PSC in Children and Adolescents: Similarities and Differences with PSC in Adults

Michael Narkewicz MD

Professor of Pediatrics Hewit-Andrews Chair in Pediatric Liver Disease

Medical Director Pediatric Liver Center

Children's Hospital Colorado

Affiliated with
University of Colorado
Anschutz Medical Campus

Children's Hospital Colorado

Goals

- Describe the epidemiology of PSC in Children and Adolescents (Pediatrics)
- Describe key features and how they differ from PSC in Adults
- Describe outcome features

Key Concepts Pediatric PSC

- Incidence is 1/5th that of Adults
- Accounts for 2-3% of liver transplants in children (<18 years of age)
- Unlike adults there are many disorders that can mimic “Primary” Sclerosing Cholangitis which are called Secondary SC

Children's Hospital Colorado

Key Concepts

- AST and ALT (liver enzymes) generally higher in PSC in Pediatrics than in Adults
- PSC in Pediatrics is a much more immunologic / inflammatory disease than in adults
  - Treatment with medications to suppress inflammation / immune response more commonly used in Pediatrics

Key Concepts

- Autoimmune hepatitis (AIH) in Pediatrics often can have bile duct inflammation and injury
- In England
  - All children with AIH have testing for bile duct involvement and colitis
  - ~40 have bile duct involvement (autoimmune sclerosing cholangitis: ASC)

Key Concepts

- The bile ducts inside the liver are more commonly affected than outside the liver
  - Dominant Strictures are less common

- Cancer of the bile ducts is VERY RARE in PSC in Pediatrics

PSC Incidence Pediatrics

- **Incidence: Number of new diagnosed cases in a defined period of time**
  - **Utah incidence per 100,000 children in 25 years**
  - **PSC: 0.2**
  - **ASC: 0.1**
  - **AIH: 0.4**

Hepatology 58:1392, 2013

PSC Prevalence

- **Prevalence: Measure that tells us the risk of developing a disease (higher than incidence): Measures all cases**
- **Utah: Prevalence / 100,000 Pediatric Patients for 25 years**
  - **PSC: 1.5**
  - **ASC: 0.6**
  - **AIH: 3.0**

Hepatology 58:1392, 2013

Children's Hospital Colorado

Average Age at Diagnosis

	Avg Age (yrs)	% Male
PSC	13	76
ASC	11	50
AIH	10	34

- Like adults, most are males
- Mayo: 2/3s male, 1/3 female
- Male/Female about the same for ASC

- 80% with PSC have IBD

Hepatology 58:1392, 2013 and 38:210, 2003

Progression of Liver Disease

- Development of complications in 5 years
- PSC 37%
- ASC 25%
- AIH 15%
- 5 year survival with native liver (no transplant)
  - PSC: 78%
  - ASC: 90%
  - AIH: 87%

Net 85% 5 year survival with native liver

Hepatology 58:1392, 2013

IBD and PSC: Similar to Adults

- My child has IBD, what is their risk of developing PSC?
- 1.5% of 1009 children with UC had PSC (JPGN 51:140, 2010)
- 9.5% (Utah) – 35% (Houston) of pediatric patients with UC had PSC
- 0.6% of pediatric patients with Crohn disease developed PSC
- Most diagnosed with PSC after IBD diagnosis

Hepatology. 2001;33:544 & Clin Exp Gastro 6:77, 2013

Children's Hospital Colorado

Pediatric PSC Treatment Differences with Adult PSC

- Autoimune involvement, some have a good response to immunosuppression (ASC)
- Histologic changes of SC with no associated radiologic changes (small duct SC) Thus stents less useful
- Ursodeoxycholic acid: no controlled study of ursodeoxycholic acid in children: still used and guidelines do not give direction

Children's Hospital Colorado

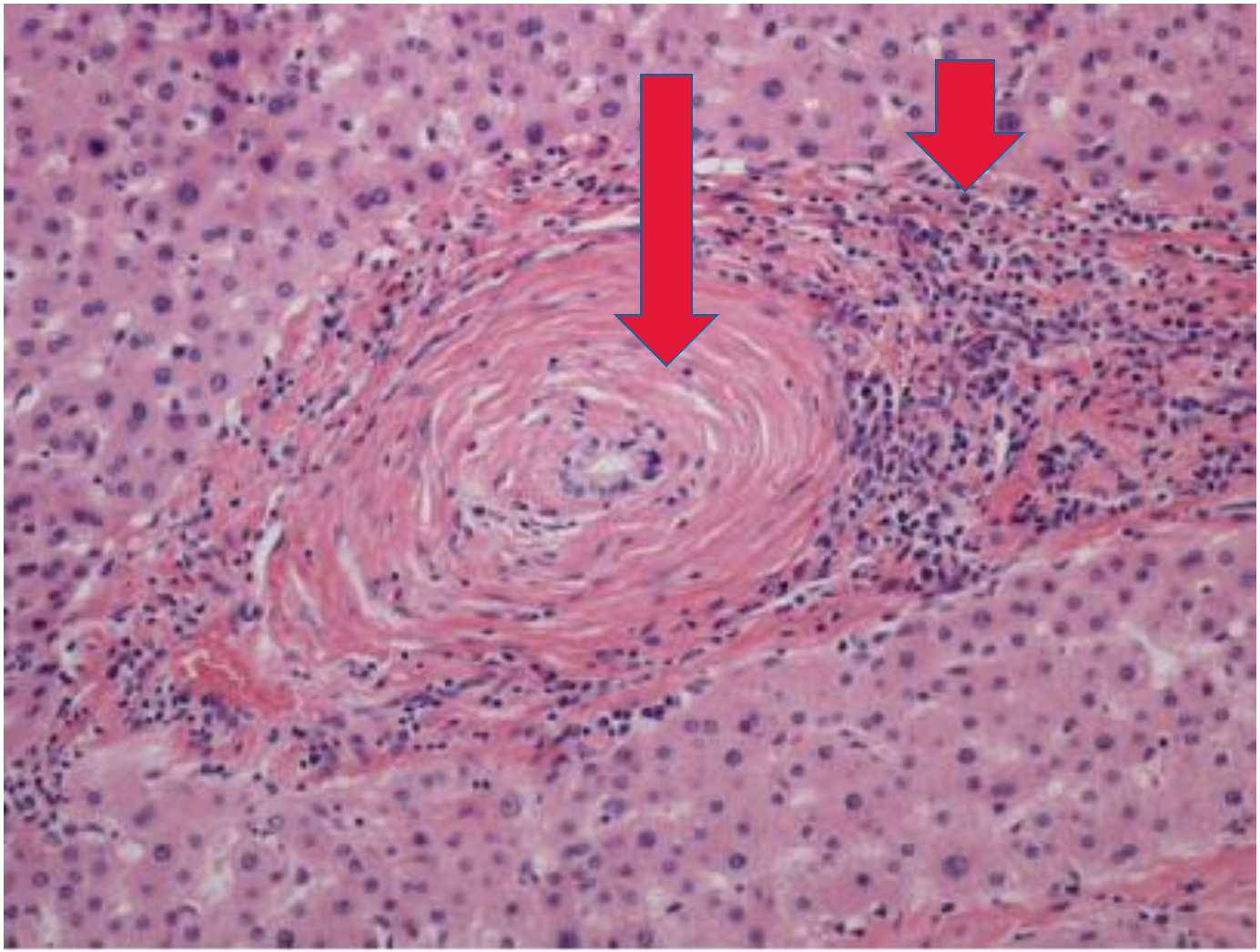
Bile duct involvement common in AIH in children

- 55 patients with AIH
- ERCP/MRCP and sigmoidoscopy
- 23 ERCP/MRCP abnormalities 40% ASC
- Autoimmune Sclerosing Cholangitis:
  - More IBD 44% vs 18%
  - More ANCA positive 74% vs 36%
  - More cholangitis on biopsy: 35% vs 12%

Hepatology. 2001;33:544

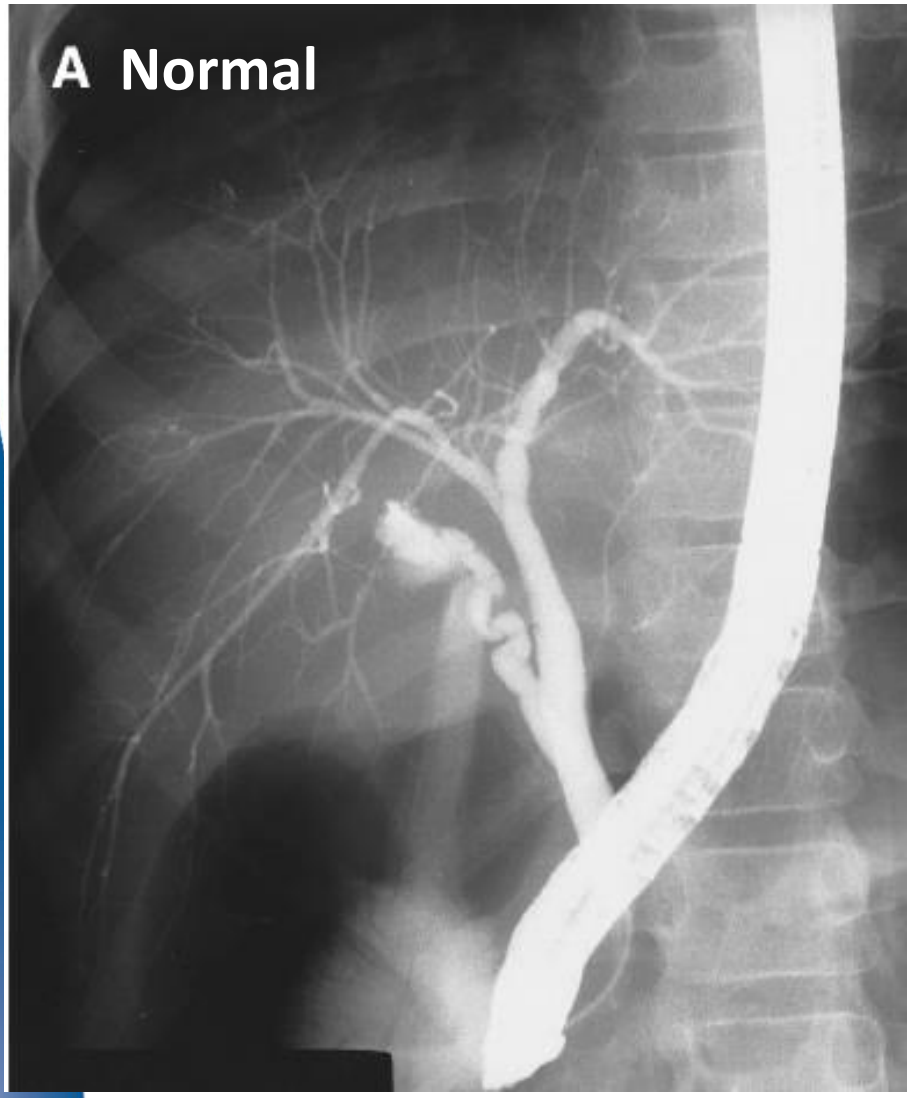
Children's Hospital Colorado

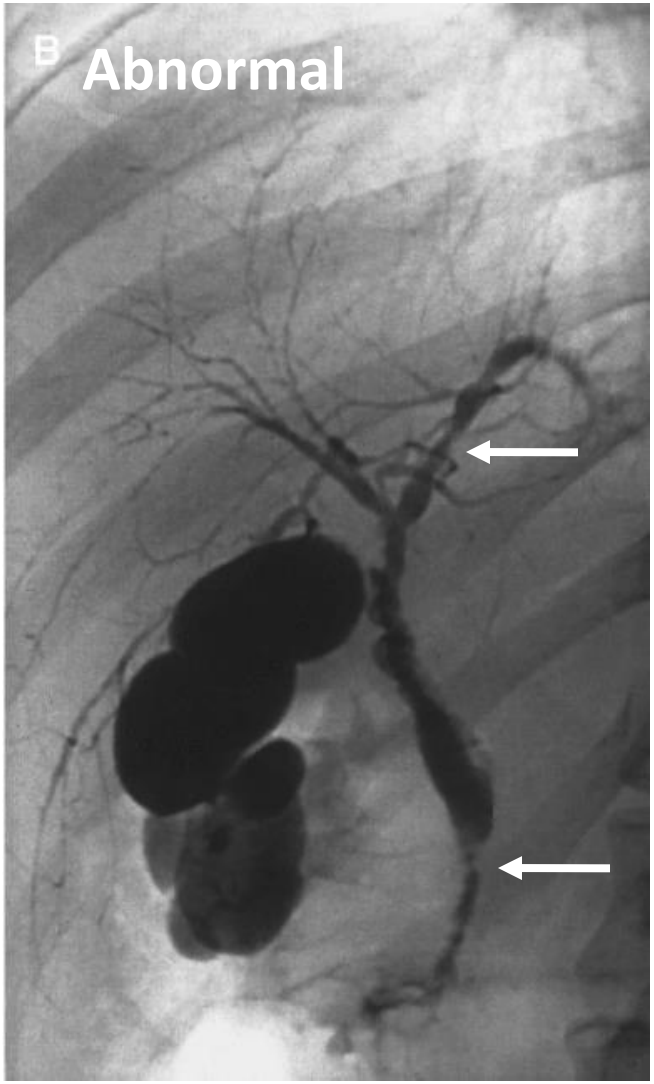
Liver biopsy



Children's Hospital Colorado

ERCP in AIH





Hepatology. 2001;33:544

Children's Hospital Colorado

Pediatric AIH/PSC

- Pediatric patients with AIH
- Large percentage have ERCP/MRCP abnormalities
- UK recommends ERCP/MRCP on all patients with AIH
- Alternative approach: ERCP/MRCP if signs of biliary involvement
- Overlap of inflammation between liver cell injury and bile duct injury is more common in children

Cholangiocarcinoma

- "Rare" in Pediatric PSC
- 6.9 % prevalence in Utah study (2 cases)
- Other rare case reports in the literature
- All in the older adolescent population

- Need a good partnership with adult PSC team to help sort this out

Children's Hospital Colorado

IgG4 Sclerosing Cholangitis

- IgG4-related sclerosing disease
- Immunoglobulin G4-related sclerosing cholangitis (IgG4-SC) **RARE**
- Characterized by sclerosing inflammation with abundant IgG4-positive plasma cells
- Most cases associated with pancreatitis
- IgG4/IgG1 cells elevated in Autoimmune PSC
- Elevated IgG4 cells (>10/HPF) present in ampulla and bile duct biopsy in 52%

JGastroenterol Hepatol. 2010;25:1648, J Gastroenterol. 2010;45:732

Children's Hospital Colorado

Liver Transplant

- ~500 liver transplants per year in pediatrics
- ~2.6% of pediatric transplants due to PSC (10-20 per year)
- Excellent 1 year (98.7%) and 5 year (86.6%) patient survival rates
- About 10% have recurrent bile duct injury/PSC

Children's Hospital Colorado

Summary

- Compared to PSC in Adults, Pediatric PSC has
- More immune / inflammation
- May respond better to immunosuppression
- Involves the small bile ducts more than the large bile ducts
- May have a better outcome overall and a better transplant survival

Children's Hospital Colorado

QUESTIONS?

Model for Intestinal Inflammation Promoting Autoimmune Disease