Primary Sclerosing Cholangitis in Pediatrics

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PSC in Children - Definition

- Chronic liver disease of unknown etiology
- Probable autoimmune process
- Irregular damage and scarring of extrahepatic and medium to large intrahepatic bile ducts
- Progresses to biliary cirrhosis
Differences: Children vs. Adults

- Cause
- Age and Course
- Auto-antibodies
- Response to immunologic suppression therapy
Causes of Sclerosing Cholangitis in Children

• Immune deficiencies
• Cystic Fibrosis
• Infections of bile ducts
• Autoimmune
  - 30-50%
• Primary SC
  \[\text{Associated with Ulcerative colitis or Crohn’s disease} = 50-80\%\]
Clinical Differences
Child vs. Adult

- **Incidence**
  - < 18 years old: .23 per 100,000
  - Adults: 1.11 per 100,000

- Males = Females in young children
- Females > Males in teens
- Males > Females in adults
Symptoms of PSC in Children

• **Initial Symptoms**
  - Fatigue, poor appetite, nausea, weight loss, itching
  - Delayed puberty
  - Jaundice is rare
  - No symptoms – elevated liver blood tests found on testing
    • Ulcerative colitis and Crohn’s disease
  - Large liver or spleen on exam
  - Gastrointestinal bleeding
Diagnosis

• Blood tests suggestive (elevated GGT)
• Imaging of bile ducts
  – Ultrasound
  – CT scan
  – Magnetic resonance cholangiography (MRCP)
  – Endoscopic retrograde cholangiography (ERCP)
• Liver biopsy
  – look for damage to bile ducts
  – how much scarring is present?
  – exclude other liver diseases
Autoimmune SC (overlap) – common in children

• **Autoimmune Hepatitis (AIH)**
  – chronic liver disease
  – NO bile duct injury!!!
  – elevated IgG
  – presence of autoantibodies in blood
  – characteristic appearance to liver biopsy
  – teen age girls – most common
  – associated with other autoimmune diseases (40%) such as IBD
  – felt to be a true autoimmune disease
Autoimmune SC (overlap)

- **ASC/overlap**
  - About one third or more of PSC children present with picture of AIH (vs. 10% of adults)
  - elevated IgG
  - liver biopsy - AIH
  - auto antibodies present
    - ANA, anti-smooth muscle antibody,
    - p-ANCA, rarely anti-LKM
  - Eventually, evidence of bile duct injury and strictures present on MRCP or ERCP
Teen with ulcerative colitis

AIH

Normal Bile Ducts

8 Years

PSC

Red arrows indicate changes over 8 years.
Autoimmune SC (overlap)

- Treatment Response of ASC
  - Steroids and Imuran: 70-90% normalized
  - Liver Blood Tests
  - Progression of bile duct injury can still happen in many
Treatment

• If ASC/AIH overlap
  – Treat for AIH component (not done in adults)
  – Corticosteroids and Imuran (azathioprine)
  – If normal blood tests for 1-2 years, attempt to wean off therapy if liver biopsy is normal

• Ursodeoxycholic acid: 10-20 mg/kg/day
  – no proof of long-term benefit, but improves liver blood tests and some symptoms
Treatment

- Fatigue
  - Exclude low thyroid or adrenal gland function, or other autoimmune disease
  - Exclude anemia
  - Daytime somnolence
  - Did not work: fluoxetine, ondansetron

- Itching
  - Urso, rifampicin, cholestyramine, others
  - Exclude bile duct stricture that needs to be dilated

- ? Use of probiotics, Remicaide, others
Treatment

- **Complications of PSC**
  - strictures
  - cholangitis

- **Complications of Cirrhosis**
  - Varices
  - Ascites
  - Fatigue
  - Others

- **Bile Duct cancer extremely rare in children**

- **Liver Transplantation**
Liver Transplant

- Ultimate treatment for majority, if not all, children with PSC
- Outcome very good
  - SPLIT data under evaluation
- Surveillance for Colitis and its complications post-liver transplant
- Recurrent disease a concern, as in adults
Survival in Children with PSC

Fig. 2. Survival analysis.

Liver 1999;19:228

9 patients
Fig. 1. Actual survival of children with PSC and the expected survival for a cohort of a U.S. Caucasian population matched by age and sex and

Hepatology 2003;38:210

52 patients
Survival - PSC vs. ASC

Fig. 3. Actual survival free of liver transplantation in children with PSC alone (dashed line) and those with PSC/AlH overlap (solid line). \( P = .2 \).
Fig. 2. Actual survival free of liver transplantation in treated (solid line) and untreated (dashed line) children with PSC. $P = .2$. 

Hepatology 2003;38:210
Bottom Line

- PSC is a Rare Disease in children
- No controlled clinical trials yet performed
- Need multi-center collaboration to learn more about cause, ASC overlap, why disease progresses, test treatments
- STOPSC study is now attempting to do this