CLINICAL VIGNETTE

Endocarditis in a Patient with Hereditary Hemochromatosis

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Case Presentation

A 55-year-old man with hereditary hemochromatosis initially presented to his primary care doctor with unintentional weight loss over several months. On further interview, he revealed having intermittent low-grade fevers and worsening dyspnea on exertion during this time. Outpatient evaluation included upper endoscopy and colonoscopy, which were unremarkable and a transesophageal echocardiogram, which revealed severe mitral regurgitation secondary to a perforated/flail mitral valve leaflet. He was scheduled for elective left heart catheterization to prepare for mitral valve replacement. He was febrile and the elective heart catheterization was canceled. He was positive for COVID-19 and blood cultures were also drawn. His fever was thought to be secondary to his COVID-19 infection and he was discharged with Paxlovid. However, blood cultures subsequently returned positive and he was admitted.

At admission, he was afebrile with normal vital signs. Physical exam, noted the patient as thin but not cachectic. There were no significant skin changes. Cardiac exam was notable for a 3/6 systolic murmur heard best in the left lateral decubitus position. He has no jugular venous distension, crackles in his lungs or lower extremity edema. During hospitalization he had multiple episodes of supraventricular tachycardia. Transthoracic echocardiogram again showed severe mitral regurgitation with flail mitral valve leaflet as well as mobile echodense masses on multiple leaflets of the mitral valve with nodular masses concerning for aortic valve vegetations. These findings were confirmed on repeat transesophageal echocardiogram. He was started on broad spectrum parenteral antibiotics for bacteremia. Blood cultures grew Granulicatella adiacens and the patient underwent both aortic and mitral valve replacements. His blood cultures cleared and he completed an extended course of intravenous antibiotics without any further evidence of infection.

Discussion

Hereditary hemochromatosis is caused by a number of different genetic mutations. The most common mutation is homozygosity in the C282Y mutation of the HFE gene, which has an overall prevalence of about three in one thousand, though not everyone who is homozygous for this mutation will develop clinical hemochromatosis.[1] Iron overload can also be caused by other conditions, mostly secondary to red blood cell transfusion dependence in conditions that cause chronic anemia (i.e. sickle cell disease, MDS, thalassemia). Common complications from iron overload syndromes include liver disease, diabetes, skin pigmentation and cardiomyopathy.[2] However, chronically increased iron stores may also increase infection risks.

Iron is found in nearly all living organisms and is considered critical component of vital enzymatic reactions. Thus, microorganisms have developed ingenious techniques for obtaining iron not only from the environment, but also from their hosts. Because of the ability to extract iron, human iron stores may help certain bacteria flourish. Over time, our immune systems have developed defense mechanisms that can prevent bacteria from accessing iron. For example, the protein lactoferrin, which is secreted by cells including neutrophils and mucosal epithelial cells, chelates and sequesters iron so it cannot be accessed by microbes.[3] Mice who lack lactoferrin have a higher incidence of spontaneous Staphylococcal abscesses,[4] indicating that blocking bacteria from iron stores is an effective immune system method to prevent infection. Our bodies have also developed methods to decrease concentration of iron in the extracellular space as part of our inflammatory cascade. This emphasizes the importance of access to iron for bacterial survival.

It is important to remember that iron overload states may predispose to infection. These infections can often be otherwise clinically silent. This patient presented initially with subacute constitutional symptoms including unintentional weight loss and night sweats. Broad, thorough evaluation was started for these symptoms, including a detailed gastrointestinal and cardiac testing. However, given the patient's history of hereditary hemochromatosis, although the patient did not report overt clinical signs/symptoms of infection, infectious etiology should have been considered. Earlier recognition of infectious links could potentially prevent more serious sequelae of delayed infectious diagnosis such as abscess formation, valvular disease, stroke, or even death.

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