CLINICAL VIGNETTE

G6PD Deficiency and a Family's Myth of Medication Allergies

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Case Presentation

A 46-year-old Italian female presented for follow-up and complained of profound fatigue. She was recently seen at urgent care for a urinary tract infection and treated with Trimethoprim/sulfamethoxazole. She was on day-5 of the treatment when she presented. The patient suspected her fatigue may be an allergic reaction to Trimethoprim/sulfamethoxazole and mentioned that she experienced similar reactions to other medications she thought she was allergic to. These include Nitrofurantoin, Phenazopyridine, Ciprofloxacin, Levofloxacin, and Ibuprofen. She also noted that "medication allergies" were a common problem in her family.

The patient's urinary tract infections were frequently triggered by sexual intercourse, and treatment with antibiotics often made her feel worse than the infection itself. She reportedly developed profound fatigue and became "much sicker" after taking antibiotics. Stopping the medication early often made her feel better.

Physical Exam

Overall, the patient appeared fatigued. Scleral icterus was noted. Rest of exam including cardiovascular, lung, abdomen, back, and skin exams were normal.

Laboratory Data

Initial labs showed decreased blood count: Hemoglobin 11, hematocrit 33, and elevated Bilirubin. G6PD deficiency was suspected with her new onset anemia and showed decreased levels. Importantly, the G6PD testing was performed after her hemolysis had resolved since false negatives can arise during acute hemolysis.

Treatment

The repeat urine test was negative for infection. Trimethoprim/sulfamethoxazole was discontinued, and the patient recovered in a few days.

After the patient's G6PD deficiency diagnosis, she made her annual trip back home to Sicily and shared the diagnosis with her family. At least five family members, mostly males, were later diagnosed with G6PD deficiency.

Discussion

Glucose-6-phosphate dehydrogenase (G6PD) is an enzyme that helps defend red blood cells against oxidative stress, thus deficiency can cause hemolytic anemia. G6PD deficiency is the world's most common enzyme deficiency and affects more than 400 million people. It is X-linked and more common in people of Mediterranean, African, and Asian descent.[1] Discovery occurred during the 1950s when patients developed hemolysis after treated with primaquine.[2] Most affected patients are asymptomatic, and symptoms affect males more often than females due to the X-linked inheritance pattern. Nevertheless, female carriers can still be clinically susceptible depending on the degree of lyonization, a process in which an X chromosome is randomly inactivated in each cell.[3] Symptoms vary and include fatigue, pallor, jaundice, abdominal pain, back pain, and dark urine.

Acute anemia in G6PD deficiency is precipitated by stress, most commonly from infections, medications, and fava beans. Primary treatment is avoiding the trigger.[2] While drug-induced anemia is a common adverse effect in patients with G6PD deficiency, there are conflicting reports over which medications clearly trigger hemolysis. Hemolysis thought to be triggered by certain medications may, in fact, be caused by the infection itself.[2,4,5] Medications with sufficient evidence for precipitating G6PD hemolysis are primaquine, dapsone, nitrofurantoin, phenazopyridine, methylene blue, and rasburicase.[4,5] Notably, nitrofurantoin and phenazopyridine are common UTI treatments for female patients as seen in our patient above.

Medications that were previously considered unsafe but now have been considered to be possibly safe by some sources include fluoroquinolones and cotrimoxazole. Youngster et al[4] recently conduct a systematic evidence-based review of the literature to identify medications safe for G6PD deficiency patients. They conclude that insufficient evidence exists for hemolysis caused by normal dosages of fluoroquinolones or cotrimoxazole.[4] However, Luzzatto and Seneca disagree and argue that even isolated reports of adverse effects should be taken seriously. To them, convincing case reports exist to support avoiding quinolones and cotrimoxazole.[5-7] These medications' safety thus requires further study.

Since G6PD deficiency is not part of routine newborn screening in the US, it should be suspected when patients develop symptoms of acute hemolysis after exposure to oxidative medications and infections. This applies even to female

patients. G6PD deficiency is often missed since carriers can remain asymptomatic, but asymptomatic patients may still experience hemolytic anemia. UTI is common in women, and the drugs of choice, nitrofurantoin, and phenazopyridine are hemolytic medications. Therefore, vigilance toward possible G6PD deficiency is warranted when prescribing these medications in the primary care setting.

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Submitted October 25, 2016