Hepatitis

Better yet, how to answer those questions on the test about the liver…

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Overview

- Liver function tests and liver enzymes
- Properties and pearls about enzymes
- Acute and chronic hepatitis
- Specific types of hepatitis (and other liver problems you may see on the test)
- Review questions

Liver Enzymes

- Liver enzymes
  - SGOT/AST
  - SGPT/ALT
  - Alkaline phosphatase
  - GGT
  - Bilirubin

Strictly speaking liver "function" tests refer to PT/INR and albumin. Why???
Liver “functions”

- Just a few things made by the liver...
  - All the coagulation factors except vWVIII
  - Albumin
  - Fibrinogen
  - Haptoglobin
  - Alpha-1 anti-trypsin
  - Ceruloplasmin
  - Transferrin

Liver also involved in protein, carbohydrate and fat metabolism as well as drug metabolism

How to look at liver enzymes

Need to decide which of 2 broad categories that the patient fits into…

Hepatocellular injury
Cholestasis or obstruction

Hepatocellular Injury

- Mostly has elevation of SGOT and SGPT

- Alkaline phosphatase and bilirubin may be up also, but to a lesser degree
Cholestasis or Obstruction

- Mostly gives elevation of bilirubin and alkaline phosphatase
- Transaminases often elevated but to a lesser degree

Alkaline Phosphatase

- Sources bone and liver
- Source also placenta in 3rd trimester
- Elevation usually suggests cholestasis, but can be up a bit with hepatocellular injury
- If elevated may check GGT to help pinpoint source since GGT not produced by bone.

GGT

- GGT mostly used to tell if elevated alk phos is from liver or bone.
- If alk phos phos high but GGT normal it suggests the source of the alk phos is bone since GGT not produced in bone
- Many things cause high GGT however…alcohol use and abuse, liver disease, DM, MI, CHF, and drugs such as phenobarbital and dilantin
- GGT is the most sensitive enzyme to detect liver damage from alcohol use
SGOT and SGPT

SGOT
- source heart, liver, skeletal muscle, kidney

SGPT
- source liver, heart, skeletal muscle
- absolute amount in muscle < SGOT
- more specific for liver damage than SGOT

Ratio of SGOT/SGPT

- Normally SGOT/SGPT is around 0.8
- SGOT/SGPT greater than 2:1 is highly suggestive of alcoholic hepatitis

Transaminases over 1000

1. Viral hepatitis
2. Ischemic or shock liver
3. Toxins such as acetaminophen, mushrooms
4. Rarely, there is a fourth cause which can occur with passage of a gallstone and a very abrupt rise and drop of the transaminases
Watch out for Rhabdomyolysis!

- Patients with rhabdomyolysis can have markedly elevated CPKs...
- This skeletal muscle injury therefore will also have very high SGOTs and SGPTs
- Don’t be fooled...if a patient has very high SGOT and SGPT but normal bilirubin and alkaline phosphatase think about rhabdomyolysis and order a CPK

Acute or Chronic

- Acute hepatitis less than 6 months
- Chronic hepatitis longer than 6 months
- Some conditions cause acute which can develop into chronic hepatitis

Hepatitis

- Refers to broad category of conditions caused by a variety of illnesses or injuries
- All tend to have in common
  - Hepatocellular necrosis
  - Inflammatory cell infiltration of the liver
  - Remember that hepatocellular necrosis or injury translates primarily into an elevation of the serum transaminases
Causes of Acute Hepatitis

- Viruses (A,B,C,D,E,EBV,CMV)
- Alcohol
- Toxins (amanita phalloides, carbon tet)
- Drugs

Alcoholic Hepatitis

- Can be acute or chronic
- #1 precursor of cirrhosis in the USA
- Risk of cirrhosis variable…genetics, sex (women more susceptible,) presence of chronic hepatitis, possibly nutritional factor
- Presentation can range from an asymptomatic person to a critically ill one

Alcoholic Hepatitis

- Typical is a patient who has been drinking heavily, has anorexia and nausea, has tender hepatomegaly and jaundice, possibly fever
- SGOT rarely over 300s
- Ratio SGOT/SGPT>2
- Alk phos rarely more than 3 times normal
- Bilirubin level quite variable depending on severity…can be 10 or higher
- PT/INR also may be elevated
- Differential includes cholecystitis, cholelithiasis
Drug induced Liver Disease
4 subtypes

- Direct hepatotoxic group
- Idiosyncratic reactions
- Cholestatic reactions
- Acute and chronic hepatitis

Direct hepatotoxic Group
- Could happen to all of us!
- Dose related severity
- Latent period after exposure

Examples… acetaminophen, alcohol, carbon tetrachloride, niacin, vitamin A

Idiosyncratic Reactions
- Sporadic and rare
- Not dose related
- Occasionally fever and eosinophilia suggesting an allergic type reaction

Examples… seizure meds, INH and PZA, methyldopa, quinidine, ketoconazole, halothane
Cholestatic Reactions

- Non-inflammatory (direct effect on bile secretion) ... examples estrogens, anabolic steroids, azathioprine
- Inflammatory (portal areas with cholangitis) often with allergic features ... examples erythromycin, ampicillin-clavulanic and semi-synthetic penicillins, chlorpropamide

Chronic Hepatitis

- Viral ... B, C, D
- Autoimmune hepatitis
- Drug related ... methyldopa, amiodarone, nitrofurantoin, INH
- Genetic and Metabolic disorders ... Wilson's disease, alpha-1 antitrypsin deficiency, nonalcoholic steatohepatitis (NASH)

Autoimmune Hepatitis

- Generally affects young females (less often post-menopausal)
- ANA and anti-smooth muscle antibodies each present in 70%
- Hypergammaglobulinemia
- Extrahepatic manifestations are clues ... amenorrhea, thyroiditis, acne, Sjogrens, arthritis, Coomb-positive hemolytic anemia, nephritis
- Old name was Lupoid Hepatitis
Treatment of Autoimmune Hepatitis
- Prednisone +/- azathioprine
- Watch for improvement in transaminases
- Cirrhosis will not reverse (remember that anything that causes cirrhosis will put patient at risk for hepatoma)
- May require transplant

Wilson's Disease
- Autosomal recessive, chromosome 13 but over 190 different mutations identified
- males=females
- Ages 10-30
- Excess absorption CU by small intestine and decreased excretion by the liver
- Excess deposition of copper is mainly in the liver, brain, cornea and kidney

Wilson's Disease Clinical Presentation
- Liver disease in adolescents (abnormal liver enzymes to cirrhosis and portal HTN) Half present this way.
- Neuropsychiatric disease in young adults (tremors, movement disorders, bulbar dysfunction, behavior and personality changes)
- Kayser-Fleischer rings (pathognomonic)
- Renal disorders (calculi, RTA)
Diagnosing Wilson’s Disease

- Low serum ceruloplasmin
- High 24 hour urinary copper level
- High hepatic copper concentration
- Kayser-Fleischer rings

Treatment of Wilson’s Disease

- Early treatment important before excess Cu can cause damage (cirrhosis)
- Restrict dietary Cu (shellfish, organ foods, legumes)
- DOC is oral penicillamine if symptomatic
- Oral Zinc for maintenance after chelation, of first line if presymptomatic or pregnant

Alpha-1 Antitrypsin Deficiency

- Patients with homozygous deficiency may develop emphysema as adults.
- About 10% of homozygous patients develop neonatal hepatitis which can progress to cirrhosis
- In adults the most common manifestation is asymptomatic which may progress and develop hepatocellular carcinoma
Alpha-1 Antitrypsin

- Can draw serum levels of alpha-1 antitrypsin
- Biopsy will show hepatocytes that contain globules that are Periodic-Acid Schiff positive

Nonalcoholic Steatohepatitis

- Classically an asymptomatic patient with chronic mild transaminase elevations in the absence of viral hepatitis, drug hepatotoxicity or alcohol use.
- Classically middle aged women
- Often seen with DM, obesity, high lipids
- Cause unclear, possibly nutritional
- Large-droplet steatosis and inflammation on biopsy that resembles alcoholic hepatitis

NASH continued

- Course usually benign, a few may progress to cirrhosis and liver transplant
- No specific treatment exists
- Focus on control of DM, weight loss, and treatment of lipid disorder
Two more things you’d better know for the test that aren’t hepatitis

- Hemochromatosis
- Primary Biliary Cirrhosis

Hemochromatosis

- Most common autosomal recessive disease in the USA, chromosome 6
- 10% caucasians are heterozygous
- Accumulation and deposition of iron in liver, skin, pancreas, heart, pituitary, testes, and joints
- Often presents age 40-50 in males, females later

Hemochromatosis

- Liver…mildly abnormal liver tests, eventually cirrhosis
- Skin pigmentation…slate-gray or brown
- Pancreas…glucose intolerance, diabetes
- Joints…arthralgias, especially 2nd and 3rd MCP joints
- Restrictive cardiomyopathy +/- CHF
- Amenorrhea, impotence
Diagnosing hemochromatosis
- Lab clues may be lacking. Early may have normal liver enzymes.
- Transferrin saturation >50% highly specific
- Ferritin often elevated but not specific
- Ultimately will need liver biopsy
- Treatment is phlebotomy, chelation if unable

Primary Biliary Cirrhosis
- Chronic cholestatic disease that destroys intrahepatic bile ducts
- Classically middle aged women who present with pruritus and fatigue
- Disease may have been present for years asymptotically
- Exam may show HSM, xanthomas
- Jaundice and portal HTN are late

PBC continued
- Liver studies reflect cholestasis
- Mostly elevated alkaline phosphatase and cholesterol, later bilirubin
- 95% have Anti Mitochondrial Antibodies
- Elevated serum IgM levels
- Treat with ursodeoxycholic acid, possibly MTX
- Many need liver transplantation
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