Primary Sclerosing Cholangitis

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Acknowledgment

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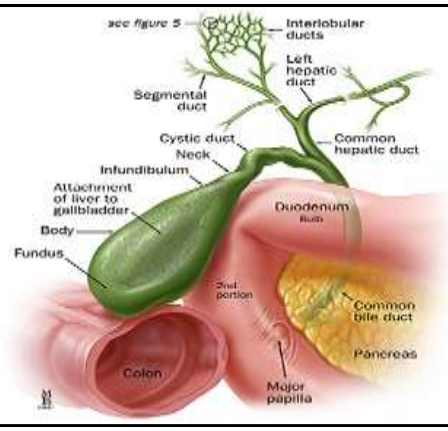
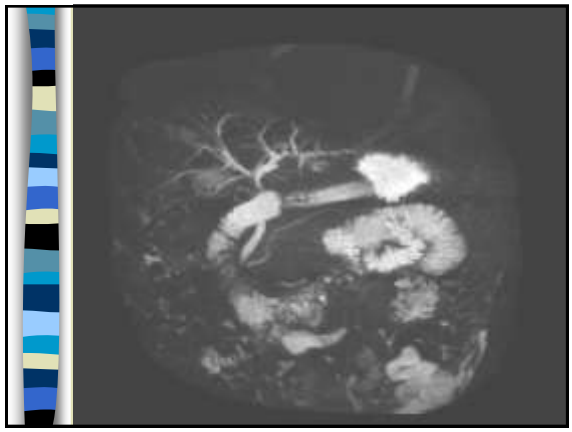
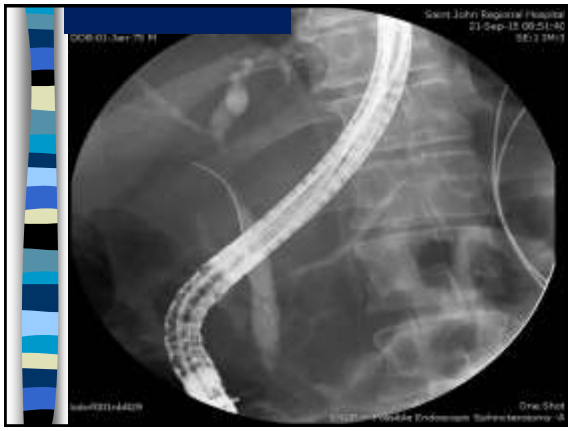
Introduction

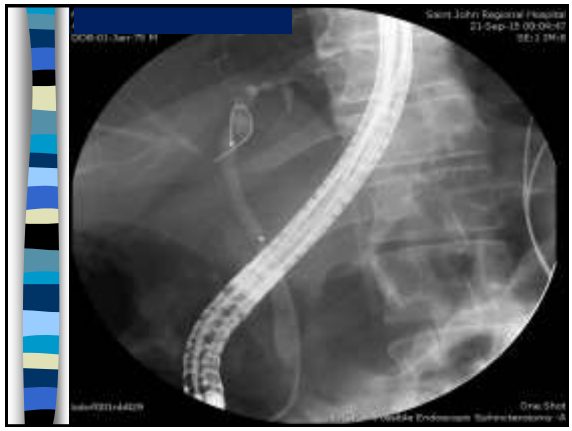
- Epidemiology
- Pathogenesis
- Clinical Manifestations
- Diagnosis
- Prognosis
- Treatment

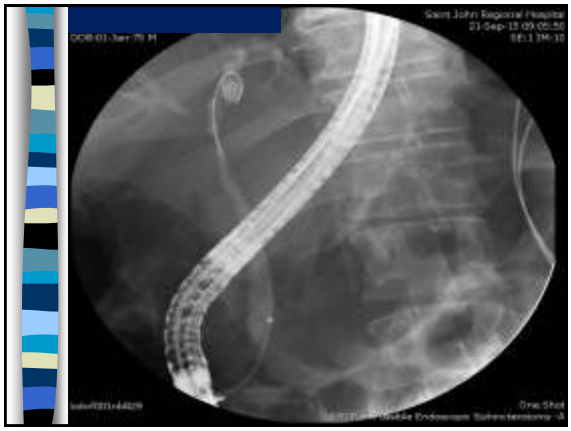


Case









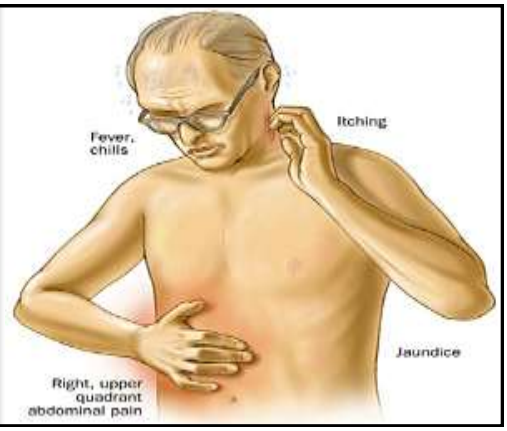
- Definition
  - Primary sclerosing cholangitis is an idiopathic condition defined as the presence of beading and stricture formation of the intra-and/or extrahepatic bile ducts that cannot be ascribed to another cause.

Epidemiology

- 5% of ulcerative colitis
- Males with pan colitis > Left sided colitis
- 1-16 per 100,000
- 60-70% of patients with PSC and UC are males
- Mean age of diagnosis 30-40 years
- PSC with no IBD Female > Male

Pathogenesis

- Unclear
- Genomic studies have identified genotypic associations and HLA haplotype associations
- Presumed autoimmune phenomenon

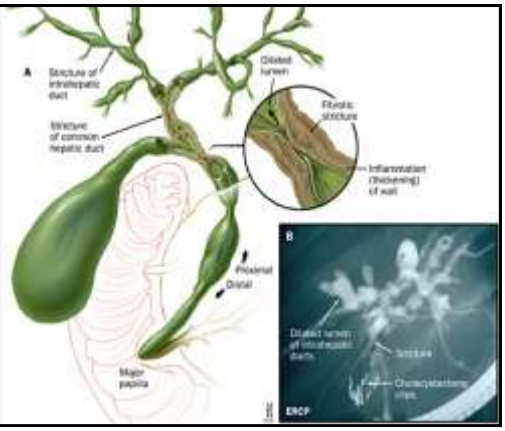


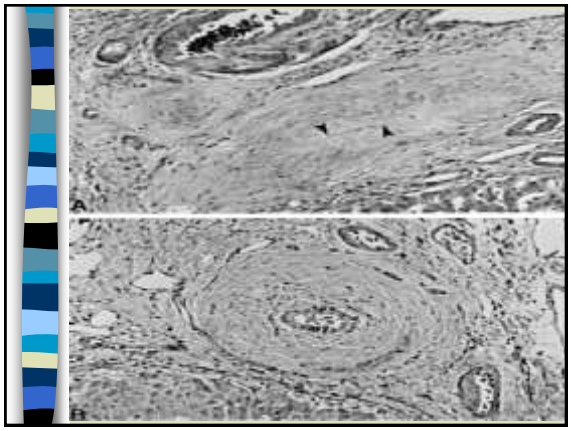
Signs and symptoms

- Abnormal liver enzymes
- Fatigue
- Pruritus
- Jaundice
- Portal hypertension

Diagnosis

- Cross-sectional imaging with ultrasound/CT to rule out biliary obstruction
  - Obstructed---ERCP with intervention
  - Nonobstructed—MRCP preferred
- Liver biopsy
  - Not necessary if suspected PSC on cholangiographic findings
  - Recommended to make diagnosis in patients with suspected small duct PSC or to exclude other conditions





- Anti –mitochondrial antibodies
- ANA
- IgG4

Medical Therapy

- Ursodeoxycholic acid
  - Doses >28mg/kg per day should not be used

*other treatments have been tested without any proven benefit

Azathioprine, budesonide, methotrexate, metronidazole, minocycline, MMF, Trental, prednisolone, tacrolimus, vancomycin

Olsson et al. Gastro 2005;129:1464-1472

- RCT
- N=219
- Urso 17-23mg/kg
- End pt– death or liver transplant
  - 7.2 VS 10.9% (7 vs. 11)
  - No statistical benefit

Farkkila et al. Hepatology 2004;40:1379-1386

- RCT
- N=80
- Urso 15mg/kg and Flagyl 600-800mg/d
- 3years
- Improved ALP, New mayo score, but no statistically significant effect on disease progression

Endoscopic Management

- Recommendations
  - ERCP with balloon dilation is recommended for PSC with dominant strictures and pruritus and/or cholangitis
  - PSC with dominant stricture seen on imaging should have ERCP with cytology, biopsy and FISH
  - PSC patients undergoing ERCP should have antibiotic prophylaxis
  - Routine stenting after dilation of a dominant stricture is not required or as short term stenting may be required in severe stricturing

- Dominant stricture
  - Stenoses<1.5mm CBD
  - <1mm hepatic ducts
  - 45% of patients

ERCP
Dominant strictures

Baluyut,AR et al, Impact of endoscopic therapy on survival of patients with PSC. Gastrointest Endo 2001;53:308-12

- 63pts
- Balloon dilation of dominant strictures
- 5 yr observed survival was greater than predicted
- 83vs 65%

Stiehl A, et al, Development of dominant bile duct stenoses in patients with PSC treated with URSO: outcome after endoscopic treatment. J Hepatol 2002;36:151-6

- 55pts
- Balloon dilation
- 5 yr survival 94 vs 78%

- Stent placement can lead to more frequent complications of cholangitis but stenting for short durations may be necessary
- Prophylactic antibiotics preoperatively and postoperatively for 3-5 days have been advised [quinolone or cephalosporin]

Dominant strictures and Cholangiocarcinoma

- Cholangiocarcinoma should be considered in all dominant strictures
- In a series of 128 patient's with PSC, 80 head dominant strictures and 21 [26%] developed a cholangiocarcinoma

- Lindberg B, et al. Diagnosis of biliary strictures in conjunction with ERCP with special reference to patients with primary sclerosing cholangitis. Endoscopy 2002; 34:909-16

- Brushing and biopsy
  - Specificity very high, sensitivity below 30%
- FISH
  - Increases sensitivity to 64% and perhaps higher with sequential samples

- Direct cholangioscopy
  - Direct visualization and biopsy
  - Specificity and sensitivity greater than 90%
- Confocal laser microscopy
  - Sensitivity 98%, specificity 67%
    - Strictures in general not specifically studied for PSC

Alternate drainage

- Percutaneous
  - Second line therapy
  - Primarily used for failures or intrahepatic
  - Altered gastrointestinal/biliary anatomy
- Surgical
  - Biliary reconstruction allows prolonged improvement with resolution of jaundice but has significant risks of cholangitis and increased rates of mortality

Liver transplantation

- Recommended when possible over medical or surgical drainage in patient with decompensated cirrhosis
- Referral when Meld score exceeds 14
  - Median time for progression from diagnosis to death/transplant 10-12 years
  - Liver transplant 5 year survival 80-85%

Fosby, E et al. recurrence and rejection in liver transplantation for PSC. World J Gastro 2012;18:1-15

Colonic Neoplasia

- Ulcerative colitis and PSC had an absolute cumulative risk of developing colorectal cancer or dysplasia at 10, 20, and 25 years of 9%, 31%, and 50%, respectively
- Ulcerative colitis alone, the corresponding risk was 2%, 5%, and 10%, respectively.

Colonic surveillance

- Full colonoscopy at time of diagnosis
- Annual colon surveillance preferably with chromoendoscopy
- Risk of colorectal dysplasia and cancer 4-5 fold higher amongst PSC plus IBD compared to IBD alone
  - Soetikno, RM et al. increased risk of colorectal neoplasia in patients with PSC and ulcerative colitis colon a meta-analysis. Gastrointestinal endoscopy 2002; 56:48-54

Complications

- ***Nutritional***
- ***Secondary Biliary Cirrhosis***
- ***Bleeding***
- ***Biliary Tract Calculi***
- ***Pancreatic Disease***
- ***Cholangiocarcinoma***
- ***Hepatocellular Carcinoma***
- ***Colonic Neoplasia***
- ***Pouchitis***

Hepatobiliary malignancy and gallbladder disease

- Regular screening for cholangiocarcinoma with cross-sectional imaging [ultrasound/MRI]and serial CA 19-9 every 6-12 months
- Cholecystectomy in patient's with PSC and gallbladder polyps greater than 8 mm

Special situations

- Further testing for autoimmune hepatitis/overlap is recommended in patients less than 25 or those with higher-than-expected aminotransferases
- MRCP is recommended for patients less than 25 with autoimmune hepatitis who have elevated serum ALP

PSC-AIH overlap

- May coexist and the prevalence in PSC is approximately 10% but has ranged from 1.5-17%

IgG4 associated cholangitis

- Increasingly recognized in patients with PSC
- Should be screened with ANA and IgG4 levels [greater than 140 mg/dL]
- Liver biopsy may also identify a classic lympho-plasmacytic infiltrate

General considerations

- Pruritus can be treated with local creams, antihistamines and bile acid sequestrants. Second line therapy includes rifampin and naltrexone
- Screen for varices if platelet count less than 150
- Bone mineral density at diagnosis and every 2-4 years
- Screen for fat-soluble vitamin deficiencies

Summary Management of PSC

Measure IGG4 at diagnosis.
Assess for varices in PLT <150
Assess BMD
Assess for fat Soluble vitamin deficiency if jaundiced

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Monitor Liver tests every 3-4 mths

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Consider screening for Cholangiocarcinoma with US/MRI and Ca19-9 Q6-12 mths

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Colonoscopic Surveillance Annually in those with IBD

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If Deterioration and dominant stricture, ERCP with balloon dilation with Abx and stent if needed

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Refer for transplant if MELD >14 or for cases suspected of Cholangiocarcinoma


Gastroenterologists
Are...