10-MINUTE CONSULTATION

Haemochromatosis

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BMJ 2008;336:506

doi:10.1136/bmj.39357.698889.94

A 45 year old man presents with gradually increasing fatigue and joint pains. Physical examination is unremarkable, and results of basic laboratory tests are normal except for high concentrations of hepatic transaminase. Should he be evaluated for haemochromatosis?

What you should cover

What is haemochromatosis?

Hereditary haemochromatosis (HH) is an iron overload disorder that is most commonly due to mutations in the HFE gene. Healthy adults typically have 35 mg/kg (women) to 45 mg/kg (men) total body iron. Normally the 1-2 mg of iron lost daily through sweating and sloughing of epithelium is balanced by duodenal iron absorption. Mutation of the HFE gene (genetic HH) can increase duodenal absorption of iron, leading to iron overload (biochemical HH) and organ damage (clinical HH).

Who gets it?

The predominant HFE mutation is C282Y. About 0.4% of people of white, northern European ancestry are homozygous for C282Y, and 75% of these people will develop iron overload. A smaller percentage will develop liver disease (30% of men and 7% of women) or diabetes (2-5%). People who are heterozygous for C282Y do not have a greater risk of clinical HH. Over 85% of patients with clinical HH are homozygous for C282Y. Clinical HH is 2-10 times more common in men than in women.

What are the signs, symptoms, and sequelae?

Early iron overload from biochemical HH is usually asymptomatic, but chronic iron overload can damage several organ systems, resulting in clinical HH. Organ damage may include hepatic cirrhosis and hepatocellular carcinoma; dilated cardiomyopathy or cardiac conduction disturbances; diabetes; hypogonadism; non-inflammatory osteoarthritis; and skin bronzing. Although nearly half of all biochemical HH is diagnosed by laboratory tests, common presenting symptoms that may lead to clinical diagnosis of HH include fatigue, arthralgia, and loss of libido.

How do you diagnose hereditary haemochromatosis?

Diagnosis requires clinical suspicion, biochemical testing, and genetic confirmation. Liver enzymes, transferrin saturation, and ferritin concentration should be measured. If the transferrin saturation and ferritin concentration are high, genetic testing for mutations of the HFE gene is warranted. A patient who is homozygous for C282Y and has elevated transferrin saturation and ferritin has confirmed clinical HH.

What you should do

- Take a thorough history and physical examination whenever a patient has unexplained fatigue, arthralgias, loss of libido, or atypical cardiac disease or diabetes. Does the patient show weight loss, enlarged liver, arthritis, heart failure or dysrhythmias, hypogonadism, hypothyroidism, or abnormal skin pigmentation? Has he a family history of haemochromatosis?
- If clinical evaluation is unrevealing, measure his transferrin saturation and his hepatic transaminase and ferritin concentrations. If his transferrin saturation is >45% and the ferritin concentration is high (>300 µg/l in men or >200 µg/l in women), or if he has a first degree relative with HH, then you should order genetic testing for mutations of the HFE gene or refer him to a gastroenterologist for such testing.
- A patient who is homozygous for C282Y, aged <40 years, and has a ferritin concentration <1000 µg/l should be treated with regular phlebotomy. This will reduce iron concentrations and prevent the long term consequences of HH.
- In patients with asymptomatic iron overload, other reasonable measures would include electrocardiography and chest radiography to screen for cardiac involvement and a fasting blood sugar test for diabetes. Any abnormalities apparent from history taking or examination (weight loss, arthritis, hypogonadism, or hypothyroidism) should be evaluated.
- Any patient who is aged ≥40, has a ferritin concentration >1000 µg/l, or has a raised hepatic transaminase concentration should be referred for liver biopsy to evaluate for cirrhosis.
- A patient who is not homozygous for C282Y or does not have elevated transferrin saturation and ferritin concentration should be referred to a gastroenterologist for investigation of other causes of liver disease or iron overload, such as porphyria, sideroblastic anaemia, or viral or alcoholic hepatitis.

Competing interests: None declared.

Provenance and peer review: Not commissioned; externally peer reviewed.

This is part of a series of occasional articles on common problems in primary care. The BMJ welcomes contributions from GPs.

Useful reading

Clinical reviews

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