Hereditary Haemochromatosis

Background

- Hereditary Haemochromatosis (HH – also Genetic Haemochromatosis or HFE-related Haemochromatosis) can usually be diagnosed via a blood test
- 1 in 200 Caucasians are homozygous for C282Y mutation in the HFE gene
- 'Homozygotes' may have normal iron indices, biochemical iron loading only, symptoms and/or organ damage
- Expression depends on age, gender, other iron losses, alcohol use

Symptoms/signs

- Typical symptoms include fatigue, arthralgia and loss of libido
- Typical signs: hepatomegaly, pigmentation, arthropathy (hips, knees, ankles, 2^{nd} / 3^{rd} metacarpophalangeal joints and base of thumbs)
- Diabetes can be a feature but more commonly now is unrelated type 2 DM

Investigating suspected haemochromatosis

- Consider iron indices in asymptomatic ALT elevation and/or clinical suspicion
- If raised ferritin and transferrin saturation (fasting ideally), send an EDTA sample for 'simple HFE genotyping' to Molecular Genetics
- Modest hyperferritinaemia with normal tf sat common, usually fatty liver related, improves with lifestyle changes – see ferritin pathway (GP guidance)
- Genotypes compatible with HH: C282Y/C282Y (homozygous – 90% of HH) or C282Y/H63D (compound heterozygote = milder form)
- If homozygous then family screening as below

When does the Hepatologist need to see them?

- Happy to provide advice for all new cases of HH or unexplained high ferritin
- Should see all HH with ferritin > 1000 mcg/l or raised ALT as risk of fibrosis
- To coordinate Venesection or blood donation (latter is preferable for those with normal presenting ferritin and who are otherwise, and those who require maintenance phlebotomy)

Family screening (C282Y homozygous primarily)

- Can refer to Clinical Genetics Department
- Siblings should have HFE / iron indices sent
- Children only need testing in adulthood - alternatively test other parent to see if carrier (90% chance of not being and children therefore carriers only)
- Parents if young or symptoms suggestive of HH

Treatment

- HH genotype + ferritin in normal range: can monitor initially 1-3 yearly (less frequent if female, compound heterozygote, stable indices), advise blood donation especially for homozygotes
- C282Y/C282Y + raised ferritin: therapeutic venesection
- C282Y/H63D + raised ferritin: blood donation/lifestyle, refer if >1000 mcg/l
- Non-HH iron overload – venesection if significant (secondary care decision)

Useful info: Haemochromatosis UK www.haemochromatosis.org.uk

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