

A Rare Case of Hemochromatosis and Wilson's Disease Coexisting in the Same Patient

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Wilson's disease and hereditary hemochromatosis are two inherited diseases with life-threatening complications. Early recognition and prompt treatment may be instrumental in reducing such complications associated with these disorders. Although both Wilson's disease and hereditary hemochromatosis are genetic in nature, the two conditions have distinct, unrelated genetic etiologies. Two distinct, separate mutations are required for simultaneous existence of the two diseases. As such, the likelihood of the two conditions coexisting is exceedingly rare. Here we report a case of a 23-year-old male with hereditary hemochromatosis with coexistent Wilson's disease. Only two reported cases exist in which this dual diagnosis was present simultaneously. In our patient, laboratory evaluation demonstrated elevated ferritin, transferrin saturation >90%, and subsequent liver biopsy demonstrated diffuse fibrotic changes. Confirmatory genetic analysis revealed the patient to be a compound heterozygous for C282Y and H63D gene mutations. Given the patient's young age and the improbability of hemochromatosis-induced hepatic damage at that age, an alternative diagnosis was sought. Further analysis revealed reduced serum ceruloplasmin along with elevated urinary copper excretion. Subsequent ophthalmologic exam revealed bilateral Kaiser Fleischer rings. In conclusion, Wilson's disease and genetic hemochromatosis both involve inherent flaws in the transportation of heavy metals and their accumulation in hepatocytes. Although both diseases arise from distinctly different genetic mutations, the coincidence of the two disorders can, in rare cases, occur.

Key words: hemochromatosis ■ Wilson's disease ■ liver ■ transplantation

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CASE REPORT

A 23-year-old white male recently diagnosed with hemochromatosis presented with fever and neck stiffness. He was evaluated at the emergency department and, following negative blood cultures and unremarkable lumbar puncture, was sent home with a diagnosis of poorly defined viral infection. Upon arriving at home, the patient began experiencing diffuse abdominal pain associated with watery diarrhea four times a day. He returned two days later with worsening abdominal pain, fever and chills that did not respond to over-the-counter ibuprofen. On admission, the patient complained of diffuse abdominal pain and severe bloating but denied any shortness of breath, chest pain, hemoptysis, hematemesis or melena. The patient also denied any family history of liver disease or hemochromatosis. He denied illicit drug use or tobacco use but admitted to drinking up to five beers daily for a six-month period while stationed in Iraq.

The patient was diagnosed with hemochromatosis three months prior to admission after being referred for evaluation of abnormal liver enzymes. At that time, the patient had a ferritin level of 1,188 ug/L and transferrin saturation >90%. A liver biopsy was obtained and demonstrated extensive inflammation and fibrosis associated with elevated iron stores. Notwithstanding, the hepatic iron index (HII) was only slightly above normal and noted to be 1.3. A subsequent genetic analysis confirmed that he was compound heterozygous *HFE* genotype C282Y/H63D. He was subsequently placed upon a treatment regimen that included weekly phlebotomy.

The physical examination showed a well-built 23-year-old Caucasian male in moderate distress. He was febrile with a temperature of 102.2°F, tachypneic, tachycardia with normal blood pressure. No jaundice was appreciated, but mucous membranes appeared dry. Lung fields were clear to auscultation bilaterally, and no murmurs, rubs or gallops were noted. Abdominal distension was observed and palpation revealed diffuse tenderness in the abdomen. Rebound tenderness was appreciated in all four quadrants. On account of severe tenderness, abdominal percussion was not conducted. However, bowel sounds were hypoactive. Neurological evalua-

tion revealed an alert, oriented patient with intact cranial nerves, normal symmetrical power and reflexes with preserved sensation. The patient had normal gait with no evidence of tremors or rigidity.

Laboratory evaluation revealed mildly elevated white blood cell count with anemia. Aminotransferases were elevated two times the normal limit, and alkaline phosphatase was 190. Follow-up coagulation evaluation revealed international normalized ratio of 1.5. Abdominal ultrasound revealed ascites, prompting further investigation. A subsequent CT scan demonstrated ascites, and the patient subsequently underwent a paracentesis that was notable for white blood cell (WBC) count of 5,000 with 84% neutrophils—findings consistent with spontaneous bacterial peritonitis. Gram staining came back negative, and cultures did not show any growth. The CT of the abdomen also demonstrated heterogeneous, irregular liver parenchyma and micronodular cirrhosis, but no hepatosplenomegaly was appreciated on imaging studies. The patient was subsequently admitted and placed on intravenous antibiotics.

Following admission, additional laboratory tests were ordered, revealing decreased serum ceruloplasmin level alongside increased urinary copper excretion, which raised the suspicion for Wilson's disease. Given the findings, ophthalmologic evaluation was obtained and was significant for Kaiser-Fleischer rings, confirming the diagnosis of Wilson's disease.

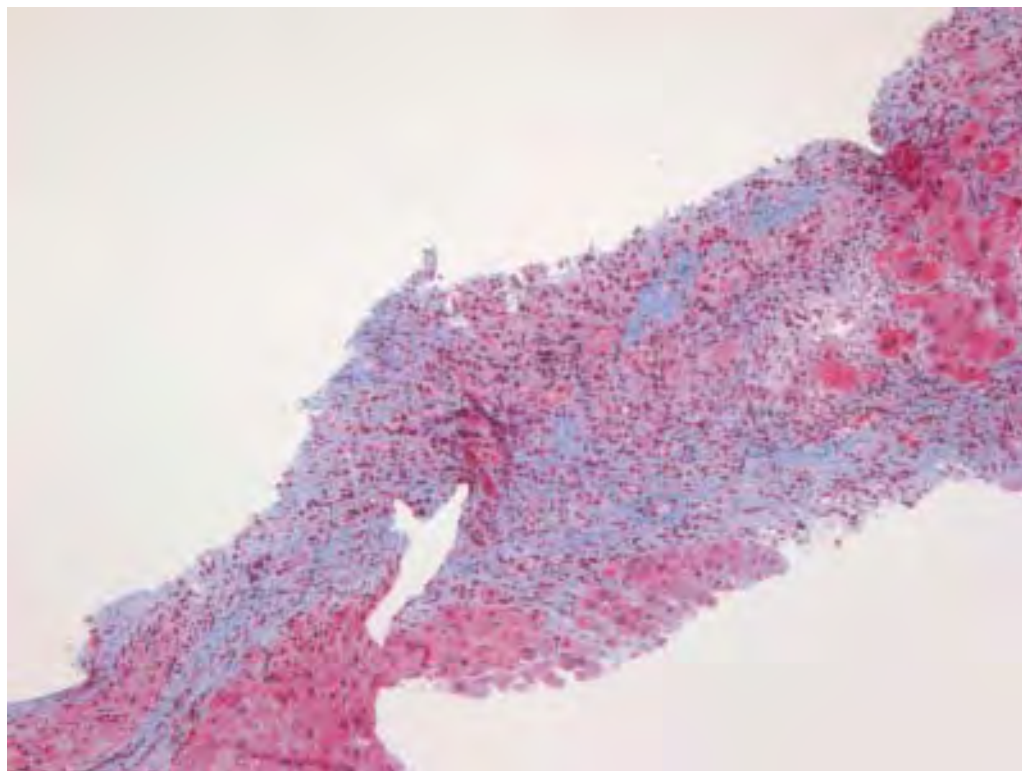
DISCUSSION

Wilson's disease and hereditary hemochromatosis are two inherited diseases with life-threatening complications. The fact that they are both treatable diseases makes early recognition and prompt diagnosis essential to minimizing such complications. Hereditary hemochromatosis results from a genetic mutation that disrupts absorption of dietary iron. Wilson's disease is caused by inappropriate copper homeostasis, which yields copper overload. Both conditions have been implicated in causing end-organ damage. Wilson's disease tends to cause damage to tissues of the central nervous system and visceral organs, while hereditary hemochromatosis primarily wreaks havoc on visceral tissues with little or no neurological involvement.

Hemochromatosis is a clinical condition characterized by iron overload. It can be genetic or secondary in nature. The hallmark of the disorder is extensive deposition of iron in multiple tissues, most notably the skin, liver, pancreas, thyroid and heart.¹ Deposition of iron in the aforementioned organs places the affected individual at increased risk of complications, including decompensated cirrhosis, diabetes mellitus, cardiomyopathy and hepatocellular carcinoma.^{1,2}

Confirming the diagnosis of both Wilson's disease and hereditary hemochromatosis involves simple, noninvasive procedures. Arriving at a diagnosis of Wilson's disease requires testing serum ceruloplasmin and cop-

Figure 1. Liver biopsy demonstrating excessive iron deposition in our patient



per levels.³ Additionally, evaluation of urine copper excretion, together with slit-lamp examination of the eyes to detect the presence of Kaiser-Fleischer rings, is also indicated.^{1,3} Definitive diagnosis of iron deposition oftentimes necessitates invasive procedures such as direct tissue biopsy (Figure 1).^{1,3} The reference ranges for the two heavy metals in liver biopsies are 10–55 µg/g dry weight for copper and 300–1,800 µg/g dry weight for iron with an iron index of 1.0.^{3,4} However, because of its invasive nature, many experts do not agree on the use of liver biopsy as a means of diagnosing either Wilson's disease or hereditary hemochromatosis.^{4,5}

The association of Wilson's disease and genetic hemochromatosis in the same patient is rare and has only been described twice.⁵ The onset of complications associated with hemochromatosis before the age of 40 is exceedingly rare. Both hemochromatosis and Wilson's disease should be suspected in all patients presenting with unexplained chronic liver disease.⁵ Although liver dysfunction is common in both conditions, hepatocellular carcinoma is extremely rare in patients with Wilson's disease in comparison to those with hereditary hemochromatosis.^{6,7} This may be secondary to the reduced life expectancy in untreated Wilson's disease patients, which means less time for the development of a carcinoma.⁷ However, with improved survival associated with Wilson's disease in western countries, this incidence may increase.

Chelation therapy can be highly efficacious in preventing manifestations of Wilson's disease.⁹ In the case of hereditary hemochromatosis, however, it is important to permit therapeutic phlebotomy to commence before the onset of complications.¹⁰ Therapy for iron overload consists of phlebotomy and chelating agents such as deferoxamine which increase iron excretion in the urine and bile.⁸ Likewise, in case of copper overload, the treatment includes penicillamine, which increases the urinary copper excretion, and zinc, which decreases the absorption of copper in the gastrointestinal tract and increases the excretion in the stool.⁸ In patients with liver failure secondary to the aforementioned metabolic diseases, liver transplantation has improved survival and prognostic outcomes.⁴ However, similar to treatment of Wilson's disease and hereditary hemochromatosis, early diagnosis of the two disorders is key to successful outcome of transplantation surgery.^{4,10}

The existence of both diseases in the same patient warrants dietary consultation, considering the fact that excess copper and iron content can be induced by excessive dietary input.^{5,9} The coexistence of both diseases should not be confused with iron overload in patients with Wilson's disease, a condition that has been described in male patients with the disease.¹⁰

CONCLUSION

Though this patient had the laboratory and genetic data that fit with hereditary hemochromatosis, his young age made his clinical presentation less likely a function of hemochromatosis. In an effort to reveal the probable causes of his hepatic damage, alternative diagnoses were sought and Wilson's disease was ultimately diagnosed. Wilson's disease and hereditary hemochromatosis both involve inherent flaws in the transportation of heavy metals and their accumulation in hepatocytes. Although both arise from distinctly different genetic mutations, the coincidence of the two primary disorders can, in rare cases, occur.

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