a body weight of 72 kg diagnosed with bladder cancer in the urology clinic underwent a nephrostomy revision with 60 mg of prilocaine under local anesthesia. The patient who developed desaturation during the procedure was consulted with us. In the evaluation of the patient; Her general condition was good, she was conscious, oriented, and cooperative, her arterial blood pressure was 120/70 mmHg, her pulse rate was 82/min, rhythmic, and her respiratory rate was 17/min. He had mild cyanosis of his lips. Respiratory examination and heart sounds were normal in the patient, whose SpO_2 was 82%, measured with pulse oximetry in room air. The patient had no active respiratory complaints. SpO_2 was 88% with 5 L/min oxygen support with a nasal cannula. Respiratory and other system examinations were normal, and ECG was sinus rhythm.

In laboratory tests; hemoglobin 9.7 g/dL, hemat-

ocrit 31.2%, MCV 91.0 fL, leukocytes 13080/µL, and platelets 274000/µL. Blood gas taken with a nasal cannula 5 L/min oxygen support revealed pH 7.45, PaO_2 126, FO_2Hb 88%, pCO_2 36 mmHg, HCO_3act 21 mmol/L, MetHb 9.2%. No pathology was detected in the chest X-ray.

The patient was in good general condition and asymptomatic, and he was followed up with nasal cannula oxygen support. MetHb was found to be 1.4% and FO_2Hb 95% in the blood gas taken 6 hours later. The follow-up of the patient, whose methemoglobin level was within the normal range and had no symptoms, was terminated.

CASE 4

A biopsy was planned for a 30-year-old female patient with a body weight of 58 kg due to a mass in the anterior mediastinum. A needle aspiration biopsy was performed from the mass under local anesthesia with 60 mg of prilocaine. The patient, who became desaturated and cyanotic during the procedure, was admitted to the clinic. The general condition of the patient was good, conscious, oriented and cooperative, arterial blood pressure was 110/75 mmHg, heart rate was 76 beats/minute rhythmic, and respiratory rate was 18/minute. His lips had a cyanotic appearance. In the respiratory examination of the patient, whose SpO_2 was 75%, measured by pulse oximetry in room air, respiratory sounds were decreased in the lower zones and heart sounds were deep. His ECG was in sinus rhythm and wave amplitudes were decreased.

In laboratory tests; hemoglobin: 9.7 g/dL, hematocrit 36.3%, MCV 92.0 fL, leukocytes 5300/µL, platelets 84000/µL. In the blood gas taken under the support of 6lt/min oxygen with mask, pH 7.46, PaO_2 120, FO_2Hb 76%, pCO_2 37 mmHg, HCO_3act 25 mmol/L, MetHb 10.2%. In the chest X-ray, the cardiothoracic ratio increased in favor of the heart and bilateral costophrenic sinuses. Watched off. In the echocardiography of the patient, pericardial effusion was present and the same amount of fluid was present as in the previous evaluations. There was no increase in the amount of pleural effusion compared to previous imaging.

The patient, who did not show any change compared to the previous ones and was clinically stable, was evaluated as methemoglobinemia and was monitored and followed up with oxygen support with a nasal cannula. MetHb was 5.3%, FO_2Hb 90%; MetHb was 0.8% and FO_2Hb was 96.4% in the blood gas taken at the 24th hour. The follow-up of the patient, whose methemoglobin level was within the normal range and had no symptoms, was terminated. The pathological diagnosis of the patient was concluded as "High-Grade Large B Cell Lymphoma".

DISCUSSION

Prilocaine, an amide compound frequently used as a local anesthetic, may also cause methemoglobinemia [3].

When the literature is examined, prilocaine-induced methemoglobinemia cases are frequently seen in newborns and early pediatric ages. It is a rare condition in adults. As a local anesthetic drug, the therapeutic dose of prilocaine has been reported as 1-2 mg/kg. Cyanosis is generally not observed in cases of methemoglobinemia occurring at therapeutic doses. The maximum safe dose of prilocaine is 8 mg/kg [2]. However, there are cases that develop methemoglobinemia in the administration of a lower than the safe dose [4].

There are few adult cases reported in our country. A case of methemoglobinemia due to prilocaine applied before epilation, and a case of methemoglobinemia developed with prilocaine before subclavian artery thromboendarterectomy draws attention [5, 6]. Apart from this, the majority of the cases reported from in country are pediatric patients [7-11].

There are adult cases reported in the literature, who were administered local anesthesia with prilocaine before liposuction, local anesthesia with prilocaine before intracardiac defibrillator implantation, and developed methemoglobinemia [12-14].

Gray-blue central cyanosis unresponsive to oxygen therapy is a valuable clinical finding. In mild cases, clinical signs and symptoms may not be observed; however, in severe cases, cyanosis, tachypnea, hypotension, tachycardia, and confusion may occur. Advanced cases can be fatal [5]. Additional comorbidities in which oxygenation is compromised, such as anemia, lung diseases, infection, and hemoglobinopathies can cause severe symptoms even at lower methemoglobin levels [15].

In cases with methemoglobinemia, varying degrees of cyanosis associated with blood methemoglo-

bin levels may be observed. The level of methemoglobin in the blood is below 1% under normal conditions. Peripheral cyanosis becomes prominent when blood methemoglobin levels exceed 10%, and tissue hypoxia and diffuse cyanosis are seen in cases with methemoglobin levels ≥35%. When methemoglobin levels approach 70%, the patient falls into a coma and may be mortal if left untreated [3, 16].

The gold standard in diagnosis is the demonstration of high or normal partial oxygen pressure and high methemoglobin level in blood gas analysis. The discrepancy between pulse oximetry and partial oxygen pressure is due to the presence of methemoglobin in the blood [15].

The recommended first-line treatment for drug-induced methemoglobinemia is methylene blue infusion. Even if patients with methemoglobin levels above 30% are asymptomatic, treatment should be considered when the methemoglobin level is 20% in a symptomatic patient [17]. Methylene blue therapy is contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency as it results in hemolysis and, paradoxically, methemoglobinemia, in these patients ascorbic acid can be given [17]. Methylene blue is given as 1-2 mg/kg intravenously over 3-10 minutes. If the methemoglobin level is greater than 50% or the clinical condition worsens, a higher initial dose of methylene blue (2 mg/kg) may be given. The dose may be repeated if symptoms do not improve or if elevated methemoglobin levels persist [18]. Hyperbaric oxygen therapy and exchange transfusion can be tried in cases with methemoglobin levels above 70% [19].

What was remarkable in our cases was that all four cases had an underlying malignancy and concomitant anemia. In addition, prilocaine was administered to these patients at a therapeutic dose without exceeding the safe dose recommended in the literature, but methemoglobinemia developed and cyanosis was observed.

CONCLUSION

Methemoglobinemia due to prilocaine, which is used as a local anesthetic in minimally invasive surgical procedures, is very rare and is fatal if not taken care of. In the case of blue-gray cyanosis unresponsive to oxygen therapy in the clinic after the use of local anesthetics, methemoblobinemia should be considered first and methylene blue should be considered in the treatment in appropriate cases together with oxygen therapy. All four of our patients were followed closely with only oxygen support and their follow-ups were terminated without any complications.

Authors' Contribution

Study Conception: MY; Study Design: MY, LCM; Supervision: LCM; Funding: N/A; Materials: MY, Aİ; Data Collection and/or Processing: MY, Aİ; Statistical Analysis and/or Data Interpretation: MY, Aİ; Literature Review: MY; Manuscript Preparation: MY and Critical Review: MY.

Informed Consent

Written informed consent was obtained from the patients for publication of this case series and any accompanying images or data.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

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