COMPLICATIONS OF CIRRHOSIS: CASES

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Defining Cirrhosis

- Histological diagnosis
- Nodules of regenerating hepatocytes surrounded by fibrous tissue
- Common final result of diverse, chronic inflammatory processes affecting the liver
- Fixed architectural distortion of the liver that results in organ dysfunction and portal hypertension
Normal Liver Blood Flow

- Dual blood supply: portal vein and hepatic artery
- Mixed blood joins in the hepatic sinusoid
- Drain from venules, into hepatic veins into IVC
- In a healthy liver, this is a low resistance circuit
Blood Flow in Cirrhosis

- Distorted architectural leads to increased resistance
- As resistance increases, veins that drain into portal reverse flow
- Spleen enlarges and sequesters platelets
- A previously low resistance circuit becomes a high one
Portal Hypertension/Ohm’s Law

- Pressure = Flow x Resistance

- Increased Pressure in the liver (Portal Hypertension) can result from an increase in blood flow to the liver or an increase in resistance.

- Cirrhosis creates a static, fixed resistance.

- An increase in dynamic resistance and flow compound the problem.
Nitric Oxide outside the Liver

• Elevated portal pressure leads to an increase in sheer stress in splenic vasculature

• There is an INCREASE in nitric oxide in the splanchnic vasculature promoting vasodilation

• Vasodilation INCREASES blood flow to the liver
Portal Hypertension/Ohm’s Law

- Resistance x Flow = Pressure

- Fixed: structural changes
- Dynamic: Decrease NO in the liver
- Increase NO in splanchnic vasculature
Portal hypertension leads to splanchnic and systemic arteriolar vasodilation which leads to:

- Decreased effective arterial blood volume
- Upregulation of sodium-retaining hormones (renin-angiotensin-aldosterone axis)
- Water retention
Pathogenesis

- Replacement of healthy liver tissue with fibrous, scar tissue
- Architectural distortion leads to loss of function and resistance of blood flow through the liver
- Responses are maladaptive as NO goes down in the liver but increases in the periphery
- As the disease and pressure progresses the effects are systemic: decreased effective circulating volume and activation of the RAAS
Measuring Portal Hypertension

- Portal hypertension is equated to the hepatic venous pressure gradient (HVPG)
  - HVPG=Wedged-Free
  - HVPG=3-5 is normal
  - With cirrhosis HVPG rises and so do complications
Cirrhosis: The Big Picture

Natural History of Chronic Liver Disease

- Chronic liver disease → Compensated cirrhosis
- Compensated cirrhosis → Decompensated cirrhosis
- Decompensated cirrhosis → Death

Development of complications:
- Variceal hemorrhage
- Ascites
- Encephalopathy
- Jaundice
Question 1:

- 60 year old male with history of HCV cirrhosis presents with hematemesis. No hx of NSAIDS. No previous bleeding history.

Vitals: Afebrile, HR: 90, BP: 90/60, 100% RA
Exam: ATOx3, icterus, ascites, mild edema, melenic stool in rectal vault
Labs: Hgb: 8 g/dL, plts: 25,000, INR: 1.6, Alb: 2.8
IV access established, Type and screened

Which of the following is the next most appropriate course of management:
- A) Platelet transfusion for goal >100,000
- B) Vitamin K 10mg IV
- C) Initiation of ceftriaxone IV
- D) Consult for placement of transjugular intrahepatic portosystemic shunt
- E) Initiation of propranolol BID titrated to a resting heart rate in the 50s
Variceal Bleeding

• Portal hypertension leads to reversal of blood flow away from the liver

• Gastroesophageal varices are present in approximately 50% of cirrhotic patients

• Prevalence increases with the severity of liver dysfunction/portal hypertension

• Vessels are under high pressure

• Rupture is a MEDICAL EMERGENCY
Acute Variceal Bleeding

- Initial steps are same for all upper GI bleeds
- Avoid over resuscitation
- Initiation of ceftriaxone IV 5-7 days
- Octreotide 50 microgram bolus and continued as 50 micrograms/hr (probably 72 hrs)
- Urgent endoscopy with intent of variceal band ligation
- If rebleeding, consider repeat endoscopy or TIPS
Preventing Variceal Bleeding

- **Screening**: EGD with new diagnosis of cirrhosis
  - EGD at cirrhosis diagnosis
  - If 2 negative exams 1-2 years apart can d/c
  - Reconsider if clinical status changes
  - No role for non selective beta blockers

- **Primary Bleed Prophylaxis (Present, no bleed hx)**:
  - Size matters; generally EGD annually

- **Secondary Bleed Prophylaxis (Varices have bled)**:
  - Variceal Banding + NSB
  - TIPS
A 59 year old man with hx of alcohol dependence presents with new onset abdominal distension. AVSS. Exam notable for: temporal wasting, palmar erythema, shifting dullness, fluid wave, non tender to palpation, LE edema. Labs notable for: Alb: 2.3, INR: 1.6, AST: 100, ALT: 40, Tbil: 3.8, Platelets: 50,000

You elect to perform a diagnostic paracentesis with the following results: ANC: 150 cells, Alb: 1.0, Tprot: 1.8. No orgs on G/S

Which of the following is correct:

- A) SAAG of 1.3 implicates nephrotic syndrome and 24 hr urine protein should be collected
- B) ANC of 150 confirms the diagnosis of SBP and admission is warranted
- C) SBP is unlikely as there is no abdominal pain
- D) Restriction of dietary salt intake is expected to be beneficial
Ascites
Ascites may be due to several causes but cirrhosis is the most common.

- The clinical workup of ascites starts with calculation of the Serum-Ascites Gradient or SAAG.
- The SAAG correlates directly with sinusoidal pressure.
- A SAAG > 1.1 implicates portal hypertension or cirrhosis as the cause.
Ascites Complications

- Spontaneous Bacterial Peritonitis
  - Translocation of gut flora from the intestine into ascitic fluid
  - Diagnosed by cell count/differential in ascitic fluid
    - >250 pmns
    - Initiation of cefatoxime or ceftriaxone
  - Albumin given as adjunct
    - 1.5 grams/kg BW day 1; 1 grams/kg BW day 3

Prophylaxis to prevent second episode
Ascites Management

- Dietary salt restriction (around 2 grams daily)

- Initiation of diuretics
  - Furesomide and aldactone

- Paracentesis
  - Albumin replacement >5 L
  - Between 5 and 10 g of albumin per liter of fluid removed……No study has compared doses

- TIPS
Question 3:

- 58 y/o WM hx of HCV Cirrhosis, listed for liver transplantation presents with altered level of consciousness. He is arousable to noxious stimuli. AVSS. Ascites on exam, abd non tender.
  Labs: INR: 1.8, Na: 130 Cr: 1.6 (at baseline), Tbil: 2.8, Dx tap: ANC=78 cells
  Head CT: unremarkable

- Which of the following is true regarding hepatic encephalopathy?
  - A) Degree of hepatic encephalopathy correlates directly with serum ammonia level
  - B) Degree of hepatic encephalopathy correlates directly with MELD score
  - C) Documentation of hepatic encephalopathy (requiring hospital admission and daily medical therapy) disqualifies active drivers license in some states
  - D) Restriction of dietary protein is recommended as first line therapy
Hepatic Encephalopathy

- Ammonia is a product of bacterial action and digestion
- Faulty metabolism or shunting through collaterals allows ammonia to reach the brain
- Ammonia crosses blood-brain barrier which modulates GABA receptors
- GABA modulation leads to clinical syndrome of confusion and lethargy
- Ammonia levels DO NOT correlate to degree of encephalopathy
- Other decompensating events often precipitate encephalopathy
Reasons for Encephalopathy

- Lactulose deficiency is a diagnosis of exclusion

- Search for other causes:
  - Infection
  - GI Bleeding
  - Overdiuresis, azotemia
  - Hepatocellular Cancer
  - Portal vein thrombus (new)
Encephalopathy Treatment

- Treatment: identify and correct precipitant
- Lactulose: reduces ammonia causing bacteria, NH3 excretion, promotes catharsis
- Rifaxamin/Xifaxin 550mg BID: non absorbable antibiotic
Question 4:

- 62 y/o WM with HCV Cirrhosis presents with hepatic encephalopathy. Dx tap reveals SBP. Admission creatinine was 1.0. Received antibiotic therapy per protocol and albumin at day 1 and 3. On day 4 of hospitalization Cr rises to 3.5. Over the following day, diuretics held, re-tap shows treated SBP, given volume expander and kidney ultrasound is unremarkable. Day 5: Cr: 4.2, and spot urine Na<15.

Which of the following is false regarding hepatorenal syndrome (HRS):

- A) HRS is characterized by extreme sodium retention
- B) Explanted kidneys are structurally normal
- C) It is often precipitated by SBP
- D) Recognition should lead to consideration of liver transplantation
- E) A trial of IV lasix should be given to assess urine output
Hepatorenal Syndrome

- Renal failure in advanced chronic liver disease characterized by marked renal vasoconstriction and decreased GFR (Cr > 1.5, Cr < 40)
- Diagnosis of exclusion
- High sodium avidity, low urine sodium
- Fluid challenge helps distinguish from pre-renal
- Type 1: rapidly progressive, Type 2: slower
- Albumin, midodrine and octreotide
- Dialysis
  - Is the patient a transplant candidate?
Question 5:

- 55 y/o with HCV related cirrhosis comes to see you for progressive dyspnea on exertion. He complains of diffuse chest pain related to activity and progressive fatigue. Physical exam is notable for: clubbing, a loud P2, right ventricular heave and TR murmur. At rest Pox: 92%

- You get a cardiac echo with bubble study that is negative for shunt, estimated PASP on the echo is 45. CXR: borderline cardiomegaly; lungs clear

- The patient is excited because Dr. Wong said he was nearing the top of the transplant list. You call Dr. Wong but he’s out of town.

- The appropriate next step is:
  - Consider right heart catheterization to evaluate for portopulmonary hypertension
  - Observation, this is hepatopulmonary syndrome that will be helped with transplant
Hepatopulmonary Syndrome

- Advanced liver disease, increased A-a gradient, intrapulmonary vascular dilations
- Often asymptomatic, but can have orthodeoxia (desats sitting up) or platypnea (increase in SOB sitting up)
- Diagnosis made with Echo: delayed bubble entry into the left atrium (3-6 cardiac cycles)
- Often improved by liver transplantation
Portopulmonary Hypertension

- Advanced liver disease and pulmonary hypertension
  - PASP>35, normal wedge pressure
- Vasconstriction
- Signs of right heart failure
- Look for other causes
- Right heart catheterization
- Generally a contraindication to transplant if mean PA pressure >35
Summary

- Cirrhosis represents the common final result of prolonged liver injury from diverse causes.
- Architectural distortion causes loss of function and triggers mechanisms that lead to portal hypertension.
- Portal hypertension is the driving force for complications with cirrhosis.
- Decompensation of cirrhosis is diverse and lethal.