Inflammatory Bowel Disease

Jason Ryan, MD, MPH
Inflammatory Bowel Disease

- Two chronic autoimmune bowel diseases
  - Crohn’s disease
  - Ulcerative colitis
- Both have **relapsing, remitting course**
  - Patients have “flares”
  - Increased medication requirements
Inflammatory Bowel Disease

• Similar symptoms both disorders
  • Recurrent episodes
  • Abdominal pain
  • Bloody diarrhea
Inflammatory Bowel Disease

- Slight female predominance in most studies
- Age of onset usually **15 to 40 years**
  - Some studies suggest second spike in 50 to 80 year olds
- More common among **whites**
- More common among **Jewish populations**
- Classic presentation
  - White woman in 30s
  - Jewish descent
Bloody Diarrhea

• Many causes other than IBD especially infection
• Typical studies sent when considering IBD
  • Stool cultures (Salmonella, Shigella, Campylobacter, Yersinia)
  • Testing for E. coli O157:H7
  • Other stool studies (C. diff, Ova and parasites)
Ulcerative Colitis

Pathologic Features

- **Ulcers** form in intestinal tract
  - Inflammation of mucosa and sometimes submucosa
  - Importantly NOT full thickness inflammation
Ulcerative Colitis

Pathologic Features

• **Always starts in rectum** → works upward
  - Always has rectal involvement
  - **Left lower quadrant pain** is common

• **Never involves small intestine**
  - “Colitis”
Ulcerative Colitis

Gross Morphology

- **Pseudopolyps** (healing of ulcers)
Ulcerative Colitis
Gross Morphology

- **Loss of haustra** *(lead pipe appearance on X-ray/CT)*

*Common findings and pseudolesions at computed tomography colonography.* Colégio Brasileiro de Radiologia e Diagnóstico por Imagem. Giuseppe D'Ippolito et al. Used with permission.
Ulcerative Colitis

Microscopy

- Crypt abscesses
- PMN infiltration of crypts
Ulcerative Colitis
Extra-intestinal Features

- **Pyoderma gangrenosum**
  - Deep, necrotic skin ulceration
- Primary sclerosing cholangitis
  - Inflammation of spine
- Uveitis
  - Inflammation of middle layer eye
Toxic Megacolon

- Rare complication of UC (also infectious colitis)
- Cessation of colonic contractions
  - Evidence that nitric oxide inhibits smooth muscle tone
- Leads to intestinal dilation → rapid distention occurs
- Wall thins → prone to rupture
- Can cause perforation
Toxic Megacolon

- Presentation
  - Abdominal pain
  - Distention
  - Fever
  - Diarrhea
  - Shock

Hellerhoff/Wikipedia
Ulcerative Colitis

Adenocarcinoma

- **Significant risk in UC**
- Risk based on two key factors
  - *Duration of disease* (>10 years before most cancers form)
  - *Extent of disease* (more disease = more risk)
  - Involvement into right colon = more disease
  - “Right sided colitis” or “pancolitis” are risk factors
- Screening colonoscopy recommended
  - Multiple biopsies taken
- **Colectomy** sometimes required
Antibody Tests

- **p-ANCA**
  - Antibody seen in vasculitis syndromes
  - Churg-Strauss and Microscopic Polyangiitis
  - Also seen in ulcerative colitis

- Anti-*Saccharomyces cerevisiae* antibodies (ASCA)
  - *Saccharomyces cerevisiae*: type of yeast
  - Elevated antibody levels seen in Crohn’s

- Both tests suggested to distinguish forms of IBD
- Not reliable for routine clinical use
Crohn’s Disease
Pathologic Features

- **Granulomatous inflammation**
- Entire wall affected ("transmural")
- Any portion of the GI tract can be affected
  - “Mouth to anus”
  - Oral ulcers can be seen
Crohn’s Disease
Pathologic Features

- Terminal ileum is common location
- **Malabsorption**
  - Vitamin deficiencies (B12)
  - Malabsorption of bile salts
  - **May have non-bloody diarrhea** due to malabsorption
- May have **right lower quadrant pain**
- Often spares the rectum
- Often “skips” sections
Crohn’s Disease
Pathologic Features

• Terminal ileum is common location
• **Malabsorption**
  • Vitamin deficiencies (B12)
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  • *May have non-bloody diarrhea* due to malabsorption
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Crohn’s Disease
Pathologic Features
Crohn’s Disease

Microscopy

• Non-caseating granulomas

Nephron /Wikipedia
Crohn’s Disease

Gross Morphology

- Cobblestone mucosa
Crohn’s Disease

Gross Morphology

- Fistulas
  - Peri-anal
  - Abdominal
  - Bladder ("enterovesical fistula")
Crohn’s Disease

Gross Morphology

• **Creeping fat**
  - Transmural inflammation heals
  - Condensed fibrous tissue pulls fat around bowel wall
  - Can wrap around bowel

• **Strictures**
  - Healing leads to fibrous tissue
  - Dense fibrous tissue narrows lumen
  - “String sign”
Adenocarcinoma

- Risk only **when colon involved**
- When colon involved, surveillance colonoscopy
Crohn’s Disease
Extra-intestinal Features

• Migratory polyarthritis
  • Most common extra-intestinal manifestation
  • **Arthritis of large joints** (knees, hips)

• Erythema nodosum
  • Inflammation of fat tissue under skin
Crohn’s Disease

Extra-intestinal Features

• **Kidney stones**
  • Calcium oxalate stones
  • High oxalate levels seen in Crohn’s
  • Fat malabsorption → Fat binds to calcium
  • Oxalate free to be absorbed in the gut

• Ankylosing spondylitis

• Uveitis
Immunology

• **T-cells**: major contributor both disorders

  • Ulcerative colitis
    • Th2 mediated disorder
    • No granulomas

  • Crohn’s disease
    • Th1 mediated disorder
    • Granulomatous disease
Smoking

- **Improves** outcomes in UC
- **Worsens** outcomes in Crohn’s
IBD Treatments

- Corticosteroids
- Azathioprine
- Methotrexate
- 6-MP
- Infliximab/adalimumab
- Sulfasalazine
- 5-ASA
Sulfasalazine

Not active until reaches colon
Perfect for UC!

Sulfapyridine

5-aminosalicylic acid (5-ASA)
Sulfasalazine
Side Effects

• GI upset (nausea, vomiting)
• Sulfonamide hypersensitivity
• Oligospermia in men
  • Mechanism unclear
  • Reversible with drug cessation
  • Problem for men trying to conceive on therapy
5-ASA

Mesalamine

- Many side effects of sulfasalazine due to sulfa
- sulfasalazine - sulfa moiety = 5-ASA
- Less side effects BUT absorbed in jejunum
- Less delivery to colon
- Modified 5-ASA compounds resist absorption
  - Coating or delayed release capsules
  - Asacol, Pentasa

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5-aminosalicylic acid (5-ASA)