Benzocaine Induced Methemoglobinemia: A Potentially Fatal Complication of Transesophageal Echocardiography

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ABSTRACT

Transesophageal echocardiography (TEE) is a relatively safe procedure with complications including bleeding, esophageal perforation, and respiratory failure being rare. One of our patients recently developed severe cyanosis despite pulse oximetry of 85% following TEE. This directs our attention to a rare, easily treatable, but potentially fatal complication of this procedure.

INTRODUCTION

Due to its many advantages over the transthoracic echocardiogram, referrals for transesophageal echocardiography (TEE) are increasing. Major complications of TEE, including bleeding, perforation, and severe respiratory failure, are rare. However, we recently observed a rare and potentially fatal complication of TEE involving severe cyanosis despite pulse oximetry of 85%.

CASE REPORT

A 50-year-old male, postautologous bone marrow transplant for diffuse large cell lymphoma, was admitted to Ochsner Foundation Hospital with fever and right lower extremity abscess. The abscess was drained, but the fever persisted and TEE was requested to assess for evidence of infective endocarditis. At the time of the procedure, the patient was on oxacillin, levofloxacin, senna, docusate sodium, acetaminophen, omeprazole, and phosphorous.

TEE was performed after sedation with intravenous versed and pharyngeal local anesthesia with benzocaine spray. Following the procedure, the patient developed marked cyanosis while the pulse oximeter reading was 85%. The patient was in no acute distress, and seemed to be remarkably stable considering his severe cyanosis. Oxygen was administered with a 100% nonrebreather mask. Arterial blood gas with co-oximetry performed on 100% oxygen demonstrated a pH 7.39, PCO_2 46 mm Hg, PO_2 33 mm Hg, HCO_3 28 mg/dl, oxygen saturation 69%, and methemoglobin of 37%. The patient was transferred to the intensive care unit, where he was treated with intravenous methylene blue. The post-methylene blue arterial blood gas with co-oximetry on 4L/min O_2 demonstrated a pH 7.43, PCO_2 39 mm Hg, Po_2 89 mm Hg, HCO_3 25 mg/dL, and methemoglobin of only 1.5%. The patient made an uneventful full recovery over the next few hours and was stable when transferred to a nonmonitored floor bed the following morning.

DISCUSSION

Marked cyanosis after TEE can raise the possibility of ominous complications such as aspiration or rupture of esophagus or trachea. Patients with such complications, however, usually appear to be in severe acute distress.

Topical anesthetics, such as benzocaine and lidocaine, are known to occasionally cause toxic methemoglobinemia (1-4), which may produce cyanosis. This is considered to be a rare adverse effect with the incidence estimated in the pulmonary literature to be approximately one in every 7,000 bronchoscopies (5). Methemoglobin is oxidized hemoglobin with ferric rather than the normal ferrous iron, thus shifting the oxygen-dissociation curve to the left, preventing hemoglobin from releasing oxygen to the tissues. While methemoglobinemia may be an inherited hemoglobin abnormality, various drugs and chemicals may also induce it (Table 1). The acquired form of this disorder reverses upon withdrawal of the causative agent. Toxic blood levels of benzocaine, aberrant hemoglobin, and NADH-methemoglobin reductase deficiency are thought to be some of the predisposing factors favoring the onset of benzocaine-induced toxic methemoglobin. However, local application of benzocaine can cause methemoglobinemia in the absence of such risk factors.

Methemoglobin greater than 15% of the total hemoglobin can cause cyanosis that is unresponsive to oxygen administration, but the patients may be asymptomatic. Major symptoms, including fatigue, headache, tachycardia and dizziness, occur with levels exceeding 20%-30%. Levels above 30%-40%, as demonstrated in our patient, can be life threatening, and levels beyond 70% are usually rapidly fatal.

Table 1. Agents known to cause toxic methemoglobinemia. Adapted from Prchal JT, Jenkins MM. Hemoglobinopathies, methemoglobinemias, polycythemias and unstable hemoglobins. In: Goldman L, Bennett JC, eds. Cecil Textbook of Medicine. 21st ed. Vol 1. Philadelphia, PA; W B Saunders Company; 2000:890.

Medications	Chemicals
Acetaminophen	Acetanilide
Dapsone	Aniline dyes
Flutamide	Nitric oxide
Metoclopramide	Nitrite
Nitroglycerine	Amyl nitrite
Paraquat	Sodium nitrite
Phenazopyridine	Nitrates
Primaquine	Nitrobanzenes
Sulfamethoxazole	Nitrofurans
Benzocaine	4-amino-biphenyl
Cetacaine	Isobutyl nitrite

The first step in managing this complication is discontinuing the toxin causing methemoglobinemia. Intravenous methylene blue is indicated for methemoglobin levels above 30% and may need to be administered at lower levels of methemoglobin in patients with anemia, manifestations of hypoxia, or cardiovascular disease.

Measuring methemoglobin level by co-oximetry, which is available as a feature of some arterial blood gas analyzers, easily provides the diagnosis. When placed on filter paper, blood with methemoglobin is chocolate colored as compared to normal blood. The pulse oximeter, on the other hand, may falsely read the oxygen saturation to be 85%, despite a much lower actual oxygen saturation. This discrepancy occurs because pulse oximeters translate the ratio of absorbance for the two wavelengths (660 nm and 940 nm) into oxygen saturation; absorption characteristics of methemoglobin are very similar to those of oxyhemoglobin. For this reason, as with the patient that we are presenting, the patients in many published case reports of toxic methemoglobinemia had pulse oximeter readings of around 85% (6,7). Failure to recognize this phenomenon and strict reliance on pulse oximetry in these cases can prove fatal.

Those performing TEE, as well as those responsible for postoperative care of these patients, should be aware of this potentially fatal complication. The information in this report should also be applicable to specialists in pulmonary diseases, critical care, gastroenterology, and various general physicians and surgical subspecialists who perform esophageal and endotracheal procedures. As pulse oximeter monitoring is typically performed during TEE, any significant fall in oxygen saturation calls for careful evaluation of the patient. A sudden drop of pulse oximeter reading to 85% in any patient, especially with cyanosis, should prompt one to consider toxic methemoglobinemia.

References

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