

## Case Report

# HEREDITARY HEMOCHROMATOSIS: A RARE DISEASE IN IRAN

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**Hereditary hemochromatosis is a common cause of chronic liver disease in western countries. No report of this disease has appeared from Iran and the few studies which have focused on chronic liver disease have failed to identify a single case of hemochromatosis. In this report, we present the first case of hereditary hemochromatosis during our 25 years of gastroenterology practice in Iran.**

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**Keywords:** Hemochromatosis • hereditary • Iran • liver disease

## Introduction

**H**ereditary hemochromatosis (HH) is a disease in which the body cannot handle iron properly and results in a state of severe iron overload. It is inherited as an autosomal recessive trait and is very common among Caucasians (1 in 400 individuals are homozygote and 1 in 10 – 20 are heterozygote).<sup>1, 2</sup> The frequency varies widely between populations. The defective gene, identified as the HFE gene, is on the short arm of chromosome 6 and the two major HFE mutations are H63D and C282Y.<sup>1, 2</sup> The iron overload affects multiple organs resulting in organ failure if not treated appropriately. This disease is commonly reported from western countries. In Iran, secondary hemochromatosis is not uncommon and is usually seen in patients with thalassemias, but in our 25 years of experience in gastroenterology practice, we have not encountered a single case of proven HH and, to the best of our knowledge, there are no published case reports of HH from Iran. Wilson's disease (WD), a genetic

defect in copper metabolism, is not uncommon in Iran.<sup>3, 4</sup> In one multicenter study performed in 6 referral centers in two cities in Iran over a period of 10 years, 84 cases of WD, but no cases of hemochromatosis, were found.<sup>3</sup> In two other studies on 439 and 191 cases of chronic liver disease, no cases of hemochromatosis were identified either.<sup>4, 5</sup> The frequency of C282Y mutations is also very low in Iran.<sup>6</sup> Even the few cases reported with homozygous H63D mutation did not have any abnormality in iron metabolism.<sup>7</sup>

## Case Report

A 43-year-old gentleman from Ardabil was referred with abnormal liver function tests. During the prior year, he had been treated for heart failure with a progressive and refractory course. He was diagnosed as having refractory cardiomyopathy. He was also being treated with insulin for diabetes mellitus since 8 months prior to referral.

On physical examination, the patient had tachycardia, a darkly-pigmented skin, lower extremity edema, fine rales in the base of his lungs, hepatosplenomegaly, and ascites. Hemoglobin electrophoresis was reported to be normal. Laboratory findings on presentation are shown in Table 1. Echocardiography showed severe left ventricular dysfunction with an ejection fraction of 15%. An upper GI endoscopy performed 4 months earlier revealed two rows of grade I esophageal

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**Table 1.** Laboratory data.

AST*	122 IU/L	WBC	5600/cmm
ALT*	88 IU/L	Hgb	15.2 g/dL
ALP**	879 IU/L	Plat	133000/cmm
T.Bil	2 mg/dL	FBS	523 mg/dL
D.Bil	0.5 mg/dL	Cr	1.3 mg/dL
HBs Ag	Negative	T.Prot	6 g/dL
HCV Ab	Negative	Alb	3.2 g/dL
		PT	19

\* Normal = < 40 IU/L; \*\* Normal = 80 – 306 IU/L.

varices. Abdominal CT scan and MRI of the liver are shown in Figures 1 and 2, respectively.

HH was suspected and serum iron, total iron-binding capacity (TIBC), and ferritin were measured. The results were:

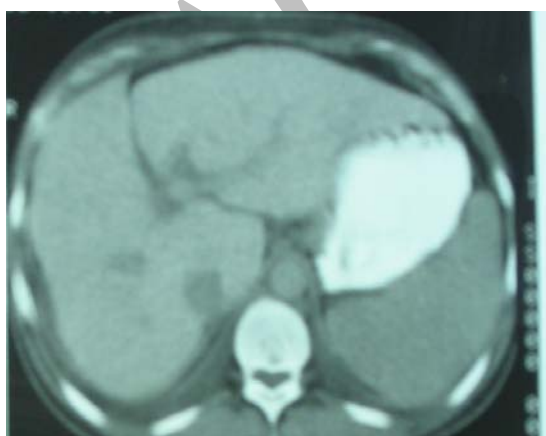
Serum iron: 190 µg/dL (normal: 65 – 170); TIBC: 259 µg/dL (normal: 230 – 440); ferritin: 2444 ng/mL (normal: 32 – 501); and transferrin saturation: 72%.

Genetic testing failed to demonstrate the H63D or C282Y mutation.

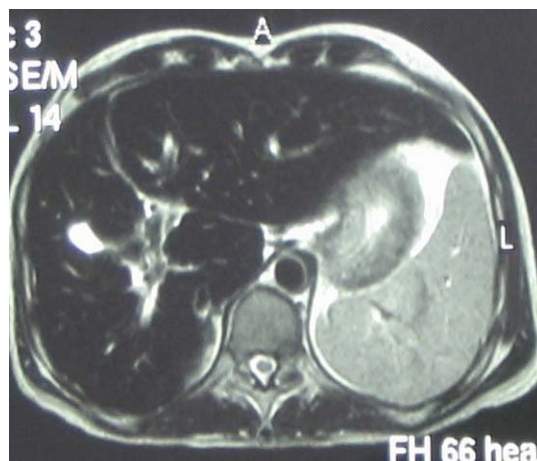
Low-volume phlebotomy (because of severe heart failure) was initiated with 250 mL every two weeks. After three months, the ferritin level decreased to below 1000 ng/mL and the patient's general condition improved dramatically. The left ventricular ejection fraction rose to 45% and the patient's dyspnea almost disappeared.

## Discussion

The diagnosis of iron overload can be made using a variety of methods.<sup>7</sup> The most sensitive method of diagnosis is to measure the iron content of a liver biopsy sample. Identifying mutations in the C282Y and H63D genes is also helpful.<sup>7</sup> Another method frequently used for screening



**Figure 1.** Abdominal CT scan showing high attenuation of the liver as compared with the spleen. Mild ascites is also noted.



**Figure 2.** MRI of the upper abdomen (T1-weighted) showing dark hypointense liver with normal-looking splenic texture.

purposes is transferrin saturation. Values above 50% are reported to be 98% specific for C282Y homozygosity in Caucasians. Radiologic techniques, especially MRI, are very helpful in diagnosing hemochromatosis. The dark hypointense appearance of the liver in T1-weighted MRI is quite characteristic (Figure 2). Clinical response to iron depletion is also occasionally used to confirm the diagnosis.

Due to the risks associated with liver biopsy in a cirrhotic patient with a prolonged prothrombin time, liver biopsy was not performed and the hepatic iron content is not available. Nevertheless, considering the clinical and laboratory findings available, the diagnosis of hemochromatosis appears to be secure.

Although conditions such as hemolytic anemia, multiple transfusions, alcoholic liver disease, nonalcoholic steatohepatitis, porphyria cutanea tarda, and chronic HCV infection can also lead to iron overload, none of these applies to the patient in this case report. A normal CBC, especially a hemoglobin of 15.2 g/dL, normal hemoglobin electrophoresis, and the T1-weighted MRI finding of normal splenic texture along with a classic hypointense liver image, are adequate evidence to exclude secondary hemochromatosis. Therefore, we can safely assume that our patient has HH.

HH occurs worldwide<sup>9–11</sup>; in Europe it is endemic and occurs with a prevalence close to 1 per 200 population. Looking at PubMed, EMBASE, and Persian journals, we did not encounter any report of HH from Iran, and we assume that our patient is the first case of HH in Iran.

In this patient, we did not find the classic H63D

or C282Y mutation. Thus, it's quite possible that with such a different epidemiology in Iran, other mutations may be involved. Mutations other than H63D or C282Y have been described in the literature.<sup>1</sup> These include mutations in transferring receptors, ferroportin, hepcidin, and others. None have been extensively studied and all are only rarely reported.

Therefore, maintaining a high index of suspicion for HH in clinical practice is recommended in order not to miss this treatable chronic debilitating disease in Iran.

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