Outline

- Microscopic colitis
- Ischemic colitis
- Eosinophilic colitis
- Drug-induced colitis
Case Report

- 65 F with chief complaint diarrhea
- Onset 10 wk ago, slowly progressive
- 3-5 watery BM/d, 1-2 over night
- Urgency, mild pain, relief after BM, mucus but no blood, incontinence
- Has lost 10 pounds

Discussion Points

- What is your differential diagnosis?
- How likely does she have MC?
- Does she meet criteria for IBS?
- What additional history do you want?
- Does she need colonoscopy?
Microscopic Colitis - Clinical Features

- Chronic watery diarrhea
- 50% with abdominal pain, mild weight loss
- Arthralgias, autoimmunity common, sprue
- Overlap with IBS
  - 50-70% in Olmsted County
  - 28-65% in analysis of RCTs
- Association with NSAIDs and other meds

Celiac sprue

- 1/3 of patients with sprue have MC-like changes on colon biopsies
- In largest studies, sprue-like small bowel changes in 2-9% of MC
- Serologies may be less sensitive in MC
- Consider sprue if steatorrhea, IDA, non-response to MC medications

1) Limsui IBD 2007  2) Madish World J Gastro 2005
Epidemiology

- 7-15% of chronic watery diarrhea
- Incidence ~5-10/100,000 each
- Typically 6th-7th decade
  - e.g. in Calgary, age >65 RR = 5.6
- Female predominance (CC>LC in most studies)
Case Report

- PMH: HTN, ↑cholesterol, GERD, depression
- Meds: Olmesartan, simvastatin, omeprazole, paroxetine
- Denies aspirin, NSAID use
- FHx: No IBD, IBS, celiac sprue, colon cancer or polyps

Discussion Points

- Thoughts?
- Plan?
Drug-induced Microscopic colitis

- **High level evidence**
  - acarbose, aspirin, NSAIDs, PPI, SSRI, ticlopidine

- **Intermediate level evidence**
  - carbamazepine, flutamide, lisinopril, simvastatin

Beaugerie and Pardi APT 2005

Drug-induced Microscopic colitis

- **Collagenous colitis**
  - Associated with NSAID, SSRI

- **Lymphocytic colitis**
  - B-blockers, SSRI, statins, bisphosphonates
  - not NSAID

- **Watery diarrhea**
  - SSRI, statins

Fernandez-Banares Am J Gastro 2007
Drug-induced Microscopic colitis

- Collagenous colitis
  - a/w lansoprazole, aspirin, B blocker
  - Negative a/w ARB
- Lymphocytic colitis
  - Sertraline, omeprazole, aspirin
  - Negative a/w oral anti-diabetic drugs

Fernandez-Banares Inflamm Bow Dis 2013

Drug-induced Microscopic colitis

- Danish population-based retrospective study
- 3474 CC and 2277 LC diagnosed 2005-2011
- 100 matched controls per case
- PPI, NSAID, Statin, SSRI use a/w both CC and LC
- PPI and SSRI a/w diarrhea
- Adjusting for a/w diarrhea weakened a/w MC but still PPI:CC and SSRI:LC

Bonderup Inflamm Bow Dis 2014
Olmesartan and Sprue

Case Report

- Meds stopped for 6 weeks, loperamide up to 16 mg/d, no improvement
- Colonoscopy: Grossly normal
- Biopsies: next slide
Discussion Points

- Diagnosis?
- Treatment?
Recommended Treatment Approach

D/C NSAIDs, other drugs

Antidiarrheals

Bismuth subsalicylate

Cholestyramine
Prednisone

Budesonide

Azathioprine/6-MP/MTX

Anti-TNF
Surgery

Case Report

• Bismuth subsalicylate, 3 TID for 6 weeks, no better
• Budesonide 9 mg/d, sx better after 3 days, resolved after 1 week
• D/C after 8 weeks
• 3 weeks later, symptoms return
Discussion Points

• What is going on?
• Does she need repeat colonoscopy with biopsies?
• Treatment?

Natural History of Steroid-treated MC

• 80 patients rx with steroids (37%)
  • 50% LC, 50% CC
  • Prednisone 21%, budesonide 79%
  • Remission 76%, response 20%
• Remission: 83% vs 53% (p = 0.02)
• Response: 14% vs 41%, NR: 3% vs 6%
• Recurrence: HR 0.38 (95% CI 0.18-0.85)

Gentile, Pardi DDW 2012
Budesonide Maintenance in Collagenous Colitis

- Two RCTs (N=82), 9 mg/d x 6 wks, remission 87-96%
- Budesonide 6 mg/d or placebo x 6 mo
- Relapse: 13-23% budesonide, 61-88% placebo

Bonderup Gut 2009
Mielke Gastroenterology 2008

Budesonide Maintenance in Collagenous Colitis: Cochrane Meta-Analysis

<table>
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<th>Study or sub-category</th>
<th>Budesonide n/N</th>
<th>Placebo n/N</th>
<th>OR (fixed) 95% CI</th>
<th>Weight %</th>
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<td>13/17</td>
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<td>Mielke 2008</td>
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<td>24.37 (5.31 – 115.45)</td>
<td>81.60</td>
<td>5.31 (1.50 – 18.84)</td>
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Total 85% CI

Test for heterogeneity: χ² = 1.77, df = 1 (P = 0.18), P = 43.6%
Test for overall effect: Z = 4.00 (P < 0.0001)

**Discussion Points**

- What do you monitor for with long term budesonide?
- What dose do you use?
- Any special instructions?
- Alternative treatments?

**Azathioprine for Microscopic Colitis**

- 9 patients (2.3%), 8 CC, 1 LC
- Steroid dependent, refractory, or intolerant
- Median dose 2 mg/kg/d, f/u 26 months
- 7 tapered off steroids, no-mild symptoms
- 1 intolerant to steroids responded
- 1 non-responder: colectomy

Methotrexate in Collagenous Colitis

- N = 19, 5 mg/wk orally, increased by 2.5 mg increments
- Median dose 7.5-10 mg QWk, range 5-25 mg/wk
- Response complete in 74%, partial in 11%

Summary

- Incidence of MC appears to have stabilized
- 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 with budesonide is effective
Ischemic colitis

Case 4

24-year-old farmer develops moderately severe crampy LLQ abdominal pain with several diarrhea, then bloody, loose stools. Her only medication is a birth control pill. She appears dehydrated, with moderate LLQ tenderness to palpation. At colonoscopy, patchy areas of edema, erythema and superficial ulceration are noted throughout the sigmoid colon. Biopsies are read as “consistent with ischemic colitis”.
Discussion Points

• What do you think is going on?
• Treatment?

Case 4 Q & A

• Which of the following is most likely?

A. She has idiopathic ischemic colitis
B. She has IMA thrombosis
C. She has a stenosis of IMA
D. She has E. coli O157:H7 infection
E. She has Salmonella colitis
Case 4 Q & A

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Ischemic Colitis

• Sx: Acute pain, urgency, diarrhea, bleeding
• Diagnosis: Plain film, CT scan show edema
  • Colonoscopy: colitis, sometimes suggestive
  • Biopsies can be very helpful
• Epidemiology
  • Most common in older subjects
  • Women > men
• Involvement: Watershed areas (where?)
Ischemic Colitis: Etiology

- Low-flow states
  - Dehydration, long-distance running, A fib, CHF, vasoactive medications, smoking
- Occlusion/ligation of IMA
- IMA stenosis (uncommon) or embolism (rare)
- Vasculitis
- Hypercoagulable states, including meds (OCP)
- Idiopathic (28-72% with prothrombotic state)
Ischemic Colitis: Etiology

- Isolated right sided involvement (more pain, less bleeding, worse outcome, esp if SMA lesion)
- Mimics: C. difficile, E. coli O157H7, CMV, Klebsiella oxytoca, IBD (biopsy should help)
- Drugs: vasoconstriction, constipation, chemo, volume-depletion, procoagulant
- More than one cause (2 hits)

Ischemic Colitis: Medications

- Digitalis
- Vasopressin
- Gold
- Cocaine
- Amphetamines
- Pseudoephedrine
- Blood pressure
- Danazol
- Alosetron/tegaserod
- Birth control pills
- Psychotropics
- Ergot
- Triptans
- Diuretics
Ischemic Colitis: Therapy

• Optimize cardiac output, volume status
• Antibiotics?
• D/C smoking, OCP, other meds
• Surgery: uncontrollable bleeding or sepsis, necrosis, perforation, stricture, chronicity

Ischemic Colitis: When to work up

• Thrombophilia work up
  - younger age, other PMH or FHx clotting
• CTA/angiography if right colonic involvement or recurrent (why?)
Eosinophilic colitis

- EGIDs are rare disorders characterized by eosinophilic infiltration of GI tract
- Eosinophilic colitis is least common, esp in adults
- Three variants
  - Mucosal: primarily diarrhea, some pain, less commonly bleeding
  - Muscular: Abdo pain, obstruction
  - Serosal: Eosinophilic ascites
Eosinophilic colitis: Pathophysiology

- In infants usually food allergy (milk, soy)
- Less clear in adults
- Associations with allergies, atopic diseases
- Parasites
  - Enterobius, Strongyloides, Trichuris
- Medications

Eosinophilic colitis: Pathophysiology

- Hypereosinophilic syndrome
- Connective tissue disorders
  - Scleroderma, DM/PM
- IBD
Eosinophilic colitis: Diagnosis

- May or may not have peripheral eosinophilia
- Endoscopic findings variable and nonspecific
- Biopsy required
  - Separate left and right side if diffuse involvement
- Stool O&P

Eosinophilic colitis: Treatment

- Rule out secondary causes
- Role of food allergy testing, elimination diets unclear in adults
- Typically steroid responsive, but high relapse rate
- Possible treatment with steroid sparing agents
  - Ketotifen, montelukast, cromolyn
Eosinophilic colitis: Summary

- EC is rare in adults
- Three variants with different presentations
- Allergic and infectious etiologies should be considered
- Treatment with steroids effective
- ?steroid sparing therapies

Drug-induced colitis
Drug-induced colitis

- The most important thing is to consider it!
- Careful review of medication list, including OTC and illicit drugs, is mandatory in most GI patients
- DIMC and ischemic colitis discussed above
- Few reports of drug-induced eosinophilic colitis
  - Clozapine, carbamazepine, gold, rifampicin
- NSAIDs, chemotherapy, 5-ASA, mycophenolate

Drug-induced colitis

- When in doubt, cut it out
Summary

- Microscopic colitis is a common cause of chronic watery diarrhea, especially in the elderly
- Several treatment options that usually allow for good symptomatic control
- Eosinophilic colitis is rare, especially in adults
- Allergic or atopic conditions are often present in patients with eosinophilic colitis
- Also consider secondary causes

Summary

- Ischemic colitis is a common cause of acute hematochezia and abdominal pain, especially in the elderly
- Ischemic colitis is most often caused by a low-flow state, and mesenteric angiography is usually not helpful
- Drug-induced colitis is uncommon, but a careful review of the medication list is indicated in any patient with colitis
Thank you