Elevated Liver Tests and Common Liver Diseases

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OBJECTIVES

- To define blood tests that evaluate liver/biliary tract injury
- To identify measures of liver function
- Review PSC images
MEASURES OF LIVER CELL INJURY

- AST (SGOT)
- ALT (SGPT)
- Alkaline phosphatase
- Gamma-glutamyltransferase
ASPARTATE AMINOTRANSFERASE (AST)

- formerly known as serum glutamic oxaloacetic transaminase (SGOT)
- enzyme found in hepatocytes
- marker of liver cell injury – when cells are lysed open
- also found in cardiac muscle, brain, pancreas, and kidney cells
ALANINE AMINO-TRANSFERASE (ALT)

- formerly known as serum glutamic pyruvic transaminase (SGPT)
- enzyme found exclusively in hepatocytes
- marker of liver cell injury
ALKALINE PHOSPHATASE
(alk phos)

- enzyme found on the hepatocyte membrane bordering bile canaliculi (the smallest branches of the bile ducts)
- widely distributed throughout tissue including liver, bone, intestine, kidney, placenta, leukocytes, various neoplasms
- most useful in detecting cholestasis
- may be increased in bone disorders, pregnancy, chronic renal failure, malignancy
- can be fractionated to determine source – liver, bone, intestine
GAMMA-GLUTAMYL-TRANSFERASE (GGT)

- similar to alkaline phosphatase
- found in kidney, spleen, heart, lung, brain
- etiologies include MI, neuromuscular disease, pancreatic disease, pulmonary disease, diabetes, ingestion of ethanol
- may be used to corroborate liver origin when elevated in setting of elevated alk phos
MEASURES OF HEPATIC SYNTHETIC FUNCTION

- Prothrombin time
- Albumin
PROTHROMBIN TIME (PT)

- measures proteins produced by the liver which are involved in clotting of blood
- dependent on Vitamin K intake, absorption, and production
- elevated PT may be due to malnutrition, malabsorption, antibiotics, medications, disseminated intravascular coagulation, liver disease
ALBUMIN

- quantitatively the most important protein synthesized by the liver
- regulated by changes in nutritional status, osmotic pressure, systemic inflammation, thyroid and glucocorticoid hormones
MEASURES OF CLEARANCE OF METABOLITES

- Liver is strategically placed to remove toxins from the blood.
- Function may be compromised due to loss of parenchymal cells, obstruction of bile flow, impaired cellular uptake, reduced hepatic blood flow.
MEASURES OF CLEARANCE OF METABOLITES

- Bilirubin
- Ammonia
BILIRUBIN

- derived primarily from the degradation of hemoglobin released from RBCs
- primarily conjugated hyperbilirubinemia (direct) is more typical for patients with hepatocellular dysfunction or cholestasis
- unconjugated hyperbilirubinemia (indirect) results from either increased bilirubin production (hemolysis) or from inherited or acquired defects in hepatic uptake or conjugation (Gilbert’s phenomenon)
AMMONIA

- potentially toxic substance produced by colonic bacteria
- absorbed into portal circulation, removed by the liver, metabolized and secreted by the kidneys
- rises in the setting of severe liver disease or portosystemic shunting
- used to confirm hepatic encephalopathy
screening of healthy, asymptomatic individuals reveals that 6 to 25% of people will have abnormal liver tests

often one time elevations

prevalence of liver disease in general population is significantly lower
TERMINOLOGY

- Hepatitis: inflammation of the liver
**TERMINOLOGY**

- **Cirrhosis:**
  - Permanent scarring of the liver
  - Associated with a spectrum of clinical manifestations
  - May be asymptomatic
GROSS IMAGE OF A NORMAL AND A CIRRHOTIC LIVER

Normal

Cirrhosis

Irregular surface

Nodules
Complications of cirrhosis

» **Esophageal varices:**
  - 20% of patients with esophageal varices will bleed
  - Each bleeding episode carries a 20-30% mortality rate
  - Patients who have had one bleed are likely to have a recurrence
  - Can be treated with variceal banding, sclerotherapy, shunts, or liver transplantation.
  - May be prophylactically treated with beta blockers or serial bandings.
Varices Increase in Diameter Progressively

Merli et al. J Hepatol 2003;38:266
THE NORMAL LIVER OFFERS ALMOST NO RESISTANCE TO FLOW
Cirrhotic Liver

**Distorted sinusoidal architecture leads to increased resistance**

- **Portal vein**
- **Portal systemic collaterals**
- **Splenomegaly**
Complications of cirrhosis

**Splenomegaly:**
- Portal hypertension leads to congestion of spleen, usually asymptomatic. May lead to hypersplenism with thrombocytopenia, leukopenia, and anemia.
- Splenectomy not indicated.

**Collateral vessels:**
- Due to increased resistance in the liver - portal blood seeks alternative routes to get to the heart.
- The most important collaterals are esophagogastric varices.
- Collaterals may be seen on ultrasound or CT scan.
Complications of cirrhosis

» ascites:
  – due to sodium retention by kidney in response to vasodilatation. Hypoalbuminemia exacerbates fluid retention.
  – Treated with sodium restriction and diuretics.

» portal systemic encephalopathy:
  – disturbances range from subtle mental status changes to coma.
  – associated with an elevation of serum ammonia.
  – Predisposing factors include gastrointestinal bleed, infection, and electrolyte abnormalities.
Hepatic Encephalopathy
Precipitants

- Excess Protein
- GI Bleeding
- Sedatives/Hypnotics
- TIPS
- Temperature
- Infections
- Diuretics
Cholestatic Disease

- predominantly affect the biliary system
- alkaline phosphatase is most important marker
Primary Sclerosing Cholangitis

Definition

- Chronic cholestatic liver disease
- Unknown etiology, frequently associated with IBD
- Diffuse inflammation and fibrosis of the biliary tree
- Leads to biliary cirrhosis and portal hypertension
Diagnosis - Cholangiography

- ERCP most commonly used
- Percutaneous cholangiography infrequently used
- Magnetic resonance cholangiography
  - non-invasive
  - no radiation
  - cost-effective
Classic Case of PSC
Comparison of ERC and MRC
Small-Duct PSC

- 5% of PSC
- Normal cholangiogram but biopsy showing PSC
- Can progress to classic PSC
- May exist with or without colitis