CLINICAL VIGNETTE

Congestive Heart Failure in a Woman with Profound Anemia

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Case Presentation

A 67-year-old woman with no known prior medical history presented to the emergency department with three weeks of bilateral leg swelling with associated dyspnea on exertion while walking five feet. By two to three days prior to admission, she stated that she was no longer able to fit into her jeans. Upon further questioning, the patient volunteered that she had been having progressive fatigue for about two years with no other associated symptoms.

She denied any past medical history at the time and stated that she had not seen a physician in over ten years. She took no medications or over-the-counter remedies. The patient lived alone, had never married, had no children, and no close friendships in the area. She had three siblings, and her mother was still alive. She denied any history of tobacco, alcohol, or illicit drug use.

On her initial evaluation, the patient was afebrile, had a blood pressure of 95/50, a heart rate of 90, respirations of 27, and an oxygen saturation of 98% on room air. She was found to have anasarca with severe, bilateral leg edema and decreased breath sounds at the bases on lung exam. A stool guaiac test was positive, but there was no overt blood in the stool. Laboratory exams were remarkable for a hemoglobin level of 1.9. Iron studies showed a ferritin of 7, total iron-binding capacity of 391, and serum iron of 10. Other lab tests were not suggestive of other metabolic deficiencies or hemolysis. A chest x-ray showed small bilateral pleural effusions with bibasilar opacities. Echocardiogram indicated a moderately increased left ventricle size and moderately reduced systolic function.

Her initial diagnoses were profound iron deficiency anemia and new onset heart failure. She received five units total of packed red blood cell transfusions during her hospitalization with subsequent stabilization of hemoglobin to 9. On admission, the most likely etiology for this patient's iron deficiency anemia was gastrointestinal blood loss, but neither esophagogastroduodenoscopy nor colonoscopy showed any sources of bleeding. A consulting gastroenterologist suggested pill enteroscopy to find sources of bleeding in the small intestine, but the patient declined the procedure. The patient's heart failure stabilized in the hospital with intravenous furosemide and with improvement in leg edema and shortness of breath. She was discharged on 40 mg per day of furosemide, in addition to carvedilol and lisinopril. Discharge medications also included iron sulfate at 325 mg twice a day.

Because of the patient's persistent debility and problems with gait, she was transferred to a skilled nursing facility after her hospitalization, for physical and occupational therapy. There, her peripheral edema resolved with only intermittent and mild shortness of breath on ambulation. At the time of discharge from the skilled nursing facility, approximately one month after her admission to the hospital, she was able to ambulate with a front-wheeled walker. Upon discharge, her hemoglobin level was 8.9.

The patient attended her first outpatient visit with a new primary care physician approximately two months after hospital admission. At that time, she stated that she was not taking her medications as prescribed. Specifically, she stopped taking iron eight days after discharge from the skilled nursing facility. Her exam was remarkable for mild-moderate edema to the legs with a normal lung exam. Hemoglobin at the time was 8.4, serum iron was 28, ferritin was 38, and iron-binding capacity was 351.

Discussion

Iron deficiency anemia is the most common source of anemia, both in developed and developing countries. The prevalence of iron deficiency anemia in the United States in men over 50 is 1-2%, while it is 2% in women of that age cohort.[1] The prevalence of iron deficiency is greater in developing countries. Severe anemia of any kind can induce cardiac pathophysiologic changes that lead to left ventricular (LV) dysfunction and heart failure. However, severe iron deficiency, in and of itself, can add to the cardiac dysfunction in cases of anemia.

When anemia develops, cardiac output increases to maintain adequate oxygen delivery. Cardiac output increases through increases in blood volume, preload, heart rate, and stroke volume, as well as a decrease in afterload.[2] If the anemia is more severe, this increased blood volume contributes to congestion with eventual development of peripheral and pulmonary edema. This type of cardiomyopathy is known as high output heart failure. In high output heart failure, low afterload results in low or borderline arterial blood pressure, and elevated cardiac filling pressures.[3] Though systemic vascular resistance is low, sympathetic activation results in increased renovascular resistance and reduced renal blood flow and glomerular filtration, leading to retention of salt and water.[4] Despite this sympathetic activation, beta blockade has not been found to improve symptoms in high output heart failure. One study performed in rats with iron-deficient rats with heart failure used beta blockers but failed to prevent cardiac decompensation.[5]

Another mechanism by which anemia may contribute to cardiomyopathy is with poor oxygen supply to tissues, which can then lead to myocyte dysfunction in the heart.[6] Myocardial contractility decreases as hemoglobin drops below 7 g/dl.[7] In addition to the drop in hemoglobin, the iron deficiency itself may affect cardiac muscle function. Because iron binds to myoglobin, a total-body iron deficit could impair myocytes' ability to extract oxygen from circulating hemoglobin.[6] In fact, iron replacement has been shown to improve cardiac function even before significant increases in hemoglobin.[8]

Anemia rarely causes heart failure on its own, and it often accompanies other cardiac abnormalities such as valvular diseases or ischemic heart disease. On its own, however, it can lead to left ventricular dysfunction. One early study found that normal cardiac hemodynamics were maintained with hemoglobin values as low as 7 g/dl. At this level, cardiac output increased, and heart failure did not occur. It was only with levels lower than 5 g/dl that heart failure developed in the absence of underlying heart disease.[9]

The cardiomyopathy of iron deficiency can be reversed through repletion of red blood cells. Gradual transfusion of packed red blood cells can reverse clinical failure within hours, but if done too rapidly, it can precipitate pulmonary edema.[6] Even iron replacement alone has been shown to improve cardiac function, as evidenced by the reduction in heart rate by infusion of iron-dextran in one study.[8] Loop diuretics can be indicated if pulmonary edema is clinically present.[6] Because peripheral vascular resistance is already low, the use of angiotensin-converting enzyme inhibitors may not have a role in treatment.

Our patient had both profound anemia and iron deficiency when she initially presented to the hospital. Her hemoglobin levels were well below the threshold of 5 g/dl, that is associated with heart failure in the absence of underlying heart disease. Her echocardiogram did not suggest valvular disease or other structural cardiac abnormalities that would have precipitated heart failure in the absence of profound anemia. Thus, it is very likely that high output heart failure from iron deficiency anemia was the mechanism for her presentation with pulmonary edema and anasarca. Her symptoms improved in the hospital through transfusions of packed red blood cells, the aggressive use of loop diuretics, and repletion of iron. Follow-up after discharge from a skilled nursing facility indicated that she had not been adherent to prescribed iron treatment. Thus, it is uncertain whether she will be able to avoid recurrences of congestive heart failure.

Conclusion

Iron deficiency anemia can lead to left ventricular dysfunction and congestive heart failure, especially if hemoglobin drops below a threshold of 5 g/dl. The left ventricular dysfunction can be reversible through gradual transfusion and repletion of iron stores. The use of loop diuretics may be warranted in the case of pulmonary edema, but vasodilators and beta blockers may be unnecessary.

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