Case Presentation

- 20 year old man with several months of gradually worsening RLQ abdominal pain and diarrhea
- Now has developed pain and swelling near the anus
- Has chills and fever to 102°F
- Physical exam: moderately tender in RLQ, small perirectal abscess
- Labs: Hgb 10 g/dL, MCV 75, WBC 11, CRP 23
Case (continued)

• Small abscess is drained

• Colonoscopy: aphthous and deeper ulcers in TI, scattered aphthous ulcers in colon, greatest in distal rectum
  • Bx: moderately active chronic ileitis, focal acute colitis

• MR enterography: bowel wall thickening and mural hyperenhancement of distal 15 cm of TI, no proximal dilation

Question

• For this young man with Crohn’s disease who presented with a perianal abscess and ileocolonic disease with ulcers, what is the most appropriate therapy?
  • Mesalamine 2000 mg PO BID?
  • Metronidazole 250 mg PO TID for 7 days?
  • Azathioprine 150 mg PO daily?
  • Natalizumab 300 mg IV every 4 weeks?
  • Anti-TNF therapy plus azathioprine?
  • Anti-TNF therapy plus methotrexate?
Presenting Features of Ulcerative Colitis

- Increased stool frequency
- Urgency or incontinence
- Rectal bleeding and/or mucus
- Incomplete evacuation/tenesmus
- Abdominal cramping
- L-sided/proctitis: constipation
- Fever, fatigue, weight loss

Presenting Features of Crohn’s Disease

- Much more varied
- Abdominal pain (transmural inflammation, strictures)
- Diarrhea
  - Fluid secretion/impaired absorption
  - Bile salt diarrhea
  - Steatorrhea
- Bleeding (less common than UC)
- Constipation
- Fatigue is a cardinal symptom
- Fistula symptoms
- Extraintestinal manifestations (skin, eyes, joints/bones, liver)
- Other complications (vitamin B12 deficiency, gallstones, kidney stones, thromboembolism)
Differential Diagnosis of IBD: “Challenge the Diagnosis”

- Irritable bowel syndrome
- Lactose intolerance
- Celiac disease
- Collagenous or lymphocytic colitis
- Infectious colitis (Shigella, Salmonella, E. coli O157H7, Yersinia, C. diff, amoeba, parasites, CMV)
- Ischemic colitis
- Diverticulitis


Triggers of IBD

- Infection (CMV, C. diff)
- NSAIDs
- Smoking (or quitting smoking)
ACG Classification of UC Severity

• **Mild**
  - <4 stools daily +/- blood, normal ESR, no systemic toxicity

• **Moderate**
  - ≥4 stools daily +/- blood, minimal systemic toxicity

• **Severe**
  - >6 stools daily, blood, toxicity (fever or tachycardia or anemia or elevated ESR

• **Fulminant**
  - >10 stools daily, continuous bleeding, toxicity, abdominal tenderness/distension, needs transfusion, colon dilation on xray


ACG Classification of Crohn’s Disease Severity

• **Mild to moderate (CDAI 150-220)**: tolerate PO intake, no systemic toxicity, tenderness, mass, obstruction or >10% wt loss

• **Moderate to severe (CDAI 220-450)**: fever, weight loss, abdominal pain or tenderness, intermittent nausea/vomiting, or significant anemia

• **Severe to fulminant (CDAI >450)**: high fever, persistent vomiting, evidence of obstruction, peritoneal signs, cachexia or evidence of abscess

**CD – Clinical Patterns**

- Inflammatory
- Fibrostenotic
- Fistulizing

**IBD: Systemic Complications**

- Eye inflammation*
- Lower bone density*
- Liver and bile duct inflammation
- Gallstones
- Skin lesions
- Growth failure in children
- Kidney stones
- Subfertility*
- Ovaries
- Uterus
- Arthritis and joint pains

*Higher incidence in women.*
Initial Evaluation

• Labs
  • Serum inflammatory biomarkers (Hgb, WBC, albumin, CRP)
  • Hepatic biochemistries
  • Creatinine
  • Iron studies/vitamin B12/vitamin D
  • Consider TPMT
  • Consider PPD or interferon-gamma release assay for *Mycobacterium tuberculosis*
  • Viral hepatitis serologies

• Stool studies
  • C diff toxin (preferably PCR-based)
  • Enteric pathogens culture
  • Consider *Giardia/Cryptosporidium* antigen in N. Amer.

• Colonoscopy

• Small bowel imaging if Crohn’s suspected (CTE or MRE)

Risk Stratification: What Do Natural History Studies Tell Us?

• Young age at diagnosis

• Crohn’s
  • Fistulizing disease at diagnosis
  • Ileal or ileocolonic or upper GI involvement

• Ulcerative colitis
  • Male gender
  • Early need for hospitalization
  • Early need for corticosteroids
  • Extensive colitis at diagnosis
Selection of Initial Medication

• Ulcerative colitis
  • Low-risk patient with mild symptoms: 5-ASA
  • Moderate to severe symptoms: steroids
  • Fulminant symptoms: IV steroids; anti-TNF?

• Crohn’s disease
  • Low-risk patient: budesonide taper then observe?
  • High-risk patient: consider immunosuppressive and anti-TNF rx

Dr. Katz’ Key Management Points for UC

• Challenge the diagnosis
• Rule out cancer and dysplasia
• Confirm active disease (scope, CRP, fecal calpro)
• Customize therapy to disease severity
• Add topical therapy to control tenesmus, regardless of extent
• Adherence (once or twice daily meds)
• Watch for predictors of relapse (CRP, fecal calpro, etc)
• All steroids need exit strategy (IMM or biologic)
• C. diff, Quantiferon, TPMT, vaccinate
• Earlier use of biologics and IMM (cautious with combo therapy in the elderly and males under 30 years)
Crohn’s Disease Clinical Decision Support Tool

Assess Inflammatory Status

- Assess inflammatory status
- Perform clinical lab testing:
  - CBC
  - CRP
  - CMP
  - Fecal calprotectin
  - ESR
- Select imaging modalities (if indicated)
  - Perform endoscopy
  - Identify symptoms without inflammatory markers
  - Identify symptoms with inflammatory markers
  - Perform CT-enterography OR magnetic resonance enterography

Assess Current and Prior Disease Burden

- Identity as low-risk patient
- Perform treatment for patient in remission (low-risk)
- Perform treatment for patient not in remission (low-risk)

- Identity as moderate/high-risk patient
- Perform treatment for patient in remission (mod/high risk)
- Perform treatment for patient not in remission (mod/high risk)

Assess Comorbidities and Disease and Therapy Related Complications


*Selection depends on local expertise and experience with imaging modalities. Magnetic Resonance Enterography is preferred due to the reduction in ionizing radiation, particularly for younger patients. If patient is less than 50 years of age, we suggest using Magnetic Resonance Enterography.

*Consideration could be given as to whether to make treatment decisions based on inflammatory markers versus confirming with colonoscopy. This may depend on whether there was historically good correlation between the biomarker selected and colonoscopy in the specific patient.

Assess Comorbidities and Complications

![Diagram]

- Infections
- Stricture/remodeling
- Symptoms related to prior surgery
- Adverse reaction to medical therapy
- Abdominal abscess or fistula
- Perianal abscess or fistula

- C. difficile, CMV, food poisoning
- Abnormal imaging (bowel dilation)
- Obstructive symptoms
- Weight loss
- Bile acid diarrhea
- Bacterial overgrowth
- Steatorrhea/fat malabsorption
- Recent introduction of new agent: drug holiday
- Pain, fistula drainage, fever


Assess Current and Prior Disease Burden

![Diagram]

- Identify patient as low risk
  - Age at initial diagnosis > 30 years
  - Limited anatomic involvement
  - No perianal and/or severe rectal disease
  - No prior surgical resection
  - No stricturing and/or penetrating behavior

- Identify patient as moderate/high risk
  - Age at initial diagnosis < 30 years
  - Extensive anatomic involvement
  - Perianal and/or severe rectal disease
  - Deep ulcers
  - Prior surgical resection
  - Strictures and/or penetrating behavior

**Initial Treatment of the Low-Risk Patient**

- **Low risk patient**
  - Ileum and/or proximal colon - none to minimal systemic symptoms
  - Options:
    - Budesonide 9 mg per day with or without AZA
    - Tapering course of prednisone with or without AZA
  - Diffuse or left colon - none to minimal systemic symptoms
  - Options:
    - Tapering course of prednisone with or without AZA


**Further Treatment of the Low-Risk Patient Who Achieved Remission with Initial Therapy**

- **Low risk patient**
  - Options:
    - Stop therapy and observe (high chance of relapse over 1 year)
    - Budesonide 6 mg/day (median time to relapse prolonged by approximately 114 days, but no difference in remission rates versus placebo at 1 year) *
    - Immunosuppressive therapy (AZA, 6MP, and MTX have been shown to be effective for maintaining steroid-induced remissions with prednisone or prednisolone, but are associated with rare risk of infection and lymphoma)
  - *Consider bone mineral density monitoring

Further Treatment of the Low-Risk Patient Who Didn’t Achieve Remission with Initial Therapy

Options:
- Immunosuppressive
- Assess drug levels
- Consider anti-TNF therapy\(^{(13)}\)


Initial Treatment of the Moderate-to-High-Risk Patient

Moderately severe Crohn’s Options:
- Use anti-TNF monotherapy over no therapy or thiopurine monotherapy\(^{(13)}\)
- Use anti-TNF + thiopurine over thiopurine monotherapy or anti-TNF monotherapy\(^{(15)}\)
- Use methotrexate for patients who do not tolerate purine analog in combination with anti-TNF

\(^5\) Combination therapy with immunosuppressant and anti-TNF biologic offers improved efficacy and durability compared with anti-TNF monotherapy and should be considered for mod/high risk patients requiring 2\(^{nd}\) or 3\(^{rd}\) biologic

Further Treatment of Moderate-High-Risk Patient Who Achieved Remission with Initial Therapy

- Steroid induced remission
  - Options: Use immunomodulator (thiopurine or MTX) over no immunomodulator
  - Use anti-TNF +/- thiopurine over no anti-TNF

- Anti-TNF or anti-TNF + thiopurine induced remission
  - Use anti-TNF +/- thiopurine over no anti-TNF

- Remains in remission for 6 months

- Does not remain in remission for 6 months
  - Define resolution of inflammation and ulcers
  - Re-assess inflammatory markers every 3 months

Combination therapy with immunosuppressant and anti-TNF biologic offers improved efficacy and durability compared with anti-TNF monotherapy and should be considered for mod/high risk patients requiring 2nd or 3rd biologic


Further Therapy for the Moderate-High-Risk Patient Who Didn’t Achieve Remission with Initial Therapy

- Mod/high risk patient

- Options
  - Use anti-TNF monotherapy over no therapy or thiopurine monotherapy
  - Use anti-TNF + thiopurine over thiopurine monotherapy or anti-TNF monotherapy

- Failure to respond
  - Low or undetectable drug concentration and low or undetectable anti-drug
  - Increase drug dose

- Positive response
  - Low or undetectable drug concentration and high anti-drug antibody
  - Switch within drug class
  - Assess inflammation

  - Therapeutic drug concentration and low or undetectable anti-drug antibody
  - Assess inflammation
  - Inflammation present
    - Continue drug at current dose and look for other causes
  - Inflammation not present
    - Switch to another drug class

Before Starting Therapy

- Immunization update
  - Tdap
  - Pneumovax
  - Influenza
  - HBV or HAV if seronegative
  - Consider HPV vaccine
  - Consider herpes zoster vaccine

Conclusions

- Serum inflammatory biomarkers, stool studies, and endoscopy are best way to assess initially
- Rule out infectious triggers
- Make assessment of prognosis
- Start effective therapy
- Reassess and adjust therapy accordingly