Interpretation of Abnormal Liver Injury Tests

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Clinical manifestations of liver disease:
- Fatigue, anorexia, malaise, weight loss, fevers, fetor hepaticus, spider angiomata, palmar erythema, jaundice, pruritis, xanthomas, testicular atrophy, gynecomastia, RUQ pain, GI bleeding, ascites, hepatosplenomegaly, encephalopathy

Liver Injury Tests:
- Aminotransferases (AST/ALT)
- Alkaline Phosphatase
- Gammaglutamly Transpeptidase (GGTP)
- Bilirubin
- Total Protein/Albumin/Globulin
- Prothrombin Time (INR)
Interpretation of Abnormal Liver Injury Tests

- Liver Injury Tests commonly used as Liver Function Tests (LFT's)
- Not a direct measure of liver function
- May be abnormal in the healthy liver
- May be normal in the diseased liver (cirrhosis)

Abnormal Liver Injury Tests

- Air Force Recruit Study
  - 99/19877 (0.5%) had abnormal LIT's
    - 12/99 had a specific cause found
    - 87/99 had no specific diagnosis

Interpretation of Abnormal Liver Injury Tests

- Epidemiology of Abnormal LIT's:
  - 249 blood donors with abnormal LIT's
    - Alcoholic liver disease, NAFLD (NASH), HCV
    - 2%-8% had no specific diagnosis
Interpretation of Abnormal Liver Injury Tests

- Epidemiology of Abnormal LIT's:
  - Liver Biopsy Studies
    - 81/1124 biopsies in abnormal LIT's
    - 84% has steatosis/steatohepatitis
    - 6 had fibrosis/cirrhosis
    - 8 had normal histology

- European Study
  - 151 pts. With abnormal LIT's > 6 months had a liver biopsy performed
    - Chronic HCV – 15.3%
    - NASH (NAFLD) – 45%
    - Chronic hepatitis – 24%
    - AIH/PBC – 1.5%
    - Alpha-1 antitrypsin deficiency – 0.7%

- In the majority of patients, non-invasive testing will suggest the diagnosis
- In the majority of patients, the diagnoses will be: alcoholic liver disease, steatosis, steatohepatitis
- Most of these study were done before the HCV testing era
Interpretation of Abnormal Liver Injury Tests

- Evaluation of the pt. with abnormal LIT's:
  - Detailed history
  - Accurate physical examination
  - Laboratory testing
  - Pattern of the abnormal LIT's
  - Isolated hyperbilirubinemia??

Interpretation of Abnormal Liver Injury Tests

- History
  - Medication (prescription/OTC's/illicit drugs/herbal preparations)
  - ETOH use (CAGE questions where indicated)
  - Blood transfusions?/tattoos?/travel?
  - Occupation, past/present
  - Family history

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- Physical Examination:
  - Stigmata of chronic liver disease
  - Muscle wasting/testicular atrophy
  - Hepato-splenomegaly
  - Pleural effusions
  - Ascites
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- Patterns of abnormal LIT’s:
  - Hepatocellular: AST/ALT (levels/ratio)
  - Cholestatic: Alkaline Phosphatase, GGT, Direct Bilirubin
  - Mixed

Liver enzymes:
- ALT: cytosol (liver, muscle)
- AST: cytosol/mitochondria (liver, heart, skeletal muscle, blood cells)
- Alk. Phos: microvilli of bile canaliculus (bone, intestine, kidney, placenta)
- GGTP: membrane of cells (liver, kidney, pancreas, intestine, prostate)

Interpretation of Liver Injury Tests

- Hepatocellular causes of abnormal LIT’s:
  - Chronic viral hepatitis
  - Hemochromatosis, Wilson’s, alpha-1 antitrypsin deficiency
  - Autoimmune hepatitis
  - Celiac Disease
  - NAFLD/steatohepatitis
  - ETOH related liver diseases
Interpretation of Liver Injury Tests

- Non-hepatic causes of abnormal LIT’s:
  - Hemolysis
  - Myopathies
  - Thyroid disease
  - Strenuous exercise

Interpretation of Abnormal Liver Injury Tests

- Viral Hepatitis:
  - HBV/HCV positive serology
  - Viral load can be determined (copies/ml)
  - AST/ALT >1000 IU/l indicates acute hepatitis or acute toxicity such as acetaminophen
  - AST/ALT >2000 IU/l –fulminant failure
  - AST/ALT may be normal in advanced cirrhosis

Interpretation of Abnormal Liver Injury Tests

- Cholestatic causes of abnormal LIT’s:
  - PBC/PSC
  - Drugs
  - Viral hepatitis
  - Extra-hepatic biliary obstruction
  - Infiltrative liver disease (high AP)
  - TPN
  - Familial cholestasis
Interpretation of Abnormal Liver Injury Tests

- Cholestatic LIT’s in Biliary Obstruction:
  - AST/ALT - 1-5x nl
  - Alk. Phos. - 2-20x nl
  - Bilirubin – 1-30x nl
  - Pro-time (INR) – prolonged

- Role of Liver Biopsy:
  - Diagnostic and prognostic information
  - Safe as an out-patient procedure
  - Complications – 0.1% - 0.3%
    - Bleeding/pneumothorax/bile peritonitis
  - Mortality: 9/100,000
  - Transjugular biopsy

- Frequently encountered clinical problems:
  - Asymptomatic ALT/AST elevation
    - common problem, frequently sent from screened blood donors
    - elevation of bilirubin and AP increases likelihood of liver disease
  - Far East/Egypt/Africa: HBV, schisto, malaria
  - USA: CAH, steatosis, ETOH, drugs, metabolic
Interpretation of Abnormal Liver Injury Tests

- Approach to pt with asymptomatic elevation of aminotransferases:
  - Evaluation guided by clinical history, physical examination, and pattern of LIT’s
  - Focus on medication (OTC/Rx), ETOH use, occupational exposure, risk factors for hepatitis, family history of liver disease
  - Focus on treatable etiologies: viral, Cu, Fe

- Cholestatic liver disease:
  - Differentiating intra vs extra hepatic cholestasis can be difficult at times.
  - Medical vs surgical cholestasis can be difficult to differentiate from routine biochemical tests and clinical history/physical examination
  - Indirect tests: CT, US
  - Direct tests: ERCP, PTC, Liver biopsy

- Isolated hyperbilirubinemia
  - Unconjugated:
    - Gilbert’s syndrome
    - Hemolysis
  - Conjugated:
    - Dubin-Johnson syndrome
    - Rotor syndrome
  - Extra-hepatic causes
Interpretation of Abnormal Liver Injury Tests

Summary:
- Take a *detailed* history that includes all risks for hepatic disease.
- Perform an *accurate* physical examination
- Order appropriate laboratory
- Perform indicated imaging studies
- Consider liver biopsy if definitive diagnosis cannot be established from non-invasive testing