

PRIMARY SCLEROSING CHOLANGITIS – 2

Definition: Chronic progressive disorder of unknown etiology characterized by:

- Progressive inflammation
- Fibrosis
- Strictureing of intrahepatic/extrahepatic bile ducts

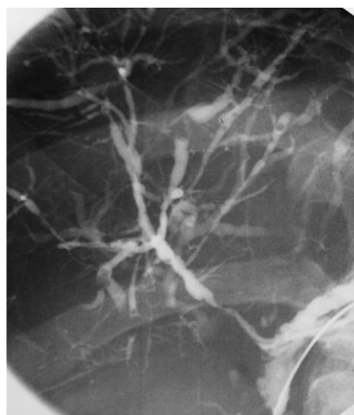
**Leads to cirrhosis, portal HTN, end stage liver disease → transplant

Stages (by liver bx):

- I. Portal triad edema, scarring, enlargement w/ piecemeal necrosis and isolated BD damaged, mono/polynuclear cells infiltrate
- II. Expansion of portal triads w/ fibrosis into parenchyma
- III. Bridging fibrosis
- IV. Cirrhosis

Epidemiology

- PSC occurs in 5% of patients with UC
- UC occurs in 60-75% of patients with PSC
- PSC more common in men (2/3) than women
- Present most commonly in 40's
- Median survival 10-12yrs
- **Increased risk of developing cholangiocarcinoma – 1%/yr (occurs in 10-15%)



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Etiology

- Unknown
- Associated w/ UC → abnormal colonic mucosa predisposes to portal bacteremia?
- Immunologic → 25% of patients have 1 autoimmune disorder outside colon/liver

Clinical

- Asymptomatic w/ hepatomegaly or elevated LFTs
- Fatigue
- Pruritis
- Cirrhosis
- Fevers, chills, night sweats
- RUQ pain
- Jaundice

Diagnosis

- Labs: alk phos, ANA, P-ANCA (80%), HLA B8/DR3
- ERCP, MRCP
- Liver biopsy – staging, demonstrates “onion skin” pattern (obliteration of small BD w/ concentric replacement by connective tissue)

Treatment

- Ursodeoxycholate – lowers serum bilirubin, AST/ALT (does NOT improve symptoms or delay progression)
- Stenting, resection of extrahepatic biliary tree w/ b/l hepaticojejunostomy – can delay need for transplant, has no effect on long term prognosis
- TRANSPLANT → only cure, 10% require re-transplant (PSC accounts for 10% of all liver transplants)

Grucela and Steinhagen. *Restorative proctocolectomy and ileal pouch-anal anastomosis for UC after liver transplant for PSC: case report and review of literature*. American Surgeon 2005.

- Case report: 45M with 15year history of UC (prednisone) and 10 year history of PSC → liver transplant for end-stage cirrhosis (MELD 30). Post-op prednisone/tacrolimus. Progressively worse colitis resulted in IPAA 1year later.
- Review of literature:
 - Despite the fact that UC and postop immunosuppression after OLT use similar drugs (prednisone, cyclosporine, azathioprine, tacrolimus, mycophenolate mofetil) it has been reported that UC has more aggressive course after transplant
 - Patients with PSC and UC are at increased risk for developing colorectal cancer than those with UC alone
 - Increased risk of pouchitis after RPC/IPAA for UC in patients with PSC
 - Penna et al. demonstrated increased risk at 1, 2, 5, 10 years after IPAA in patients with PSC than those with normal hepatic function
 - Aitola et al. demonstrated increased risk in patients after RPC with biopsy proven PSC (with or without symptoms)
 - Prior transplant at time of RPC may lead to increased risk of pouchitis

Gwoe-Tzer Ho et al. *The clinical course of UC after orthotopic liver transplantation for PSC: further appraisal of immunosuppression post transplantation*. Eur J Gastroenterology/hepatology 2005.

- Methods
 - 20 patients with OLT for PSC and UC
 - Examined the course of UC using:
 - Relapse rate – increased stool frequency requiring increased medication dose or addition of second agent (+/- endoscopic/histologic evidence)
 - Number of steroid courses/year (excluding steroids for OLT rejection)
 - Documented steroid dependency (inability to wean steroids)

- Results
 - Rate of relapse of UC is higher after OLT → does transplanted liver create a new balance of immunoregulation and restore competence of immune system?
 - 1 relapse/3.3 years → 1 relapse/year (p=0.007)
 - 38% in 6mos, 50% in 1yr, 69% 2yrs after OLT
 - Requirement of steroids for UC is higher after OLT
 - Steroids/year 0.10 → 0.4 (p=0.003)
 - 40% patients required steroids for UC → 75% after OLT
 - 4 patients dependent after OLT
 - Colectomy rate after OLT
 - 3.46 years average
 - ¾ with IPAA had recurrent pouchitis
 - High rate of neoplasia in PSC/UC patients
 - 19% developed neoplasia
- Weaknesses
 - Heightened awareness of patients' condition after OLT
 - Steroids for OLT were withdrawn 3months after transplant
 - The patients received lower doses of azathioprine for postop immunosuppression than that recommended for IBD (1.02mg/kg vs. 2mg/kg)

Melissa Alvarez, M.D.
March 20, 2006