Actualités et controverses en gastroentérologie
2 mars 2017

Colites microscopiques

Alain Schoepfer, MD, PD+MERClin
Médecin adjoint
Division of Gastroenterology and Hepatology
CHUV
Microscopic colitis

- Definition
- Epidemiology
- Diagnosis
- Etiology and pathophysiology
- Treatment
- Challenges
Microscopic colitis

• Definition
• Epidemiology
• Diagnosis
• Etiology and pathophysiology
• Treatment
• Challenges
Definition

- Chronic inflammatory disease of colon
- Characterized by watery diarrhea
- F > M
- Middle-aged patients
- Subtypes:
  - Lymphocytic colitis (LC): IEL >20/hpf
  - Collagenous colitis (CC): subepithelial collagen band >10µm
  - Incomplete MCi: MC not otherwise specified, does not fulfill histologic criteria for either LC or CC
- Limited knowledge as of yet

Microscopic colitis

• Definition
• Epidemiology
• Diagnosis
• Etiology and pathophysiology
• Treatment
• Challenges
Epidemiology

• Incidence **LC**: 1.1-5.2/100,000/yr
• Incidence **CC**: 3.1-5.5/100,000/yr
• Prevalence: 103/100,000 persons
• Mean age at Dx 65 yrs
• 25% of pts diagnosed before 45 yrs
• Dx in 10% of pts investigated for chronic diarrhea
• Rare in children
• F > M

Pardi DS, et al. GUT 2007;56;504
## Epidemiology

<table>
<thead>
<tr>
<th>Region and study period</th>
<th>Collagenous colitis</th>
<th>Lymphocytic colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Örebro, Sweden 1984–1988&lt;sup&gt;21&lt;/sup&gt;</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Örebro, Sweden 1989–1993&lt;sup&gt;21&lt;/sup&gt;</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>Örebro, Sweden 1993–1995&lt;sup&gt;1&lt;/sup&gt;</td>
<td>3.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Örebro, Sweden 1996–1998&lt;sup&gt;1&lt;/sup&gt;</td>
<td>6.1</td>
<td>5.7</td>
</tr>
<tr>
<td>Örebro, Sweden 1999–2003&lt;sup&gt;2&lt;/sup&gt;</td>
<td>4.7</td>
<td>5.1</td>
</tr>
<tr>
<td>Örebro, Sweden 2004–2008&lt;sup&gt;2&lt;/sup&gt;</td>
<td>5.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Terassa, Spain 1993–1997&lt;sup&gt;22&lt;/sup&gt;</td>
<td>1.1</td>
<td>3.1</td>
</tr>
<tr>
<td>Terassa, Spain 2004–2008&lt;sup&gt;19&lt;/sup&gt;</td>
<td>2.6</td>
<td>2.2</td>
</tr>
<tr>
<td>Iceland 1995–1999&lt;sup&gt;16&lt;/sup&gt;</td>
<td>5.2</td>
<td>4.0</td>
</tr>
<tr>
<td>Olmsted County, Minnesota, USA 1985–1997&lt;sup&gt;3&lt;/sup&gt;</td>
<td>1.6</td>
<td>2.7</td>
</tr>
<tr>
<td>Olmsted County, Minnesota, USA 1998–2001&lt;sup&gt;3&lt;/sup&gt;</td>
<td>7.1</td>
<td>12.6</td>
</tr>
<tr>
<td>Calgary, Canada 2002–2004&lt;sup&gt;23&lt;/sup&gt;</td>
<td>4.6</td>
<td>5.4</td>
</tr>
<tr>
<td>Calgary, Canada 2004–2008&lt;sup&gt;18&lt;/sup&gt;</td>
<td>7.2</td>
<td>14.0</td>
</tr>
<tr>
<td>Zeeland, Denmark 2002–2010&lt;sup&gt;17&lt;/sup&gt;</td>
<td>10.8</td>
<td>6.7</td>
</tr>
</tbody>
</table>

Epidemiology

Crohn’s disease: 1/1,000
Ulcerative colitis: 1/1000
Microscopic colitis: 1/1000
EoE: 1/2000

Microscopic colitis

• Definition
• Epidemiology
• Diagnosis
• Etiology and pathophysiology
• Treatment
• Challenges
Diagnosis: Clinical presentation

- chronic, nonbloody diarrhea
- Sudden diarrhea onset in 40% of pts
- Average bowel frequency 4-9/day
- Diarrhea volume up to 2 liters/day
- Fecal urgency in 70%
- Incontinence in 40%
- Nocturnal diarrhea in 50%
- Abdominal pain in 50%
- Extraintestinal manifestations possible (arthralgia, uveitis, etc)

Diagnosis: laboratory findings in MC

- Typically non-specific
- Mild anemia
- Auto-antibodies in 50% of pts: RF, ANA, AMA, ANCA, ASCA
- Rarely protein-losing enteropathy
- Fecal exam: eosinophil protein X, myeloperoxidase, and tryptase may be elevated
- Fecal calprotectin: conflicting results regarding use as surrogate marker for microscopic activity

Diagnostic workup

Laboratory
• Search for fecal parasites
• Fecal culture (Salmonella, shigella, campylobacter)
• Toxin test for C. Difficile

Endoscopy:
• Normal-appearing mucosa
• Unspecific findings: edema, erythema

Diagnostic workup: endoscopy

• Severity of histologic changes declines from proximal to distal colon
• Rectosigmoid biopsies miss Dx of CC in 40% of cases
• Highest dx yield if Bx taken from transverse colon (83%) and right colon (70%)
• Lowest Dx yield in bx from rectosigmoid (66%)
• Endoscopy is generally safe
Endoscopy in MC

Normal colon

Mosaic pattern in CC
Endoscopy in MC:
« fractured colon » in CC

CC

EoE
Diagnostic workup: histology

**LC:** increased IEL in CD3 staining
(≥20 IEL/100 surface epithelial cells)
CC: increased subepithelial collagenous layer (EvG), inflammation of lamina propria, intraepithelial infiltration with lymphocytes and epithelial lesions
Microscopic colitis

- Definition
- Epidemiology
- Diagnosis
- Etiology and pathophysiology
- Treatment
- Challenges
Etiology and Pathophysiology: Risk factors

Microscopic colitis

### Etiology and Pathophysiology

#### Risk factors: Drugs

<table>
<thead>
<tr>
<th>High likelihood</th>
<th>Intermediate likelihood</th>
<th>Low likelihood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acarbose (^{123})</td>
<td>Carbamazepine (^{11,128-131})</td>
<td>Cimetidine (^{132})</td>
</tr>
<tr>
<td>Aspirin and NSAIDs (^{118,133-136})</td>
<td>Celecoxib (^{137})</td>
<td>Gold salts (^{138})</td>
</tr>
<tr>
<td>Clozapine (^{139})</td>
<td>Duloxetine (^{140})</td>
<td>Piascledine (^{141})</td>
</tr>
<tr>
<td>Entocapone (^{142})</td>
<td>Fluvastatin (^{137})</td>
<td></td>
</tr>
<tr>
<td>Flavonoid (^{124,137,143-147})</td>
<td>Flutamide (^{29,138})</td>
<td></td>
</tr>
<tr>
<td>Lansoprazole (^{125,148-151})</td>
<td>Oxetorone (^{152,153})</td>
<td></td>
</tr>
<tr>
<td>Omeprazole/Esomeprazole (^{126})</td>
<td>Madopar (^{154})</td>
<td></td>
</tr>
<tr>
<td>Ranitidine (^{122})</td>
<td>Paroxetine (^{11})</td>
<td></td>
</tr>
<tr>
<td>Sertraline (^{11,127,137})</td>
<td>Simvastatin (^{155})</td>
<td></td>
</tr>
<tr>
<td>Ticlopidine (^{29,138,156-159})</td>
<td>Stalevo (^{160})</td>
<td></td>
</tr>
</tbody>
</table>

---

\(^{a}\) This paper used the 'French algorithm' to evaluate causality assessment of adverse drug reactions. This implies the evaluation of seven criteria belonging to two groups: chronological and semiological. Chronological criteria are: Time to onset, dechallenge, and rechallenge. Semiological criteria are: Search for non-drug related causes, evocative semiology of drug responsibility and/or risk factors for drug reaction, and specific validated laboratory test. A bibliographic score taking into account how often the adverse reaction has been reported was used to calculate the total likelihood score of causality.

\(^{b}\) Venotonic drugs containing flavonoids (diosmin, rutin, or hesperidin).

\(^{c}\) Anti-parkinsonian drugs, containing levodopa and benserazide (Madopar\(^R\)) and carbidopa, levodopa and entocapone (Stalevo\(^R\)).

Etiology and Pathophysiology

Risk factors: smoking

- OR 2.1 (95% CI 1.6-2.9) for smokers for developing MC
- Smokers develop MC 10 years earlier than non-smokers

Yen EF, et al. IBD 2012;18:1835
Etiology and Pathophysiology

Risk factors: genetics

• Familial cases of MC are described
• Different members of family developed either LC or CC => supports similar underlying pathomechanism
• Association of MC with HLA-DQ2 or DQ1/3

Pathogenesis

Pathogenesis is unclear, it is likely multifactorial, involving mucosal immune responses to luminal factors in genetically predisposed individuals.

- Abnormal collagen metabolism
- Altered epithelial barrier function
- Diarrhea mechanisms:
  - Inflammatory
  - Secretory
  - Osmotic
  - Bile acid malabsorption

Ung KA, et al. Gut 46:170
Associated conditions

Microscopic colitis

Ung KA, et al. Gut 46:170
4.3% of celiac disease patients have microscopic colitis.

Ung KA, et al. Gut 46:170
Link with Crohn’s disease or UC?

- Rarely microscopic colitis can precede the development of overt IBD (mainly Crohn’s disease)
- In CD rarely lymphocytic and collagenous gastritis are reported

Microscopic colitis

- Definition
- Epidemiology
- Diagnosis
- Etiology and pathophysiology
- Treatment
- Challenges
Treatment

Treatment

No role for the following drugs

• Prednisone (lower response rates than for budesonide)
• Aminosalicylates
• Methotrexate
• Octreotide
• E. coli Nissle

Long-term evolution

• Chronic intermittent course
• Relapses are common (30-60% within 12 months)
• 10-year FUP in CC: diarrhea resolved in 50% of pts (under anti-inflammatory treatment)
• No transformation between LC and CC
• No increased risk for colorectal cancer

Bonderup OK, et a. Eur J Gastroenterol Hepatol 1999
Microscopic colitis

- Definition
- Epidemiology
- Diagnosis
- Etiology and pathophysiology
- Treatment
- Challenges
Pathogenesis
Epidemiology
Randomized clinical trials
Natural history
Thèse: «prévalence et incidence des colites microscopiques dans les cantons de Vaud, Neuchâtel, et Fribourg»

Hugo Maye
Thanks for your attention!