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CLINICAL VIGNETTE

Methemoglobinemia: A Case from Primary Care

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Case

A 25-year-old female presented to her primary care provider an unusual bluish discoloration on the tip of her nose and nails, which she had noticed while putting on makeup before going to work. She panicked and rushed to her doctor's office. Three days prior, she had developed dysuria and started taking phenazopyridine (Pyridium) which she had at home left over from prior urinary tract infections. Her recent symptoms of dysuria started on a Friday and she could not get in touch with her doctor to start antibiotics until Monday, when the unusual skin discoloration was noticed.

The patient believed she took 4-5 pills of pyridium per day for the last 3 days, as her dysuria was quite severe. In the past, she was averaging 3-4 urinary tract infections per year, which were always treated with antibiotics and pyridium. Her past medical history was otherwise unremarkable. Her only regular medication was Lo-Loesterin with iron. She denied using tobacco and was a social drinker having 1-2 drinks per week. She denied allergies to medications. Her family history was unremarkable. On review of systems she denied fevers, chills, shortness of breath, or palpitations. She still had persistent dysuria, although it was improving.

Upon physical examination, she appeared anxious but in no pain or respiratory distress. Her vital signs were within normal limits with a blood pressure of 120/75mmHg, heart rate of 90 beats per minute with a regular pulse. She had a normal respiratory rate and oxygenation of 97% on room air. She was afebrile. A bluish discoloration was noted on the tip of the nose, lips and nail beds. The rest of the physical examination was unremarkable, and a diagnostic test was performed.

Discussion

Methemoglobinemia can be either congenital or acquired. The acquired version usually results from ingestion of medications that increase the production of methemoglobin. Methemoglobin occurs when the ferrous ions of heme become oxidized. Once in the ferric state, oxygen is irreversibly bound and unable to be delivered to local tissue. The resulting effect is a reduction of functional hemoglobin. Infants and those with

deficiencies of cytochrome b5 reductase are especially susceptible, as this is one pathway to convert methemoglobin back to hemoglobin.¹

In most individuals, there is a small amount of methemoglobin due to oxidative stress, however, compensatory mechanisms in the body keep the levels at less than 1%.² Methemoglobinemia results in impaired oxygen delivery which presents as dyspnea, tachycardia, headache, and ultimately cyanosis. Symptoms usually begin when greater than 20% of hemoglobin is affected. Methemoglobin concentrations greater than 40% can result in altered mental status, shock, and death. In addition to stopping the causative agent, treatment of methemoglobinemia requires administration of agents that can accept electrons and convert ferric iron to its reduced functional ferrous state. Methylene blue or vitamin C are used, with the former being preferred due to more rapid onset and better efficacy. However, methylene blue is ineffective in patients with G6PD deficiency, as G6PD is required in the NADH-dependent process. Blood transfusion is another option for treatment.

Acquired methemoglobinemia with benzocaine is well known and described, typically in the setting of procedures that utilize topical benzocaine.² Dapsone and nitrates are other medications that are well known to cause methemoglobinemia. One of the major metabolites of phenazopyridine is aniline, a drug that is known cause of methemoglobinemia. Despite this, methemoglobinemia is a rare occurrence after commonly prescribed doses of pyridium. Of interest, aniline-induced methemoglobinemia is less responsive to treatment with methylene blue than nitrate-induced methemoglobinemia.³

The patient was sent to the lab for determination of her methemoglobin percentage, which was 12.3% of total hemoglobin. In this case, as her symptoms were mild and mostly cosmetic, no treatment was prescribed other than cessation of pyridium. The patient was referred to urology to evaluate her frequent urinary tract infections.

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