University of Virginia Fellow Presentations

Patrick Northup, MD, MHS
GI and Hepatology Fellowship Program Director
Presenters: Andrew Copland, MD and Darius Jahann, MD

Conflicts: None
Off label discussion: Indomethacin, mycophenolate, budesonide, rituximab, tacrolimus, infliximab
Patient Presentation

A 78y/o female presented with several weeks of jaundice

She was experiencing RUQ pains, nausea, and acholic stools.

Exam was notable for palpable mass in the RUQ, scleral icteris, and jaundiced skin

Admitting labs were notable for: AST 328, ALT 452, AlkPhos 568, and tBili 11.6
Initial Imaging
EUS did not reveal adequate window for FNA so bile duct brushing were obtained.
Risk factors for Post ERCP Pancreatitis

**Patient characteristics**  
- Female gender (OR 2.5)
- Young age (OR 2.1)
- Hx of PEP (OR 5.4)
- Normal bilirubin (OR 1.9)
- Suspected SOD (OR 1.9-2.6)

**Procedural Characteristics**  
- Difficult bile duct cannulation (OR 3.4)
- Balloon dilation of biliary sphincter (OR 4.5)
- Precut Sphincterotomy (OR 4)
- Pancreatic duct injection (OR 1.7)
- Pancreatic sphincterotomy (OR 3.1)

Freeman et al. Gastrointest Endosc 2001;54:425-34.
Post Procedure: Pancreatitis

- Our patient experienced abdominal pain, fever, and leukocytosis
- Lipase was elevated at 2469
- CT scan was obtained...

Preventing ERCP pancreatitis

- Patient selection
- Wire-guided cannulation
- Indomethacin
- Pancreatic duct stents
- IV Fluids
**Indomethacin**

- Randomized placebo controlled trial of indomethacin vs placebo.
- Demonstrated 45-50% risk reduction of PEP regardless of PEP risk factors.


---

**Pancreatic Duct Stents**


<table>
<thead>
<tr>
<th>Study Name</th>
<th>Year Published</th>
<th>RR (95% CI)</th>
<th>S. Weight</th>
<th>RR w/ PD Stent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td></td>
<td>0.32</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild to Mod PEP</td>
<td>0.36</td>
<td>0.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe PEP</td>
<td></td>
<td>0.23</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Would our patient have benefited from a pancreatic duct stent?

Indomethacin and PD stents

- Elmunzer et al (AJG 2013) made a post-hoc analysis of their indomethacin trial data with multivariate regression controlling for patient risk factors.

- Indomethacin alone was superior to Indomethacin + Stent and Stent alone strategies.

- Indomethacin strategy also yield significant cost savings.

Aggressive Hydration

- Pilot study w/ 2:1 randomize to aggressive hydration vs standard hydration (62 patients).
- 75% of cases were for stones.
- Average tbili was ~4.

Protocol:
- 3ml/kg/h during ercp
- 20ml/kg bolus after ercp
- 3ml/kg/h for 8hrs after

Buxbaum et al Clinical Gastroenterology and Hepatology 2014;12:303–307

Take Home Points

- Indomethacin is a simple, cheap way to reduce a patients risk of pancreatitis by as much as 50%.

- The risk of pancreatitis is never zero.

- Concurrent use of indomethacin and pancreatic duct stents remains a grey area in the literature and future studies may significantly affect our ERCP practice.
A 58-year-old Woman with Fatigue

Darius Jahann, MD
Gastroenterology Fellow
University of Virginia

Patient Presentation

- **HPI**: 58 y/o female who presented with several weeks of fatigue.
- **PMH**: Hypothyroidism.
- **SHx**: Infrequent EtOH. No drugs or tobacco.
- **Meds**: Levothyroxine.
- **FHx**: Celiac disease in a sibling.
Patient Presentation

**Physical Exam:** Unremarkable

- **HEENT:** No scleral icterus. **Cardiopulmonary:** wnl.
- **Abd:** non-tender, no hepatosplenomegaly. **Neuro:** non-focal, no asterixis.

**Labs:**
- AST 558
- ALT 670
- AP 109
- Tb 1.2

Diagnostic Algorithm

Liver Disease of Unknown Cause

- ANA, SMA, LKM-1, AMA

- Conventional tests negative
  - F-actin, SLA/LP, LCT1, LKM3
  - PDH-E2, pANCA

- Atypical pANCA+
  - AIH
  - PSC

- AIH
  - PBC

- Cryptogenic chronic hepatitis

Manns et al. Hepatology 2010; 51: 2193-2213
Moderator: Patrick G. Northup, MD, MHS
Presenters: Andrew Copland, MD and Darius Jahann, MD

Patient Presentation

- Viral Hepatitis panel: negative
- Iron panel: wnl
- Anti-smooth muscle Ab: positive
- ANA: negative
- AMA: negative
- Anti-actin Ab: positive
- Anti-soluble liver Ag: negative
- Anti-liver kidney microsome: negative

Liver Biopsy
Autoimmune Hepatitis

Autoimmune Hepatitis (AIH) is a liver disease characterized by the destruction of liver cells by the body's immune system. It is typically diagnosed through a combination of laboratory tests (Labs), autoimmunity markers, and histological examination (Histology).

Scoring System


Table 3: Simplified diagnostic criteria for the diagnosis of autoimmune hepatitis (AIH)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cut-off</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA or SMA</td>
<td>≥140</td>
<td>+1</td>
</tr>
<tr>
<td>ANA or SMA</td>
<td>≥80</td>
<td>+2*</td>
</tr>
<tr>
<td>LKM</td>
<td>≥840</td>
<td></td>
</tr>
<tr>
<td>SLA/LP positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver histology (evidence of hepatitis)</td>
<td>Compatible with AIH</td>
<td>+1</td>
</tr>
<tr>
<td>(evidence of hepatitis is a necessary condition)</td>
<td>Typical AIH</td>
<td>+2</td>
</tr>
<tr>
<td>Serum immunoglobulin G levels</td>
<td>≥Upper normal limit</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>&gt;1.1 upper normal limit</td>
<td>+2</td>
</tr>
<tr>
<td>Absence of viral hepatitis</td>
<td>Yes</td>
<td>+2</td>
</tr>
<tr>
<td>Sum</td>
<td>≥6: probable AIH</td>
<td>≥7: definite AIH</td>
</tr>
</tbody>
</table>
Treatment

• Induction of Treatment and Maintenance of Remission
  • Prednisone monotherapy (60 mg/day)
  OR
  • Prednisone (30 mg/day) + Azathioprine (50mg)
  • Our patient was started on prednisone mono tx

Prednisone taper

• No clear guidelines for management
• Start with Prednisone 40 – 60 mg/day
• ↓ by 10 mg every 2 weeks for goal of 20 mg
• Then ↓ by 2.5 mg every 3-4 weeks
• Start azathioprine with a confirmed response in LFTs
Moderator: Patrick G. Northup, MD, MHS  
Presenters: Andrew Copland, MD and Darius Jahann, MD

### Treatment Course

<table>
<thead>
<tr>
<th>Month 0</th>
<th>Month 3</th>
<th>Month 4</th>
<th>Month 7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone</td>
<td>Pred + AZA</td>
<td>Pred + MMF</td>
<td>MMF</td>
</tr>
</tbody>
</table>

**LFTs normalized over 2 months**

- Prednisone tapered to 15 mg/day
- GI side effects after 8 weeks
- AZA stopped

**LFTs WNL**

- MMF 500 mg BID added
- AST 89
- ALT 113

**LFTs rising**

- Prednisone tapered off over next 4 months

### Challenging patients

<table>
<thead>
<tr>
<th>Method</th>
<th>Features</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mathematical models</td>
<td>MELD &gt; 12 on presentation</td>
<td>Sens 97% / Spec 68% for tx failure</td>
</tr>
<tr>
<td>Clinical phenotype</td>
<td>≤ 30 y/o HLA DRB1<em>03 &lt; 60 y/o HLA DRB1</em>04</td>
<td>Tx failure 24% Cirrhosis 33% Tx response 95%</td>
</tr>
<tr>
<td>Rapidity of Tx response</td>
<td>Multilobular necrosis, ↑ bili, tests unimproved or worse within 2W of tx</td>
<td>98% mortality within 6 months</td>
</tr>
<tr>
<td>Serological markers</td>
<td>Anti-SLA</td>
<td>Severe histological changes Longer tx duration ↑ relapse rate ↑ Txp / death</td>
</tr>
<tr>
<td>Ethnic background</td>
<td>Non-white N. American or N. European</td>
<td>Cirrhosis at presentation Cholestatic features</td>
</tr>
</tbody>
</table>

Treatment Course: next step

- Options:
  - Increasing MMF dosage to 1000 mg BID
  - Addition of low dose prednisone or budesonide
  - Transition to tacrolimus for refractory disease

- Outcome:
  - LFTs normalized within 4 weeks
  - Currently at month 33, LFTs have remained normal

Budesonide vs Prednisone

- **Non-cirrhosis**: Budesonide effective in combination with AZA & lower incidence of corticosteroid-induced side effects
  - Budesonide + AZA: 47% 6-month remission w/o s/e
  - Prednisone + AZA: 18.4% 6-month remission w/o s/e

- **Cirrhosis**:
  - Efficacy of budesonide may be reduced.
  - Incidence of corticosteroid-side effects increased

Manns et al. Gastroenterology 2010; 139 1198-1206.
Alternative therapeutic options

- **Cyclosporine**
  - Limited data, most in adolescents and children (Alvarez et al 1999)
  - Side effects: nephrotoxicity, HTN, infections, malignancy

- **Tacrolimus**
  - Effective as salvage therapy at low doses (Tannous et al 2013)
  - Side effects: diabetes, neurotox, nephrotox, diarrhea

- **Rituximab**
  - Case report data: successfully used in AIH cases associated with B-cell driven diseases
  - Rare, series side effects: neutropenia, pneumonitis, PML

- **Infliximab**
  - TNF-α is essential in induction of AIH
  - Promising results in a case series of 11 patients (Weiler-Normann et al 2013)
  - 7/11 had infectious complications (UTIs, PNA, herpes)

Summary

- AIH is a heterogeneous disease that often requires a combination of labs, serological markers, and histology for diagnosis.

- Clinical and laboratory characteristics may help identifying which patients are difficult to treat.

- About 20% of patients will not respond to conventional therapies and may require alternative treatments to achieve remission.
Thank You