Abnormal Liver Tests

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Talk Outline

• Understanding Liver Tests

• Examples of Liver Diseases

• Case Studies
Blood Tests for the Liver

• LFTs = Liver Function tests
  – Hepatocyte damage (ALT, AST)
  – Cholestasis (ALP, GGT, BR)
  – Synthetic function (albumin, protein)
Limitations of Liver Enzymes

• With **acute** disease, enzymes are useful to track liver disease on a day to day basis
  
  *But don’t correlate with disease severity or prognosis*

• With **chronic** disease, liver enzymes are **not** useful in assessing the severity or progression of liver disease

• There are **extrahepatic** causes of abnormal liver enzymes
Signs of liver dysfunction

- **Examination** – palmar erythema, spider naevi, small liver, big spleen, ascites, hepatic encephalopathy
- **Imaging** – nodular liver edge, portal hypertension
- **Endoscopy** – varices, hypertensive gastropathy
Real Liver Function Tests

• Synthetic function (prothrombin time, large molecules)
• Measures of portal hypertension (platelet count)
• Measures of excretion (bile acids, dye clearance tests)
• Measures of functional reserve (breath tests, lignocaine conversion)
Avoid saying “Liver Function Tests”

Use “Liver tests” or “Liver enzymes” instead
The enzymes

- **Alanine Aminotransferase (ALT)**
  - Hepatocytes
  - Longer half life than AST

- **Aspartate Aminotransferase (AST)**
  - Hepatocytes, cardiac muscle, skeletal muscle, kidney, brain, pancreas, lung, blood cells

- ALT and AST > 1000 = *ischaemic hepatitis, viral hepatitis, paracetamol*
- AST > ALT = *alcohol, drugs, cirrhosis*
The enzymes

• **Alkaline phosphatase (ALP)**
  – Group of enzymes (isoenzymes can be measured)
  – Biliary epithelium, bone, placenta, kidneys, gut

• **Gamma-Glutamyl Transpeptidase (GGT)**
  – Liver and other viscera
  – Main role is to help interpret ALP

- ALP >> GGT = *bone disease, pregnancy*
- GGT >> ALP = *alcohol, medications*
Bilirubin

• *With* elevated liver enzymes: reflective of liver disease or biliary obstruction

• *Without* elevated liver enzymes:
  – Haemolysis
  – Gilbert’s syndrome
  – Severe liver disease
Approach to Abnormal Liver Tests

- Decide on the pattern
- Assess liver function
- Old liver tests
- Imaging
- Ask about:
  - **New** – pain, systemic illness, viral
  - **Old** – viral, autoimmune, metabolic
  - **Always** – alcohol, medications, toxins, risks for viral hepatitis
Acute abnormalities

With abdominal pain
  • Gall stones
Without abdominal pain
  • Viral hepatitis
  • Medications and Toxins

With systemic illness
  • Ischaemic hepatitis
  • Cholestasis of sepsis
Choledocholithiasis

- Biliary pain
- Initially – elevated ALT and AST. Rapid fall
- Later – elevated ALP and GGT and almost always bilirubin
- Rapid rise and fall
- Confirm with
  - US or CT
  - CT cholangiogram, MRCP, EUS, ERCP
Acute Viral Hepatitis

• Hepatitis A (also E, EBV, CMV, sometimes C)
• Mild – Moderate symptoms
• ALT > 1000
• Jaundice peaks after ALT does
• Confirm with antibody against virus (IgM first then IgG which persists)
Acute on Chronic Viral Hepatitis

• Hepatitis B +/- D (NOT hepatitis C)
• Elevated ALT, sometimes > 1000
• Jaundice and coagulopathy are signs of severity
• Confirm with HBV sAg positive, HBV cIgG positive, HBV cIgM positive
Acute Alcoholic hepatitis

• An acute liver complication of alcohol toxicity
• Elevated AST > ALT with BR and INR.
• Doesn’t have to follow a binge
• Tender hepatomegaly, low grade fever
• Discriminant function calculated from BR and PT and predicts prognosis
• Even with steroids, recovery is very slow.
Paracetamol

Toxicity is:
Possible
>150mg/kg or 8g

Likely
>250mg/kg or 12g

Almost certain
>350mg/kg or 16g

*Single dose*
Paracetamol Toxicity

- Initially: nausea and normal liver tests *but need to start NAC now*
- Next few days: RUQ symptom and elevated AST and ALT > 1000. Raised BR, PT, creat and acidosis are poor prognostic signs.
- Later that week: Liver failure, multiorgan failure
- Biochemical recovery takes weeks
Drug Induced Liver Injury (DILI)

- 10% of all adverse drug reactions
- Most frequent reason for medications being withdrawn from the marketplace
- Highly variable presentation
- BR > 50 with ALT >100 has mortality of 10%
Drug Induced Liver Injury (DILI)

- Timing can be misleading
- Can be extrahepatic manifestations
  - Fever, rash, eosinophilia (eg penicillin hypersensitivity)
  - EBV like syndrome (eg sulfonamides, phenytoin)
Some of the Drugs

- **Cholestatic** – clavulanate, carbamazepine, chlorpromazine, ezetemibe, erythromycin, ketoconazole, rifampicin, rosiglitazone, Bactrim, steroids, oestrogen

- **Hepatocellular** – phenytoin, isoniazid, diclofenac
Some of the Drugs

- **Steatosis** – HIV drugs, amiodarone, valproate
- **Bland fibrosis** – methotrexate
- **Vascular** – OCP, azathioprine
- **Granulomatous hepatitis** – allopurinol, carbemazepine, cepahlexin, amiodarone,
- **Neoplasia** – OCP, anabolic steroids
Ischaemic Hepatitis

• Impairment of liver perfusion
• Portal vein > hepatic artery
• Clinical context usually obvious (shock, hypoxia)
• Sudden rapid rise in AST and ALT. Jaundice modest and late, ALP usually normal. LDH very very high
• If underlying cause treated, AST falls very quickly (halves every day)
Cholestasis of Sepsis

- Extrahepatic infection – cytokine mediated liver damage
- Modest rise in ALP/GGT, mild rise in ALT/AST, variable rise in BR (conjugated)
- Parallel’s course of illness
- Exclude antibiotics and cholangitis
Chronic abnormalities

**Hepatocellular** (ALT >5XULN, ALP <2X ULN)
- Viral
- Autoimmune

**Cholestastatic** (ALP>5XULN, ALT<2XULN)
- Obstruction
- Infiltration

**Variable / Mixed**
- Fatty liver disease
- Medications
Chronic Viral Hepatitis

• Hepatitis B and C
  – Elevation of ALT and AST. Other normal.
  – B fluctuates, C is stable
  – Confirm with HBV sAg and HCV Ab (+/- HCV RNA)
  – Ask about risk factors but test anyway
Autoimmune hepatitis

• Elevated ALT and AST. Rarely >1000. Fluctuate.
• Often other autoimmune diseases
• Confirm with serology (ANA, ASMA, Anti LKM Ab) then usually with liver biopsy.

• Elevated BR and ALP can indicate “overlap syndrome”
Extrahepatic Bile Duct Obstruction

- Elevated BR and ALP/GGT
- When painless – think malignancy (pancreas, GB, cholangiocarcinoma, ampulla)
- The higher the BR the more likely a malignant cause
- Confirm with imaging (CT better than US if malignancy suspected, US best for screening)
- The longer the BR took to rise, the slower it will fall once bile duct drained
Intrahepatic Biliary Obstruction

• **Primary Biliary ‘Cirrhosis’**
  – Middle aged women
  – Elevated ALP, rarely BR
  – Confirm with AMA. Biopsy not usually necessary

• **Primary Sclerosing Cholangitis**
  – Usually associated with IBD
  – Elevated ALP and sometime BR if there are dominant strictures
  – US, CT and biopsy can be normal
  – Confirm with cholangiogram (MRCP, ERCP)
Infiltration

- Elevated ALP/GGT with less impressive BR
- Causes include malignancy, granulomatous inflammation, abscess, TB, sarcoid,
- CT with contrast best initial test although US can detect multiple smaller lesions better sometimes
Fatty Liver Disease (NAFLD)

- Associated with metabolic syndrome
- Commonest Western liver disease
- Elevated ALT > AST, sometimes ALP
- Confirm with imaging (US)
- Hard to distinguish from steatohepatitis (NASH) from bland steatosis without a biopsy
Clinical Examples
Case 1

- Elderly man
- Painless jaundice
- HT, DM, CKD

- BR 328 ↑↑↑
- ALT 111 ↑
- AST 139 ↑
- ALP 739 ↑↑↑
- GGT 314 ↑↑

- INR/plt Normal
- Albumin low
Case 1

- Old liver tests:
  - BR / ALT / AST normal
  - ALP 200-450 for > 3 years
  - GGT 200-400 for > 3 years
Case 1

- CT (non con) = Normal biliary tree. Strandling around CBD.
- US = CBD 5mm. Diffuse liver process. Gall stone. Splenomegalgy.
- ERCP
Case 1

- pANCA 1:80
- Brief fever with GNR in BC
- Ascites
- Further info – biliary stricture dilated at ERCP years before

- Diagnosis = Primary Sclerosing Cholangitis with cirrhosis
Case 2

- 65 year old male
- Otherwise well
- 4 weeks of high fevers, altered bowel habits, hiccups
- Cultures negative
- Antibiotics no help

- BR 11
- ALT 30
- AST 84 \[^{\uparrow}^{\downarrow}^{\downarrow}^{\downarrow}\]
- ALP 820 \[^{\uparrow\uparrow\uparrow}\]
- GGT 468 \[^{\uparrow\uparrow\uparrow}\]

- INR normal
- Plt high
- Alb low
Case 2

- Old liver tests normal
- CT = a few sclerotic boney lesions. Liver and bile ducts normal
- Bone Scan = normal
Case 2

- Developed tender hepatomegaly
- US = possible diffuse process
- Repeat CT = no focal lesions
- Became coagulopathic, tachycardic

- Liver biopsy – multiple lesions seen – adenocarcinoma
- **Diagnosis = liver infiltration by cancer**
- Died 2 days later
Case 3

- 58 year old male
- Background of gout, hereditary spherocytosis, alcohol
- Severe epigastric and chest pain
- Cardiac investigations normal

- BR 75  ↑↑
- ALT 34
- AST 30
- ALP 86
- GGT 83  ↑

- Alb, INR, plt normal
Case 3

• US = single gall stone. Normal CBD

• Old liver tests
  – BR 50-80
  – ALT/AST/ALP/GGT mildly abnormal at times
Case 3

- Reticulocyte count high
- LDH high
- Haptoglobin low

- Diagnosis = jaundice due to haemolysis (and a painful gall stone)
Case 4

- 59 year old female
- Previous well
- Severe epigastric pain
- US = gall stone. N CBD
- Booked for elective cholecystectomy
- Liver tests - normal
Case 4

- Represents with nausea 1 month later
- US = gall stone in gall bladder. Normal CBD

- BR 174 ↑↑
- ALT 234 ↑↑
- AST 201 ↑↑
- ALP 789 ↑↑↑
- GGT 735 ↑↑↑

- Alb, INR, plt normal
Case 4

• Further history
  – Recent sinusitis
  – Prescribed Augmentum
  – Eosinophils 0.9 (<0.6)

• Diagnosis = Augmentum induced cholestasis

• Progress
  – BR 174 → 190 → 157 → → 12
Case 5

- 42 year old man
- Excessive alcohol
- Noticed by a drinking buddy to be jaundiced
- Lower grade fever

- BR 420 ↑↑↑
- ALT 48
- AST 217 ↑↑
- ALP 192 ↑
- GGT 96 ↑
- INR 2.3 ↑↑
- Albumin 18 ↓↓
- Platelets 87 ↓↓
Case 5

- Old liver tests – elevated GGT but otherwise normal
- US = normal CBD. Portal HT

- Diagnosis = acute alcoholic hepatitis complicating cirrhosis
- Progress – stabilised briefly with prednisone, then deteriorated and died
Case 6

- 49 year old female
- Healthy
- Routine bloods

- BR 13
- ALT 381 ↑↑
- AST 184 ↑↑
- ALP 64
- GGT 14

- Alb, INR, plt normal
Case 6

• Old liver tests
  – Infrequent
  – BR / ALP / GGT – normal
  – ALT and AST fluctuate from normal to 300s

• Caucasian, never used drugs
• Autoimmune markers negative
• No medications
Case 6

- HCV Ab negative
- HBV sAg positive
eAg positive
HBV DNA log 7.7
- Liver biopsy – cirrhosis
- **Diagnosis = chronic hepatitis B with cirrhosis**
- Progress – commenced on entecavir, liver tests and DNA normalised
Case 7

- 27 year old female
- Substance abuse issues
- G7 P6
- Now ?23 weeks
- Fevers and malaise

- BR 81 ↑↑
- ALT 4017 ↑↑↑
- AST 3466 ↑↑↑
- ALP 161 ↑
- GGT 45

- INR 1.6
- Alb low
- Plt normal
Case 7

• Old liver tests
  – Normal
• Liver US normal
• Baby US ≥24 weeks

• Transferred to Sydney
Case 7

- HCV Ab positive (was negative 2006)
- HCV RNA positive
- HAV / HBV / autoimmune markers negative

- Diagnosis = acute hepatitis C

- Settled. Baby OK.
Case 8

- 53 year old female
- Recent bowel and ovarian cancer
- 30g alcohol per day
- Polyarthritis

- BR 15
- ALT 743 \(\uparrow\uparrow\)
- AST 417 \(\uparrow\uparrow\)
- ALP 68
- GGT 42

- Globulins 54 \(\uparrow\)
- Alb, INR, plt normal
Case 8

- Old liver tests
  - BR normal
  - ALT 200-700
  - AST 100-400
  - ALP <200
  - GGT <200

- US normal
Case 8

- ANA 1280
- dsDNA 10 (<7)
- ENA negative
- ANCA 80 (MPO and PR3 negative)
- SMA 640 – t subtype
- LKM Ab negative

- Liver biopsy – chronic active hepatitis, mild fibrosis
- Diagnosis = type 1 autoimmune hepatitis
- Settled with prednisone and azathioprine
Case 9

- 88 year old lady
- Severe abdo pain
- Fever
- Previously normal LFTs
- US = bile duct dilation

- BR 78
- ALT 68
- AST 65
- ALP 357
- GGT 350
Approach to Abnormal Liver Tests

• Decide on the pattern
• Assess liver function
• Old liver tests
• Imaging
• Ask about:
  - **New** – pain, systemic illness, viral
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  - **Always** – alcohol, medications, toxins, risks for viral hepatitis