Microscopic Colitis

Darrell S. Pardi, MD
Inflammatory Bowel Disease Clinic
Mayo Clinic
Disclosure

• Research
  – Astra Zeneca, P&G, Salix*

• Consulting
  – Salix*

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Overview

• Background and Nomenclature
• Clinical features
• Epidemiology
• Clinically relevant pathophysiology
• Treatment
Background

• Two subtypes, originally called CC (1976) and MC (1980)
• Microscopic colitis used as umbrella term
  - subsets collagenous, lymphocytic colitis
• Very similar clinically and histologically
• Can coexist or change over time
• Unclear if distinct or parts of a spectrum
Which of the following is true regarding patients with microscopic colitis?

A) Abdominal pain is uncommon
B) Weight loss is uncommon
C) Fecal leukocytes are uncommon
D) Most meet Rome criteria for IBS
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Clinical Features

- Constant or intermittent watery diarrhea
- 50% with abdominal pain, mild weight loss
- Arthralgias, autoimmune disorders, sprue
- Overlap with IBS
  - 50-70% in Olmsted County cohort\(^1\)
  - 28-65% in secondary analysis of RCTs\(^2\)

1) Limsui IBD 2007  2) Madish World J Gastro 2005
Clinical Features

- Association with NSAIDs and other meds
- 50% have fecal WBCs
- Mucosa usually grossly normal
- No known ↑ risk colon cancer
Which of the following is true regarding the epidemiology of microscopic colitis?

A) Incidence less common than Crohn’s
B) It is about as common as IBS
C) The incidence is increasing significantly
D) It accounts for 30-40% of watery diarrhea
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Epidemiology

• European and Canadian studies: Incidence ~5/100,000 each

• Typically 6th-7th decade
  – e.g. in Calgary, age >65 RR = 5.6

• Female predominance (CC>LC in most)

• 7-15% of chronic watery diarrhea
Olmsted County Incidence Data

1985-2001
CC 3.1/100,000
LC 5.5/100,000

1997-2001
CC 6.2/100,000
LC 12.9/100,000
Incidence of Microscopic colitis, Olmsted County 1985-2001
Pathophysiology

- NSAIDs and other drugs
- Abnormal fluid/salt secretion/absorption
- Bile acid malabsorption
- Abnormal collagen synthesis/degradation
- Infection
- Autoimmunity
- Reaction to luminal antigen
Drug-induced Microscopic colitis

• High likelihood
  – acarbose, aspirin, NSAIDs, PPI, SSRI, ticlopidine

• Intermediate likelihood
  – Carbamazepine, flutamide, lisinopril, simvastatin

Beaugerie and Pardi APT 2005
The best treatment for severe microscopic colitis is:

A) Loperamide
B) 5-aminosalicylate
C) Budesonide
D) Prednisone
E) Azathioprine
The best treatment for severe microscopic colitis is:

A) Loperamide
B) 5-aminosalicylate
C) **Budesonide**
D) Prednisone
E) Azathioprine
Treatment

• Few controlled trials
• Many anecdotal reports/case series
• Consider drug-induced microscopic colitis
  – If any doubt, stop drug and observe diarrhea
Budesonide RCTs

- 3 DB, PC, RCTs in CC, 1 in LC
- 9 mg/d x 6-8 weeks, +/- taper
- N=93 with CC, 41 with LC
- Response 57-100% (~80%) vs. 12-40%
- Relapse ~80%

Natural History of Budesonide-treated CC

During 16 month median f/u of a budesonide RCT cohort with CC, 61% had recurrent diarrhea

Figure 1. Cumulative probability of clinical remission of collagenous colitis after budesonide therapy.

Miehlke APT 2005
Natural Hx of Budesonide-treated CC

• 34 pts, 9 mg/d x 6 wks, remission 87%
• Randomized to budesonide 6 mg/d or placebo x 24 wks
• Relapse: 23% budesonide, 88% placebo
• After 30 wks treatment with budesonide, relapse 77%

Bonderup Gut 2008
Natural Hx of Budesonide-treated CC

- 48 pts, 9 mg/d x 6 wks, remission 96%
- Randomized to budesonide 6 mg/d or placebo x 6 mo
- Relapse: 13% budesonide, 61% placebo
Natural History of Steroid-treated MC

- 70 patients rx with steroids
  - Prednisone 65%, budesonide 35%
- Response: 87% prednisone, 100% budesonide (p = 0.15)
- Relapse: 91%

Abdalla DDW 2008 abstract
Bismuth subsalicylate RCT

- 1 DB, PC, RCT (1999 abstract only)
- 9 tabs/d x 8 weeks
- N=14 (9 collagenous, 5 lymphocytic)
- Response 100% vs. 0% (?)
- Histologic improvement in 86% vs. 17%
- Relapse 25%, all successfully retreated

Fine, Gastro 1999:A880
Mesalamine RCT

- N = 64
- 2.4 gm/d +/- cholestyramine
- Remission 85% in LC (+ or – cholest.)
- In CC: 73% w/o vs. 100% with cholestyramine

Calabrese J Gasto Hep 2007
## Open Label Treatment Responses

### Complete and Partial Response

<table>
<thead>
<tr>
<th>Colitis type (N)</th>
<th>¹LC (170)</th>
<th>²LC (199)</th>
<th>³CC (163)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidiarrheals</td>
<td>73%</td>
<td>70%</td>
<td>71%</td>
</tr>
<tr>
<td>Bismuth</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestyramine</td>
<td>65</td>
<td>57</td>
<td>59</td>
</tr>
<tr>
<td>5-ASA</td>
<td>42</td>
<td>37</td>
<td>35</td>
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<tr>
<td>Steroids</td>
<td>87</td>
<td>88</td>
<td>82</td>
</tr>
</tbody>
</table>

1) Pardi Am J Gastro 2002  
2) Olesen Gut 2004  
3) Bohr Gut 1996
Other Treatment Studies

• **BSS:** N=12, response 92%; mean time to response 2 weeks, 75% MOR for 7-28 months \(^1\)

• **Mesalamine:** N=81, ~3 gm/d, response 86% in LC, 42% in CC \(^2\)

• **AZA:** N=9, steroid refractory or dependent; response 89% \(^3\)

• **Methotrexate:** N = 19, 7.5-10 mg PO QWk; response ‘good’ in 74%, ‘partial’ in 11% \(^6\)

1) Fine, Gastro 1998  
2) Fernandez-Banares, AJG 2003  
3) Pardi, Gastro 2001  
4) Riddell, J Gastro Hep 2007
Recommended Treatment Approach

D/C NSAIDs, other drugs, dairy products

- mild
  - Antidiarrheals
  - Bismuth subsalicylate

- moderate
  - Cholestyramine
  - Aminosalicylates

- severe
  - Budesonide
  - Azathioprine / 6-MP
  - MTX
  - Surgery
Summary

• Microscopic colitis is relatively common cause of diarrhea, particularly in elderly
• Consider celiac disease if suggestion of steatorrhea or significant weight loss
• Consider drug-induced MC
• Treat with bismuth or budesonide
  -Right dose and right duration
• Maintenance therapy may be necessary