Primary Sclerosing Cholangitis
and
Cholestatic liver diseases

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I have nothing to disclose
Educational Objectives

• What is PSC?
• Understand the cholestatic liver diseases
  – Signs, symptoms, blood work, imaging and diagnosis
• Management plan and long term follow up.
• Appreciate conditions associated with PSC.
• Difference in PSC and PBC
• 35 year old male referred for jaundice, itching, fatigue and weakness.
• Patient has h/o diarrhea and rectal bleeding off and on for a year. Recent diagnosis of Ulcerative colitis.
• F/H of Ulcerative colitis.
• H/O Iron deficiency anemia
• On mesalamine and MVI. H/O iron supplement.
Hepatocellular vs cholestatic liver Disease

• Hepatocellular liver disease is due to damage to hepatocytes.
  • Increase in ALT and AST.

• Cholestatic liver disease due to disease of Bile ducts and process where Bile acid flow is restricted.
  • Increase in ALP and GGT.
PSC

- PSC 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.
- PSC is characterized by inflammation, fibrosis, and stricturing of medium and large ducts in the intrahepatic and/or extrahepatic biliary tree.
- Many, if not most, cases of PSC are associated with inflammatory bowel disease (IBD) up to 75%.
- 12-15% will develop cholangiocarcinoma over life time.
- Male to female ratio is 2:1.
Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver and biliary tract disease that has a highly variable natural history.

Pathogenesis is not understood. Disease symptoms and complications are due to fibrosis and strictures of CBD.

PSC may be asymptomatic for long periods but may also have an aggressive course, leading to recurrent biliary tract obstruction, recurrent episodes of cholangitis, and may progress to end-stage liver disease.

The typical cholangiography findings include focal stricturing and saccular dilatation of the bile ducts, which may lead to a “beaded” appearance.
Signs and Symptoms

- A large number (>50%) of patients present without symptoms
- Fatigue
- Pruritis
- Jaundice
- Rectal bleeding, diarrhea.
- RUQ pain
Types of PSC

• Classic PSC

• Small duct PSC
Diagnosis

1. MRCP is preferred over endoscopic retrograde cholangiopancreatography (ERCP) to establish a diagnosis of PSC.

2. Liver biopsy is not necessary to make a diagnosis in patients with suspected PSC based on diagnostic cholangiographic findings.

3. Liver biopsy is recommended to make a diagnosis in patients with suspected small duct PSC or to exclude other conditions such as suspected overlap syndrome with autoimmune hepatitis, PBC.
Serologic findings in patients with PSC

- Hypergammaglobulinemia – 30 percent
- Increased serum immunoglobulin M (IgM) levels – 40 to 50 percent
- Atypical perinuclear antineutrophil cytoplasmic antibodies (P-ANCA) – 30 to 80 percent
- Human leukocyte antigen DRw52a – 0 to 100 percent in various reports
Normal ERCP and CBD
ERCP image in PSC
Differential diagnosis of primary sclerosing cholangitis

- Secondary sclerosing cholangitis
- Cholangiocarcinoma
- IgG4-associated cholangitis
- Histiocytosis X
- Autoimmune hepatitis
- HIV syndrome
- Bile duct strictures
- Choledocholithiasis.
- Primary biliary cirrhosis
- Papillary tumors
Small duct PSC Differential Diagnosis

• Liver biopsy is recommended to make a diagnosis in patients with suspected small duct PSC or to exclude other conditions such as suspected overlap with autoimmune hepatitis.

• Antimitochondrial autoantibody testing can help exclude (PBC) primary biliary cirrhosis.

• Patients with PSC should be tested at least once for elevated serum immunoglobulin G4 (IgG4) levels.
PSC
Histology
**PBC**

- **Interlobular bile duct destruction**
- Prevalence: 0.6–40 per 100,000
- Gender: F:M, 10:1
- Age at onset: 50–60 years
- Smoking increases risk
- >28 known risk genes
- Autoantibodies (AMA)
- Known T cell targets

**PSC**

- **Intra-/extrahepatic bile ducts**
- Prevalence: 0.2–14 per 100,000
- Gender: F:M, 1:2
- Age at onset: 30–40 years
- Smoking decreases risk
- >16 known risk genes
- Autoantibodies (ANCA?)
- Unknown T cell targets

**Shared hepatic features:**

- Autoimmune hepatitis (~10%)
- Cholestatic liver cirrhosis
- Pruritus
- Fatigue
- Cancer
- Inflammatory bowel disease
PSC and IBD

- Annual colon surveillance preferably with chromoendoscopy is recommended in PSC patients with colitis beginning at the time of PSC diagnosis.

- A full colonoscopy with biopsies is recommended in patients with PSC regardless of the presence of symptoms to assess for associated colitis at time of PSC diagnosis.

- Some advocate repeating the exam every 3–5 years in those without prior evidence of colitis.
Medications

- Ursodeoxycholic acid
1. ERCP with balloon dilatation is recommended for PSC patients with dominant stricture and pruritus, and/or cholangitis, to relieve symptoms.

2. PSC with a dominant stricture seen on imaging should have an ERCP with cytology, biopsies, and fluorescence in-situ hybridization (FISH), to exclude diagnosis of cholangiocarcinoma.

3. PSC patients undergoing ERCP should have antibiotic prophylaxis to prevent post-ERCP cholangitis.

4. Routine stenting after dilation of a dominant stricture is not required, whereas short-term stenting may be required in patients with severe stricture.
Complications of PSC

- Fat-soluble vitamin deficiencies (A, D, E, and K)
- Metabolic bone disease
- Dominant biliary strictures
- Cholangitis and cholelithiasis
- Cholangiocarcinoma
- Gallbladder cancer
- Hepatocellular carcinoma (in patients with cirrhosis)
- Colon cancer (in patients with concomitant ulcerative colitis)
Liver Transplant

- Liver transplantation, when possible, is recommended over medical therapy or surgical drainage in PSC patients with decompensated cirrhosis, to prolong survival.
- Patients should be referred for liver transplantation when their Model for End-Stage Liver Disease (MELD) score exceeds 14.
- Outcomes for liver transplantation in PSC compare favorably to transplants for other indications,
special circumstances in which liver transplantation may be indicated despite low MELD score

• Recurrent or refractory cholangitis
• Intractable pruritus
• Peripheral or hilar cholangiocarcinoma <3 cm in diameter (in the context of a clinical trial)
CANCER SCREENING

• Gallbladder carcinoma and cholangiocarcinoma
  • An annual ultrasound examination to detect mass lesions in the gallbladder.
  • Ultrasound or magnetic resonance imaging (MRI) to look for evidence of cholangiocarcinoma every 6 to 12 months.
  • Serum levels of the tumor marker cancer antigen (CA) 19-9 every 6 to 12 months to detect cholangiocarcinoma.
  • Cholecystectomy in patients found to have a gallbladder polyp >8 mm (of note, some guidelines recommend cholecystectomy for gallbladder masses of any size.
  • Evaluation for cholangiocarcinoma in patients with deterioration of constitutional performance status or liver biochemical tests.