Hereditary Hemochromatosis: Gastrointestinal Features

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Hemochromatosis is a disease defined by iron overload. Hereditary hemochromatosis is an autosomal recessive disease with a prevalence of 2 per 1,000 in those of European ancestry. It most commonly presents with liver disease but can also affect many other organ systems [1].

Gastrointestinal symptoms often include [1]:

- Abdominal pain
- Symptoms related to complications of cirrhosis and portal hypertension
- Hepatomegaly
- Cirrhosis/end-stage liver disease with portal hypertension
  - Ascites/fluid retention
  - Esophageal/rectal varices
  - Portal hypertensive gastropathy
  - Hemorrhagic diathesis
  - Hepatic encephalopathy
- Diabetes mellitus/"bronze diabetes"
- Cardiomyopathy
- Impotence from hypogonadotropic hypogonadism due to pituitary involvement
- Development of hepatocellular carcinoma
- Elevated aminotransferase levels

The pathogenesis is based on genetic mutations that affect transport of iron. The most common involve HFE, a regulator of hepcidin, the major serum signaling protein [2–4]

- Autosomal recessive
- Mutation of *HFE* gene
  - Homozygous at *C282Y* (80% of cases have mutations at this locus)
  - Compound heterozygote mutation of *C282Y* and *H63D* plus another risk factor for iron overload
  - Homozygous H63D not clinically significant for development of iron overload
  - Leads to inappropriately high levels of iron absorption and deposition in the liver and other organs

The pathology of iron overload of the liver can show [1]:

- Liver biopsy (see Fig. 71.1)
  - Two to 4+ or more hepatocellular iron stores on staining with higher density in the periportal area
  - Severe iron storage shows 4+ staining with fibrosis
  - Hepatic iron index of 1.9 μmol/g/year
  - Hepatic iron concentration of >71 μmol/g/dry weight

The diagnosis is made with [1]:

- Transferrin saturation >45%
- Elevated ferritin
- C282Y and H63D mutation genetic testing
- Abnormal liver enzymes
- Hepatomegaly
- Liver biopsy
- Hepatic magnetic resonance imaging

The differential diagnosis of hemochromatosis should include [1]:

- Secondary iron overload
  - Sideroblastic anemia
  - Thalassemia major
  - Sickle cell anemia
  - Excess alcohol consumption
  - Parenteral iron overload from transfusions
- Nonalcoholic steatohepatitis

The treatment involves removal of iron and reduction of iron body stores [1]:

- Phlebotomy to remove excess iron stores performed weekly until
  - Ferritin is <50 ng/mL
  - Transferrin iron saturation <50%

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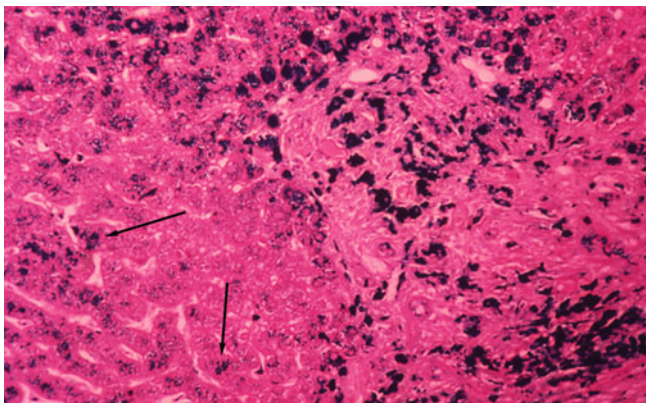

Fig. 71.1 A photomicrograph of a liver biopsy specimen stained with Prussian Blue showing iron overload liver parenchymal (hepatocytes) (*arrows*) typical of hemochromatosis. In addition, because of heavy overload, there is also iron present in epithelium of bile educts, Kupffer cells, and stroma of portal areas (High-power magnification)

- Chelation with deferoxamine, deferasirox, or deferiprone, if anemia and iron overload are present concomitantly
- Avoidance of vitamin C, which enhances iron toxicity
- Liver transplant; screen for hepatocellular carcinoma if cirrhosis is present

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