Diagnosis and Management of Crohn’s Disease of the Ileal Pouch

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Cleveland Clinic
December 5, 2008
Indications for Colectomy
Ileal Pouch-anal Anastomosis (IPAA)
Ileal Pouch Disorders and Associated Complications

**Surgical/Mechanical**
- Anastomotic leaks
- Pelvic sepsis
- Pouch sinuses
- Pouch fistulae
- Strictures
- Afferent limb syn.
- Efferent limb syn.
- Infecundity
- Sexual dysfunction
- Portal vein thrombi
- Pouch prolapse
- Foreign bodies

**Inflammatory/Infectious**
- Pouchitis
- Cuffitis
- Crohn’s dis.
- Small bowel bacterial overgrowth
- Inflammatory Polyps

**Functional**
- Irritable pouch syn.
- Anismus
- Poor pouch compliance
- Pseudo-obstruction
- Hypersensitive suture line

**Dysplastic/Neoplastic**
- Pouch dysplasia or cancer
- ATZ dysplasia or cancer
- Lymphoma
- Squamous cell cancer

**Systemic/Metabolic**
- Anemia
- Bone loss
- Vitamin B12 deficiency
Crohn’s Disease in Patients with IPAA

Cumulative Frequency %

<table>
<thead>
<tr>
<th>Study</th>
<th>Frequency %</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yu 2000</td>
<td>2.7</td>
<td>1519</td>
</tr>
<tr>
<td>Duetsch 1991</td>
<td>3.5</td>
<td>272</td>
</tr>
<tr>
<td>Fazio 2003</td>
<td>4.1</td>
<td>1816</td>
</tr>
<tr>
<td>Neilly 1999</td>
<td>4.8</td>
<td>171</td>
</tr>
<tr>
<td>Gemlo 1992</td>
<td>7</td>
<td>196</td>
</tr>
<tr>
<td>Keighley 2000</td>
<td>9</td>
<td>222</td>
</tr>
<tr>
<td>Peyregne 1999</td>
<td>13</td>
<td>54</td>
</tr>
</tbody>
</table>
Risk Factors for Crohn’s Disease of the Pouch

- Younger age
- Female
- Smoker
- Family history of Crohn’s disease
- Preoperative diagnosis of indeterminate colitis
- Sero-positive anti-*Saccharomyces cerevisiae*-IgA

(different risk factors for clinical phenotypes)

Phenotypic Classification

Inflammatory

Fibrostenotic

Fistulizing

Shen B, CGH 2008
Diagnosis
Terminology

- Crohn’s disease
- Crohn’s disease of the pouch ✓
- Crohn’s-like
- Or a totally “unknown” disease entity
“Hallmarks” of Crohn’s Disease

- Granulomas
- Skip lesions
- Transmural inflammation
- Fistula

- pseudogranulomas
- ischemia
- chronic pouchitis
- Surgery-related
Granulomas in Crohn’s Disease of IPAA

Cumulative Frequency %

<table>
<thead>
<tr>
<th>Condition</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>12</td>
</tr>
<tr>
<td>N = 25</td>
<td></td>
</tr>
<tr>
<td>Fibrostenotic</td>
<td>12</td>
</tr>
<tr>
<td>N = 17</td>
<td></td>
</tr>
<tr>
<td>Fistulizing</td>
<td>10</td>
</tr>
<tr>
<td>N = 31</td>
<td></td>
</tr>
</tbody>
</table>

Shen B, et al AJG 2006
Foreign-body Granulomas
N = 110
Sensitivity = 63.8% ; Specificity = 96.2%
Likelihood ratio = 16.7
Pouch failure: 12.8% in PGM+ vs. 1.4% in PGM- (P = 0.02)

Kariv R. et al/ DDW 2007
Causes of Afferent Limb Inflammation (Ileitis)

- NSAID induced
- Backwash ileitis from diffuse pouchitis
- Surgery-related ischemia or ischemic ileitis
- Crohn’s ileitis
Differential Diagnosis of Distal Ileitis

Backwash ileitis from diffuse pouchitis

NSAID induced

CD

Afferent Limb  Pouch Inlet  Pouch Body
Segmental Pouchitis-Pattern of Ischemic Injury
Extracellular Pigments in Ischemic Pouchitis

### Features of Ischemic Pouchitis

<table>
<thead>
<tr>
<th></th>
<th>Ischemic Pouchitis (N = 10)</th>
<th>CD Pouch (N = 15)</th>
<th>Antibiotic-responsive Pouchitis (N = 15)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom score</td>
<td>3 (0, 5)</td>
<td>3 (2, 4)</td>
<td>4 (2, 4)</td>
<td>0.66</td>
</tr>
<tr>
<td>Pouch endoscopy score</td>
<td>2.5 (2, 4)</td>
<td>1 (0, 3)</td>
<td>4 (3, 5)</td>
<td>0.014</td>
</tr>
<tr>
<td>A-limb endoscopy score</td>
<td>0 (0, 0)</td>
<td>2 (0, 3)</td>
<td>0 (0, 0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Cuff endoscopy score</td>
<td>0 (0, 2)</td>
<td>0.5 (0, 3)</td>
<td>0 (0, 2)</td>
<td>0.78</td>
</tr>
<tr>
<td>Any response to antibiotics</td>
<td><strong>2 (20.0%)</strong></td>
<td>13 (86.7%)</td>
<td><strong>15 (100%)</strong></td>
<td><strong>0.001</strong></td>
</tr>
<tr>
<td>Granulomas</td>
<td>0</td>
<td>2 (15.4%)</td>
<td>0</td>
<td>0.17</td>
</tr>
<tr>
<td>Pyloric gland metaplasia</td>
<td>0</td>
<td>3 (23.1%)</td>
<td>2 (13.3%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Histologic ulcers</td>
<td>4 (40.0%)</td>
<td>2 (15.4%)</td>
<td>3 (20.0%)</td>
<td>0.4</td>
</tr>
<tr>
<td>Extracellular pigment</td>
<td><strong>8 (80.0%)</strong></td>
<td>4 (30.8%)</td>
<td>2 (13.3%)</td>
<td><strong>0.003</strong></td>
</tr>
</tbody>
</table>

## Distinction between Ischemic and Crohn’s Stricture

<table>
<thead>
<tr>
<th>Feature</th>
<th>Ischemia</th>
<th>CD Pouch</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of strictures</td>
<td>Ileostomy site, inlet/outlet</td>
<td>Anywhere</td>
</tr>
<tr>
<td>Fistula</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Granulomas</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Pyloric gland metaplasia</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Extracellular pigment</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Response to medicines</td>
<td>-</td>
<td>+/-</td>
</tr>
<tr>
<td>Response to endoscopic tx</td>
<td>+</td>
<td>+/-</td>
</tr>
</tbody>
</table>
Optical Coherence Tomography for Transmural Inflammation

Normal Pouch

Acute Pouchitis

Shen B. DDW 2009
Optical Coherence Tomography for Transmural Inflammation

Chronic Pouchitis

Crohn’s Pouch

Shen B. *DDW* 2009
Transmural Inflammation-A Sign of Crohn’s?

Chronic Pouchitis

Crohn’s Disease of Pouch

Shen B. *DDW* 2009
## Histopathology of Pouch Resection Specimens

<table>
<thead>
<tr>
<th>Condition</th>
<th>Crohn’s (N = 16)</th>
<th>Chronic Pouchitis (N = 10)</th>
<th><em>P</em> value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulomas</td>
<td>19%</td>
<td>0</td>
<td>0.14</td>
</tr>
<tr>
<td>Pyloric gland metaplasia</td>
<td>50%</td>
<td>50%</td>
<td>1.0</td>
</tr>
<tr>
<td>Intraepithelial lymphocytosis</td>
<td>0</td>
<td>0</td>
<td>NA</td>
</tr>
<tr>
<td>Transmural inflammation</td>
<td>13%</td>
<td>35%</td>
<td>0.27</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>0</td>
<td>10%</td>
<td>NA</td>
</tr>
<tr>
<td>Fistula</td>
<td>38%</td>
<td>0</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Shen B. *DDW* 2009
Fecal and Serum ASCA in Distinction of CD from Other Pouch Conditions ROC Curve

Tang L, et al. CCFA Miami 2008
Causes of Fistula/Sinus

- Surgical leaks
- Cryptoglandular abscess
- Iatrogenic
- Crohn’s disease
Not All Pouch-vaginal Fistulae Are From Crohn’s

Courtesy of Dr. Victor Fazio
Identification of Internal Os of Fistula
Perianal Fistula / Pouch-vaginal Fistula
A Sign of Crohn’s Disease?
Location and Timing Are the Key

Above the anastomosis
At the anastomosis
Below the anastomosis

J pouch

Cut-off: 6 - 12 months after ileostomy take-down
Diagnostic Algorithm

Pouch Endoscopy & Biopsy

- Iatrogenic Complications, fistula, leaks)
- Pouchitis/Ileitis
- Cuffitis

5-ASA Failure

- Antibiotic Failure

- Crohn’s Disease Suspected
- Crohn’s Disease Confirmed

Contrasted Enema
CTE/MRE
MRI Pelvis, EGD

Diagnostic/
Therapeutic EUA

Trial of
Biologics

Shen B. IBDJ 2008
Treatment
Management Algorithm for Crohn’s Pouch

Crohn’s Disease Pouch

Inflammatory
- Medical Therapy
  - Antibiotics?
  - 5-ASAs, Corticosteroids, Immunomodulators, Biologics

Fibrostenotic
- Medical Therapy
  - Antibiotics?
  - 5-ASAs, Corticosteroids, Immunomodulators, Biologics?
  - Endoscopic Therapy

Fistulizing
- Medical Therapy
  - Antibiotics, Immunomodulators, Biologics
  - Endoscopic Therapy?

Surgery
- Incision & Drainage, Seton, Stricturoplasty, Fistular Repair, K Pouch, Diversion, Pouch Excision

Shen B, IBDJ 2008
Infliximab for CD of the Pouch

- N = 26 (ileitis=5; ileitis-fistula=7; fistula =14)
- Concurrent immunomodulator = 15
- Median f/u = 22 months

Fistular closure= 50% (9/18)

Colombel JF, et al. AJG 2003
## Adalimumab for Crohn’s Disease of Pouch

<table>
<thead>
<tr>
<th>Factor</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Symptom Improvement</strong></td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>6 (35.3)</td>
</tr>
<tr>
<td>Complete</td>
<td>7 (41.2)</td>
</tr>
<tr>
<td><strong>Endoscopic Inflammation Improvement</strong></td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>4 (28.6)</td>
</tr>
<tr>
<td>Complete</td>
<td>7 (50.0)</td>
</tr>
<tr>
<td><strong>Fistular Response (N=5)</strong></td>
<td></td>
</tr>
<tr>
<td>Partial</td>
<td>1 (20.0)</td>
</tr>
<tr>
<td>Complete</td>
<td>1 (20.0)</td>
</tr>
<tr>
<td><strong>Adverse Effect</strong></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>3 (17.7)</td>
</tr>
<tr>
<td>Injection Site Reaction</td>
<td>1 (5.9)</td>
</tr>
<tr>
<td>Pouch Failure</td>
<td>3 (17.7)</td>
</tr>
</tbody>
</table>

N = 17; 4 wk induction therapy

Shen B, et al APT 2009
Needle Knife “Stricturoplasy”

Shen B. IBDJ 2008
Needle Knife “Fistulotomy”
Pouch-cutaneous Fistula: EndoClip
Natural History and Prognosis
Clinical Setting of Crohn’s Disease of Pouch

- **Intentional CD pouch**: in a selected group of patients with a preop diagnosis of Crohn’s colitis
- **Incidental CD pouch**: in patients with a missed diagnosis of Crohn’s disease
- **De novo CD pouch**
  (Diagnosis of pouch conditions can change over time)
Early vs. Late-onset of Crohn’s Disease of the Pouch
Pouch Failure in Patients with Crohn’s Disease

Cumulative Frequency %

- Fazio, 1995 (N = 67)
- Peyregne, 1999 (N = 79)
- Duetsch, 1991 (N = 19)
- Sagar, 1996 (N = 37)
- Gemlo, 1992 (N = 13)
- Tulchinsky, 2003 (N = 13)
- Keighley, 2000 (N = 23)
- Neilly, 1999 (N = 8)

Values: 25.4, 42.9, 44.4, 45.9, 46.2, 46.2, 47.8, 100
Phenotypes of Crohn’s Disease and Pouch Survival

Shen B, et al. IBDJ 2008

Probability of Pouch Survival
(p-value = 0.054)

Proportion w/o Pouch Failure

Years of Follow-Up

Inflammatory
Stricture
Fistulizing
Pouch Survival in Different Settings

- UC or Indeterminate colitis: N = 2,630
- Incidental CD: N = 97
- De novo CD: N = 87

Crohn’s Disease and Cancer Risk

- Prevalence: 10/2700 with IPAA underlying UC
- Poorly-differentiated cancer: 4
- Concurrent Crohn’s disease: 6
- Precolectomy dysplasia: 7
- Mucosectomy not necessarily protective: 3
- “Missed dysplasia” in routine surveillance: 3/7
- 1-year mortality: 40%
Conclusions

- CD of the pouch can occur in patients with a preoperative diagnosis of UC or IC.
- Natural history varies.
- Diagnosis and differential diagnosis can be challenging, and a combined assessment of clinical, endoscopic, imaging, and histologic features is often needed.
- Phenotypic classification may be useful for "targeted" therapy and prognosis.
THE INFLAMED POUCH
Anatomy of Pelvic Pouch

- Afferent limb (neo-terminal ileum)
- Tip of “J”
- Efferent limb
- Outlet/cuff

**“J”**
- Inlet
- Efferent limb
- 15-20 cm

**“S”**
- 15 cm

**“W”**
- 12 cm
Sinus vs. Crohn’s Fistula