INFLAMMATORY BOWEL DISEASE

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Background

- IBD includes ulcerative colitis and Crohn's dis.
- Chronic inflammation in various parts of GI tract
- Extra-intestinal manifestations may exist
- Most common in Western countries
- Family history is very strong risk factor (CD > UC)
- Both sexes affected equally
- Peak incidence = 2nd or 3rd decades of life, and again between 60-80 years of age
- Significant morbidity and decreased quality of life

Etiology

- Multifactorial and poorly understood, may involve any or several of the following factors:

1. Immunologic
   - Inappropriate T-cell response by epithelium to antigens and microorganisms
   - Symptoms suppressed by anti-inflammatories
2. Infectious
   - Lesions tend to be dominated by heavy flora
3. Genetics
   - CD > UC

Etiology

4. Diet/Smoking
   - Refined sugars and chemical food additives linked to IBD
   - Smoking is protective for UC but worsens CD
   - Risk of developing CD in smokers is 40% less that in non-smokers
5. NSAIDs
   - Use may trigger occurrence or lead to flares
   - Impairment of mucosal healing mechanism
   - Use based on risk:benefit

Ulcerative Colitis

- Production of pro-inflammatory cytokines by T-helper type 2 cells in response to unknown antigen
- Limited to colorectal region
  - Proctitis Vs. proctosigmoiditis Vs. pancolitis
- Continuous, superficial inflammatory pattern
- Crypt abscesses common
- Advanced inflammatory response may result in mucosal friability and significant GIB

Crohn's Disease

- Atypical inflammatory response mediated by T-helper type 1 cells
- May affect any part of the entire GI tract
- Most common site is small intestine
- Discontinuous pattern
- Transmural involvement may lead to strictures, fistulas, and perforations
- Rectal involvement is less common than UC

Presentation and Diagnosis

- Symptoms of IBD: diarrhea (more bloody in UC than CD) or constipation, abdominal pain/ cramping, malnutrition and weight loss, rectal bleeding..
- Signs: fever, arthritis, fistulas or anal fissures..
- Extra-intestinal manifestations: ocular, joint, skin, kidneys, liver, chronic anemia, bones
- Labs: leukocytosis, elevated CRP and ESR, positive fecal occult blood..
- Tests/procedures: colonoscopy, EGD, imaging
- Classification: mild, moderate, severe, fulminant

UC Vs. CD

Feature	CD	UC
Malaise, fever	Common	Uncommon
Rectal bleeding	Uncommon	Common
Abdominal pain	Common	Unusual
Fistulas	Common	Absent
Distribution	Discontinuous	Continuous
Rectal involvement	Uncommon	Common
Ileal involvement	Very common	Rare
Strictures	Common	Rare
Crypt abscesses	Rare	Very common

Treatment of IBD

- Goals: suppression of inflammation in acute flares, and maintenance of remission
- Large percentage of IBD pts relapse even on maintenance therapy
- Non-pharmacologic therapy
  - No specific diet, address needs case-by-case, enteral or parenteral nutrition in severe cases
  - Maintenance of bone health, Ca + Vit D in all pts on steroids
  - Surgery per indication case-by-case (fistula, obstruction, abscess..)

Treatment of IBD: Pharmacologic

- Drugs to avoid:
  - Anti-diarrheal meds (loperamide, diphenoxylate/ atropine): may cause toxic megacolon
  - Anticohlinergics: may cause toxic megacolon
  - Opiates: may cause obstruction
  - NSAIDs: may worsen IBD symptoms

Treatment of IBD: Pharmacologic Aminosalicylates

- Sulfasalazine, mesalamine, olsalazine, balsalazide
- Induction and maintenance of some forms of IBD
- Various delivery mechanisms for 5-ASA (mesalamine) to areas of inflammation in GI tract
  - Oral formulation: linked to carrier molecule or pH-dependent release
- Sulfasalazine
  - Prototypical agent
  - Colonic bacteria breaks bond with carrier molecule
  - AEs: mostly due to sulfapyridine carrier, include HA, GI symptoms, fatigue
  - C/I in sulfa allergy pts

Treatment of IBD: Pharmacologic Corticosteroids

- Rapid suppressors of inflammation in IBD
- Prednisone, prednisolone, methylprednisolone, HC, budesonide..
- Should be used for short-term only, however many pts end up being dependent on them
- AEs: hyperglycemia, cataracts, HTN, skin atrophy, adrenal suppression, osteoporosis, infection risk..
- Budesonide is released in terminal ileum, minimizes systemic exposure and AEs
- Usually requires tapering off prior to D/C

Treatment of IBD: Pharmacologic
Immunosuppressants

- Azathioprine, 6-MP
  - Inhibit inflammation
  - Slow onset (up to months)
  - Most effective for long-term maintenance and sparing corticosteroids
  - Thiopurine methyltransferase (TPMT) activity test for AZA and 6-MP
  - Toxicity includes pancreatitis, lymphomas, nephrotoxicity, leukopenia
- MTX: maintenance of remission
- Cyclosporine: active fulminant IBD

Treatment of IBD: Pharmacologic
Biologic Agents

- TNF-α-targeting antibiodies
- Infliximab, adalimumab
- Infliximab may suffer loss of efficacy over time 2/2 antibody development
- All are administered IV/SQ and are expensive
- Serious AEs: infusion-related reactions, infections, lymphomas

Treatment of IBD: Pharmacologic
Mild-Moderate Ulcerative Colitis

- Active distal disease (left sided and proctitis)
  - Topical aminosalicylates (mesalamine) are first line for inducing remission
  - Enema for left-sided disease
  - Suppositories for proctitis
  - Oral and topical mesalamine may be combined in left sided disease
  - Topical corticosteroids are indicated if no response to topical mesalamine (2nd line)

Treatment of IBD: Pharmacologic
Mild-Moderate Ulcerative Colitis

- Active proximal disease (transverse colon and up)
  - Oral aminosalicylates (sulfalazine or mesalamine) are first line for inducing remission
  - Oral corticosteroids are indicated if no response to aminosalicylates (2nd line)
  - Azathioprine or 6-MP, or infliximab are 3rd line if unresponsive to steroids or become steroid-dependent

Treatment of IBD: Pharmacologic
Severe-Fulminant Ulcerative Colitis

- Hospitalization often required
- IV corticosteroids for 7-10 d
- Cyclosporine continuous IV 2nd line if unresponsive to 7-10 d of IV steroids
- Fulminant disease may require surgical intervention

Treatment of IBD: Pharmacologic
Maintenance of Remission in UC

- Life-long maintenance therapy often required
- Topical mesalamine (supp. or enema) preferred for distal disease
- Oral mesalamine or salfasalazine for maintenance in pts with extensive or proximal disease
- Topical *and* low-dose oral mesalamine may be combined together in some cases
- Oral or topical corticosteroids are not recommended for chronic maintenance of UC remission
- Azathioprine, 6-MP, or infliximab are 2nd line to mesalamine

Treatment of IBD: Pharmacologic Mild-Modearte Crohn's Disease

- Oral mesalamine, sulfasalazine, or budesonide are options for inducing remission
  - Budesonide preferred for ileal and/or ascending colon disease (not released past it)
- Metronidazole or ciprofloxacin have been used as 3rd line agents but no good data

Treatment of IBD: Pharmacologic Moderate-Fulminant Crohn's Disease

- In moderate-severe cases, oral corticosteroids (prednisone) or budesonide or anti-TNF-α therapy can be used to induce remission
  - Corticosteroids more potent and effective than budesonide, generally first line
  - Anti-TNF-α therapies may be used as alternatives to corticosteroids
  - Anti-TNF-α therapies effective in fistulae treatment
- Severe-fulminant cases
  - Hospitalization is often required
  - IV corticosteroids and/or infliximab may be used

Treatment of IBD: Pharmacologic Maintenance of Remission in CD

- Indefinite maintenance therapy often needed
- Immunosuppressants (e.g., azathioprine) or biologics (e.g., infliximab) are preferred
- Aminosalicylates have no role in maintenance
- Corticosteroids not effective for maintenance and associated with AEs
  - However up to 50% of pts who are placed on corticosteroids for acute episodes become dependent on them for prevention