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IBD for the Internist


PELOTON

Objectives

- Compare and contrast UC vs CD
- List most common extra-intestinal manifestations of IBD
- Understand basic treatment plan, including management of flares
- Describe risk factors for cancer, osteoporosis, infections and recommended screening

A 25-year-old woman is evaluated for a 1-month history of intermittent, loose, bloody bowel movements associated with pain in the left lower quadrant before defecation. The bleeding occurs with and without bowel movements. She reports no fever, chills, night sweats, arthralgia, eye pain, or rash. The patient works in a day care center and has not traveled or used antibiotics recently. She takes no medication.

On physical examination, vital signs are normal. The abdomen is scaphoid and soft, with suprapubic tenderness. The remainder of the physical examination is normal.

Stool testing for bacterial enteropathogens, including *Clostridium difficile*, is negative.

Colonoscopy results show patchy erythema and ulceration in the cecum, ascending colon, descending colon, and sigmoid colon with no involvement of the transverse colon or rectum. Mucosal biopsies of the involved mucosa reveal distorted and branching colonic crypts with lymphocytic and neutrophilic infiltration. Ileal examination is normal.

What is the most likely diagnosis?

A. Ulcerative colitis

B. Crohn’s disease

C. Giardiasis

D. Microscopic colitis

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Definitions

- Ulcerative Colitis (UC): chronic idiopathic inflammatory disorder of colonic mucosa. It is characterized by superficial mucosal intestinal inflammation that extends in a contiguous fashion beginning at the anal verge to involve a portion of the colon or the entire colon.
- Crohn's Disease (CD): A chronic idiopathic disorder of the GI tract characterized by transmural intestinal inflammation that has a propensity to involve almost any portion of the GI tract, from the mouth to the anus.
  - Typically w/ ileum, has "rectal sparing," patchy distribution

Epidemiology

- UC- Incidence among Caucasians ranges from 1.2 to 24.3 cases per 100,000 people annually, with a worldwide prevalence of 7.6– 505 per 100,000 depending on the region
- CD- Incidence ranges from 0.03 to 20.2 per 100,000 people per year, with prevalence rates of 3.6–322 cases per 100,000 people per year
- The incidence rate of UC is slightly higher in men, there is a higher incidence rate of CD in women.
- Diagnosis of CD peaks at ages 20- 30 years, the peak age of diagnosis for UC is 30-40 years.
  - Some studies also describe a second peak of onset at 60-70 years

Risk Factors

- Family history
  - First degree relatives have greatest risk
- Most commonly among Caucasians and in decreasing order of prevalence among African-Americans, Hispanics, and Asians
- Ashkenazi Jewish descent
- Tobacco use*
- Increased risk for the development of IBD in patients exposed to OCP compared with patients not exposed to OC

Differentials

- “Colitis” and “enteritis” are non-specific and denote histologic or radiologic colonic and small intestinal changes, respectively, resulting from any etiology

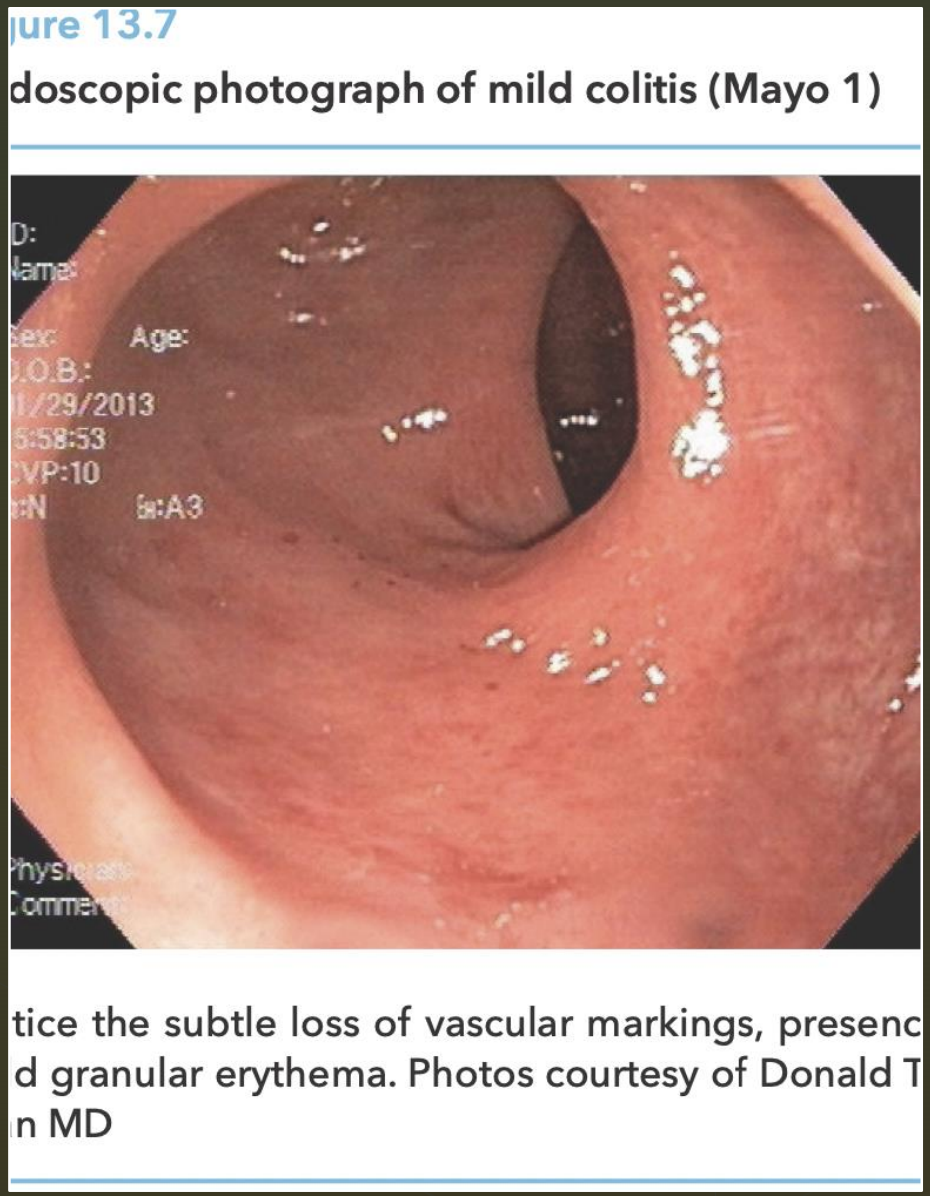
Table 13.1

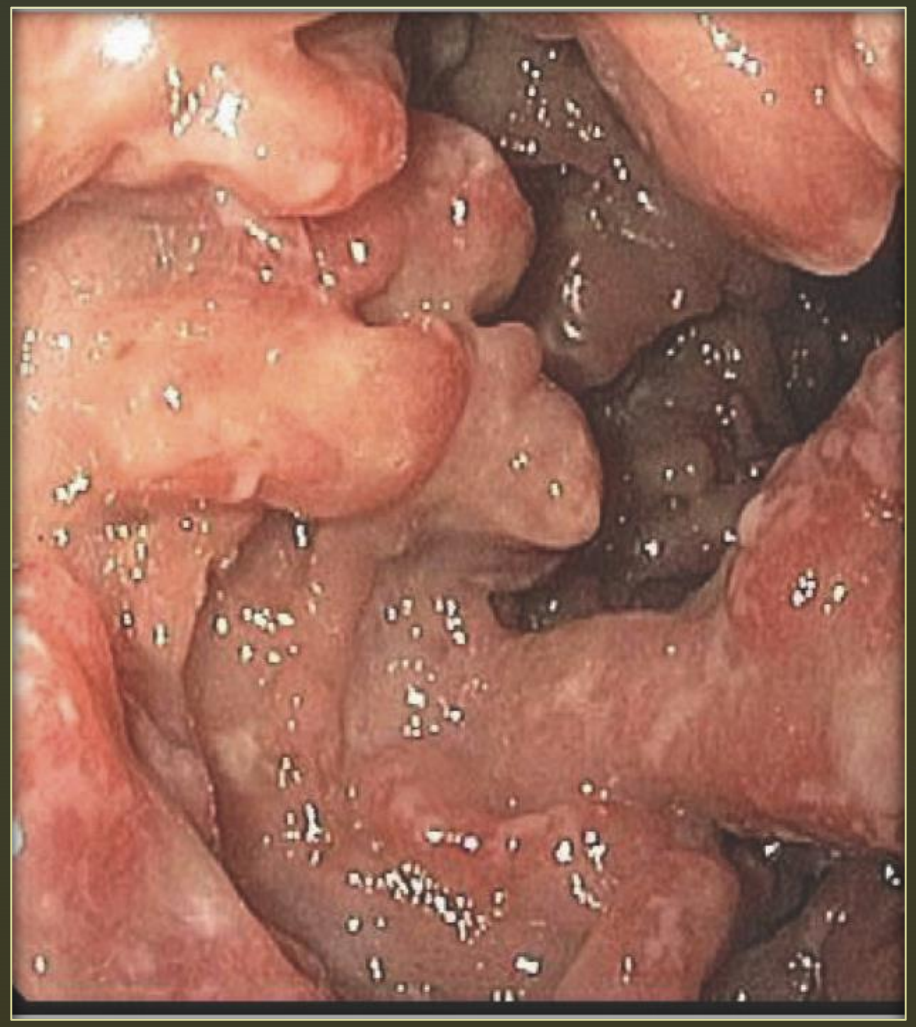
Differential diagnosis of intestinal and colonic inflammatory diseases

Infectious Conditions	Noninfectious Conditions
Bacteria	Collagenous colitis
Bacterial toxins	Lymphocytic colitis
Toxigenic E. coli	Segmental colitis associated with diverticulosis (SCAD)
Clostridium difficile	Diversion colitis
Bacterial invasion	Ischemic colitis
Salmonella	Medication-induced colitis
Shigella	NSAID-induced enterocolitis
Campylobacter	Gold-induced enterocolitis
Yersinia	Chemical colitis
Mycobacterium	Glutaraldehyde-induced colitis
Gonorrhea	Radiation enterocolitis
Aeromonas	Appendicitis
Lymphogranuloma venereum	Neutropenic enterocolitis/ typhlitis
Parasites	Solitary rectal ulcer syndrome
Amebiasis	Carcinoma
Chlamydia	Lymphoma
Schistosomiasis	Leukopenia
Viruses	Mesenteric venous thrombosis
Cytomegalovirus	
Herpes simplex	
Adenovirus	

Features of UC

- Begins in the rectum and extends proximally to involve all or part of the remaining colon in a continuous fashion
- Symptoms can be gradual or sudden and include: increase in stool frequency and bloody diarrhea, fecal urgency, and abdominal cramping which is typically partially of completely relieved with defecation
- Nocturnal stools (not specific to UC but important to ask for IBD)
- Abdominal pain is not a common feature





Features of UC

- Endoscopic findings include include loss of the normal vascular markings, mucosal granularity, friability, mucus exudate, and focal ulceration
- Colonic mucosa appears reddened, granular, and friable
- The inflammation in UC is predominantly confined to the mucosa
- Path features of UC include the presence of crypt architecture distortion, crypt atrophy, increased inter-crypt spacing to less than six crypts/mm, irregular mucosal surface, basal lymphoid aggregates, and a chronic inflammatory infiltrate

Features of Crohn's Disease

- Any segment of the GI tract can be involved, from the mouth to the anus, although the disease most commonly affects the terminal ileum and cecum. Ileocecal region is most commonly involved, and symptoms therefore are notable for cramping right lower quadrant abdominal pain and diarrhea
- 10-15% present with perianal CD- perirectal abscesses, painful and edematous external hemorrhoids, anal fissures, perianal fistulas, or rectovaginal fistulas
- Up to 1/3 present before age 20yo
- CD can commonly have fissures, fistulas, abscesses; small bowel involvement
- Endoscopic features do not always correlate with disease severity, can be helpful to see "skip lesions," in which diseased areas alternate with grossly normal bowel segments

A 26-year-old woman is evaluated for a 2-month history of diarrhea characterized by two to three semibloody stools per day associated with cramping lower abdominal pain. She reports no fever, chills, nausea, vomiting, or weight loss. She has not traveled internationally. She takes no medication.

On physical examination, vital signs are normal. Abdominal examination shows left and right lower abdominal tenderness to palpation. Rectal examination is remarkable for bright red blood.

Stool testing for enteric pathogens is negative.

Results of colonoscopy show inflamed mucosa characterized by granularity, erythema, friability, and loss of vascular pattern that starts at the anorectal verge and extends proximally in a continuous and symmetric fashion to the splenic flexure where there is an abrupt transition from affected to normal mucosa. The terminal ileum is normal. Biopsy results for the inflamed mucosa reveal crypt abscesses along with distorted and branching colonic crypts.

Which is the most likely diagnosis?

A. Chronic Entamoeba histolytic infection

B. Crohn’s Colitis

C. CMV

D. Ulcerative Colitis

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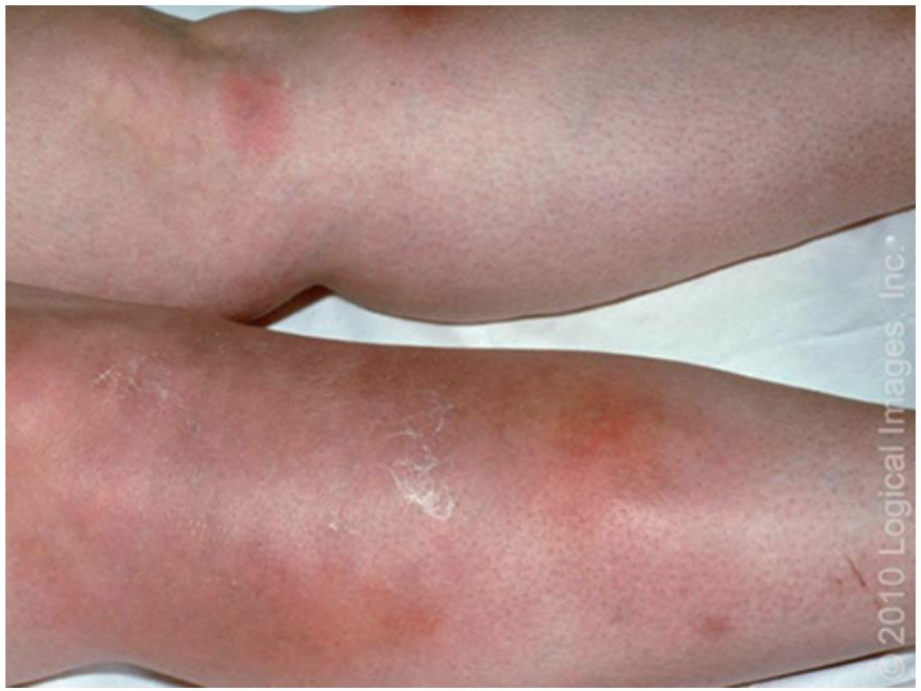
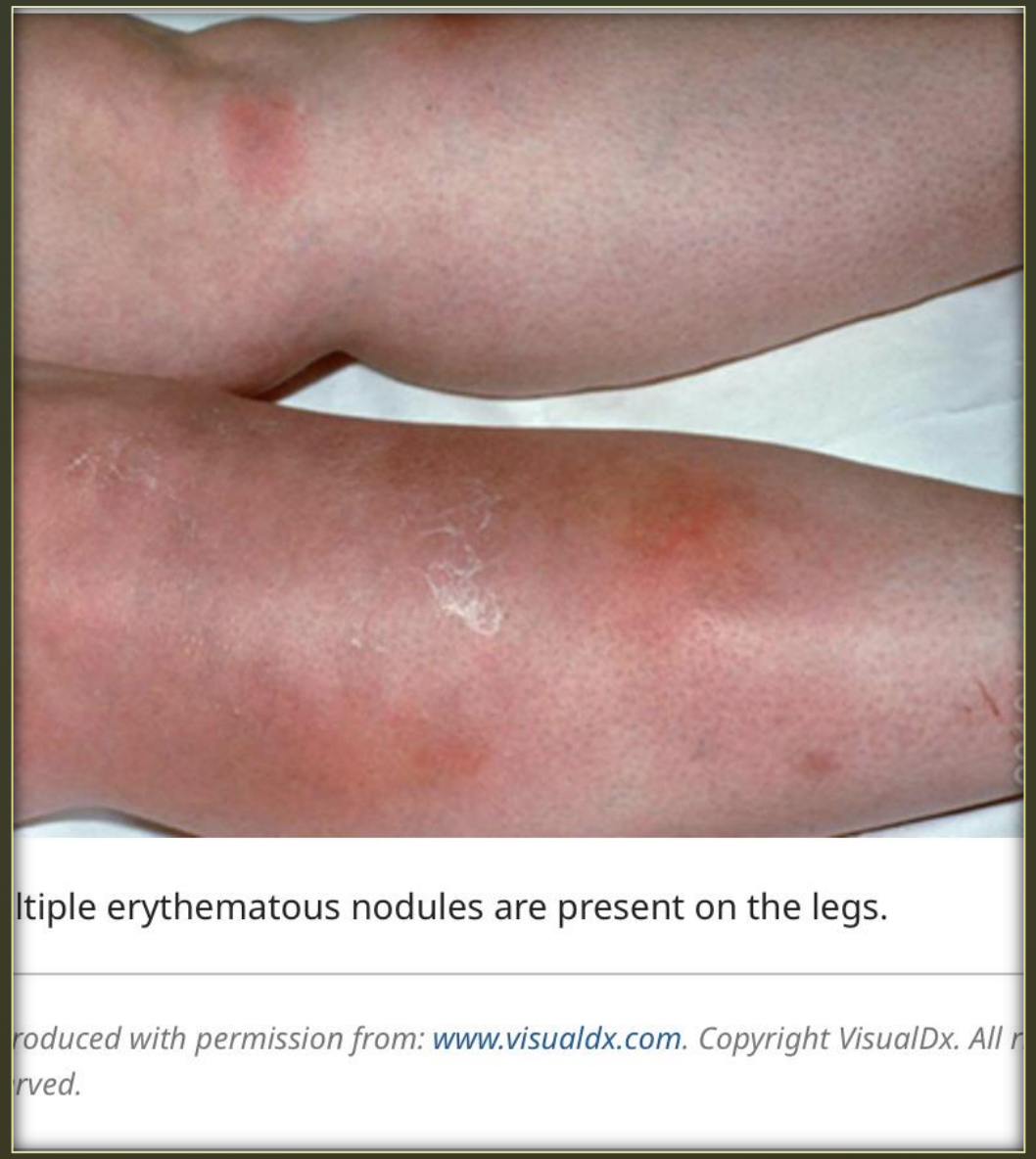
EIM- DERM



Multiple erythematous nodules are present on the legs.



EIM- DERM

- Erythema Nodosum
  - 5% prevalence
  - Painful, raised nodules on extensor surfaces
  - PARALLELS disease activity
  - Waxing/waning course

-

EIM-DERM

- Stomatitis
  - Parallels, painful
- Sweet syndrome
  - Parallels disease activity, non-pruritic, tender nodules/plaques
- Pyoderma gangrenosum
  - 0.5-2%
  - Can parallel or be independent of disease activity
  - Pustules, can progress to deep ulcers and dermal necrosis
  - Pathergy

EIM-MSK

- -Peripheral arthropathy
  - type 1
  - type 2
- -Central (axial) arthropathy
- -Enthesitis and dactylitis

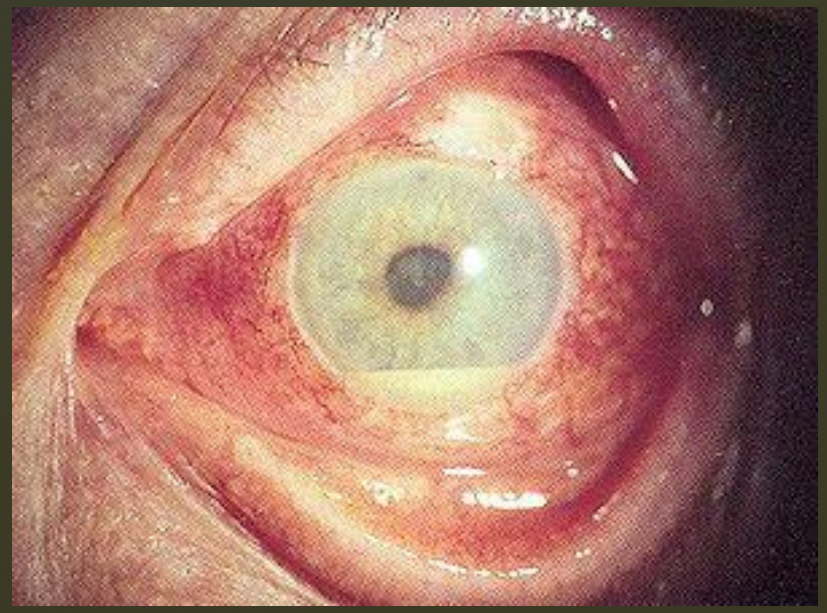
EIM-MSK

- PERIPHERAL
- 5-20% of IBD patients
- Seronegative (-RF/ANA)
- Non-destructive/erosive
- Type 1 and 2
- 1: <5 joints, typically large joints, acute onset/self-limited, asymmetric and migratory, PARALLELS disease
- 2: >5 joints, MCP/small joints affected, can persist for years, INDEPENDENT of disease activity

- AXIAL
- Seen in ~5% of IBD patients
- Crohn's >UC
- Ankylosing Spondylitis
- Sacroiliitis
- Tx: MTX, NSAIDS, anti-TNF,
- INDEPENDENT of disease activity

OCULAR EIMS

1.



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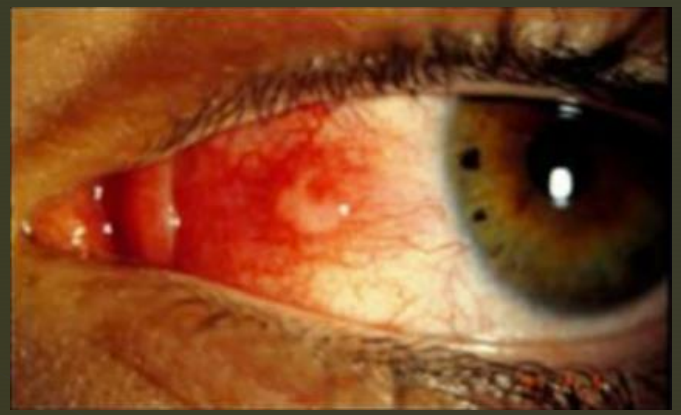

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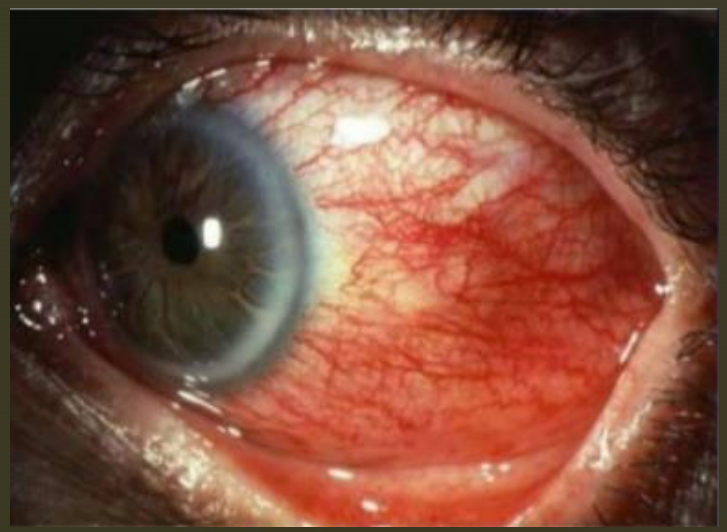

OCULAR EIMS

- -Episcleritis-inflammation of episclera, burning/itching, PARALLELS disease. Tx: eyedrops, NSAIDs, topical steroids
- -Scleritis-severe pain w/ movement, photophobia, INDEPENDENT of disease. Needs urgent optho eval
- -Uveitis-photophobia, blurry vision, usually w/ Crohn's, INDEPENDENT of disease. Needs urgent optho eval.
- -RARE: Keratopathy, retinopathy

Treatment

- Goals of therapy:
  - Induce remission
  - Maintain remission
  - Alleviate intestinal and EIM symptoms
  - Therapy with minimal toxicity
  - Adequate nutrition, improved QOL

A 30-year-old man is evaluated after being hospitalized for an acute flare of extensive ulcerative colitis. He reports six to eight bloody bowel movements daily with prominent urgency and lower abdominal cramping for the past 2 weeks. He has been taking prednisone daily for 1 week. His only other medication is mesalamine.

On physical examination, vital signs are normal. Abdominal examination reveals lower abdominal tenderness. The abdomen is not distended and bowel sounds are normal. Blood is seen on digital rectal examination.

Hemoglobin level is 10 g/dL (100 g/L). He remains hemodynamically stable.

Which of the following is the most appropriate venous thromboembolism prophylaxis for this patient?

A. SCDs

B. ASA

C. Heparin

D. Graduated compression stockings

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A 26-year-old woman with Crohn disease is evaluated for a 2-week history of worsening abdominal pain in the right lower quadrant. She reports passage of one to two formed and nonbloody stools per day with no changes in bowel habits. The patient has required three courses of prednisone for disease flares over the past year. Her only medication is azathioprine.

On physical examination, temperature is 37.7 °C (99.9 °F) and pulse rate is 115/min; other vital signs are normal. Abdominal examination shows fullness and tenderness in the right lower quadrant with no distinct mass. The remainder of the examination is unremarkable.

Laboratory studies show a hemoglobin level of 10.5 g/dL (105 g/L) and a C-reactive protein level of 32 mg/dL (320 mg/L). Leukocyte count and liver chemistry tests are normal.

CT enterography shows asymmetric mural thickening and mucosal inflammation of a long segment of distal ileum without luminal narrowing.

Which of the following is the most appropriate treatment?

A. Budesonide

B. Infliximab

C. Mesalamine

D. Prednisone

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Disease activity	Ulcerative colitis	Crohn's disease
Mild	Oral aminosalicylate Topical aminosalicylate Hydrocortisone enemas Hydrocortisone suppositories	Oral aminosalicylate (?; see text for discussion) Hydrocortisone enemas Metronidazole Ciprofloxacin
Moderate	Oral aminosalicylate Topical aminosalicylate Azathioprine/6-mercaptopurine Nicotine patch Oral corticosteroids Parenteral corticosteroids Infliximab	Aminosalicylate (?; see text for discussion) Oral corticosteroids Azathioprine/6-mercaptopurine Metronidazole/ciprofloxacin Methotrexate Infliximab, adalimumab, or certolizumab pegol
Severe	Oral/IV corticosteroids Cyclosporine Infliximab	Oral / IV Corticosteroids Cyclosporine (?) Infliximab, adalimumab, or certolizumab pegol
Maintenance	Aminosalicylate Azathioprine/6-mercaptopurine Infliximab	Azathioprine/6-mercaptopurine Methotrexate Infliximab, adalimumab, or certolizumab pegol
Fistulizing Crohn's Disease		Ciprofloxacin Metronidazole 6-Mercaptopurine/azathioprine Infliximab, adalimumab, or certolizumab pegol Methotrexate (?)

Pharmacotherapies

5-Amionsalicylates

- Ex: mesalamine
- SE: fever, rash, nausea, vomiting, and headache. Monitor renal function
- Males- fertility
- UC patients with mild-to-moderate disease activity, oral aminosalicylates have been shown to be superior to placebo for induction of remission
- Not effective in CD

Steroids

- A mainstay of therapy for moderate and severe IBD (both in CD and UC)
  - IV/oral
  - Budesonide
- Useful for inducing remission, not maintenance due to SE
- SE: insomnia, emotional lability, difficulty concentrating, hyperglycemia, fluid retention, moon face, acne, weight gain hypertension, metabolic bone disease, osteonecrosis

Pharmacotherapies

AZA, 6-MP

- Azathioprine and 6-MP are effective for the treatment of active luminal CD, fistulizing CD, and for both steroid-sparing and maintenance of remission in CD
- Check TPMT activity
- Increased risk of lymphoma
- Can be combined w/ biologics

MTX

- Methotrexate is effective in inducing remission in patients with moderate-to-severe CD and has a significant corticosteroid- sparing effect
- UC efficacy is not established
- Not associated w/ increased lymphoma risk
- Females, teratogenicity

Pharmacotherapies

Cyclosprine

- Potent immunosuppressive, rapid onset of action
- Best for: severe UC refractory to corticosteroids, such as those who have failed to respond to three to five days of adequately dosed IV corticosteroid therapy
- Primarily used as a bridge, not effective for maintenance of remission

Anti-TNFs

- anti-TNF agents infliximab, adalimumab are most commonly used
- Check for underlying infections before initiating
- Combo therapy w/ immunomodulators more effective
- Check Ab’s
- Vedo (monoclonal-severe UC, crohn’s)

Pharmacotherapies

JAK-2

- Potent immunosuppressive, rapid onset of Tofacitinib (UC salvage)
- Increased risk of infection, in particular non-systemic zoster and possibly lymphoma

Anti- IL2/23

- Ustekinumab is a fully human monoclonal anti- body
- Ustekinumab is approved for the treatment of CD, and is given via a one-time, weight-based IV infusion, followed by subcutaneous injection

A 25-year-old female with a history of ileocolonic Crohn's disease with perianal phenotype presents for clinic follow up. She recently learned she is six weeks pregnant and wants to discuss her Crohn's management during pregnancy. Her Crohn's disease was initially diagnosed at age 16 years when she presented with recurrent perianal abscesses. Evaluation confirmed perianal fistula as well as luminal Crohn's disease involving the rectum and ileocecal region. She was treated initially with a prednisone taper and then placed on infliximab monotherapy with good response. However, four years later, she developed recurrent symptoms and was found to have high anti-infliximab antibodies with no detectable drug level. At that time, she was placed on combination therapy with adalimumab and azathioprine, which she has maintained until now. Clinically, she feels well with no diarrhea or rectal bleeding. She continues to have intermittent drainage from the perianal fistula that she manages with short courses of antibiotics, the last three months ago.

Which of the following is the most appropriate medical management for this patient during pregnancy?

A. Intermittent use of ciprofloxacin for perianal fistula symptoms

B. Stop adalimumab and continue azathioprine during pregnancy

C. Continue both adalimumab and azathioprine during pregnancy

D. Stop azathioprine and continue adalimumab monotherapy

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Treatment

- Antibiotics- no trials showing efficacy in CD
- Probiotics- VSL3 for UC
- Nutritional therapy
- Surgery- 30% of UC will need, CD up to 75%
  - Remember biologics after surgery in CD

Healthcare Considerations

- Increased risk for vaccine-preventable illnesses (flu, 13 valent pneumococcal, 23 valent pneumococcal)
- Live vaccines contraindicated for immunosuppressed patients
- Yearly pap smear- women
- Increased risk for metabolic/bone disease- ca/vit D supplementation (DEXA for age appropriate, those w/steroid use, or as baseline)
- Routine depression screening
- Yearly derm, optho exams

A 22-year-old man with a history of extensive ulcerative colitis diagnosed three years ago presents for evaluation. He is currently in clinical remission, maintained on oral mesalamine 2.4 g/day in divided doses. He was noted to have persistent elevation of serum alkaline phosphatase on blood samples drawn three months apart. Magnetic resonance cholangiopancreatography (MRCP) revealed alternating narrowed and dilated segments of the intrahepatic and extrahepatic biliary ducts consistent with primary sclerosing cholangitis (PSC).

Which of the following is recommended at this time?

A. Repeat MRCP 6mo for screening

B. Surveillance colonoscopy now and yearly thereafter

C. First surveillance colonoscopy in 5 years, then yearly thereafter

D. High dose UCDA should be started

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IBD and cancer

- Increased risk of melanoma and non-melanoma skin cancer
- CRC
  - 8yrs postdx , then q 1-2 years
- PSC and GB cancer w/ UC
  - CRC screen at dx of PSC
  - Yearly GB w/ PSC

References

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THANK YOU!