

A rare cause of cyanosis and hypoxia that should not be forgotten after implantable cardioverter defibrillator implantation

İmplant edilebilir defibrilatör yerleştirilmesi sonrasında hekimlerin aklından çıkmaması gereken siyanoz ve hipoksinin nadir nedeni

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Summary– Transvenous pacemaker or implantable cardioverter defibrillator (ICD) implantation procedures are usually performed under local anesthetic, and prilocaine is the most common agent to be used. The data regarding methemoglobinemia after cardiac device implantation are scarce. Thus, presently described is the case of a 47-year-old female patient with arrhythmogenic right ventricular cardiomyopathy/dysplasia who underwent ICD implantation for secondary prophylaxis and developed cyanosis as a result of prilocaine-associated methemoglobinemia. Prilocaine was administered during the procedure. To our knowledge, this is the second case in the literature presenting methemoglobinemia due to local anesthetic after transvenous cardiac device implantation.

Özet– Transvenöz kalp pili ya da implant edilebilir defibrilatör (ICD) yerleştirilmesi işlemleri yerel anestezi altında yapılır ve prilokain çoğunlukla tercih edilen anestetik ajandır. Kalp cihazı yerleştirilmesi sonrası methemoglobinemi ile ilişkili veriler azdır. Bu nedenle, bu yazıda 47 yaşında ikincil korunma amaçlı ICD yerleştirilen aritmojenik sağ ventrikül kardiyomiyopatisi/displazisi bulunan, işlem sırasında kullanılan prilokaine bağlı methemoglobinemi ve siyanoz gelişen kadın hasta sunulmuştur. Bilgilerimize göre, bu hasta literatürde transvenöz kalp cihazı yerleştirilmesi sonrasında yerel anestezi ilacına bağlı methemoglobinemi gelişen ikinci hastadır.

Local anesthetic agents are used for various cardiovascular procedures, including coronary angiography, transesophageal echocardiography, and permanent pacemaker implantation. Although methemoglobinemia developing after the administration of a local anesthetic is rare, the toxicity can be dangerous, and even fatal.^[1] Therefore, practicing cardiologists should be aware of this rare but important complication of local anesthetics. Only one report was located presenting methemoglobinemia after the administration of high-dose (1400 mg) prilocaine during permanent pacemaker implantation.^[2] Presently described is a case of

Abbreviations:

ARVC/D	Arrhythmogenic right ventricular cardiomyopathy/dysplasia
DeoxyHb	Deoxyhemoglobin
Hb	Hemoglobin
ICD	Implantable cardioverter defibrillator
MHb	Methemoglobin
OxyHb	Oxyhemoglobin
SaO ₂	Arterial oxygen saturation

methemoglobinemia developing in a patient after administration of 800 mg prilocaine during implantable cardioverter defibrillator implantation.

CASE REPORT

A 47-year-old woman with the diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) and documented unstable ventricular tachycardia episodes underwent ICD implantation for secondary prevention at our cardiovascular interventional laboratory. According to the standard protocol in our pacemaker unit, ICD implantation was performed under conscious sedation, achieved with 2 mg of intravenous midazolam bolus (Dormicum; F. Hoffmann-La Roche AG, Basel, Switzerland) and subcutaneous injection of 2 small bottles (40 mL, a total dose of 800 mg) of prilocaine hydrochloride (Priloc 2%, Vem İlaç Sanayi ve Ticaret Ltd. Şti, Tekirdağ,

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Turkey) as a local anesthetic agent into the left pectoral region. The implantation procedure was performed uneventfully. The patient was well, and pulse oximetry indicated that peripheral oxygen saturation was normal (~95–98% without nasal oxygen supplementation) on room air throughout the procedure. She was wide awake when transferred to the coronary care unit for follow-up after the procedure. However, notable central cyanosis with peripheral oxygen saturation of 80% developed 1 hour after the beginning of the implantation procedure. Apart from anxiousness and looking tired, she remained free of symptoms with 100% oxygen supply via a non-rebreather mask, yet oxygen saturation did not improve. Physical examination revealed blood pressure of 130/80 mmHg, oxygen saturation (SpO₂): 80% using pulse oximetry, pulse rate of 102 bpm, normal heart and lung sounds without any abnormality, prominent central cyanosis, and neurological examination was normal. Electrocardiography indicated no abnormality. Morphological complications, including pneumothorax, pericardial effusion, and cardiac perforation, were immediately ruled out by serial transthoracic echocardiography and chest radiography. Arterial blood gas analysis revealed dark brown blood with pH: 7.43, SaO₂: 98.3%, pO₂: 113 mmHg, bicarbonate: 25.7 mEq/L, oxyhemoglobin (OxyHb): 80.2% (n=90–95%), hemoglobin (Hb): 13.8 g/dL, and methemoglobin (MHb) level of 23.5% (n≤0.8%). The patient was diagnosed as methemoglobinemia and methylene blue 1 mg/kg (over 10 minutes) was immediately injected intravenously. One hour later, the patient was much more alert and repeat arterial blood gas analysis displayed improved MHb level of 3% with oxygen saturation of 92%. Two hours later, arterial blood gas analysis yielded MHb level of 0.6% with complete resolution of cyanosis and oxygen saturation of 96%. The patient was discharged uneventfully from the hospital the day after the procedure.

DISCUSSION

The rate of cardiovascular electronic device (pacemakers and ICDs) implantation has seen a significant incremental trend over the years. However, surgeons should be aware of both major and minor potential complications of the procedure. In addition to frequent, well-known complications, very rare causes of complications should also be kept in mind during

follow-up of the patients in wards or coronary care units. A sudden drop in peripheral oxygen saturation measured by pulse oximetry should be evaluated immediately and carefully. There are several conditions in differential diagnosis of peripheral hypoxia that should be excluded by simple measures, such as anxiety due to pocket pain, acute pulmonary embolism, pneumothorax, methemoglobinemia, and acute pulmonary laceration.^[3] Clinical, physical examination, and laboratory findings should be assessed in combination to reach a definitive final diagnosis. Clinical well-being except for central cyanosis, unresponsiveness to nasal oxygen supplementation, normal echocardiographic and radiographic examinations, discrepancy between peripheral SaO₂ measured with pulse oximetry and pO₂ in arterial blood gas analysis, and increased MHb concentration in arterial blood gas helped us to diagnose our patient as methemoglobinemia, which was successfully treated with intravenous methylene blue. MHb is the oxidized form of Hb and does not bind to oxygen effectively. Less than 2% MHb level can be present under normal physiological conditions and does not cause any symptoms. However, in case of genetic (enzymatic defects, etc.) and/or acquired (drugs, toxins, etc.) reasons, the level of MHb can be increased. MHb concentration of 10% to 20% is tolerated well, but greater levels are often associated with symptoms. In the literature, there were several reports of increased MHb level and clinical diagnosis of methemoglobinemia after the administration of local anesthetic agents, including prilocaine hydrochloride.^[4–6] However, methemoglobinemia observed after the administration of 600 mg prilocaine hydrochloride during a pacemaker implantation was only reported in 1 patient.^[2] It has been reported that the administration of >600 mg of prilocaine hydrochloride to adults may cause non-acute 15% methemoglobinemia via the formation of the o-toluidine metabolite. Thus, the advice given by the US Food and Drug Administration (FDA) is that 600 mg is the maximum safe dose of prilocaine in a normal healthy individual.^[7] The main clinical characteristics of the disease include central cyanosis that is unresponsive to oxygen supplementation and blood the color of dark chocolate. CO-oximetry is the gold standard for definitive diagnosis, but arterial blood gas paired with pulse oximetry and serum MHb levels can confirm the diagnosis clinically. A diagnostic CO-oximeter has the capacity to measure light absorption at 4 wavelengths,

in contrast to a traditional pulse oximeter, which measures at only 2 wavelengths: red (660 nm) and infrared (940 nm). The absorption spectra of red and infrared wavelengths by oxy and deoxyHb is different; thus, the absorbance ratio of oxyHb/deoxyHb at 2 different wavelengths yields the saturation percentage in traditional pulse oximetry. However, the light absorption spectrum for MHb is 631 nm; therefore, at 660 and 940 nm 100% MHb will result in an oxygen saturation reading of only 85%. CO-oximetry is preferred in multiple hemoglobinopathies due to the capacity to analyze the peak light absorption spectrum of a blood sample. Treatment of the methemoglobinemia includes the removal of the responsible agent, aggressive oxygen supplementation, and treatment with the first-line antidote, methylene blue. Methylene blue activates nicotinamide adenine dinucleotide phosphate methemoglobin reductase, which reduces methylene blue to methylene leucoblue, which then transforms MHb to deoxyHb through a non-enzymatic mechanism. Exchange transfusion and hyperbaric oxygen treatment are second-line options for patients with severe methemoglobinemia whose condition does not respond to methylene blue or who cannot be treated with methylene blue (e.g., with glucose-6-phosphate dehydrogenase deficiency). Intravenous ascorbic acid can also be used for treatment.^[1]

Due to the rarity of the condition, a good history and a high level of suspicion are required to make the definitive diagnosis. Thus, clinicians should be cautious when evaluating a patient with peripheral hy-

poxia after cardiovascular electronic device implantation. In addition, the dose of prilocaine hydrochloride as a local anesthetic agent should not exceed the amount recommended by FDA (<600 mg).

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REFERENCES

1. Cortazzo JA, Lichtman AD. Methemoglobinemia: a review and recommendations for management. *J Cardiothorac Vasc Anesth* 2014;28:1043–7. [CrossRef]
2. Sari C, Aslan AN, Bastug S, Bayram NA. An unusual complication after permanent pacemaker implantation: Methemoglobinemia. *Turk Kardiyol Dern Ars* 2015;43:468–71.
3. Alter P, Waldhans S, Plachta E, Moosdorf R, Grimm W. Complications of implantable cardioverter defibrillator therapy in 440 consecutive patients. *Pacing Clin Electrophysiol* 2005;28:926–32. [CrossRef]
4. Lata K, Janardhanan R. Methemoglobinemia: a diagnosis not to be missed. *Am J Med* 2015;128:45–6. [CrossRef]
5. Awasthy N, Khan N, Radhakrishnan S. Methemoglobinemia: arterial blood gas as a diagnostic tool. *Indian Heart J* 2014;66:394–5. [CrossRef]
6. Kaendler L, Dorszewski A, Daehnert I. Methaemoglobinemia after cardiac catheterisation: a rare cause of cyanosis. *Heart* 2004;90:51. [CrossRef]
7. US Food and Drugs Administration. (Accessed, <http://www.fda.gov/default.htm> <http://www.fda.gov/default.htm>).

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Anahtar sözcükler: Kardiyovasküler elektronik cihaz; komplikasyon; methemoglobinemi.