Board Review Liver and Biliary Track Disease

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- 1) 44 yo woman presents with a 4 week history of anorexia, nausea and abdominal pain. She stopped drinking alcohol 2 weeks ago because she felt to sick to drink. PMH: Alcohol abuse X 24 years, depression, hypothyroidism. Meds: Fluoxetine and levothyroxine. PE: T- 38.2 P 120

  BP 90/60 Eyes: sclera icteric . Skin- jaundiced, spider angioma present

  Liver is enlarged and tender. Ext- trace edema

  Neuro- OX2, no asterixes

- Lab: AST 100, ALT 35 Alk phos- 200 (normal <160), T bili- 40.9 D bili- 19 alb-2.6 (Nl> 3.5)

PT-19.8, INR 2.4, plt-90, HCT 38 WBC-11.2 MCV 104

What is the most likely diagnosis?

A) Autoimmune hepatitis
B) Primary biliary cholangitis
C) Drug-induced liver injury
D) Budd-Chiari syndrome
E) Alcoholic hepatitis
F) Acute cholecystitis

AST/ALT Ratio

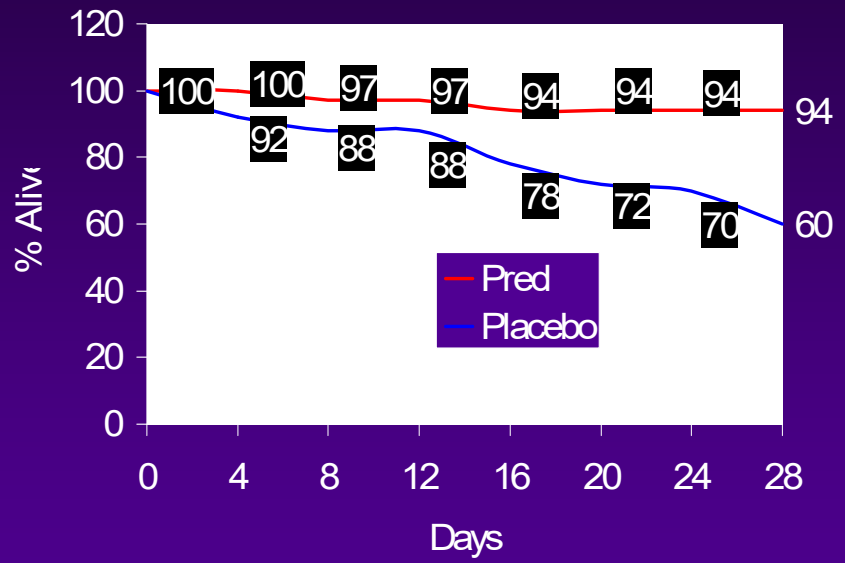
- Greater than 2:1 suggests alcoholic liver disease
- The ratio is almost always less than 1 with viral hepatitis UNTIL cirrhosis occurs, at which time the ratio rises to 1 or slightly greater than 1.

Alcoholic Hepatitis Case

- 2) What might improve survival?
  - A) cyclosporine therapy
  - B) Propothiouracil therapy
  - C) Protein restriction
  - D) Corticosteroids
  - E) Antibiotics

Alcoholic Hepatitis Case

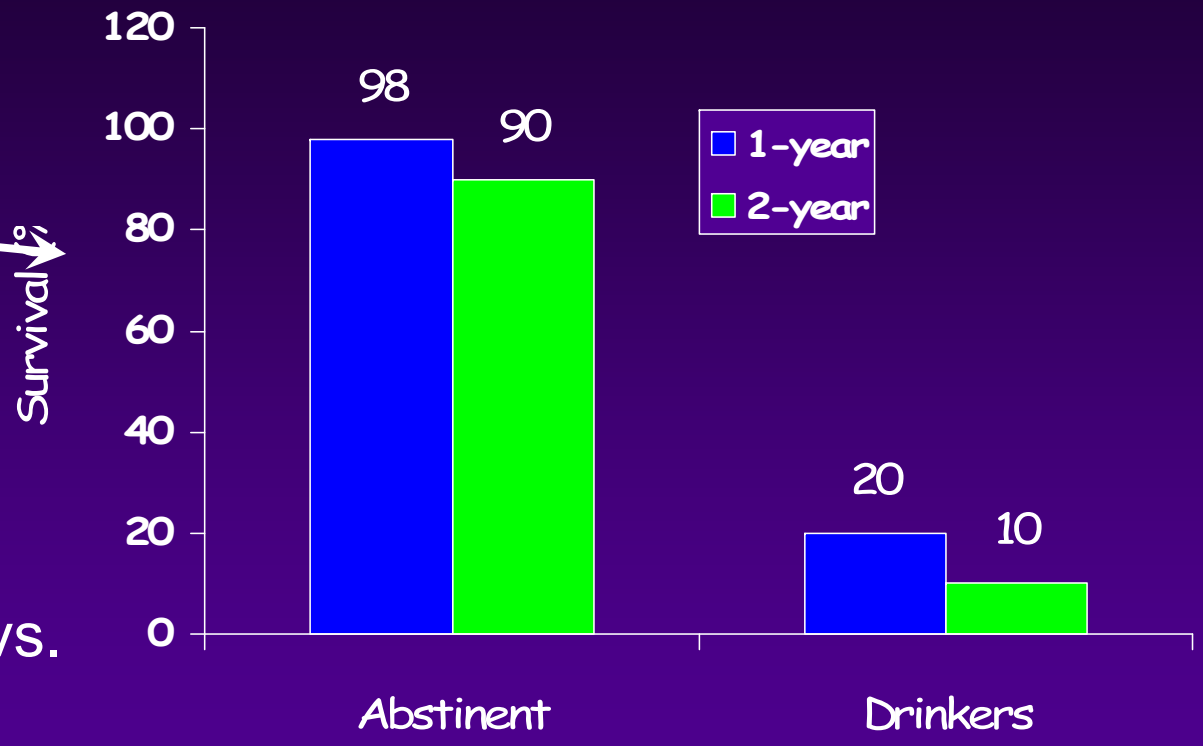
- **Pearls**
  - survival benefit at 1 and 6 months in selected patients if steroids used when DF >90
  - do NOT use steroids if
    - gastrointestinal bleeding
    - renal failure
    - concomitant infection
  - dose
    - 40 mg x 4 weeks then taper



Survival with Alcoholic Hepatitis

Treatment

- Abstinence
- Good Nutrition
- Corticosteroids
- Pentoxifylline
  - mortality 24.5% vs. 46.1%
- Liver Transplantation



- 3) A 51 yo man presents with increasing pain in his hands. He has found it harder to keep working at his job as a mechanic. PMH: DM, HTN and hyperlidemia. He has a distant history of nasal cocaine use. On exam He has swelling over the metacarpal-phalangeal joints of his hands. Labs: Hb 14 HCT 42 ALT 66 AST 100 Alb 3.0 , Hand films shown

What is the Most Likely Diagnosis?

A) Alcoholism

B) Hepatitis C

C) Porphyria Cutanea Tarda

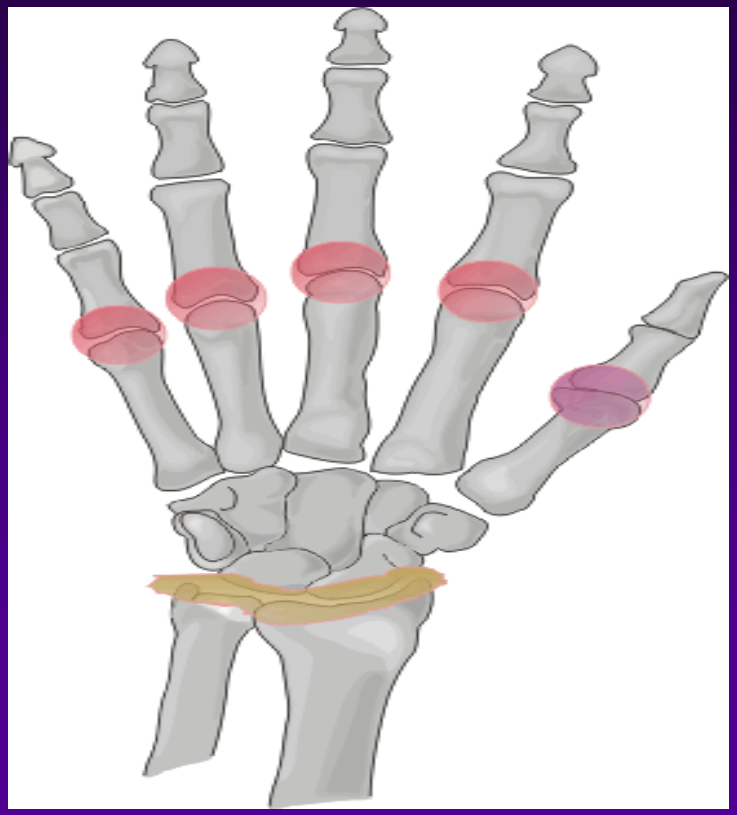
D) Hemochromatosis

E) Sarcoid

Hemochromatosis on the Boards

- Look for funny arthritis involving the metacarpal- phalangeal joints of the hand
- Diabetes + Cardiomyopathy and a sprinkling of Liver issues
- Hypogonadism
- Beware the patient with “alcoholic cardiomyopathy”

Arthritis in Hemochromatosis



Hemochromatosis

- Classic presentation rare (“bronze diabetes”)
- Important clinical features: Fatigue (74%), Cardiomyopathy, liver disease (75%), hypogonadism (45%) (small tests an important pearl in men), arthritis (44%), odd skin color (70%), Diabetes (48%))
- Best screening test is iron and TIBC (iron saturation), ferritin
- Liver biopsy, genetic testing (C282Y/C282Y) to confirm
- Treatment- Phlebotomy

- 4) 35 yo man denied insurance due to increased liver enzymes. Feels well, no symptoms
- PMH – none Meds – none FHx - negative
- Substance use – 3 glasses wine/day; no tobacco
- Exam
  - 120/80 50 6'0" 176# BMI 23.9
  - exam – no abnormalities
  - AST **68** ALT **70** AP 120 Tbili 1.0

What is the Most Appropriate Management?

A) ultrasound

B) CT scan

C) liver biopsy

D) repeat in 1-2 months after abstinence

E) No need to do anything

Pearls

- first step in evaluating elevated liver enzymes
  - discontinuation of all EtOH and suspect drugs
- abnormal enzymes should never be ignored
  - normal or minimally abnormal liver tests do NOT preclude significant liver disease, even cirrhosis

Follow up

- 5) Patient returns in 2 months
  - AST 55 ALT 78 AP 109 Tbili 0.8
- Patient now admits to Injection drug use in his 20s
- Next tests?

A) ultrasound

B) CT scan

C) HCV / HBV serologies

D) HCV PCR

E) HBV PCR

Pearls

- history/labs most consistent with viral disease
- ultrasound/CT *not* helpful in diagnosis
  - unless you suspect biliary etiology or steatosis
- serologies measure past exposure
  - if negative, points you a different way

Evaluation of Elevated Transaminases

Step 1

Stop all alcohol, possible offending drugs/supplements and then recheck in a month

Step 2

Test for Hep B/C, hemochromatosis (Fe/TIBC) and consider NASH (U/S)

Step 3

Consider non-hepatic causes

Step 4

Look for zebras

Step 5

Watchful waiting if transaminases <2X ULN, Bx if persistently higher than that

Non Hepatic Causes of Increased Transaminases

- Muscle disorders – usually high AST, but ALT can go up, and several days after injury ratio is close to 1
- Thyroid disorders
- Celiac disease –ALT usually greater than AST, goes to normal on gluten free diet
- Adrenal insufficiency
- Anorexia Nervosa

Follow up

- 6) Patient's results return
  - HBsAg (-), Anti-HBs (+), Anti-HBc (+)
  - anti-HCV (+)
- Interpretation?

A) chronic HBV and chronic HCV

B) chronic HBV and past HCV

C) past HBV and past HCV

D) past HBV and probable HCV

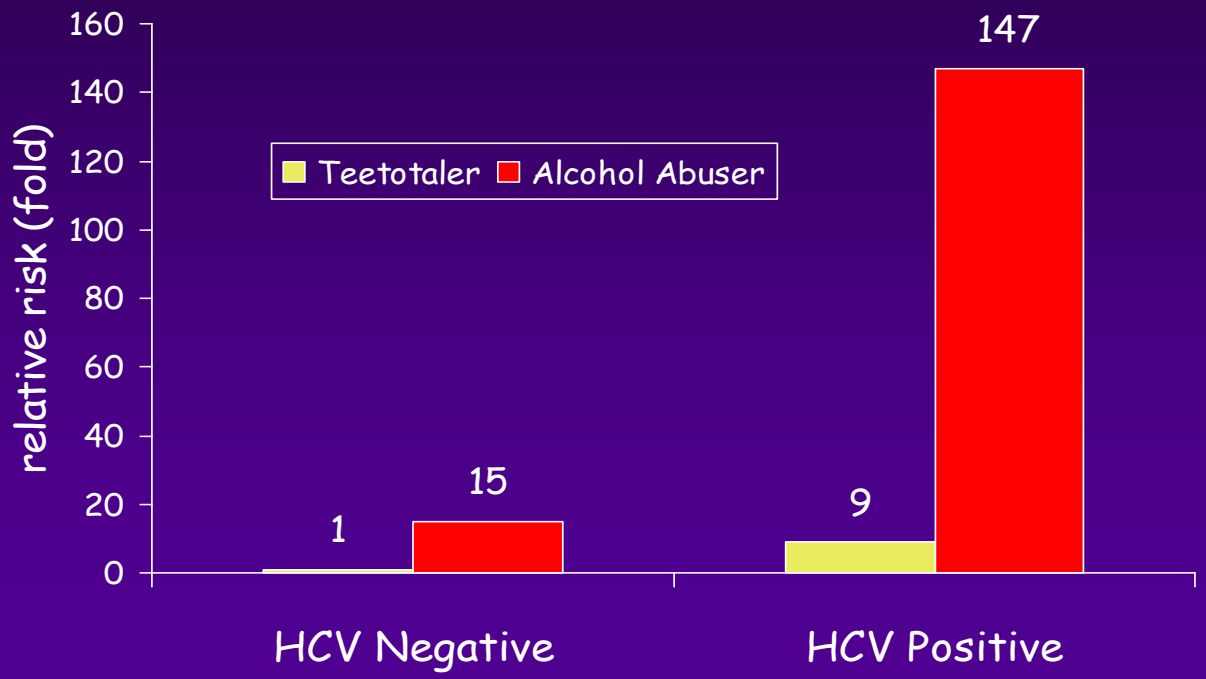
Pearls

- Antibodies for sAb and cAb = past HBV infection
  - now immune
- ELISA testing is for hepatitis C antibodies only
  - Sensitivity >99% in high risk population
    - Usually diagnostic if
      - liver enzymes elevated and risk factors present
  - sensitivity <50% in low risk population

Establishing the Diagnosis

- Next step:
  - verify infection → HCV viral measurement
    - Remember – antibody test does not confirm active infection

Effect of Alcohol on Cirrhosis in Hepatitis C



Lancet 1997;349:825-832.

More Pearls About Hepatitis C

- standard-of-care treatment for HCV

For genotype 1 hepatitis C treatment with Glecaprivir- pibrentasvir for 8 weeks, Ledipasvir-sofosbuvir regimens leads to a >95% sustained viral response. Can treat for 8 weeks if patient is without cirrhosis and viral load is <6 million, treat for 12 weeks if cirrhosis and/or viral load > 6 million

For genotype 2 hepatitis C, for treatment naive and treatment experienced non cirrhotic patients 12 weeks of sofosbuvir plus velpatasvir therapy leads to SVR 99-100%

For genotype 3 hepatitis C, treatment naïve and treatment experienced non cirrhotic patients treatment with 12 weeks of sofosbuvir plus velpatasvir had 98% SVR

- HCV patients are NOT at risk for liver cancer <u>until</u> cirrhosis develops
- Once cirrhosis develops, it generally takes about 8-15 years for a liver to "fail"

Management of Patients With ESLD

- 8) A 47 yo man with ESLD presents for evaluation. He has a history of MI and has osteoarthritis and gout. Which of these medications should be avoided in this patient?

A) Statins
B) NSAIDS
C) Acetaminophen
D) Prednisone

Medications and ESLD

- Acetaminophen is ok, maximum dose should be 2 g a day
- Statins are fine, might even be beneficial at sustained virologic response in hep C patients
- NSAIDS should not be used

- 9) A 45 yo man with ESLD presents with abdominal pain. On exam he has T 38.3, P100, BP 90/60 . Abdomen with shifting dullness, ascites on hand held US. Tender to palpation and with shaking abdomen. Lab WBC 14,000 Na 128 Alb- 2.3 Cr 1.2, Bili- 4.4 Paracentesis fluid- WBC 1000/ul with 80% polys. Alb- 1.0. What do you recommend?

  A) Ampicillin + tobramycin

  B) Levofloxacin

  C) Cefotaxime + Albumin

  D) Levofloxacin + metronidazole

  E) Ceftriaxone

Spontaneous Bacterial Peritonitis

- More common in patients with ascites and high SAAGs (>1.1)
- > 250 polys/ul has high sensitivity
- Treatment of choice cefotaxime (or other 3rd generation cephalosporin) for 5 days
- If Cr > 1, Bili >4 or Bun >30, should give 1.5g/kg albumin on day 1and 1g/kg on day 3

- 10) A 44 yo woman with ESRD and refractory ascites and esophageal varices on EGD 6 months ago presents for follow up. She has been receiving large volume paracentesis weekly X 6 weeks to try to manage ascites. Medications: Ciprofloxacin 750 mg weekly , Propranolol 10 mg bid, Vitamin D. Lab: Cr 1.2, Na 128, Alb 2.4 peritoneal fluid TP 1.1. VS: BP 88/60 P 66 What do you recommend?

  A) stop Ciprofloxacin

  B) Increase ciprofloxacin to 500 mg daily

  C) Increase propranolol to 20 mg BID

  D) Stop propranolol.

Prophylaxis for Patients with ESLD

- Quinolones for SBP prophylaxis if prior SBP or if ascites fluid TP is< 1.5 and serum Na < 130 or Cr >1.2, or Bun >25
- Non selective B blockers for variceal hemorrhage prophylaxis if varices on EGD (ever). Avoid in patients with refractory ascites because of increased mortality in this group who receive B blockers

- 11) A 60 yo woman with a history of end stage liver disease presents with worsening confusion. She has a hx of hepatic encephalopathy. Her family brings her in today because she has had 3 falls in the past 24 hours, including one this morning that was unwitnessed (her daughter found her on the floor). PE: T 36.6 P 90 BP 90/60. Skin- skin is jaundiced Abd- soft, nontender. No fluid wave present, stool heme negative. Lab: WBC 6.0 HCT 44 Bun 8 Cr .8, Ua- normal

What Is The Most Appropriate Next Test?

A) Abdominal CT scan
B) Non contrast head CT
C) Ammonia level
D) Liver function tests
E) D-Dimer

Testing in the Liver Patient With AMS

- Ammonia testing will not be the correct answer- no utility in following ammonia levels, an it is of little value in patients with known past hepatic encephalopathy diagnosis
- Always look for infection/GI bleeding (blood cultures/tap ascites)
- Head CT only if unwitnessed falls or head trauma /diagnostic uncertainty

To Recap

- Don’t choose ammonia level
- Only get a head CT if you have to (falls/trauma)

- 12) A 57 yo woman with ESLD due to hepatitis C presents for follow up. She was last seen 2 years ago. What testing do you recommend for her?

A) Hepatic Ultrasound

B) Hepatic Ultrasound and alpha-fetoprotien

C) Hepatic CT scan

D) LFT's and alpha fetoprotein

E) Serum ammonia

Screening for HCC

- Cirrhosis is a risk factor for HCC- all with cirrhosis should be screened with q6 month ultrasounds
- Risk is highest with hepatitis B and C as well as hemochromatosis
- Alpha fetoprotein screening alone is no longer recommended
- Screen patients with chronic Hep B-A) if active
- B) asian men >40 C) Asian women >50 D) African or African American men

- 13) A 50-year-old male with a history of alcoholism presents with severe RUQ pain, nausea, and fever.
- Lab: AST 45, ALT 35, alk phos 200, WBC 17,000. Ultrasound shows 3–4 small gallstones, no pericolic fluid.

What additional test would best help in diagnosing acute cholecystitis?

A) Abdominal CT scan

B) Abdominal MRI scan

C) HIDA scan

D) Bilirubin

E) Liver/Spleen scan

Hepatic Tc^{99} — Iminodiacetic Acid Scan (HIDA Scan)

- Specific test for acute cholecystitis
- Positive scan shows filling of biliary tree and not gallbladder
- Good for diagnosing acalculous cholecystitis

- 14) A 54 yo woman presents with severe abdominal pain X 2 hours. The pain came on suddenly and was 10/10 in severity. It was in her RUQ radiating to her back. She has had a 50 # weight loss in the past year. She is evaluated in the ED and labs show AST 450 ALT 500 Alk phos 100 bilirubin 1.2. She receives morphine for her pain with minimal relief. A ultrasound shows multiple gallstones but no dilated ducts. A HIDA scan shows no signs of acute cholecystitis. Her pain resolves 3 hours after arriving in the ED, repeat labs 15 minutes after pain resolution: AST 900 ALT 1000 Alk phos 130 Bili 1.2.
- What is the most likely diagnosis?
- A) Acetaminophen toxicity
- B) Hepatitis A
- C) Ischemic hepatitis
- D) Liver fluke
- E) Passage of gallstone

Labs and Acute Bile Duct Obstruction

- Early on, AST and ALT are elevated to a far greater degree than alk phos or bilirubin
- Once obstruction has persisted for a number of hours, Alk phos and bilirubin increase
- GGT is the most sensitive test for obstruction

- 15) A 46 yo man presents with fatigue and pruritus , most prominently on his palms and soles, He has been more fatigued for the pas 6 months. PMH: Depression, GERD, ulcerative colitis (colectomy in 1998). Meds: Sertraline and omeprazole. PE BP 100/60, P 80 T 36.7
- Eyes- sclera non icteric
- Abdomen- liver 12cm, splenomegaly present
- No fluid wave. Skin- no spider angioma or palmer erythema. Excoriations present on arms

- Labs: AST 85 ALT 90 Alk phos 600 Tbil- 1.9

Alb- 3.0 INR 1.1 HCT 42 WBC 5.6 Plt 120,000

Bun 15 Cr 1.0

Abdominal CT- small nodular liver, splenomegaly, abdominal varices present.

What is the most likely diagnosis?

A) chronic hepatitis C

B) primary sclerosing cholangitis(PSC)

C) chronic hepatitis B

D) primary biliary cholangitis (PBC)

E) Constrictive pericarditis

Abnormal Liver Tests Case

Pearls

pruritis suggests cholestatic disease

PSC occurs most commonly in middle aged males

frequently associated with inflammatory bowel disease

- most commonly associated with ulcerative colitis (50-75%)
- can also be seen with Crohn's disease

16) What test would you do to confirm the diagnosis?

A) liver biopsy

B) HIDA scan

C) hepatic ultrasound

D) endoscopic cholangiogram

Abnormal Liver Tests Case

- Pearls
  - diagnosis of PSC is based on clinical, biochemical, and cholangiographic findings
  - typical findings → diffuse multifocal strictures of the biliary tract with areas of dilation (“beading”)

Primary Sclerosing Cholangitis

- male - 60-70% of cases are in men
- history of inflammatory bowel disease
  - 50-100% of cases associated with ulcerative colitis
    - depending on country (in USA, 75% 36% Italy 98% Norway)
  - BUT - 2.4-7.5% of those with IBD have PSC
- cholestatic features (alkaline phosphatase, bilirubin, GGT)
- positive ANCA in 80%
- signs of chronic liver disease
- typical cholangiography

17) How would you treat him?

A) ursodiol

B) colchicine

C) liver transplantation

D) Prednisone and azathiprine

Primary Sclerosing Cholangitis

Pearls

no therapy to date has shown a major impact on survival or prevention of complications

- high-dose ursodiol in trials

Management Goals

- relieve symptoms
- prevent or treat complications
- optimize timing of liver transplantation

Complications Of PSC

- Complications
  - pruritis
    - cholestyramine, rifampin, naltrexone, naloxone
  - bacterial cholangitis
    - antibiotics
  - fat-soluble vitamin deficiency
    - supplemental vitamins
  - osteoporosis (in 50%)
    - supplemental calcium and vitamin D, bisphosphonates
  - Varices
    - non-selective beta-blockers
  - cholangiocarcinoma
    - poor prognosis

Autoimmune Hepatitis

- Most commonly seen in women 20-50
- Frequently they have a history of another autoimmune disease (ITP, type 1 DM, thyroiditis, hemolytic anemia or sprue
- Most patients have hypergammaglobulinemia (picked up on an SPEP). Positive ANA and anti Smooth muscle antibodies are also seen .
- Corticosteroids (often with azathioprine) extremely effective treatment

A Few Words About Wilsons Disease

- The older the patient, the less likely it is Wilsons disease. Almost all diagnoses are made by age 40. On the boards , it would be a younger patient
- Eye manifestations- Kayser- Fleischer ring, sunflower cataracts
- Nueropsych- parkinson like tremor, clumsy gait
- Hematologic- hemolytic anemia
- Hepatic
- Rhematologic- chondrocalcinosis (esp knees)
- Initial testing- ceruloplasmin level and 24 hour urinary Cu+ slit lamp exam for K-F rings

- 19) 55 yo woman comes to you to establish care
  - fatigue
- She has a few symptoms
  - pruritis
  - dry eyes
- past history
  - hysterectomy for fibroids 10 years ago
  - no alcohol, tobacco or drug use

- exam
  - spider angiomata
  - mild splenomegaly
  - otherwise normal

- labs
  - platelets **90,000**
  - bilirubin **2.0**
  - AST/ALT normal
  - **TSH 10**
  - cholesterol **500**
  - alk phos **450** (4x ULN)
  - albumin **3.0** (nl >3.5)
  - INR **1.6**

What is the Most Appropriate Next Step?

A) ultrasound

B) CT scan

C) liver biopsy

D) further laboratory testing

E) symptomatic treatment of itching and dry eyes

Pearls

- viral and autoimmune diseases must be excluded
- imaging techniques may confirm her cirrhosis, but are not helpful in diagnosis
- if cirrhosis is already clinically evident, liver biopsy is not necessary

20) What is the Most Likely diagnosis?

A) Chronic hepatitis C

B) primary sclerosing cholangitis (PSC)

C) Autoimmune hepatitis

D) primary biliary cholangitis (PBC)

E) nonalcoholic fatty liver disease (NAFLD)

F) Wilson’s disease

Results

- Further lab testing:
  - HAV (-) HBV (-) HCV (-)
  - ANA (-) ASMA (-)
  - AMA (+) 1:2560
  - iron studies normal
- ultrasound – splenomegaly, small nodular liver, portal hypertension, no biliary dilatation, single gallstone

Primary Biliary Cholangitis Pearls

- chronic cholestatic liver disease – cause unknown
  - genetic and immunologic factors play a role
- PBC is found in all races and ~90-95% are female
- age of onset ranges from 30-70
- antimitochondrial antibody (AMA) found in 95%!!!!!!
- associated with other autoimmune disease!!!!!!!!
  - thyroid, rheumatoid arthritis, Sjögren's, scleroderma, CREST (Especially Sjogren's and autoimmune thyroiditis)

More PBC Pearls

- serum cholesterol is elevated in >50% of PBC patients
- patients with PBC are NOT at increased risk of death from atherosclerosis, despite markedly elevated cholesterol
  - most of this elevation is secondary to high HDL
  - PBC patients have low lipoprotein(a) levels

Treatment Options for PBC

- treatment with ursodiol (in pooled controlled studies)
  - 13-15 mg/kg daily
  - prolonged time before transplant was required
    - but benefit likely better in early disease
  - is safe and well tolerated

  TRANSPLANT MOST IMPORTANT AND USEFUL TREATMENT
- controversial:
  - Methotrexate
  - Colchicine

Complications of PBC

- pruritis
  - cholestyramine, colestipol, rifampin, naltrexone, naloxone, nalmefene, ursodiol, PUVB, plasmapheresis
- fat-soluble vitamin deficiency
  - supplemental vitamins
- steatorrhea
  - medium-chain TGs
- osteoporosis (in 50%)
  - supplemental calcium and vitamin D, bisphosphonates
- Varices
  - non-selective beta-blockers

- 23) A 37 yo woman with a history of alcoholism is brought to the emergency room by friends with confusion and abdominal pain. Her friends report that she has been complaining of right sided chest pain for the past 6 days. Her friends last saw her 2 days ago. On exam she is confused and drowsy. She has RUQ tenderness. Labs: WBC 13,000, Bili- 9 AST 10,000 ALT 7,000 INR 8.0

What is the Most Likely Cause of Her Symptoms?

A) Impacted stone in the CBD

B) Hepatitis C

C) Alcoholic hepatitis

D) Acetaminophen overdose

E) Hepatocellular carcinoma

Massively Elevated Transaminases

- Common Causes

Drug/toxin – usually acetominophen or toxic mushrooms

Acute hepatitis A or B (not C)

Ischemia

- Less Common

Exacerbation of autoimmune hepatitis

Acute Bud-Chiari

Hellp syndrome/Acute fatty liver of pregnancy

24) A 47 yo woman presents for evaluation of abnormal liver tests. She had tests done for a life insurance exam. The patient has no symptoms. She has a history of hyperlipidemia treated with Atorvastatin. Exam: Obese woman BP 140/70 P80. No hepatomegaly on exam. Labs: AST 88(NL <50) ALT 96 (NL <50) Alk phos 150 (NL < 130) Glucose 124. Subsequent workup Hep C ab negative. What is the most likely cause of her liver lab abnormalities?

A) Non alcoholic steatohepatitis (NASH)

B) Alcoholic hepatitis

C) Toxicity from atorvastatin

D) Hemochromatosis

E) Autoimmune hepatitis

Nonalcoholic Steatohepatitis

- Common 7-9% of liver biopsies
- More common in women
- Associated with metabolic syndrome (Obesity, type 2 DM, hyperlipidemia)
- Lab abnormalities: Usually transaminase elevations ALT slightly more than AST, not much elevation in Alk phos
- Diagnosis: Definitive by biopsy, strongly suspect in patients with right risk factors and negative hepatitis serologies
- Therapy- gradual weight loss, ? Vitamin E, ? Pioglitazone ? metformin

Board Reflexes Hepatology

- IBD history and jaundice or inc alk phos= PSC
- Middle age woman with increased alk phos, pruritus = PBC
- Antimitochondrial ab elevated most commonly in PBC
- Ant Sm Muscle Ab most commonly elevated in autoimmune hepatitis (usually with a positive ANA and hyperglobulinemia)
- Hand arthritis involving MCP joints and liver abnormalities = hemochromatosis
- Please don't order a serum ammonia

ANSWERS

- 1) E -alcoholic hepatitis
- 2) D- corticosteroids
- 3) D-hemochromatosis
- 4) D- repeat in 1-2 months after abstinence
- 5) C- HBV/HCV serologies
- 6) D- past HBV probable HCV
- 7) B- completely abstain from alcohol
- 8) B- NSAIDS
- 9) C- cefotaxime and albumin
- 10) D- stop propranolol
- 11) B- non contrast CT scan of head
- 12) A- Hepatic ultrasound

ANSWERS

- 13) C- HIDA scan
- 14) E- passage of gallstone
- 15) B- Primary sclerosing cholangitis
- 16) D-endoscopic cholangiogram
- 17) C- liver transplantation
- 19) D- further lab testing
- 20) D- PBC
- 23) D- acetaminophen overdose
- 24) A- Nonalcoholic steatohepatitis