CLINICAL VIGNETTE

Administration of High Doses of Vitamin C in a Patient with Beta Thalassemia Trait and Elevated Ferritin

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The patient is a 43-year-old man with a medical history significant for beta-thalassemia trait and nonalcoholic steatohepatitis (NASH) admitted to the hospital with Strep pyogenes sepsis due to a skin abscess. Due to his beta-thalassemia trait and ineffective erythropoiesis, the patient has had anemia and elevated ferritin level for years. Initially, the elevated ferritin was treated with occasional phlebotomy, however, this was poorly tolerated due to the anemia. More recently his treatment added intermittent iron chelation therapy.

When the patient was hospitalized, he was given the appropriate antibiotics along with high doses of Vitamin C as part of the sepsis protocol. During that hospitalization the patient also received high doses of iron in the setting of microcytic anemia with a hemoglobin of 8. Ferritin levels were measured during his hospitalization with numbers consistently in the 1300-1600 range, with a normal of less than 325.

I was consulted on this patient as he had dyspnea on exertion and there was concern about the effects of the elevated ferritin on his cardiac functioning.

The use of Vitamin C in sepsis reached wide circulation in 2017 in an article published by Marik and colleagues in CHEST.[1] This retrospective study compared the outcome of consecutive septic patients treated with intravenous Vitamin C, hydrocortisone, and thiamine during a 7-month period compared to a control group, with the primary outcome being hospital survival. With an 8.5% mortality in the treatment group compared to 40.4% in the control group, the study concluded that intravenous vitamin C, together with corticosteroids and thiamine are effective in preventing organ dysfunction, acute kidney injury, and reducing the mortality in patients presenting in severe sepsis. As these medications are readily available at a low cost and have long-safety records, this protocol is increasingly being used in hospitals in patients presenting with sepsis.[2]

Vitamin C, in addition to its antioxidant properties helps regulate cellular iron metabolism. Aside from its known ability to enhance nonheme iron absorption in the gut, Vitamin C can regulate cellular iron uptake and downstream cellular metabolism. In nonerythroid cells, iron is converted to ferritin which heteropolymerizes to form a wide range of iso-ferritins with tissue-specific distributions.[3] These tissues include hepatic tissue and cardiac tissue, where large quantities this can lead to organ dysfunction.

Traditionally when myocardial iron overload was suspected, endomyocardial biopsy was the method by which definitive diagnosis was made. This does not represent an ideal solution as it is an invasive procedure that carries significant potential risk. Additionally, if chelation therapy is prescribed it is difficult to assess the effect of therapy on the myocytes. As such, noninvasive imaging, specifically MRI is routinely being used to assess for iron overload in both hepatic and cardiac tissue, using T2* and R2 measurement techniques. This testing, which can be done in the absence of dye administration or even IV access can reliably quantify iron in the different tissues. Given the safety profile, the test can be repeated periodically if chelation treatment is prescribed or for interval surveillance in patients prone to iron overload states. Another benefit of Cardiac Magnetic Resonance (CMR) is that it can provide imaging on cardiac chamber structure and function that in skilled hands can surpass the information obtained from a transthoracic echocardiogram.

When I saw the patient in the office his vital signs were within normal limits and his clinical exam was significant for obesity and multiple healing scars on his arms and legs where he had picked at his skin. These compromised areas were believed to be the source of his Strep pyogenes bacteremia. I had referred him for a cardiac MR to assess cardiac functioning as well as myocardial iron assessment. He had incidentally also been referred for an MR of the liver to assess for iron overload in the liver. The cardiac imaging showed that ejection fraction was normal as was his cardiac structure, and there was no T2* signal dropout in the myocardium to suggest iron overload.

This patient, while having a chronically elevated ferritin and having been administered high doses of vitamin C in close temporal relation to infusion of IV iron suffered no myocardial iron overload. While the most common mechanism of iron and vitamin C absorption is synergistically in the gut, vitamin C has been shown to affect iron metabolism at a cellular level.[3] My opinion is that serious consideration should be taken when administering high doses of vitamin C to patients with a known hemoglobinopathy.

REFERENCES

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