ABNORMAL LIVER FUNCTION TESTS; A CLINICAL PERSPECTIVE

Jossi Aldridge

Objectives

- Gain an overview of the common patterns of abnormal LFTs.
- Develop a general approach to how to manage these patients.
- Explore factors on history and examination which point towards a likely diagnosis.
- Non-invasive liver screen.
- Clinical examples

WHAT ARE THE LIVER FUNCTION TESTS?

Liver function tests

- **Alanine Transferase**
- **Alkaline phosphatase**
- **Bilirubin**
- **Gamma GT**
- Aspartate Transaminase

- Platelet count
- Prothrombin time
- Urea
- Albumin
- Sodium
- Hb + MCV

One group indicate active pathology

- Ie there is ongoing/recent inflammation, obstruction etc.
- Ratios and combinations suggest aetiology.
- In simplest terms:
  - **Alanine Transferase –** inflammation/hepatocyte injury
    - ALT>1000 due to AIH, Drugs (paracetamol), Viruses (HAV, HBV) or ischaemia. (These causes can present with lower ALT rises but are the main causes of such an extreme elevation)
  - **Alkaline phosphatase -** obstruction
  - **Bilirubin –** often raised in obstruction and can indicate more severe damage in inflammation.
  - **Gamma GT –** often raised in obstruction. Also isolated raise with alcohol use.
  - **Aspartate Transaminase** – raised in inflammation. If AST>ALT this suggests alcoholic hepatitis.

- *NB As with all liver pathology, LFT interpretation is not done in isolation.*

The second group indicate synthetic function

- These can indicate severity (ie acute liver failure) and/or chronicity
  - In acute setting they can denote acute liver failure (PT, albumin)
  - In end stage cirrhosis, pt may have relatively normal ALT/Alk phos etc as there is little liver left to produce the elevations but the synthetic function is markedly impaired (Plt, Na, Albumin, PT, Hb, MCV).
- Platelet count – low (reduced synthesis and increased phagocytosis in splenomegaly)
- Prothrombin time – prolonged (NB patients are actually procoagulant but the prolonged PT is a marker of severe acute and chronic damage)
- Urea – reduced synthesis in chronic liver disease therefore supportive of cirrhosis. NB can be elevated in acute bleeds (varices)
- Albumin – reduced synthesis in chronic liver disease
- Sodium – hyponatraemia in advanced cirrhosis especially with ascites and portal hypertension. Poor prognosis.
- Hb + MCV – anaemia of chronic disease and blood loss.

CLINICAL HISTORY

What questions do you want to ask these patients?

Useful information from the history

- Sx: jaundice, pruritis, weight loss, abdominal distension, pain, duration
- Travel
- Any known liver disease ie previous diagnosis?
- Any FHx liver disease

History continued: Risk factors

- IVDU/Cocaine
- Tattoos
- From UK?
- Blood Tx/operations
- Occupational exposure
- Sexual Hx
- EtOH
- T2DM
- Hypercholesterolaemia
- BMI
- Drugs
- Herbal remedies

NON-INVASIVE LIVER SCREEN

Causes of abnormal LFTs

NILS

- Viral
  - Hep A/B/C/E (D)
  - EBV/CMV
- Autoimmune
  - Immunoglobulins
  - SMA, LKM, ANA
  - AMA
  - ANCA
- Genetic
  - A1AT
  - Iron studies
  - Caeruloplasmin
- Misc
  - Glucose
  - Cholesterol
  - TFTs
  - Coeliac serology
  - AFP

HBV serology

Serology	Result	Interpretation
HBsAg HBcAb HBsAb	-ve -ve -ve	At risk for infection (Vaccinate)
HBsAg HBcAb HBsAb	+ve +ve -ve (NB. IgM+ in acute)	Active HBV
HBsAg HBcAb HBsAb	-ve +ve +ve	Previous infection (cleared)
HBsAg HBcAb HBsAb	-ve +ve -ve	Resolved infection (distant > acute) Occult infection
HBV DNA	Numerical value	Active HBV Level guides treatment

The less complicated viruses

- HCV
  - HCV Ab+: Patient has or has had HCV. Indicates need for PCR.
  - PCR+: Active HCV
  - Genotyping: prognostic implications.
- HAV Ab+/PCR+: Acute HAV (in the right clinical context)
- HEV Ab+/PCR+: Acute HEV
- EBV Ab+: Current or previous EBV infection
  - Further testing depending on context
- CMV Ab+: Current or previous CMV infection
  - Further testing depending on context

Genetic

- Genetic testing for Alpha1 anti-trypsin deficiency
- Caeruloplasmin:
  - A screening tool for Wilsons disease:
    - Caeruloplasmin low
    - May then do urinary copper excretion which is elevated.
- Iron studies:
  - A screening tool for hereditary haemochromatosis:
    - Ferritin increased+ (Usually >1000. NB is an acute phase protein)
    - Transferrin saturation +
    - Serum iron +

Autoimmune

- Autoimmune hepatitis:
  - Raised IgG
  - Positive ANA/SMA/LKM Abs
- Primary Sclerosing Cholangitis
  - Positive pANCA
- Primary biliary cholangitis
  - Positive AMA Ab

MISCELLANEOUS

- NAFLD
  - Glucose -DM
  - Cholesterol - metabolic syndrome
- TFTs
  - LFTs can be abnormal in both hyper and hypothyroidism.
- Coeliac serology
  - LFTs can be abnormal in Coeliac disease
- AFP
  - Don’t forget HCC

CLINICAL EXAMPLES

MR. A.
Hepatology clinic referral

- Dear Doctor, please see this 46 year old man with abnormal LFTs found incidentally on review for a flu like illness. No history of excess alcohol

- ALT 134
- Alk phos 121
- Albumin 40
- Bilirubin 26
- GGT 90
- FBC N, Coag N, U+Es N

Mr A continued

- All very unexciting then….

- ‘My mum died of something with her liver’
- ‘She had to go and have blood taken out regularly’

- Ferritin 2500
- Transferrin saturation 62%
- HFE genotyping: homozygous for hereditary haemochromatosis

- Regular venesection
- Genetic counselling re family

Diagnosis

- Haemachromatosis

Mrs B Hepatology clinic referral

- Dear Doctor please see this 36y lady. She has had a recent pregnancy during which she suffered obstetric cholestasis but unlike her previous pregnancy her LFTs have remained abnormal after delivery. She has no significant alcohol history and no risk factors for viral hepatitis.

- ALT 98
- Alk Phos 87
- Bilirubin 39
- GGT 103
- Albumin 35

FBC N

Coag N

U+Es N

Mrs B cont

- Attended with husband (policeman).
- No risk factors on history
- Examination NAD
- Very anxious about chances of this happening again in subsequent pregnancies.

- NILS: HCV Ab positive – can be non specific
- HCV: PCR positive
- Brought in for consultant review in clinic
- Referred to Leeds for further treatment

Diagnosis

- Hepatitis C Virus

Miss C - Urgent Clinic referral (Psych)

- Please see this young lady with SCZ who had a baby in 4 months ago. She is on a number of antipsychotics and under specialist care. Her medication has been amended after bloods showed abnormal LFTs persistently. Please see urgently and advise.

- ALT 36
- Alk Phos 218
- Bilirubin 27
- Albumin 26
- FBC N

Na 130

Urea 4

Coag N

Miss C continued

- No IVDU
- EtOH 14units/week since delivery (and return home)
- No other RFs
- No Sx
- Examination NAD

- On review of bloods – abnormalities dated back to Feb 2015 before which they were normal.
- No changes to meds for at least 2 years
- Ideas?

Miss C cont

- Normal pregnancy
- Repeat LFTs normal
- Had had a CT scan post-partum due to obstetric complications – Liver NAD
- No need for NILS
- D/C with reassurance

Diagnosis

- Normal pregnancy

Mrs D

- Please see this lady found to have abnormal LFTS on bloods taken for abdominal pain. USS: fatty liver.

- ALT 86
- Alk phos 121
- Bili 23
- Albumin 41
- U+Es N
- FBC N
- PT N

Nil on history

O/E BMI 65

USS: fatty liver

Diagnosis?

Mrs D continued

- Most likely NAFLD due to BMI
- NILS
- Advised aggressive weight loss through diet and exercise (patient reluctant for bariatric surgery)
- Explanation
- NAFLD fibrosis score – risk categorise

Diagnosis

- NAFLD

Mrs E

- Please see this lady urgently. Bloods for flu-like illness showed ALT 2310, bili 39, alk phos 230, Albumin 32. (Remaining FBC, PT, U+Es NAD). Discussed with gastro SpR – advised acute hepatitis screen and referral.

- Bloods as above
- No RFs, Examination NAD

- Thoughts?

Mrs E cont

- Acute hepatitis E
- Remainder of NILS NAD
- Repeat LFTs normal
- GP notified diagnosis appropriately – no cause identified
- Self limiting in the majority – resolves spontaneously in 6/12
- COOK YOUR PORK!

Diagnosis

- Hepatitis E Virus

Mr F

- Please review this young man with a recent history of ulcerative colitis known to the IBD team. Noted to have persistently abnormal LFTs
- ALT 68
- Alk phos 334
- Bili 36
- Albumin 33
- U+Es N
- Hb 11
- Plt 446
- PT N

Nil else on history

Nil O/E

Thoughts?

Mr F continued

- NILS: pANCA positive
- Likely Primary sclerosing cholangitis
- For liver Bx

Diagnosis

- Primary Sclerosing cholangitis

Mrs G

Please see this patient with abnormal LFTs.

ALT 63

Alk phos 256

Bili 37

Albumin 29

Hb 9.8

MCV 101

Plt 78

Na 127

Urea 2.4

PT 13.2

Mrs G continued

- Lovely well presented lady attending with husband
- History:
  - EtOH 70 units EtOH/week (wine with meals, more when on cruises)
  - No other risk factors
  - O/E palmar erythema, spider naevi,
- Likely ALD with cirrhosis
- Mx: NILS, USS, OGD, Complete abstinence, HCC surveillance

Diagnosis

- ALD with cirrhosis

Miss H

Please see this 16 year old girl found to have abnormal LFTs on Ix for amenorrhoea

ALT 83

Alk phos 256

Bili 37

Albumin 29

Hb 9.8

MCV 101

Plt 78

Na 127

Urea 2.4

PT 13.2

Miss H cont

- Nil on history
- Nil on examination

- Thoughts?

- Bloods extremely concerning for cirrhosis but no obvious cause. ? Genetic ? AI most likely
- NILS negative
- USS – cirrhosis
- Plan – consultant review to discuss findings and need for Bx. Referred to Leeds for further Investigation and Mx.

Diagnosis

- Cirrhosis ? Cause