Autoimmune Pancreatitis and Cholangitis: A Practical Approach

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Disclosures

• None relevant
Goals

• Distinguish distinct disease types of “autoimmune pancreatitis”
• Distinguish IgG4 Associated Cholangiopathy
• Treatment strategies
The Challenge….

• Terminology
• Difficult to diagnose
  • Rare disease
  • Criteria are hard to meet (high suspicion vs. confirmed dx)
  • Histology difficult to acquire
  • Anxiety of missing malignancy
• Difficult to treat, not standardized
  • Relapse, incomplete response
  • Maintenance of remission
• Relatively newly described disease (1990s)
• Most experience is cohort series, expert consensus, etc.
When in doubt make up abbreviations

- IgG4 RD
- Type 1 AIP
- Type 2 AIP
- IDCP
- LPSP
- AIC
- IAC
- AMA neg PBC
- AIH-PBC overlap
- AIH-PSC overlap
Cholangiopathy – what are we talking about

- **AIH-PBC overlap**
  - AMA+, AIH on histology
  - ANA+ or SMA+ PBC on histology
- AMA negative PBC
- AIH-PSC overlap

**IgG4 Associated Cholangiopathy**
IgG4 Related Disease

• Immune mediated spectrum of disease with shared features
  • Pathology –
    • lymphoplasmacytic infiltrate
    • IgG4+
    • storiform fibrosis
  • Serology – IgG4
  • Presentation – pseudotumor

• Steroid responsive

• Multiple organs can be involved (including pancreas and bile duct)
Extrapancreatic manifestations of IgG4RD

- Bile duct (most common)
- Salivary glands
- Eyes (Lacrimal gland, extraocular muscles, orbital pseudotumor)
- Retroperitoneal fibrosis
- Sclerosing aortitis or periaortitis
- Thyroiditis
- Tubulointerstitial nephritis
- Lymphadenopathy
- Interstitial pneumonitis, inflammatory pseudotumor
IgG4 associated cholangiopathy (IAC)

- Part of the spectrum of IgG4 RD
- May have intrahepatic or extrahepatic strictures
- May present with jaundice
- Often associated with AIP
- Treated similarly to AIP
- Key is to exclude underlying cholangiocarcinoma
- May be difficult to distinguish between PSC
“Autoimmune pancreatitis”

- Part of a spectrum of multiorgan fibroinflammatory diseases that may or may not be associated with elevated IgG4
- Two types with some similarities and differences
- Presentation is variable and diagnosis is challenging
- Treatment is with steroids
- Can mimic (and must rule out) neoplasia
“Autoimmune Pancreatitis”

- Autoimmune pancreatitis (AIP)
- Idiopathic Duct-Centric Pancreatitis
Shared features of AIP & IDCP

- Presentation (pseudotumor, pancreas enlargement)
- Response to steroids
- Lymphoplasmacytic infiltrate
Autoimmune Pancreatitis (AIP)

• AKA AIP type I
• AKA Lymphoplasmacytic sclerosing pancreatitis (LPSP)
• Part of the spectrum of IgG4-RD
Autoimmune Pancreatitis: HISORt criteria

- **Histology**
- **Imaging characteristic (CT, Pancreatography)**
- **Serology: IgG4**
- **Organ involvement (extrapancreatic)**
- **Response to Therapy (steroids)**

Chari et al CGH 2006
Idiopathic Duct-Centric Pancreatitis (IDCP)

• AKA AIP type II
• Less common and harder diagnose
• Characteristic pathology
  • Granulocytic epithelial lesion (GEL)
• Associated with comorbid IBD
## Distinguishing features AIP vs. IDCP

<table>
<thead>
<tr>
<th>Feature</th>
<th>AIP</th>
<th>IDCP</th>
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<tbody>
<tr>
<td>IgG4</td>
<td></td>
<td>• Younger</td>
</tr>
<tr>
<td>Extrapanc involvement</td>
<td>• Relapse common</td>
<td>• Associated with IBD</td>
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<tr>
<td></td>
<td></td>
<td>• Relapse uncommon</td>
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</tbody>
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AIP vs. IDCP: Presentation

- **AIP**
  - Obstructive jaundice most common
  - Mean age >60
  - 3:1 M:F
  - Extrapancreatic involvement

- **IDCP**
  - Acute pancreatitis most common
  - Mean age 30s
  - M=F
  - Associated with IBD

Both can present as jaundice, mass, pancreatitis, PD stricture
AIP vs. IDCP: Serology

• **AIP**
  - IgG4>135: sens 95%, spec 97%
  - Elevated IgG4 alone does not rule out pancreas cancer
  - Higher levels of IgG4 more suggestive of AIP
  - Normal levels don’t exclude

• **IDCP**
  - Not associated with IgG4
  - No specific serology
AIP vs. IDCP: Imaging

• AIP
  • Diffuse parenchymal enlargement
  • Rim or halo
  • Effacement of the contour ("sausage-shape")
  • Diffuse atrophy
  • Focal mass
    • Sharp demarcation
    • Iso-attenuating
    • Lack of atrophy
  • Diffuse or segmental, multifocal duct stricturing without dilation

• IDCP
  • Focal mass
  • Diffuse enlargement
  • Interstitial pancreatitis
  • Absence of stranding
AIP vs. IDCP: Histology

- **AIP**
  - Lymphoplasmacytic infiltrate
  - Storiform fibrosis
  - Obliterative Phlebitis
  - >10 IgG4+ per HPF

- **IDCP**
  - Lymphoplasmacytic infiltrate
  - Storiform fibrosis
  - Granulocyte epithelial lesion
    - GEL
    - Intraluminal and intraepithelial neutrophils in medium and small ducts
    - Required for diagnosis in absence of IBD
Utility of EUS

- Easy access to the pancreas and safe tissue acquisition
- Exclude other diagnosis (cancer)
- Development of more reliable core needles
- EUS/FNA is not part of consensus guidelines (histology needed)
- Diffuse enlarged hypoechoic gland, concentric bile duct thickening
Autoimmune Pancreatitis during evaluation of idiopathic pancreatitis

- 3.9% pts evaluated for etiology of acute pancreatitis ended up dx with AIP by HISORt criteria
- 24% of cohort of known AIP pts had criteria for acute pancreatitis
- Suggested risk factors for AIP: younger age, jaundice, abnormal transaminases, other organ involvement
- Responsive to steroids
Treatment

- Prednisone 40 mg/d for 4 weeks
- Re-image at 2-4 weeks for improvement (i.e. exclude mass; “2 week steroid trial” in diagnostic dilemma or initial negative investigation)
- Taper 5 mg q1-2 weeks.
- Relapse: minimal dose of steroids, maintenance 5-10 mg/d, steroid sparing agents (6-MP/Aza, rituximab)
Initial diagnosis of AIP

Prednisone (40 mg/day x 4 weeks)

- Reassess disease activity

Incomplete remission or steroid intolerance

- No response
- Alternative diagnosis

Complete remission

Prednisone taper (5mg/week) w/o maintenance treatment

Relapse or recrudescence

- Consider rituximab induction with or without maintenance
- Prednisone (40mg/day x 4 weeks) +AZA/6-MP/MMF
- Taper Prednisone with 28 weeks overlap

Relapse/incomplete remission on IM

IM intolerance

Complete remission

Switch to another IM

Clinically monitor for relapse

Initial diagnosis of IDCP

Prednisone (40 mg/day x 4 weeks)

- Reassess disease activity

Incomplete remission

- No response
- Alternative diagnosis

Complete remission

Prednisone taper (5mg/week) w/o maintenance treatment

Relapse or recrudescence

Prednisone (40mg/day x 4 weeks) +Taper Prednisone
Initial diagnosis of IDCP

Prednisone (40 mg/day x 4 weeks)

- Reassess disease activity

- Incomplete remission
- Alternative diagnosis

- No response

Complete remission

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