South West Strategic Clinical Network
Somerset, Wiltshire, Avon and Gloucestershire (SWAG) Cancer Services

Raised Ferritin

Background

- 3-4g total body iron, 70% in red cells, 10-20% stored in ferritin (10% as transferrin, myoglobin, cytochrome, serum iron).
- 1-2mg lost daily from mucosal cells, but equal amount absorbed daily from diet (about 10% of total normal dietary intake).
- Ferritin binds and sequesters intracellular iron (~4500 atoms/molecule).
- Ferritin is an acute phase protein. It can also be released from cytolysis of hepatocytes such as in liver disease.
- High serum ferritin is found in a large spectrum of conditions which may or may not represent iron overload.

Table 1 Common causes of a raised ferritin

Disorder	Iron overload	Transferrin saturation
Hereditary haemochromatosis Iron loading anaemias* Transfusion related	yes	high
Advanced cirrhosis Wilson's disease	yes	high
Inflammation Infection Malignancy Metabolic syndrome Chronic hepatitis	no	low/ normal

* beta thalassemia, congenital sideroblastic/dyserythropoietic anaemia. Characterised by high levels of ineffective erythropoiesis.

Investigations

1) Important points to consider in the history include:
   - intercurrent infection
   - inflammatory/ autoimmune features
   - symptoms suggestive of underlying malignancy
   - alcohol history, other risk factors for liver disease
   - symptoms suggestive of haemochromatosis as listed above

2) Caution is needed in interpreting ferritin if patient acutely unwell. Please repeat when well with CRP, LFTs (including GGT) and a blood film. Consider autoimmune profile if clinically appropriate.

3) Look at FBC parameters and consider any features of ineffective haematopoiesis (anaemia, low MCV, film changes).

4) If obvious evidence of excessive alcohol, advise reduction in intake and repeat ferritin, GGT after 2-3 months.

5) If deranged LFTs consider ordering liver screen (including viral hepatitis serology, autoimmune profile, caeruloplasmin and USS liver) and referral to gastroenterology/hepatology team.

6) If persistently raised ferritin suggest ***fasting*** iron studies should be performed. If raised transferrin saturations present (parameters above) **only** then perform HFE gene mutation status.

7) Referral to clinical haematology is warranted if relevant HFE mutations found (listed below) confirming hereditary haemochromatosis or if iron loading anaemia suspected.

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Hereditary Haemochromatosis (HH)summary

- Genetic condition characterised by dysregulation of iron absorption
- Type 1 (accounting for >90% of all HH) associated with HFE gene mutation
- 2 mutations in HFE seen, C282Y and H63D. 1 in 8 of caucasians are carriers for C282Y, 1 in 4 carriers for H63D
- 85% of cases are due to C282Y homozygosity (high penetrance). The remainder are due to C282Y/H63D heterozygosity (10-15%) and H63D homozygosity (low penetrance)
- Clinical features include asthenia, arthralgia (esp if 2nd & 3rd MCP), pigmentation, diabetes ("bronzed diabetic"), sexual dysfunction, liver dysfunction, neurological/psychiatric disturbance and cardiomyopathy
- Laboratory diagnosis includes ferritin >300 in males or >200 in post menopausal females, ***fasting*** transferrin saturations >55% in males or >50% in females and HFE mutation present
- Treatment involves therapeutic venesection to aim for ferritin <50. Pharmacological iron chelation can be considered if venesection cannot be tolerated
- Patients in can donate blood to NHSBT when they are stablisied
- Dietary advice to reduce/abstain from alcohol and red meat (includes fortified cereals as well as Vitamin C supplements)
- Family members of affected individuals should be tested

References

British Committee for Standards in Haematology Guidelines. Genetic Haemochromatosis. 2000. http://www.bcshguidelines.com/documents/haemochromotosis_2000.pdf