Methemoglobinemia as a Cause of Unexplained Hypoxia in Neurosurgical Patients: A Report of Two Cases

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Introduction

Methemoglobin (metHb) is an abnormal hemoglobin where the ferrous iron in the hemoglobin is oxidized to a ferric state. Hemoglobin in this state cannot carry oxygen, resulting in hypoxemia, which manifests as low peripheral oxygen saturation (SpO₂). Bedside co-oximetry can identify this condition. We present here two cases of methemoglobinemia. Our experience with the first case enabled swift diagnosis of the second case. This also enabled us to prepare ourselves better in the second case if worsening of hypoxemia had occurred. Therefore, we learn here that whenever there is low SpO₂ with a normal partial pressure of oxygen, methemoglobinemia should be suspected and diagnosis should be confirmed using co-oximetry.

Keywords
► methemoglobinemia
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Abstract

In methemoglobinemia, ferrous iron in the hemoglobin is oxidized to a ferric state. Hemoglobin in this state cannot carry oxygen resulting in hypoxemia, which manifests as low peripheral oxygen saturation (SpO₂). Bedside co-oximetry can identify this condition. We present here two cases of methemoglobinemia. Our experience with the first case enabled swift diagnosis of the second case. This also enabled us to prepare ourselves better in the second case if worsening of hypoxemia had occurred. Therefore, we learn here that whenever there is low SpO₂ with a normal partial pressure of oxygen, methemoglobinemia should be suspected and diagnosis should be confirmed using co-oximetry.

Case 1

A 9-year-old child presented with complaints of headache, projectile vomiting, and weakness of the right-sided upper and lower limbs (Medical Research Council [MRC] grade 4%). Magnetic resonance imaging of the brain showed multiple serpiginous flow voids in the cervicomedullary junction. Bilateral vertebral artery angiogram showed arteriovenous malformation (AVM) measuring 19.5×13 mm, in the cervicomedullary junction, with feeders from both right and left posterior inferior cerebellar arteries (PICA), right and left vertebral arteries and draining via dilated latero-medullar-pontine veins into the petrosal vein, superior petrosal sinus, bilateral cavernous, and transverse sigmoid sinus. The patient had initially visited another hospital, where SpO₂ of 85% was documented. Chest X-ray and two-dimensional echocardiogram with bubble test for the evaluation of the cause of hypoxia were unremarkable. Given the diagnosis of brainstem AVM, hypoxia was attributed to central
hypoventilation without any confirmation by polysomnography, ABG, or pulmonary function tests.

The child visited our hospital and was scheduled for the embolization of the AVM. Preinduction, the patient’s SpO2 on room air was 88 to 90%, which improved to 98% after oxygen supplementation. After induction of anesthesia and tracheal intubation, the SpO2 dropped to 92% and cyanosis of hands and lips was seen, despite ventilation with fractional inspiratory oxygen (FiO2) of 1 (Fig. 1A). Since the patient was now being ventilated with 100% oxygen, diagnosis of central hypoventilation was ruled out. The color of the arterial blood (drawn for ABG) was chocolate brown. The PaO2 was 460 mm Hg on two consecutive samples, which were appropriate for FiO2 of 1. Due to acute angulation of the right distal PICA, navigation until the AVM nidus failed, and the procedure was abandoned. Anesthesia was reversed and the patient’s trachea was extubated. In the recovery room, SpO2 was 89 to 90%, which improved to 94 to 95% with oxygen supplementation. The cause of the mismatch between SpO2 and PaO2 and unexplained hypoxemia was evaluated using pulse co-oximetry (Radical-7, Masimo, Irvine, California, United States) and the metHb level was found to be 21.1% (Fig. 1B). Since the child was not on any medications, acquired methemoglobinemia was ruled out and a provisional diagnosis of congenital methemoglobinemia was made.

**Case 2**

A 30-year-old female presented with a 3 months history of convulsions, headache, and altered sensorium. She had been receiving antiretroviral treatment for the past 4 months. The patient was conscious, with power in right side limbs of MRC grade 3. She had neck stiffness and Kernig sign was positive. A computed tomography scan of the brain showed multiple ring-enhancing lesions in bilateral parietal lobes with significant perilesional edema suggestive of brain abscess. Burr hole and tapping of the abscess were planned on an emergent basis. Laboratory investigations were unremarkable except for the low CD4 count (15 cells per mm³).

In the operating room, her heart rate was 58 beats/minute with SpO2 of 85%, without any signs of respiratory distress. Lung and cardiac auscultation were normal. SpO2 did not rise above 90% despite preoxygenation for 5 minutes.

The tracheal was intubated after induction of anesthesia and the patient was mechanically ventilated with FiO2 of 1. However, the SpO2 did not improve beyond 90 to 91%. Arterial blood appeared dark brown with a normal PaO2 (246 mm Hg) and saturation (98.6%). The difference between PaO2 and SpO2 was investigated using co-oximeter, which showed a metHb of 18.7% (Fig. 2). The intraoperative course was uneventful except for low SpO2. After surgery and tracheal extubation, with oxygen supplementation at 6 L/min, SpO2 was maintained at 88%. A detailed history from the patient revealed the ingestion of sulfamethoxazole–trimethoprim for more than a month to treat fever. Methemoglobinemia has been reported with sulfamethoxazole–trimethoprim. The incidentally observed methemoglobinemia is most likely the acquired type due to prolonged use of sulfamethoxazole.

**Discussion**

In the first case, when low SpO2 was encountered, the presence of any cardiac and pulmonary causes was ruled out. Hypoxia was present throughout the procedure. Post-procedure, we found the cause of low saturation to be methemoglobinemia by co-oximetry. When hypoxemia occurred again in the second case, after ruling out systemic causes, co-oximetry showed a metHb level of 19%. Now, methylene blue was kept available for emergency use. The early diagnosis and adequate preparation reduced the stress and increased the confidence in managing this case.

Therefore, from these cases, we learnt that abnormal hemoglobin should be suspected whenever PaO2 is normal, with low SpO2. Generally, only patients with metHb levels above 30% are symptomatic.

Patients with unexplained hypoxia warrant co-oximetry evaluation. Co-oximetry helps determine the percentages of
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Various forms of hemoglobin in the blood in relation to total hemoglobin. These include oxygenated, deoxygenated, carboxy-, and metHb. It uses four to eight wavelengths and therefore is able to distinguish between the different hemoglobin. Blood gas analyzers with integrated co-oximetry modules are available or they can be done using noninvasive technology similar to a peripheral pulse oximeter. Indications for co-oximetry are known or suspected exposure to drugs that cause hemoglobin conversion to metHb or in patients who have been exposed to carbon monoxide. Patients with high levels of carboxyhemoglobin have normal SpO2 values because pulse oximeters cannot differentiate carboxyhemoglobin from oxyhemoglobin.4 Drug-induced methemoglobinemia can occur with drugs like nitrates and nitrite derivatives, sulfonamides, and dapsone. Dapsone is administered for the treatment of leprosy, endemic to countries like India. These patients will be asymptomatic preoperatively but will challenge the anesthesiologist preoperatively with cyanosis and desaturation.5 The use of drugs such as fentanyl, dexmedetomidine, nitrous oxide, and drugs metabolized by the P450 system is controversial and these drugs should be avoided. Remifentanil, propofol, benzodiazepines, and inhalational agents are safer choices.5 Blood transfusion or exchange transfusion can also help in improving oxygen delivery. The learning point from these cases is that hypoxia in any patient should be thoroughly investigated, and if there is any mismatch between pulse oximetry and arterial oxygen tension, suspicion of abnormal hemoglobin should be raised. This can be diagnosed with a simple bedside co-oximeter. However, availability of co-oximeter may not be possible at many centers. ABG, on the other hand, is more widely and easily available method.

Conflict of Interest

None declared.

References


Fig. 2 Co-oximetry showing elevated methemoglobin (18.9%) in the second case.