Guidelines for referring patients with abnormal liver function tests

1. Isolated rise in total bilirubin (TB) alone
2. Isolated rise in gamma glutamyl transpeptidase (GGT) alone
3. Isolated rise in aspartate transaminase (AST) alone
4. Isolated rise in alkaline phosphatase (AP) alone
5. Rise in GGT and AP with or without a rise in TB
6. Rise in GGT and AST with or without a rise in TB
7. Rise in all four parameters

1. Isolated rise in TB

...is almost always due to Gilberts disease or haemolysis. Bilirubin should always be fractionated

a) A rise in unconjugated fraction may be due to haemolysis and is suggested by relevant history, raised reticulocyte count and positive coomb's test. If there is haemolysis, patient is referred to the haematologist. If haemolysis is ruled out the diagnosis is Gilberts disease. It is an innocuous condition characterised by a deficiency of the enzymes needed to conjugate bilirubin in the liver. Patient should be reassured and no further tests are needed. They may become jaundiced when the body is stressed with illness or during fasting.

b) A rise in conjugated bilirubin alone is rare, but calls for Ultra sound abdomen and hospital referral as it may be caused by CBD stones.

2. Isolated rise in GGT

...is caused by:

a) Alcohol abuse. This is a common cause. If history is corroborative, nothing need be done, except for advice on abstinence.

b) Fatty Liver or non-alcoholic steatohepatosis (NASH). This is especially common in middle-aged overweight women. Causes include diabetes mellitus hyperlipidemia and obesity. They will need testing for fasting lipids, fasting glucose and an Ultrasound abdomen. The latter may corroborate the diagnosis. Appropriate treatment is instituted for diabetes and hyperlipidemia. Referral to dietician is needed. Hospital referral is indicated only if GGT is above 150.
c) Drugs acting as enzyme-inducers also frequently raise GGT in isolation. They include Phenytoin, Carbamazepine and Barbiturates etc. If patient is on other drugs, a check through BNF is advised or contact your pharmacist.

3. Isolated rise in AST alone

...is very uncommon in liver disease and usually points to a cardiac or skeletal muscle origin. Cardiac and skeletal muscle enzymes should be checked and the patient referred to the GI clinic only if no other cause can be found.

4. Isolated rise in AP

...is nearly always non-hepatic. A bony origin should be suspected. Rise in AP is common in growing children. Paget’s disease is a common cause in the elderly, but metastasis should also be considered and the patient tested for calcium, phosphate, proteins and ESR.

5. Rise in GGT and AP

...is usually due to fatty liver. The differential diagnosis is wide and includes alcohol, gallstones, drugs neoplasia and cholestatic forms of various infective, metabolic and immunological liver disorders. Do U/S abdomen, hepatitis serology (including Epstein-Barr virus), ferritin, auto antibodies for liver disease, immunoglobulins, ESR and refer to the GI clinic.

6. Rise in GGT and AST

...strongly points to alcohol abuse. But if there is no history of alcohol abuse, do liver disease screen as above and refer.

7. Rise in GGT, AP and AST

...with or without a rise in bilirubin entails prompt consideration. Do U/S abdomen (plus liver disease screen if no structural cause found on scan), and refer urgently.

Lastly a few observations regarding these guidelines.

- A rise in AP alone or AST alone is not in keeping with liver disease. (but … in pregnancy and certain situations …)
- Rise in TB, AP, GGT and AST always prompts early referral.
- Fluctuating rises in liver enzymes suggest alcohol abuse or gall stones. There is also a theoretical possibility of necrosing periampullary carcinoma.

References

- Jo Hull-Davies: last updated Dec 2006