Primary Sclerosing Cholangitis

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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


- 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 Endosc 2001;53:308-12
- 63 pts
- Balloon dilation of dominant strictures
- 5 yr observed survival was greater than predicted
- 83 vs 65%

- 55 pts
- 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


- 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%

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

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 if PLT <150
- Assess BMD
- Assess for fat soluble vitamin deficiency if jaundiced
- Monitor Liver tests every 3-4 mths
- Consider screening for Cholangiocarcinoma with US/MR and CA19-9 Q6-12 mths
- Colonoscopy: Surveillance annually in those with IBD
- If Deterioration and dominant stricture, ERCP with balloon dilation with biliary stent if needed
- Refer for transplant if MELD >14 or in cases suspected of Cholangiocarcinoma