Cetirizine: Old Culprit or a New Member in the Family of Methemoglobinemia?

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Methemoglobinemia is both a challenging and rewarding disease entity if diagnosed early. Treatment and preventing further recurrence by removing the culprit are equally important. We congratulate Grillo et al¹ for the first-ever reported case of cetirizine-induced methemoglobinemia. We would like to address a few additional points that might be beneficial for readers.

The young girl described in the case report had blue discoloration of the hands for a long period. Apart from cytochrome-b5 reductase deficiency, was vasculitis-related Raynaud phenomenon ruled out for this young female? We reviewed the available literature and agree that there is no reported case of cetirizine as a direct causative agent of methemoglobinemia, but we did find 3 reports of patients developing methemoglobinemia while taking cetirizine.^{2–4} In the first case report, White et al² attributed the methemoglobinemia to amyl nitrate, but the patient was also receiving an antihistaminic agent at the same time. The second case reported by Murphy and Fernandez³ described the case of a 57-year-old female who took phenazopyridine for a urinary tract infection and subsequently developed methemoglobinemia. Her medications also included amitriptyline, cetirizine, clonazepam, diclofenac gel, fluticasone, pramipexole, pregabalin, and vitamin D supplements. The third individual developed methemoglobinemia due to omalizumab. At the time the patient presented with methemoglobinemia the patient was receiving daily cetirizine 40 mg, ranitidine 300 mg, montelukast 10 mg, dapsone 50 mg, and systemic steroid bursts for urticaria. We strongly believe that cetirizine may have directly or indirectly (additive) caused methemoglobinemia in the above 3 cases. From the above reports and the novel case report by Grillo et al,¹ we concur that cetirizine should be evaluated as a cause of methemoglobinemia in any patient with this diagnosis. Given the availability of cetirizine as a non-prescription drug, practitioners should proactively ask about the use of this agent during a medication history.

Although Grillo et al¹ asked about any recent intake of green beans, carrots, beets, or spinach, it is important to also ask specifically about nitrate-based preservatives or consumption of frozen items that might have high nitrite content, as they are also an important cause of methemoglobinemia.⁵ Sodium nitrite is commonly used in the food industry as a coloring agent, preservative,

or antimicrobial agent. We assume that Grillo et al¹ did not determine the serum nitrite concentration, which might have been important in this case.

Another important point in this discussion is the fact that the patient described by Grillo et al¹ has a younger sibling with an autism spectrum disorder. It is important in this situation to determine if this is a case of undiagnosed familial methemoglobinemia. Unfortunately, the parents denied the requested laboratory studies. In this case, it would be important to inform the primary care provider about the importance of genetic testing for cytochrome-b5 reductase deficiency for this patient and her sister, as a milder version of methemoglobinemia can have neurological manifestations as well.^{6,7}

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