Letter to the Editor

Cocaine-induced methemoglobinemia

Kamal Kant Sahu[1], Ajay Kumar Mishra[1], Amos Lal[2], Ahmad Daniyal Siddiqui[1], Susan V. George[1]

[1] *MD Medicine, Saint Vincent Hospital, Worcester 10608, USA*
[2] *MD Medicine, Mayo Clinic, Rochester 55905, USA*

Corresponding Author: *Kamal Kant Sahu, Email: drkksahu85@gmail.com*

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Dear editor,

We congratulate Chowdhury et al[1] for their excellent report and successful management of a young lady suffering from cocaine-induced methemoglobinemia. Through this letter, we aim to address some additional concerns, which would certainly be helpful for a complete understanding of this topic.

Chowdhury et al[1] mentioned the top differentials for their patient's central chest discomfort as pulmonary thromboembolism, pneumothorax, significant anemia, and poisoning. We would like to mention another important differential as acute coronary syndrome (ACS) in any patient in whom there is a history of cocaine abuse due to coronary vasospasm. The study by Hollander et al[2] mentioned a very high incidence (25%) of cocaine-induced myocardial infarction (MI) in younger patients, particularly between 18 to 45 years. Cocaine-Associated Myocardial Infarction (CAMI) Study Group found that the degree of coronary artery calcification was a significant risk factor for MI in cocaine users as compared with non-users.[3] The index case reported by Chowdhury et al[1] underwent a thorough evaluation to rule out ACS. The patient's symptoms resolved completely once the underlying metabolic derangement was managed effectively. Hence, whilst ACS/vasospastic phenomenon should be in a list of differentials, it was not the main concern in the index case. We recommend to keep ACS in mind while dealing with cocaine toxicity and to evaluate with serial serum troponin levels and electrocardiogram in an appropriate clinical setting.

Although it is evident that the development of methemoglobinemia and cocaine consumption has a temporal correlation, it's important to rule out the other concurrent causes.[4] Use of e-cigarettes, nitrate/nitrite contaminated water consumption, frozen items with high nitrite/nitrate content, food items like choy sum, herbal drugs, anti-acne agents like topical and systemic dapsone, and the use of over-the-counter medications like eutectic mixture of local anaesthetics (EMLA) cream have been known to be associated with methemoglobinemia.[5-8]

Although not applicable in the index case, rarely an immediate acquired cause can uncover the underlying mild form of congenital methemoglobinemia.[9] There are no guidelines until today as when to evaluate patients for congenital causes, nicotinamide adenine dinucleotide (NADH)-cytochrome b5 reductase, or abnormal hemoglobin variants. The answer to this question requires a well-planned and probably multicentric study considering the rarity of the disease. The simple logic indicates that if methemoglobinemia recurs despite the removal of an acquired cause or exposure, it might be worth looking for congenital methemoglobinemia.

We are not clear how Chowdhury et al[1] concluded the patient's anemia to be related to anemia of chronic disease. Were there any predisposing and other medical comorbidities leading to anemia of chronic disease? One obvious reason could be the recent obstetric procedure, which could easily lead to some loss of blood and subsequent anemia. In cases, when no antecedent history of bleeding or chronic disease could be identified, the workup for intravascular hemolysis with lactate dehydrogenase level, serum haptoglobin level, absolute reticulocyte index, iron profile, and peripheral blood smear findings would be beneficial to look for methemoglobinemia-induced hemolysis. The question of inquiring the cause of anemia in this case of methemoglobinemia was important to ensure that the patient did not have any active hemolysis in addition to methemoglobinemia. There are many reports of poisoning in which patients suffer concurrent hemolysis in addition to methemoglobinemia.[10]

Chowdhury et al[1] did mention hemolysis as one of

the major side effects of methylene blue. While we agree with the discussion of the pathophysiology of the buildup of high concentrations of hydrogen peroxide inside erythrocytes leading to hemolysis, it is also important to mention that glucose 6 phosphate dehydrogenase (G6PD) deficiency is one of the contraindications to use methylene blue. In such conditions, other agents (like vitamin C and riboflavin), hyperbaric oxygen therapy, and plasmapheresis can be used along with the discontinuation of culprit agent, which was cocaine in this case.[11-14]

Also, not to forget the importance of making a follow-up plan of care for this patient as she had a psychosocial problem and drug addiction issues. Addressing her drug addiction is as equally important as managing her methemoglobinemia. This is because, unless we address her cocaine use disorder, there will always be a high chance of recurrence of cocaine-induced methemoglobinemia. Hence, the most important long-term plan for this patient is to get enrolled in a substance abuse program and to get educated about the harmful effects of cocaine use.

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