Collagenous Colitis

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History

- Collagenous colitis (CC) was first described by Lindstrom in a case report in 1976 of a woman with chronic watery diarrhea, normal mucosa macroscopically, with a thickened sub-epithelial collagen band seen microscopically.

- Subsequently clustered with lymphocytic colitis (LC) into the entity termed Microscopic Colitis.

- These two colitides are viewed as atypical IBD in some reviews and may represent the same disease process because they share so many features.
Definition

“The term collagenous colitis and lymphocytic colitis are now used to denote the association of chronic watery diarrhea with normal or near normal endoscopic findings, combined with characteristic histopathological inflammatory changes.”

- Lymphocytic and collagenous colitis may be viewed as microscopic colitis with or without collagen thickening.
Females predominate numbers of cases; from case series range from 2.7:1 to 15:1 female : male ratio.

Mean age from early fifties to mid sixties but reports in children do exist.

Incidence is estimated at 1.1 per 100,000 (Spain) persons and 4.1 per 100,000 (Iceland).

Prevalence among those with watery diarrhea who get colonoscopy is 9.5%.
Clinical Presentation

- Cardinal clinical manifestation is watery, non-bloody diarrhea – sometimes insidious (58%) and sometimes with sudden onset (42%) often confusing it with infectious causes.

- Average of six “bowel actions” per day but may have as many as 20.

- The presence of nocturnal diarrhea may help distinguish from IBS.

- Also cramping (41%), anorexia, mild weight loss (42%), urgency, fatigue (24%), and incontinence.

- Malabsorption is rare but protein losing enteropathy may be associated.
Associated Conditions

- Celiac disease (estimated at 3.8-5.0%)
- Autoimmune diseases such as thyroiditis, RA, DM-I, sarcoid, pernicious anemia, scleroderma, CREST, Sjogren’s
- Non-erosive seronegative arthritis in 10%
Colonoscopy with biopsy is diagnostic – important to sample right and left colon as the left side may have less diagnostic utility compared to the right.

U/S – not generally that useful.

Stool Studies – to diagnose secretory diarrhea; stool osmolar gap < 50 – indicates a secretory diarrhea.

Studies to rule out or rule in celiac disease may be useful especially in persons under 50.

Stool may have fecal WBC (50%) and obviously no parasites.

ESR may be slightly elevated and total IgM may be elevated.
Pathology

- At endoscopy the colon typically appears normal.
- May have mild patchy erythema, edema, and superficial erosions.
- Hallmarks include:
  - Increased density of IEL.
  - Epithelial injury.
  - Mononuclear cell infiltrate in LP – amount correlate with diarrhea severity.
  - Thickened subepithelial collagen band.
  - Sparing of crypt architecture.
# CC, LC, IBD Characteristics

<table>
<thead>
<tr>
<th></th>
<th>LC</th>
<th>CC</th>
<th>IBD</th>
<th>Acute Colitis</th>
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</thead>
<tbody>
<tr>
<td>Interepithelial lymphs</td>
<td>+++</td>
<td>+/+++</td>
<td>-</td>
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</tr>
<tr>
<td>Interepithelial PMN’s</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Crypt distortion</td>
<td>-</td>
<td>-</td>
<td>+++</td>
<td>-</td>
</tr>
<tr>
<td>Surface damage</td>
<td>++</td>
<td>+++</td>
<td>-</td>
<td>++</td>
</tr>
<tr>
<td>Lamina Propria</td>
<td>+</td>
<td>+/+++</td>
<td>+++</td>
<td>-</td>
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<tr>
<td>mononuclear cells</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Subepithelial collagen</td>
<td>-</td>
<td>++++*</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

* > or = 10μm

Adapted from Tagkalidi et. al, *Microscopic Colitis*. 2002.
Collagenous Colitis (CC) vs. Lymphocytic Colitis (LC)

<table>
<thead>
<tr>
<th>Clinicopathologic Features of Lymphocytic and Collagenous Colitis†</th>
<th>Lymphocytic colitis</th>
<th>Collagenous colitis</th>
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</thead>
<tbody>
<tr>
<td><strong>Clinical features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median age and range, years</td>
<td>58 (55 to 77)</td>
<td>58 (41 to 84)</td>
</tr>
<tr>
<td>Female-to-male ratio</td>
<td>3:1</td>
<td>15:1</td>
</tr>
<tr>
<td>Type of diarrhea</td>
<td>Secretory</td>
<td>Secretory</td>
</tr>
<tr>
<td>Mean fecal weight, grams</td>
<td>712 (317 to 1269)</td>
<td>565 (246 to 1438)</td>
</tr>
<tr>
<td><strong>Pathologic features</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percent of lamina propria space occupied by inflammatory cells</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>(normal 47±2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Types of inflammatory cells in lamina propria</td>
<td>Mainly plasma cells</td>
<td>Mainly plasma cells</td>
</tr>
<tr>
<td></td>
<td>and neutrophils</td>
<td>and neutrophils</td>
</tr>
<tr>
<td>Subepithelial collagen band (normal &lt;3.65 μM)</td>
<td>Normal</td>
<td>Abnormally thick</td>
</tr>
</tbody>
</table>

†Adapted from Lee, E, Schiller, LR, Vendrell, D, et al, Gastroenterology 1992; 103:1790.
Histopathology

**Collagenous colitis** High power view of a colonic biopsy from a patient with collagenous colitis. There is a thickened subepithelial collagenous band (arrow) associated with increased mononuclear cell infiltration and epithelial degeneration. Courtesy of Robert Odze, MD.

**Normal colon** Low (left) and high (right) power views of a biopsy of a normal colon. Low power reveals straight crypts and mild lamina propria mononuclear cell infiltration. High power shows the surface enterocytes with inter-spersed goblet cells (arrows). Courtesy of Robert Odze, MD.

From Up to Date, “Microscopic colitis”
Pathology – via U/S

Collagenous colitis Ultrasound examination of the sigmoid colon in collagenous colitis. The sigmoid colon is normal size but the layers are more pronounced. 1 = lamina muscularis; arrow = submucosa; and 2 = mucosa. The distance between the crosses is 1.7 mm. Courtesy of C F Dietrich, MD and Wolfgang F Caspary, MD.

From Up to Date, “Microscopic colitis”
Pathogenesis

- Generally viewed as an abnormal immune and tissue response to some luminal substance.

  This is supported by:
  
  - Cases where ileostomy caused remission and subsequent relapse with ileostomy takedown.
  
  - Effects of binders such as colloidal bismuth and cholestyramine – putative role for binding bacterial products.
  
  - Fecal toxicity on epithelial monolayers *in vitro*. Reversal of this phenomenon with cholestyramine.
Treatment

- **Avoidance of suspected inciting agents:**
  - Glutens – only if celiac disease is present.
  - NSAIDS, ranitidine, carbamazepine, simvastatin, lansoprazole all implicated.

- **Treat with specific drugs in a progression**
  - Anti-motility agents.
  - Colloidal bismuth, cholestyramine, sulfasalazine, mesalazine.
  - If these fail then budesonide, prednisolone.
  - If these fail then MTX, azathioprene.
  - In severe refractory cases elemental diet and iliostomy.
Prognosis

- Limited long-term studies exist to assess the natural history of CC and to a lesser extent LC.
  - No link to increased in colon CA as in other forms of IBD
  - Most cases are chronic intermittent in nature with periods of normal function
  - One study of LC showed diarrhea cessation in 93%, return to normal histology in 82%, and no progression to collagenous colitis
  - Another series of CC patient showed significant improvements in diarrhea in 74% of patients
  - The good news is the disease is not associated with increased mortality or severe deterioration.

*Up to Date,* "Microscopic colitis"