Liver Diseases

disclosure

- none

Alcoholic Liver disease

- Risk Factors for Alcoholic Liver Disease
  - Amount of alcohol consumed
  - Duration of alcohol consumption
  - Gender
  - Viral hepatitis
  - Nutrition
  - Iron overload
  - Genetics

3 Types of Liver Damage

1.Fatty Liver

2. Alcoholic hepatitis

3. Cirrhosis

Alcoholic Hepatitis

- Typically seen in malnourished patients
- Frequently precipitated by a period of binge drinking
- Prodrome: (2-3 weeks)
  - Anorexia
  - Nausea
  - Fatigue
  - Weight loss

Alcoholic Hepatitis

- Persistence of Alc. Hep. is associated with relentless progression to cirrhosis over months to years.
- Complications can be identical to those of cirrhosis.
- Poor prognostic signs:
  - Advanced age, jaundice, azotemia, and coagulopathy.

Alcoholic Hepatitis

- Clinical manifestations
  - Hepatomegaly, mild fever, jaundice
  - More severe cases: ascites, encephalopathy
- Lab
  - Increased AST&ALT→not more than 10x normal
  - Increased AST/ALT ratio (2-3:1)
  - Decreased albumin
  - Prolonged PT

Alcoholic hepatitis-treatment

- Abstinence
- Bed rest
- Nutrition
- +/- steroids

Liver question

- What is most commonly used to assess the prognosis of patients with alcoholic hepatitis?

Answer: Maddrey discriminant function analysis

- Discriminant function= 4.6(prothrombin time-control) + serum bilirubin (mg/dL)
- Discriminant function >32 effectively identifies patients whose risk of death is higher than 50%
  - Consider steroids

Nonalcoholic Fatty Liver Disease

- Clinical
  - Nonalcoholic (<20g alcohol/day)
  - Exclusion of viral, autoimmune, genetic, and drug-induced liver disease.
- . Nonalcoholic Steatohepatitis (NASH)
  - Chronic inflammatory condition in people who don’t have significant alcohol history.
    - *Characteristics: steatosis, hepatocellular necrosis, and inflammation.*

Nonalcoholic Fatty Liver Disease

- clinical manifestations
  - Central obesity (apple shaped not pear-shaped)
    - Abd. Obesity (waist >40” in men and 34.5” for women)
  - NIDDM
  - +/- hyperlipidemia
  - Most patients are asymptomatic
  - Occasional RUQ discomfort, malaise, fatigue
  - Hepatomegaly→ 75% of patients

Nonalcoholic Fatty Liver Disease

- Lab
  - Elevated aminotransferase (<300UI/L)
  - AST/ALT ratio <1
  - Mild elevation alkaline phosphatase and GGTP

Nonalcoholic Fatty Liver Disease

- Diagnosis
  - Findings of fatty infiltrate on imaging studies.
  - Exclusion of other liver diseases by history, physical, and serology.
  - Alcohol consumption should be <40g/week.
  - Liver biopsy is the definitive method of diagnosis. Not indicated in asymptomatic patients with normal AST, ALT.

Nonalcoholic Fatty Liver Disease

- Histologic finding
  - Steatosis-macrovasicular mild to severe
  - Inflammation
  - Hepatocyte injury– focal necrosis and ballooning
  - Hepatocyte degeneration– mallory hyaline
  - Fibrosis– varying degree

Nonalcoholic Fatty Liver Disease

- Management
  - Directed at associated risk factors.
  - Gradual weight loss.
  - Control of hyperglycemia and hyperlipidemia.
  - Discontinue suspected meds.
  - Alcohol use <20g/day. Alcohol abstinence if significant fibrosis
  - HAV and HBV vaccination
  - Avoid drugs that may promote steatohepatitis (amiodarone,tamoxifen)

Viral Hepatitis

Hepatitis B

A DNA virus.

- Risks in US: sexual promiscuity and IVDA
  - Many immigrants likely contracted at birth or young childhood
- Prevention:
  - Hep B immune globulin should be given to household and sexual contacts of patients with acute hepatitis B.
  - Infants and previously unvaccinated should receive hep B vaccine.

Hep B Serologic Markers

1.HBsAG	1.Current infection
2. Anti-HBs	2.Immunity (immunization or resolved infection)
3. IgM anti-HBc	3. Recent infection, occasionally reactivation
4. IgG anti-HBc	4. Remote infection
5.HBeAg and/or HBV DNA>105 viral copies/mL	5. Active viral replication

Interpretation of Hep B serologic panel- examples

- HBsAg +
- Anti-HBc +
- IgM anti-HBc +
- Anti-HBs -

Acutely infected

- HBsAg +
- Anti-HBc +
- IgM anti-HBc -
- Anti-HBs -

Chronically infected

Hep B

- Treatment –when?
  - If pt at increased risk of progression:
    - LFTs >2x normal,
    - active viral replication (HBV DNA increased),
    - and active disease identified in liver biopsy specimens

Hep B treatment

- Interferon
  - Pegylated—once weekly and better efficacy
- Oral agents
  - Lamivudine, Adefovir, Entecavir
  - Become popular for treatment of chronic hepB
  - Few side effects
    - Adefovir→ nephrotoxicity
  - Useful in pts with decompensated cirrhosis

Hepatitis C

Leading indication for liver transplantation

- Diagnostic tests
  - anti-HCV: indicates current infection or previous exposure with clearance.
  - “gold standard” presence of HCV RNA by PCR—now the preferred test, bypassing RIBA.
- Level of RNA does not correlate with severity of disease.
- Genotyping: genotype 1most common in US

Hepatitis C

Natural history and clinical presentation

- 60-85% develops chronic disease.
- Rarely do pts present with acute hepatitis
- Some pts have fatigue and mild RUQ pain
- 20% of pts with chronic Hep C will progress to cirrhosis.

HCV testing recommendations(CDC)

Adults born from 1945 through 1965) should be tested once (without prior ascertainment of HCV risk factors)

- Currently injecting drugs; Ever injected drugs
- Have certain medical conditions, including persons:
  - who received clotting factor concentrates produced before 1987
  - who were ever on long-term hemodialysis
  - with persistently abnormal alanine aminotransferase levels (ALT)
  - who have HIV infection

HCV

- Were prior recipients of transfusions or organ transplants, including persons who:
  - were notified that they received blood from a donor who later tested positive for HCV infection
  - received a transfusion of blood, blood components, or an organ transplant before July 1992
- HCV- testing based on a **recognized exposure** is recommended for:
  - Healthcare, emergency medical, and public safety workers after needle sticks, sharps, or mucosal exposures to HCV-positive blood
- Children born to HCV-positive women

Hepatitis C

Subgroup of pts likely to develop progressive liver disease

1. duration of infection
2. alcohol intake >50g/d
3. coinfection with HIV or HBV
4. male sex

Pts with cirrhosis due to HCV generally have disease >20 years.

Hepatitis C

Treatment

- Should be given to pts at highest risk of developing cirrhosis.
- Pegylated interferon with ribavirin **WAS** the standard of care (not any longer)
  - 24-48 weeks depending on genotype

- New treatments (since 2013)
  - Five highly potent DAA(direct-acting antiviral agents)oral combination regimens are recommended for patients with HCV genotype 1 infection
    - Genotype 4 and 6 treated similar to 1
    - 2 and 3 treatment is similar to different duration

Hepatitis D

- A defective virus
  - Requires the presence of HBsAg to replicate

Hepatitis E

- Single stranded RNA
- The highest incidence of HEV infection is in Asia, Africa, Middle East, and Central America.
- HEV is the second most common cause of sporadic hepatitis in North Africa and the Middle East.

Hepatitis E

- HEV is spread by fecally contaminated water in endemic areas
- Person-to-person transmission is uncommon
- HEV can be transmitted by blood transfusion, particularly in endemic areas

Portal hypertension

- an increase in hepatic venous pressure gradient.
- In cirrhosis it occurs through an increase in resistance to portal venous outflow
  - Due to distortion of liver
  - ~30% of the increase is through potentially reversible vascular factors---where pharmacotherapy targets

Esophageal varices

- risk factors for hemorrhage from esophageal varices:
  - radius of varix,
  - thickness of varix wall
  - pressure gradient between the varix and the esophageal lumen.

Esophageal varices

Recommendations for treatment of esophageal varices

- Primary prophylaxis: all patients with cirrhosis should have EGD for screening.

  If no varices repeat endoscopy in 2-3 years.

  -1st line therapy : nonselective beta blockers (propranolol or nadolol)

  -2nd line therapy: endoscopic band ligation

- Control of bleeding: best managed by endoscopic means preferable band ligation.

  - begin octreotide, continue for up to 5 days.

  -2nd line therapy: TIPS

Esophageal varices

- Secondary prophylaxis: prevent rebleeding.

  Essential—80% of patients who bleed will have a rebleed within 2 years.

  1st line therapy: endoscopy and beta blockers.

  other: liver transplantation

Ascites

- Pathogenesis: renal retention of sodium and movement of this extra fluid into the peritoneal space.
- diagnostic paracentesis is essential for patients who present with ascites.
  - the difference between serum albumin and ascitic albumin help determine portal hypertension (1.1g/dL or greater). Could be liver or heart disease. **(SAAG**)
  - A protein of 2.5g/dL or more favors heart disease.
- cell count of more than 250 neutrophils/mm3 is spontaneous bacterial peritonitis (SBP).

Management of Ascites

- low sodium diet
- fluid restriction: only necessary if serum sodium is <125mEq/L
- diuretic therapy:
  - urinary sodium excretion is used to determine the efficacy of therapy.
    - If urinary sodium excretion is more than 30mEq/d,

      spironolactone alone may be used.

      If urinary sodium excretion is between 10-30mEq/L then a combination of spironolactone and furosemide is used.

      If urinary sodium excretion is < 10mEq/L then large volume paracentesis is usually required.

Spontaneous Bacterial peritonitis

- End-stage liver disease
- No secondary source
- Clinical manifestations
  - Fever
  - Abdominal pain/tenderness
  - Altered mental status
- Index of suspicion should be high

SBP- Diagnosis

- +bacterial culture
- And/or pmn >250 cells/mm3

Hepatic encephalopathy

- Pathogenesis:
  - Ammonia and manganese considered etiologic factors for encephalopathy.
- Clinical features:
  - range from 0—no overt encephalophy to IV patient in a coma.
- Precipitating factors:
  - GI bleed, infection, large protein meal, use of sedatives, electrolyte abnormalities or hypoxia, constipation, and hypoglycemia.

Hepatic encephalopathy- Management

- dietary: limit protein based on level of encephalopathy.
  - Long-term restriction of dietary protein of < 1g/kg daily should be avoided.
- Nonabsorbable disaccharides:
  - Lactulose, may help remove dietary and endogenous ammonia.
    - Pt should have 2-3 semiformed stools/day.
- Antibiotics:
  - neomycin, metronidazole, and rifaximin have been used for treatment.

Liver diseases

Hemochromatosis

- autosomal recessive disorder with increased intestinal absorption of iron.
- Excess iron is deposited in the liver, pancreas, and other organs.
- About 1 in every 250 white persons in the US is homozygous for the mutation.

Hemochromatosis

- Suspect in pts with elevated iron sat, ferritin, or family hx.
- Most pt asymptomatic
- Cirrhosis, heart failure, hypogonadism, and arthritis
- HFE gene mutation
  - Autosomal recessive dz
    - 85% homozygous for C282Y mutation

Hemochromatosis-Treatment

- reserved for patients with evidence of iron overload, indicated by an increase in the serum concentration of ferritin.
  - therapeutic phlebotomy: simple, relatively inexpensive and effective.
  - avoid supplements with iron
  - avoid raw fish due to risk of *Vibrio vulnificus* infection
  - avoid alcohol
- If diagnosed and treated before diabetes and cirrhosis develops survival rate is normal

Wilson’s disease

- Inherited
- Excess copper
- Hepatic, neurologic, and psychiatric manifestations

- Gene mutation
  - *ATP7B* genes
- All ethnic groups
- ~1 in 30,000

Wilson’s disease

- Diagnosis
  - Reduced ceruloplasmin
  - Increased urinary excretion of copper
  - Presence of K-F rings
  - Elevated hepatic copper level
- Treatment
  - Copper-chelating medications

Wilson’s

- Kayser-Fleischer rings (KF)
- Seen with slit-lamp

Autoimmune Hepatitis

- Occurs in children and adults
  - 3.6 to 1 female to male
- All ethnic groups

Clinical Manifestations

- Asymptomatic→ liver failure
  - Subclinical
- Present with cirrhosis

Complications

- Depends on degree of liver damage

Diagnosis

- Aminotransferase elevation
- ANA
  - Anti-smooth muscle antibody
- hypergammaglobulinemia
- Histology: nonspecific
  - Portal mononuclear cell infiltration
    - Lymphoplasmacytic
  - fibrosis

Treatment –Autoimmune Hepatitis

- Liver transplant
- Prednisone
- azathioprine

Autoimmune Hepatitis: Typical lab

- Increased AST and Alt 100%
- Increased gamma globulin and IgG 90%
- Mild hyperbilirubinemia 83%
  - <3 mg/dL
- Alkaline phosphatase increase 67%
  - <2x normal
- ANA, SMA, or anti-LKM1 87%

Primary Biliary Cirrhosis (Primary biliary cholangitis)

- Cholestatic liver disease
- 90% women
- 95% will be AMA + (anti-mitochondrial Ab)
- Fatigue common
- Pruritis 30-50%
- Frequently being picked up in pts with asymptomatic lab abnormalities
- IgM high

DDx for cholestasis without biliary obstruction

- Drug-induced cholestasis
- Primary biliary cirrhosis
- Primary sclerosing cholangitis
- Idiopathic adulthood ductopenia
- Idiopathic biliary ductopenia
- Cholestasis of pregnancy
- Cystic fibrosis
- HIV-associated cholestasis
- Sarcoidosis
- Granulomatous hepatitis

Alpha1-antitrypsin (AAT) deficiency

- Autosomal co-dominant disorder with lung and liver injury
- Can cause premature emphysema and liver disease
- Pt with cirrhosis due to AAT have a significant increased risk of HCC up to 30%
- Diagnosed by phenotyping. Liver damage does NOT correlate with serum AAT levels (unlike lung). Diagnosis confirmed with biopsy
- No effective medical treatment for the liver manifestations of AAT deficiency.