The Evaluation & Treatment of a Symptomatic Patient with an Ileal Pouch

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Case Presentation

- 30 year old female with ulcerative colitis since age 18
- Annual steroid-requiring flares despite 5ASA maintenance
- TPC-IPAA and loop ileostomy for severe pancolitis unresponsive to steroids at age 25
- Path: Continuous severely active disease of the mucosa; c/w ulcerative colitis
- Loop ileostomy closed 4 months later

Risk Factors for Acute Pouchitis

- Extensive UC
- Backwash ileitis
- Primary sclerosing cholangitis
- P-ANCA
- IL-1 receptor antagonist polymorphisms
- NOD2 gene polymorphisms
- Non-smoker
- NSAID use
- Arthralgia

Cumulative Frequency of Pouchitis

- Achkar JP, et al. CGH 2005
- Shen B, et al. AJG 2005
- Meier CB, et al. IBDD 2005
- Shen B, et al. CGH 2006

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Evaluation & Treatment options

- 1. Therapeutic trial of metronidazole
- 2. Therapeutic trial of ciprofloxacin
- 3. Therapeutic trial of MTZ and Cipro
- 4. Pouchoscopy with biopsy then treat accordingly
- 5. Pouchoscopy without biopsy then treat accordingly

Diagnosis of Pouchitis

- Often based on symptoms alone with patients given empiric antibiotic therapy
- Symptoms do not correlate with endoscopy and histology
- Symptoms alone are not sufficient to make the diagnosis

Treatment of Acute Pouchitis


Frequency of Pouchitis in Symptomatic Patients


Endoscopic Spectrum of Pouchitis

The “Bacterial Theory” in Pouchitis

- Dysbiosis
- Anaerobe/aerobe↑
- Sulfate-reducing bacteria ↑
- *Clostridium difficile* in chronic pouchitis 12-18%
- *Clostridium perfringes* ↑
- *Fusobacter nucleatum* ↑

**Evolution of Pouchitis**

- Role of microbiota
- Role of Immune dysregulation
- Confounding Factors (e.g. ischemia)
- Acute pouchitis
- Chronic pouchitis

**Primary Sclerosing Cholangitis-associated Pouchitis/Enteritis**

**IgG4-associated Pouchitis**

**Autoimmune Disorder-associated Pouchitis**
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**Visceral Hypersensitivity in Irritable Pouch Syndrome**

- Gas ($P < 0.02$)
- Urge to Defecate ($P < 0.02$)
- Pain ($P < 0.05$)

```
0      1      2      3      4      5      6      7      8

Pressure in mmHg
```

- Normal Pouch (N = 11)
- Irritable Pouch Syndrome (N = 8)

Shen B, Sanmagul C, Parul M, et al. DDW 2004

**Cost of Diagnostic Strategies**

```\n| Strategy            | Cost  | Incr. Cost | Effective (Days) | Incremental Effective (Days saved) | Incremental Cost Effective. |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Flagyl-first</td>
<td>$194</td>
<td></td>
<td>12.2</td>
<td></td>
<td></td>
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<tr>
<td>Endoscopy w/o bx</td>
<td>$238</td>
<td>$44</td>
<td>27.6</td>
<td>15.4</td>
<td>$3</td>
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<tr>
<td>Flagyl-then-Cipro</td>
<td>$202</td>
<td></td>
<td>6.7</td>
<td>(Dominated)</td>
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<td>Cipro-first</td>
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<td>(Dominated)</td>
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<tr>
<td>Endoscopy w/ bx</td>
<td>$352</td>
<td></td>
<td>25.0</td>
<td>(Dominated)</td>
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</table>
```

**Cost-Effectiveness of Diagnostic Strategies**

- Serotonin 20X

Shen B. AJG 2008

**Decision Analysis**

1. Flagyl-first
2. Cipro-first
3. Flagyl-then-Cipro
4. Endoscopy w/ bx
5. Endoscopy w/o bx


**Case Presentation**

- Patient’s symptoms completely resolved on metronidazole
- Over the next few years, there were episodes of diarrhea with increasing frequency
- Multiple pouchoscopies:
  - Inflammation in the pouch c/w pouchitis
- Eventually, antibiotics no longer relieved symptoms
- Finally, pt was told a pouch excision with ileostomy was the only cure
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Case Presentation: Review of Original Colectomy Specimen

- Path slides:
  - Pancolitis
  - Ulcerations extending to muscularis externa
  - Normal terminal ileum

- Impression: Indeterminate colitis

Small Bowel Follow Through

Pouchoscopy: Pouch

Pouchoscopy: Afferent Limb

Determinants of Crohn’s Disease in Ileal Pouches

- 23 patients with Crohn’s disease diagnosed after IPAA
- 26 ulcerative colitis patients with IPAA
- Principal variable – afferent limb ulcers


ALU’s are Seen More Often in CD Patients with Pouchitis

Crohn’s Patients

<table>
<thead>
<tr>
<th></th>
<th>% w/ ALU’s</th>
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<tr>
<td>Pouchitis</td>
<td>80</td>
</tr>
<tr>
<td>No Pouchitis</td>
<td>20</td>
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(p=0.012)
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**Phenotypic Classification**

- Inflammatory
- Fibrostenotic
- Fistulizing

**Therapy?**

1. Azathioprine
2. Prednisone
3. Infliximab
4. 1 and 2
5. 1 and 3
6. Pouch excision with ileostomy

**Fecal markers of inflammation**

- **Lactoferrin**
  - Major component of cytoplasmic granules of PMNs
  - Sensitive and specific marker of fecal leukocytes in infectious colitis
  - Indicator of disease activity in IBD

- **Alpha 1-Antitrypsin**
  - Reflects enteric protein loss
  - Correlates with degree of inflammation & extent of diseased bowel
  - In one study shown to be elevated in active pouchitis

**Case Presentation**

- Prednisone and Azathioprine both started
- Patient’s symptoms decreased dramatically within several days
- Steroids were tapered over 3 months
  - Now the pt doing well on Azathioprine alone

**Evaluation & Treatment of Symptomatic Patients Ileal Pouches**

- Pouchoscopy w/o Biopsy
- D/C NSAIDs
- Cuffitis
- Pouchitis
- Irritable Pouch Syndrome
- Topical 5ASA
- Topical steroids
- Antibiotics
- Relapsing pouchitis
- Crohn’s disease (ALUs)
- Probiotics
- Long-term Antibiotics
- Anti-depressants
- Anti-cholinergics
- Fiber
- Fecal markers of inflammation
  - Lactoferrin
  - Alpha 1-Antitrypsin
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**Study Design**

- **60 Symptomatic / Asymptomatic**
- **Stool Collection**
- **Endoscopy, Histology & PDAI**
- **Cuffitis**
- **Pouchitis**
- **Crohn’s disease**
- **IPS**
- **Asymptomatic**
- **Inflammatory Group**
- **Non-Inflam Group**
- **Asymptom Group**

**Proposed Diagnostic Algorithm**

- **Symptomatic Patient with IPAA**
- **Fecal Lactoferrin < 7 mcg/g**
- **Fecal Lactoferrin > 7 mcg/g**
- **Pouch endoscopy + Biopsy**
- **IPS**
- **Pouchitis**
- **Cuffitis**
- **Crohn’s disease**
- **Dietary fiber**
- **Antispasmodics**
- **Antidepressants**
- **Ciprofloxacin or metronidazole**
- **Topical 5-ASA**
- **Topical steroids**
- **Immu. Inflammab**

**Summary**

- Pouch is not natural and complications are common
- Pouchitis is a disease spectrum and stratification of etiology is important
  - Bacteria-related (acute)
  - Immune-mediated (chronic)
  - Ischemia-related (chronic)
- Microbiome
  - Initiation of early phase of acute pouchitis
  - Superimposed infection or in late phase?
  - Ischemia/tissue hypoxia: infection of C. diff and other bugs
- Ischemia: chronic pouchitis, leaks
  - Most chronic antibiotic-refractory pouchitis is either immune-mediated or ischemia-related

**Bo Knows Pouches**

- 49 patients provided a second stool sample for AAT
- Median 18, IQR 9.3-15
- Median 15, IQR 12.25
- Median 9, IQR 9.25-29

- Cleveland Clinic