Virtual Grand Rounds

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Week 20: Management of Alcohol-Associated Liver Disease with Hepatology and Addiction Medicine
Ashwani K. Singal, MD, MS, FACG, and Jessica L. Mellinger, MD
August 6, 2020 at Noon EDT

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COVID-19: Overcoming Operational Challenges of the New Normal

Practical guidance for financial, staffing, and patient-related operational issues impacting endoscopy and practice management

MONDAY, JULY 27, 8 to 9:30 PM EDT

Moderator: ACG President Mark B. Pochapin, MD, FACG

Presenters:
Louis J. Wilson, MD, FACG
David A. Greenwald, MD, FACG
Costas H. Kefalas, MD, MMM, FACP
Melissa Latorre, MD, MS

Panelists: ACG Endoscopy Resumption Task Force

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All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.
How to Receive CME and MOC Points

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ACG will send a link to a CME & MOC evaluation to all attendees on the live webinar.

ABIM Board Certified physicians need to complete their MOC activities by December 31, 2020 in order for the MOC points to count toward any MOC requirements that are due by the end of the year. No MOC credit may be awarded after March 1, 2021 for this activity.

ACG will submit MOC points on the first of each month. Please allow 3-5 business days for your MOC credit to appear on your ABIM account.

MOC QUESTION
If you plan to claim MOC Points for this activity, you will be asked to: Please list specific changes you will make in your practice as a result of the information you received from this activity.

Include specific strategies or changes that you plan to implement. THESE ANSWERS WILL BE REVIEWED.
Disclosures:

Moderator:
Anita Afzali, MD, MPH, FACG
Consultant/Speaker/Advisory Boards: AbbVie, Janssen, Pfizer, Takeda, Bristol Myers Squibb/Celgene

Speaker:
Anne G. Tuskey, MD, FACG
Dr. Tuskey has no relevant financial relationships.

What’s New With Those “Other” Colitides

Updates on Checkpoint inhibitor colitis, Colonic ischemia, Radiation proctitis, and Microscopic colitis

Anne G. Tuskey, MD, FACG
Medical Director Digestive Health Clinics
IBD Program Director
University of Virginia Health System
Case #1

- 44-year-old man with metastatic pulmonary adenocarcinoma referred to clinic with now bloody diarrhea
- Started on pembrolizumab 6 months ago
- Developed diarrhea 2 months later: 4-5 BM/day, loose, urgent
  - C. difficile PCR and Community Pathogens PCR negative
- Treated with prednisone 100 mg daily with taper with resolution
- Diarrhea returned when pembrolizumab restarted
  - C. difficile PCR and Community Pathogens PCR negative
- Started on prednisone 100 mg (1 mg/kg) but diarrhea returned when tapered to 80 mg daily
- 7-8 BM/day, loose, urgent and blood in > 50%

What is the next best step?

A. Start loperamide
B. Check CMV viral load
C. Increase prednisone to 2 mg/kg/day
D. Endoscopic evaluation
E. IV methylprednisolone
Colonoscopy

Pathology: Active colitis. Scattered epithelial apoptotic injury. No viral cytopathic effect is identified.
Note: All of the mucosa in this biopsy series shows some evidence of inflammatory and epithelial injury. In the biopsies of the right and left colon, there are scattered areas of neutrophilic cryptitis and crypt microabscess associated with epithelial apoptotic injury consistent with colitis secondary to PD-L1 inhibitor therapy

Diagnosis: Immune Checkpoint Inhibitor Mediated Colitis (ICI-C)

Case Continued

- Diarrhea persists after 3 days of IV methylprednisolone 2 mg/kg/day

Now what is the next best step?

A. Increase to methylprednisolone 3 mg/kg/day
B. Add ciprofloxacin and metronidazole
C. Start infliximab
D. Fecal microbiota transplant
E. Consult surgery for diverting loop ileostomy
Immune Checkpoint Inhibitors

- CTLA-4 and PD1/PDL1 are regulatory pathways that inhibit the immune response
  - Associated with tolerance and prevention of autoimmunity
- Cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4)
  - Ipilimumab, Tremelimumab
- Programmed cell death receptor-1 (PD-1)
  - Nivolumab, Pembrolizumab, Cemiplimab
- Programmed cell death ligand-1 (PD-L1)
  - Atezolizumab, Avelumab, Durvalumab

Images from www.cancer.gov

Tumor cells may up-regulate suppressive signaling to T-cells via CTLA-4 and PD1 in order to evade the immune anti-tumor response

Checkpoint inhibitors BLOCK these inhibitory signals thereby re-activating the immune response to tumor cells

De Mallo RA et al. Onco Targets Ther. 2017
Immune Related Adverse Events (irAEs)

- Activated T-cells can cross-react with host antigens → unique spectrum of adverse events (irAEs)
- Most common sites
  - Skin
  - Gastrointestinal
    - Colitis (ICI-C)
    - Hepatotoxicity
  - Endocrine
  - Pulmonary

ICI-C: Severity of Colitis

<table>
<thead>
<tr>
<th>Grading Diarrhea Severity</th>
<th>Diarrhea Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Increase of &lt; 4 BM/day</td>
</tr>
<tr>
<td>2</td>
<td>Increase of 4-5 BM/day</td>
</tr>
</tbody>
</table>
| 3                         | Increase of ≥ 7 BM/day
                          | Hospitalization indicated             |
| 4                         | Life-threatening consequences
                          | Urgent intervention indicated         |

Brahmer JR et al. J Clin Oncol. 2018
ICI-C: Timing and Incidence of Colitis

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Diarrhea</th>
<th>Colitis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Any Grade (%)</td>
<td>Grade 3/4 (%)</td>
</tr>
<tr>
<td>Timing of onset, weeks</td>
<td>6-8</td>
<td></td>
</tr>
<tr>
<td>Anti-CTLA-4 monotherapy</td>
<td>23-33</td>
<td>3-6</td>
</tr>
<tr>
<td>Anti-PD-1/PD-L1 monotherapy</td>
<td>11-19</td>
<td>1-3</td>
</tr>
<tr>
<td>Combination Anti-CTLA-4 and Anti-PD-1/PD-L1</td>
<td>44-45</td>
<td>9-11</td>
</tr>
</tbody>
</table>


ICI-C: Clinical Features and Work up

- Colitis related mortality rate is 2-5%
- Watery diarrhea, urgency, incontinence, abdominal pain
- Laboratories: CBC, CMP, TSH, TTG IgA
- Stool studies: infectious work-up, fecal calprotectin
- CT scan abdomen/pelvis
  - Indications: Grade 3 or 4 diarrhea, severe abdominal pain, distension, peritoneal signs
  - Rationale: Rule out complications of colitis
  - Findings: Bowel wall thickening, fat stranding, fluid filled colon, mucosal hyper enhancement
ICI-C: Endoscopic Evaluation

- Sigmoidoscopy/Colonoscopy
  - Indications: Persistent Grade 2 diarrhea, Any Grade 3 or 4, Steroid refractory, Severe abdominal pain, Hematochezia
  - Findings: Endoscopic appearance is not specific: erythema, edema, mucosal friability, superficial ulcerations, erosions, can be segmental, can be normal
  - Histology: Not specific
  - Active colitis pattern: Neutrophilic inflammation, ↑ intraepithelial lymphocytes, ↑ apoptotic crypt epithelial cells (can resemble infectious colitis)
  - Lymphocytic colitis pattern: ↑ lamina propria lymphoplasmacytic inflammation, scattered crypt epithelial apoptosis (can resemble microscopic colitis)
Management Severe (Grade 3 / 4) ICI Colitis

- Discontinue checkpoint inhibitor
- IV fluids, electrolyte repletion
- Consider hospitalization
- High dose corticosteroids (1-2 mg/kg/day methylprednisolone)
- Evaluate for contraindications to anti-TNF therapy

Improvement

- Convert to equivalent dose of prednisone
- Taper prednisone over 6-8 weeks
- For Grade 3: may resume PD-1/PD-L1 if now Grade 1 and prednisone ≤ 10 mg

Persistent (≥ 3 days) or progressive symptoms

- Start IFX 5-10 mg/kg
- Alternative options: VDZ and MMF
- Response: Taper prednisone
- Partial response: IFX 5-10 mg/kg in 2 weeks
- No response: Colectomy for toxic megacolon or perforation

Back to Our Case

- Persistent symptoms despite discontinuation of pembrolizumab and high dose corticosteroids
- Started on infliximab 5 mg/kg

75 patients with irEC
- 52% received CS alone
- 48% received IFX + CS

Despite higher grade colitis in the IFX group (grade 3/4: 86% vs. 34%; p < 0.001), median times to diarrhea resolution were shorter
Checkpoint Inhibitor Colitis: Take Home Points

- Gastrointestinal toxicities are common irAEs of checkpoint inhibitors
  - Incidence much higher in anti-CTLA-4 than anti-PD-1/PD-L1 agents
- Early diagnosis and treatment is key to optimizing clinical outcomes
- Endoscopic evaluation indicated for: Persistent Grade 2 diarrhea, Any Grade 3 or 4, Steroid refractory, Severe abdominal pain, Hematochezia
- High dose corticosteroids are first-line therapy
- Infliximab is recommend for steroid dependent/refractory colitis
  - Data for vedolizumab or mycophenolate for IFX refractory cases

Case #2

- 70-year-old woman with hypothyroidism presents to the ED with acute onset abdominal pain followed by bloody diarrhea
- Medications: levothyroxine, conjugated estrogen
- She reports crampy abdominal pain with associated nausea and passage of 6-8 episodes of loose stool mixed with bright red blood clots
- Exam: Abdomen soft with mild tenderness in the left upper and left lower quadrants
- Laboratorues: WBC 14.3, Hgb 11.8, CMP normal, Lactic acid 0.9
- Community Pathogens PCR and C. difficile PCR negative
What is the next best step in her management?

A. Repeat *C. difficile* testing  
B. Ciprofloxacin and metronidazole  
C. CT scan abdomen/pelvis with oral and IV contrast  
D. Multiphasic CTA  
E. Colonoscopy

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Colon Ischemia (CI)

- **Reduction in blood flow due to:**
  - Acute arterial occlusion (embolic, thrombotic)
  - Venous thrombosis
  - Hypo-perfusion of the mesenteric vasculature (non-occlusive)
- **Type I**
  - Majority of cases
  - Non-occlusive small-vessel disease
- **Type II**
  - Identifiable etiology - commonly associated with systemic hypotension, decreased cardiac output or cardiac/vascular surgery

*Brandt LJ et al. Am J Gastroenterol. 2015  
Trotter JM et al. BMJ. 2016*
Colon Ischemia: Risk Factors

- Surgery: aortic or abdominal surgery, prior resection for colon cancer
- CV: HTN, CHF, atherosclerosis, PVD, Atrial fibrillation
- Pulm: COPD
- GI: Diarrhea, constipation, IBS
- Endo: Obesity, DM
- Rheumatologic disease
- Hypercoagulable disorder
- Drugs: constipation inducing drugs (opioids), immunomodulators, illicit drugs (cocaine, amphetamines)
- Extreme exercise

Brandt LJ et al. Am J Gastroenterol. 2015

Colon Ischemia: Clinical Features

- Presentation:
  - Sudden cramping, mild, abdominal pain
  - Urgent defecation, maroon/bloody < 24 hours
  - Left-sided disease: more blood, right-sided disease: more pain

- Outcomes:
  - Most cases are benign and self-limited
    - Isolated right-sided colon ischemia (IRCI) associated with higher mortality rates
    - Gangrenous colitis 10% and fulminant colitis 2.5%
  - Recurrence < 10%

Brandt LJ et al. Am J Gastroenterol. 2015
Montoro MA et al. Scand J Gastroenterol. 2011
Colon Ischemia: Laboratory Testing

- Decreased Hgb levels, low serum albumin and the presence of metabolic acidosis can be used to predict severity
- Recommended initial testing for suspected CI
  - Serum: Albumin, amylase, CBC, CMP, CK, lactate, LDH
  - Stool: *C. difficile*, Culture, O&P
- Routine testing for a coagulation disorder in most patients with CI isn’t necessary

Colon Ischemia: Imaging

- CT with intravenous and oral contrast should be ordered as the imaging modality of choice for patients with suspected CI
- Findings include bowel wall thickening, edema, and thumbprinting
- Pneumatosis and porto-mesenteric venous gas predict transmural infarction
- Vascular imaging studies not indicated in most CI patients
  - CTA should be performed on any patient with suspected IRCI or in any patient in whom the possibility of AMI cannot be excluded

Brandt LJ et al. Am J Gastroenterol. 2015
Colon Ischemia: Colonoscopy

- Early colonoscopy (48 h) with minimal air insufflation in suspected CI to confirm diagnosis
- Avoid in severe CI
  - Use CT to evaluate distribution with limited colonoscopy to confirm diagnosis as necessary; procedure should be stopped at the distal-most extent of the disease
- Biopsies should be obtained unless if gangrene
- Colonoscopy should not be performed in patients with peritoneal signs or evidence of gangrene or pneumatosis

Brandt LJ et al. Am J Gastroenterol. 2015

Colon Ischemia: Colonoscopy for Prognostication

313 cases of biopsy proven ischemic colitis:

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Entire population % (n)</th>
<th>Pancolonic % (n)</th>
<th>Right colon % (n)</th>
<th>Transverse colon % (n)</th>
<th>Left colon % (n)</th>
<th>Distal colon % (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (days, median (range))</td>
<td>7 (1-115)</td>
<td>9 (1-54)</td>
<td>10 (1-89)</td>
<td>6 (1-113)</td>
<td>5 (1-75)</td>
<td>6 (1-55)</td>
</tr>
<tr>
<td>Surgical intervention</td>
<td>19.8% (62)</td>
<td>30.4% (7)</td>
<td>44.3% (35)</td>
<td>18.8% (6)</td>
<td>5.9% (6)</td>
<td>10.4% (8)</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>11.8% (37)</td>
<td>21.7% (5)</td>
<td>20.3% (16)</td>
<td>12.5% (4)</td>
<td>6.9% (7)</td>
<td>6.5% (5)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Right colon % (n)</th>
<th>All other patterns % (n)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of stay (days, median (range))</td>
<td>10 (1-89)</td>
<td>6 (1-115)</td>
<td></td>
</tr>
<tr>
<td>Surgical intervention</td>
<td>44.3% (35)</td>
<td>11.5% (27)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Mortality rate</td>
<td>20.3% (16)</td>
<td>9.0% (21)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Brandt LJ et al. Am J Gastroenterol. 2010
<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>Criteria</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>Typical symptoms of CI with a segmental colitis not isolated to the right colon and with none of the commonly associated risk factors for poorer outcome that are seen in moderate disease</td>
<td>Observation Supportive Care</td>
</tr>
<tr>
<td>Moderate</td>
<td>Any patient with CI and up to 3 of the following factors:</td>
<td>Volume replacement Broad-Spectrum antibiotics Surgical consultation</td>
</tr>
<tr>
<td></td>
<td>• Male gender</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hypotension (systolic BP &lt; 90 mmHg)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Tachycardia (heart rate &gt; 100 beats/min)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Abdominal pain without rectal bleeding</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• BUN &gt; 20 mg/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Hb &lt; 12 g/dL</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• LDH &gt; 350 U/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Serum Na &lt; 136 mEq/L</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• WBC &gt; 15 cells/cmm</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Mucosal ulceration on colonoscopy</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>Any patient with CI and more than 3 of the criteria for moderate disease or any of the following:</td>
<td>Emergent surgical consultation Transfer to ICU Volume replacement Broad-spectrum antibiotics</td>
</tr>
<tr>
<td></td>
<td>• Peritoneal signs on physical examination</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pneumatosis or portal venous gas on radiologic imaging</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Gangrene on colonoscopy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Pancolonic distribution or IRCI on imaging or colonoscopy</td>
<td></td>
</tr>
</tbody>
</table>

Brandt LJ et al. Am J Gastroenterol. 2015

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Algorithm for the management of patients suspected of having colon ischemia

*Clinical assessment, vital signs, serology (WBC, Hgb, BUN, LDH, electrolytes)*

**Mild disease**
- Typical symptoms of CI with none of the commonly associated risk factors for poorer outcome that are seen in moderate disease
- **CT of the abdomen and pelvis**
  - Normal
  - Abnormal
  - Consider colonoscopy and biopsy
    - Consistent with CI
    - No ulceration
    - Ulceration
    - Observation and supportive care

**Moderate disease**
- Any patient suspected of CI with up to three of the risk factors associated with poor outcome (listed below)*
  - **CT of the abdomen and pelvis**
    - Non-IRCI
    - IRCI on CT (or colonoscopy)
    - Consider CTA, MRA, or mesenteric angiography
    - Vascular occlusion
    - Surgical evaluation
    - Mesenteric angiography
  - **Consider colonoscopy and biopsy**
    - Occlusion relieved
    - Occlusion not relieved

**Severe disease**
- Any patient suspected of CI with more than three of the criteria for moderate disease* or any of the following peritonial signs on physical examination, pneumatosis or portal venous gas on radiologic imaging, gangrene on colonoscopic examination and pancolonic or IRCI involvement on imaging by colonoscopy or CT
  - **CT of the abdomen and pelvis**
    - Consider CTA, MRA, or mesenteric angiography
    - Vascular occlusion
    - Surgical evaluation
    - Mesenteric angiography
  - **Consider colonoscopy and biopsy**
    - Occlusion relieved
    - Occlusion not relieved
    - Surgical intervention, if possible
  - **Supportive care, correction of cardiovascular abnormalities, volume replacement and broad-spectrum antimicrobials**
  - **Transfer to intensive care unit**
  - **Emergent surgical consultation**

* Risk factors associated with poor outcome: male gender, hypotension (SBP < 90 mm Hg), tachycardia (HR > 100 beats per min), abdominal pain without rectal bleeding, BUN > 20 mg/dL, Hb < 12 g/dL, LDH > 350 UI, serum sodium < 136 mEq/L (mmol/L), WBC > 15 x 10^9/cm³

Brandt LJ et al. Am J Gastroenterol. 2015
Colon Ischemia: Take Home Points

- CI is common and usually benign
  - IRCI is associated with worsened outcomes
- CT A/P with IV and oral contrast modality of choice for suspected CI
- Colonoscopy recommended to confirm diagnosis and prognostication
- Antibiotics for moderate to severe disease
- Emergent surgical consultation for severe disease

Case #3

- 64-year-old man with history of prostate cancer treated with external beam RT 3 years ago is referred for management of persistent rectal bleeding
- Colonoscopy confirms your suspicion for chronic radiation proctitis

Which of the following treatment options would you recommend?

A. Metronidazole
B. Butyrate enema
C. Sucralfate enema
D. Mesalamine enema
E. Oral mesalamine
Radiation Proctitis: Background

- Risk significantly greater with external beam RT > brachytherapy
- Doses < 45 Gy associated with few long term side effects
- Newer modalities for external beam XRT will hopefully minimize toxicity
- ~1-5% of patients treated with XRT for pelvic malignancy will develop chronic radiation proctitis (CRP)

Radiation Proctitis: Clinical Features

- Acute: during or within 6 weeks of radiation therapy
  - Direct mucosal damage
  - Diarrhea, mucous, urgency, tenesmus, bleeding uncommon
- Chronic: 9 months - 30 years after exposure
  - Progressive epithelial atrophy and fibrosis associated with chronic mucosal ischemia
  - Bleeding, mucous, tenesmus, urgency with incontinence, strictures
- Concomitant injury to the genitourinary tract or small bowel may lead to fistulas, SBO, or SIBO
Radiation Proctitis: Work-up

- Assess for recurrence of primary malignancy
- Endoscopic evaluation
  - Non-specific and mucosal biopsies are not diagnostic; help to exclude other causes
- Imaging: MRI if fistula suspected, CT if obstruction to exclude malignancy

CRP: Medical Treatment

- No large controlled trials for treatment options
- Topical therapy
  - Glucocorticoid enemas (e.g. hydrocortisone 100 mg twice daily) for tenesmus
  - Mixed data for SCFA enemas: some benefit with acute, not effective for chronic
  - Sucralfate enema
    - RCT: Oral sulfasalazine + prednisolone enemas vs sucralfate enemas (2 gm twice daily)
    - Sucralfate enemas better tolerated and had a significantly better clinical response after 4 weeks
    - Remission may be sustained following discontinuation
- Oral therapy
  - 5-ASA, metronidazole, pentoxifylline lacking data
  - Hyperbaric oxygen: expensive and not widely available

Paquette IM et al. Dis Colon Rectum 2018
Janss J et al. Endoscopy. 2011
CRP: Endoscopic Treatment

- APC effective in reducing short-term CRP symptoms
- Some data for bipolar electrocoagulation, radiofrequency ablation, Nd-YAG laser and cryotherapy
  - RCT: APC vs Bipolar: equal efficacy (92% vs 93%) but significantly more complications in the bipolar group (87% vs 33%)
- ASGE Guidelines endorse use of APC, bipolar electrocoagulation, heater probe and RFA

<table>
<thead>
<tr>
<th>Statement</th>
<th>Strength of recommendation</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. In patients with chronic radiation proctopathy, we suggest argon plasma coagulation, bipolar electrocoagulation, heater probe, and radiofrequency ablation for treatment of bleeding from chronic radiation proctopathy. There is insufficient evidence to recommend a specific endoscopic modality over another for treatment of bleeding from chronic proctopathy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>2. In patients with chronic radiation proctopathy, we suggest against the use of 4% formalin compared with argon plasma coagulation because of higher adverse event rates compared with argon plasma coagulation for treatment of bleeding from chronic radiation proctopathy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
<tr>
<td>3. In patients with chronic radiation proctopathy, there is insufficient evidence for or against the use of the newer-generation cryosurgical system for treatment of bleeding from chronic radiation proctopathy.</td>
<td>Conditional</td>
<td>Low</td>
</tr>
</tbody>
</table>

Lee JK et al. Gastrointest Endosc. 2019
Lena L et al. Endoscopy. 2011

Radiation Proctitis: Take Home Points

- With newer modalities for radiation therapy, < 5% patients treated with radiation for pelvic malignancy will develop CRP
- Sucralfate enemas first line therapy for persistent bleeding in CRP
- Endoscopic therapy with APC for patients with bleeding despite enema therapy
Case #4

- 60-year-old woman is referred to your clinic with a 6 month history of diarrhea
- 4-7 BM/day loose, non-bloody. No associated abdominal pain or weight loss
- Responds somewhat to over the counter anti-diarrheal medications but she is taking loperamide 4 times daily and still has occasional accidents
- No significant medical history
- Medications: MVI, sertraline
- Laboratories: CBC and CMP unremarkable, normal TSH, negative TTG IgA

What is the next best step in her work-up?

A. Hydrogen breath testing
B. Upper endoscopy with duodenal biopsies
C. Flexible sigmoidoscopy with biopsies
D. Colonoscopy with biopsies
E. CT enterography
Microscopic Colitis: Clinical Features

- Two subtypes of Microscopic colitis (MC)
  - Collagenous colitis (CC) and Lymphocytic colitis (LC)
  - Unclear if distinct or parts of a spectrum
- Most common symptom is intermittent watery diarrhea
- Almost half will have concomitant abdominal pain, wt loss or arthralgias
- Average age at diagnosis 50-70 yrs, female predominance
- Association with NSAIDs and other medications
- Association with celiac disease and other autoimmune conditions

Predictors of Microscopic Colitis

- Factors that increase the probability of MC
  - Age > 50
  - Nocturnal bowel movements
  - Weight loss
  - Diarrhea < 12 months
  - Introduction of a new drug
  - Known autoimmune disease

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of autoimmune disease</td>
<td>4.0 (2.1-7.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Introduction of new drug within 3 months of diarrhea onset</td>
<td>3.7 (2.1-6.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age &gt; 50 years</td>
<td>3.4 (1.9-6.2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Weight loss</td>
<td>2.2 (1.203.8)</td>
<td>0.008</td>
</tr>
<tr>
<td>Diarrhea &lt; 12 months</td>
<td>2.0 (1.1-3.5)</td>
<td>0.024</td>
</tr>
</tbody>
</table>
Virtual Grand Rounds

Microscopic Colitis and Celiac Disease

- Up to 1/3 patients with Celiac Disease have MC-like histologic changes on colon biopsies
  - Consider MC in patients with Celiac Disease not responding to a strict GFD
- Only 2-9% patients with MC have Celiac Disease
  - Not necessary to screen every MC patient
  - When suspected (steatorrhea, iron deficiency anemia, non-responder):
    - → obtain SB biopsies instead of celiac serologies

References:
Pardi et al. Am J Gastroenterol. 2017
Wolber R et al. Hum Pathol. 1990
Breen EG et al. Scand J Gastroenterol. 1987
Olesen M et al. Gut. 2004

Virtual Grand Rounds

Microscopic Colitis: Drug Induced

- High likelihood
  - PPIs, NSAIDs, H2RAs, SSRIs
- Intermediate likelihood
  - Carbamazepine, Flutamide, Lisinopril, Statins

References:
Pardi D et al. Am J Gastroenterol. 2017
Microscopic Colitis: Diagnosis

- Diagnosis made by histology
  - LC: > 20 intraepithelial lymphocytes/100 surface cells, mixed acute/chronic infiltrate
  - CC: intraepithelial lymphocytes less prominent, thickened subepithelial collagen band > 7µm (nl ≤ 5µm)
  - Recommend at least 8 biopsies from different segments of colon

Pardi et al. Am J Gastroenterol. 2017

Microscopic Colitis: Treatment

- Budesonide is the best-studied treatment for MC (6 RCTs)
  - Response 80% vs 20% placebo
  - Relapse common (60-80%)
  - Maintenance may be required
    - 3 RCTs showed budesonide (4.5-6 mg/day) was superior to placebo for maintenance through 6-12 months
    - Taper to lowest effective dose

Mehle S et al. Gastroenterology. 2018
Pardi DS. Am J Gastroenterol. 2017
Mehle S et al. Gastroenterology. 2018
Budesonide Non-Responders

- Incorrect diagnosis
  - Review slides with GI pathologist
- Drug-induced microscopic colitis
- Non-compliance
- Evaluate for other causes diarrhea
- Treatment options
  - Trial prednisone or a bile acid binder
  - Immunosuppressive agents
    - Recent data disappointing

Microscopic Colitis: Take Home Points

- MC is a common cause of watery diarrhea; especially in older women
- Remember association with Celiac Disease
- Remember medications associated with MC (PPIs and SSRIs)
- Diagnosis with biopsies from the right and left colon
- Induction therapy with bismuth or budesonide
- Budesonide maintenance therapy is often required
Thank you!

Questions?

Moderator:
Anita Afzali, MD, MPH, FACG

Speaker:
Anne G. Tuskey, MD, FACG
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John R. Saltzman, MD, FACG
July 30, 2020 at Noon EDT

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Ashwani K. Singal, MD, MS, FACG, and Jessica L. Mellinger, MD
August 6, 2020 at Noon EDT

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Costas H. Kefalas, MD, MMM, FACG
Melissa Latorre, MD, MS
Panelists: ACG Endoscopy Resumption Task Force

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