Complications of Cirrhosis

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What is Cirrhosis?

- The end result of chronic liver disease
- Histologically defined as regenerative nodules surrounded by fibrous septa
- Eventually disrupts architecture of entire liver
- Etiologies in Western countries: alcohol, viral, NAFLD, biliary, genetic hemochromatosis, Wilson’s, A1AT, cause in 10-15%
- Cirrhosis may lead to liver failure, portal hypertension, or development of hepatocellular carcinoma

NORMAL LIVER

CIRRHOTIC LIVER

CIRRHOTIC LIVER
Decreased clearance of Estrogen
Increased Free Estrogen due to decreased sex steroid-binding globulin

Bones
osteoarthritis
osteomalacia

PHYSICAL EXAM FINDINGS
LIVER: Blood Flow
- High Flow
  - Mesenteric vessels
- Low pressure
  - Vast network of sinusoids

Cirrhosis: Portal Hypertension
Effects on blood flow
1. Fibrosis restricts blood flow; increased portal vein pressure
2. Collaterals acquire increased pressure, affecting spleen, esophagus, stomach (varices), gastropathy
3. Ascites due to fluid shift into peritoneum
4. Shunting of blood from liver decreases metabolism of "toxins"
5. Portal bacteremia not cleared induces peritonitis
What Pressure Defines Portal HTN?
Portal Vein-Hepatic Vein Pressure Gradient

- Catheter (with deflated balloon) in Hepatic Vein measures “free HV pressure”
- Inflated Balloon in Hepatic Vein measures Portal Vein Pressure
- PV-HV pressure > 10 mmHg = “significant” portal HTN

Portal Hypertension Pathophysiology

- Increased Resistance to inflow/outflow
  - Fixed scarring of the liver
  - 7 reversible elements: sinusoidal blood vessels
- Increased Flow to portal system
  - Increased splanchnic flow (vasodilatation/NO)
  - Increased cardiac output
    » Low SVR
  - Increased blood volume
- Decreased Albumin: hepatic synthetic dysfx
  » Decreased oncotic pressure, fluid leaks out of vascular space

Esophageal Varices

- Risk of bleeding proportional to size and degree of portal hypertension
- Even with optimal therapy, death from initial bleed may be greater than 20%
- Non-selective Beta blockers (Propranalol, Nadolol)
- Use of Isosorbide Mononitrate controversial

Portal Gastropathy

- Normal
- Gastropathy

Esophageal Varices: Banding

- Used to treat bleeding
- For Acute and Chronic Therapy
- As part of variceal eradication program
- Usually combined with Beta Blockade
**Gastric Varices**

**TIPS**

**Transjugular Intrahepatic Porto-Systemic Shunt**

- Functional side to side shunt
- Produces connection from Portal Vein to Hepatic Vein
  - Increase Hepatic vein pressure, RV volume
  - Decrease Portal pressure, hepatic perfusion
- TIPS improves sodium and water handling
  - Hepatic hydrothorax
  - Refractory ascites
- Caution:
  - CHF, Bili > 4, Inc Creat, PSE, Older pt

**Surgical shunts**

- Limited indications: for endoscopic, medical failure, not OLT candidates
  - Cirrhosis: Child’s A
  - Budd Chiari syndrome
  - Non-cirrhotic portal hypertension
- Selective vs non-selective
  - Goal is to preserve portal perfusion

**Surgical Shunts**

- Porto-caval
- Meso-caval
- Spleno-caval

**Blakemore Tube**

- Historically, an important way to stabilize a patient with variceal bleeding prior to:
  - Surgery
  - Transplant
- Now, only used in emergencies
  - Prior to TIPS
  - To Transport a patient from Hospital to hospital
Ascites
Clinical Diagnosis

- **History:** increasing abdominal girth
- **Physical Examination:**
  - shifting dullness, fluid wave
  - very poor in detecting modest amounts of ascites
- **Radiology:** ultrasound, CT scan more sensitive

Ascites

- **Differential dx:**
  - Portal hypertension
  - Hepatic (or portal vein) occlusion
  - Heart failure
  - Peritoneal inflammation
    - TB peritonitis
    - Carcinomatosis (sometimes chylous ascites)
  - Ovarian Cancer
  - Nephrogenic ascites (nephrotic syndrome)
  - Pancreatic ascites
  - "Other" (Schistosomiasis, non-cirrhotic portal HTN, polycystic liver disease, etc.)
Ascites

- 26 year old woman
- Presents with abdominal pain, fever, and ascites
- Born in Africa

Characteristics of Ascites due to Portal Hypertension
- Transudate; i.e., ascites protein < 3 g/dl; most < 1 g/dl
- WBC < 50 cc/mm³; mostly mononuclear
- Normal ascitic fluid amylase
- Serum - ascites Albumin gradient (SAG) > 1.1 g/dl due to portal HTN

Ascites: Treatment
- Bedrest
  - Na⁺ restriction; 1.5-2 gms/day
  - fluid restriction: 1.5 liters if Na⁺ < 120
- Diuretics (maximum doses):
  - Spironolactone 400mg, Furosemide (200 mg)
  - Amiloride, HCTZ, Metolazone, Zaroxyln
- Large-volume paracentesis
- TIPS
- Surgery: Liver transplantation
  - LeVeen or Denver Shunt (historical value, ? if valuable now, radiologists now place these)

LeVeen/Denver peritoneo-venous shunt
- Coagulopathy:
  - DIC almost universal
  - severity can be limited by replacing ascites with saline
- Infection
  - generally requires removal of shunt
- Occlusion
  - Venous side of shunt
- Heart failure
  - Volume overload

Large-Volume Paracentesis
- Advantages: Fast, ~ hospital time, less expensive
  - Patients should have normal creatinine
  - Better if volume overloaded (peripheral edema)
- Disadvantages:
  - Precipitate renal insufficiency
  - Removes proteins (e.g., opsonins)
- Use of volume expansion
  - Albumin: 6 gms/liter of ascites removed
  - May not be required for < 2-3 liter paracentesis

Hepatic Hydrothorax
- Ascites leaks through rents in the diaphragm
- Diagnosis: Fluid should have characteristics similar to ascites
- Treatment: AVOID CHEST TUBES. Surgical repair not usually effective
- TIPS is treatment of choice for diuretic-refractory cases
- Liver transplantation
SBP
Spontaneous Bacterial Peritonitis
- Infection independent of another intra-abdominal source
- Monomicrobial
- Enteric flora enters portal circulation, not cleared
- Ascites WBC > 500 or 250 with greater than 50% polys
- Culture negative neutrocytic ascites
- Culture positive neutrocytic ascites
  - If gm negative: treat
  - If gm positive: likely contaminant

Spontaneous Bacterial Peritonitis: Prevention
- Risks:
  - GI bleeding/hypotension
  - Advanced liver disease
  - Previous history
- Early treatment of other infections
- Prophylactic antibiotics to GI bleeders
- Volume expand with Albumin
  - Effective to reduce hepato-renal syndrome
- Oral Quinolones, Bactrim can prevent recurrence when given chronically
- Liver transplantation

Spontaneous Bacterial Peritonitis: Treatment
- Most common organisms are E. coli, Klebsiella, Pneumococcus, Enterococcus
- Drug of choice for therapy:
  - Board exam: Cefotaxime
  - Real life: extended penicillin, Zosyn, Unasyn
- AVOID AMINOGYCOSIDES
- Narrow antibiotic spectrum if culture results are known
- ? re-tap after 48 hours to confirm response to therapy

Hepato-Renal Syndrome
- Etiology: Unclear, but likely an exaggeration of mechanisms involved in ascites formation
- Precipitants:
  - GI Bleed
  - Nephrotoxins (NSAID’s, Aminoglycosides, sepsis)
  - iatrogenic (diuresis, paracentesis)
- Diagnosis:
  - Euvolemic patient
  - Urine output < 800 cc/day, UNa < 10 mEq/l,
  - “clean urine sediment”
- Treatment: TIPS, MARS, Glypressin, Terlipressin, Transplantation
  - Midodrine 5-15mg po tid
  - Octrotide sq100-200 mcg sq tid

Portal Systemic Encephalopathy: Hepatic Encephalopathy
- Inability to clear “encephalopathogenic agents” (Ammonia, Gaba, Mercaptans, endogenous Benzos)
  - Cirrhosis
  - Portal Hypertension
  - Shunting (TIPS, surgical shunt)
  - Protein load
    - Usually GI bleed, Gastropathy, less common PO proteins
  - Acute Liver Failure:
    - PSE defines fulminant Hepatic Failure
    - Cerebral Edema (not in chronic!!)
    - Emergency Liver Transplantation in therapy

Liver Failure: "Pseudonephrosis"
**TX PSE**

- Decrease encephalopathic agent:
  - Lactulose 30cc po q 2 until effect (traps NH3 in colon or NH3 incorporated into bacterial proteins)
  - Rectal Tube
    - Tap water Enema
    - Lactulose 200 cc in 300 cc tap water

- Cathartic:
  - Mg Citrate, Mirilax, Go-lytely
  - Decrease production/block EA:
    - Neomycin 500 mg po q 6 (watch Creatinine and hearing)
    - Flagyl 500 mg po q 8 (neuropathy, antabuse effect)
  - “Brain Stabilizers”
    - Zinc and/or L-Carnitene

- Rifaximin
  - Poorly absorbed antibiotic
  - 400 mg po tid
  - Not FDA approved

**Indications for Liver Transplantation**

- Manifestations of Portal HTN not controlled by alternative measures
  - Esophageal and/or gastric variceal bleeding
  - Bleeding from portal hypertensive gastropathy.
  - Hepatic encephalopathy
  - Spontaneous Bacterial Peritonitis
  - Significant Ascites, hydrothorax

- Patients with HCC can be transplanted if:
  - No evidence of extrahepatic disease
  - No macroscopic vascular invasion
  - One lesion < 5 cm or
  - Three lesions, each < 3 cm