CLINICAL VIGNETTE

An Unusual Presentation of Hemochromatosis

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A 79-year-old male with a history of renal cell carcinoma, atrial fibrillation, essential hypertension and hyperlipidemia presented to primary care for evaluation after MRI showed incidental findings suggesting hemochromatosis. The surveillance MRI was obtained after ablation of renal cell carcinoma. MRI renal protocol showed diffuse low signal intensity in the liver suggesting iron deposition. The patient reported fatigue, but denied abdominal pain, arthralgias or erectile changes. He had no history of heart failure or cirrhosis. On physical exam, there was no skin hyperpigmentation or joint pain. He reported a remote history of heavy alcohol use for 10 years. Iron studies showed ferritin 900 ng/mL and transferrin saturation of 90%. HFE gene testing returned homozygous for C272 Y. Fibroscan showed F2 fibrosis. He was evaluated by hepatology and is completing phlebotomy.

Hemochromatosis is an autosomal recessive disorder in people of Northern European descent, present in 1 in 200.[1] The most common gene defect associated with hemochromatosis is a substitution of tyrosine for cysteine at amino acid position 282 (C282Y). Other less common mutations include aspartate for histidine at amino acid position 63 (H63D) and cysteine for serine at amino acid position 65 (S65C).[2] Other mutations that cause hemochromatosis are less common and include mutations in hepcidin, hemojuvelin and ferroportin.[2] All of these mutations affect iron regulation pathways in the body. Hemochromatosis results from increased absorption of iron from the intestine that results in diabetes, cardiovascular disease, cirrhosis and hepatocellular carcinoma.

The diagnosis of hereditary hemochromatosis is established by the presence of the HFE gene on genetic testing. However, only 10% of patients with homozygous C282Y will develop iron overload and the clinical manifestations of hemochromatosis.[2] Most patients are identified in the asymptomatic stage based upon screening labs.[3] Clinical features that suggest hemochromatosis include the classic triad of cirrhosis, diabetes and skin hyperpigmentation. Symptoms include fatigue, right upper quadrant abdominal pain, and arthralgias. Arthropathy typically occurs in the metacarpophalangeal joints. Cardiovascular manifestations of hemochromatosis include heart failure, conduction disturbances and sick sinus syndrome as iron is deposited into the myocardium. Heart failure associated with hemochromatosis is typically a dilated cardiomyopathy. Iron deposition in the liver leads to hepatomegaly, transaminitis and cirrhosis. Diabetes results from iron deposition into the pancreas.[4]

Patients with a family history of hemochromatosis should undergo screening. Patients with iron overload may be screened for hemochromatosis, specifically with elevated transferrin saturation >45%.[1] AASLD guidelines recommend liver biopsy to determine the stage of liver disease in patients who are C272 Y homozygotes or if ferritin is >1000 ng/mL.[2]

Other factors that impact the progression of hemochromatosis include gender, alcohol use, and blood loss. Female homozygotes are less likely to be symptomatic due to routine loss of iron with menses and pregnancy. Other concomitant liver disease can influence the degree of fibrosis associated with hemochromatosis.

Treatment of hemochromatosis is phlebotomy. Phlebotomy is used once weekly until a target ferritin of 50-100 ng/mL is reached.[2] Phlebotomy decreases the progression to cirrhosis. Hemochromatosis patients with cirrhosis require screening for hepatocellular carcinoma.

REFERENCES

1. **Powell LW, Seckington RC, Deugnier Y**. Haemochromatosis. *Lancet*. 2016 Aug 13;388(10045): 706-16. doi: 10.1016/S0140-6736(15)01315-X. Epub 2016 Mar 12. Review. PubMed PMID: 26975792.
2. **Bacon BR, Adams PC, Kowdley KV, Powell LW, Tavill AS; American Association for the Study of Liver Diseases**. Diagnosis and management of hemochromatosis: 2011 practice guideline by the American Association for the Study of Liver Diseases. *Hepatology*. 2011 Jul; 54(1):328-43. doi: 10.1002/hep.24330. PubMed PMID: 21452290; PubMed Central PMCID: PMC3149125.
3. **Adams PC, Barton JC**. Haemochromatosis. *Lancet*. 2007 Dec 1;370(9602):1855-60. Review. PubMed PMID: 18061062.
4. **Schrier S, Bacon B**. Clinical manifestations and diagnosis of hereditary hemochromatosis. Post TW, ed. *UpToDate*. Waltham, MA: *UpToDate* Inc. http://www.uptodate.com (Accessed on November 20, 2018.)