CROHN’S DISEASE
(Regional Enteritis)

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CROHN’S DISEASE

- Disease of unknown etiology characterized by **transmural inflammation of gastrointestinal tract** (primarily ileal and cecum)
  - Transmural inflammation (full thickness)
  - Any portion of gastrointestinal tract (from mouth to anus)
  - Discontinuous involvement (Skip lesions)
  - Intermittent disease activity
  - Variety of phenotypes
    - Inflammatory
    - Stricturing
    - Fistulizing/penetrating
CROHN’S DISEASE

- Initially described by Lesniowski in 1904
- Subsequently described by Crohn, Ginzburg, and Oppenheimer in 1932
EPIDEMIOLOGY

- Affects 1-10 people per 100,000 population in North America and Northern Europe (400 000-600 000 people)
- Peak age of onset at 15-30 years with a lesser peak at 55-80 years
- Female slightly > male
- Significant morbidity in pts with CD compared to general population (up to 15% rendered incapable of working after 10-20 yrs of diagnosis)
ETIOLOGY

- Interactions between environmental, microbial, and immunologic factors in genetically susceptible hosts
- Smoking—increased relative risk (2 times)
- Oral contraception—increased relative risk
- Infection
  - Mycobacterium avium paratuberculosis
  - Measles virus
ETIOLOGY

- Genetic
  - Mutations within NOD2/CARD15 gene of chromosome 16 (expressed on monocytes; role in apoptosis and activation to bacterial LPS)
    - Younger age at disease diagnosis
    - Ileal disease location
    - Ileoceleal resections
    - Higher risk of postoperative recurrence and reoperation
PATHOGENESIS

• Normally, gut suppresses inflammatory immune response to stream of microbial antigens
• In IBD, this suppression is lost
• Increased mucosal permeability (? Primary or secondary)
• Cell-mediated response predominant (excessive activation of CD4 T cells)
• Cytokine release (IL-1, IL-2, IL-6, TNF)
• Inability to induce T cell suppressor function
• Imbalance between proinflammatory and anti-inflammatory cytokines
DISTRIBUTION

• Ileocecum (50%)
• Ileum (30%)
• Colon (20%)
• Rectum and anus
• Esophagus, stomach, and duodenum
PATHOLOGY

- Deep tissue noncaseating granulomas
- Intralymphatic granulomas
- Granulomatous vasculitis
- Stiff thick-walled segment of bowel with “creeping fat” (wrapping of mesenteric fat circumferentially)
- Deep narrow linear ulcers with intervening islands of edematous mucosa (mucosal cobblestoning)
- Aphthous ulcers (developing on surface of submucosal lymphoid nodules; earliest macroscopic lesion)
- Inflammatory pseudopolyps
- Enlarged mesenteric lymph nodes (non-caseating, non-matted)
- Single or multiple colonic or enteric strictures
- Corkscrew appearance of serosal vessels
PATHOLOGY

- Sometimes difficult to differentiate between Crohn’s colitis and ulcerative colitis
- Indeterminate colitis in 5-10% of pts with colonic involvement alone
- Subsequent disease behavior
- Consideration of macroscopic, microscopic, radiologic, and endoscopic features together with history and clinical picture
Unaffected large bowel

Affected small bowel

(a) Creeping fat

(b)

Creeping fat

(a)

(b)
CLINICAL COURSE

- Location of inflammation an important determinant of the type of complications
  - Stricturing disease more likely in pts with small bowel involvement
  - Fistulizing disease more likely in pts with ileal or perianal involvement
SYMPTOMS

• Diarrhea (70-90%)
• Abdominal pain (45-65%)
• Rectal bleeding (30%)
• Perianal disease
• Tenesmus
• Fecal frequency
• Weight loss
• Extraintestinal manifestations (ocular, hepatobiliary, skin, joints)
CLINICAL COURSE

- Unpredictable phases of disease activity and quiescence
  - 75% chronic intermittent disease
  - 10% chronically active disease
  - 15% remain asymptomatic

- 50% of patients will develop complications in the form of stricturing (stenosis) or perforating (fistula, abscess) disease
DIAGNOSIS

• Barium enema/small bowel follow through/ CT scan
• Endoscopy with mucosal biopsy (sigmoidoscopy, colonoscopy)
• Serologic markers (ASCA, anti-CBir1, anti-OmpC)
• MRI/Endoanal ultrasound for evaluation of perianal disease
MEDICAL VS SURGICAL THERAPY

• Complementary therapies. Careful use of medical therapy appropriately combined with surgical therapy
MEDICAL THERAPY

- Probiotics (Lactobacillus)
- Aminosalicylates (sulfasalazine, mesalamine)
- Corticosteroids (prednisone, budesonide)
- Antibiotics (metronidazole, ciprofloxacin, rifaximin)
- Immunomodulators
  - Azathioprine/6-Mercaptopurine
  - Methotrexate
  - Cyclosporine
- Biologic therapy
  - Infliximab (Remicade)—chimeric monoclonal anti-TNF antibody
  - Adalimumab (Humira)—recombinant human monoclonal anti-TNF antibody
PRINCIPLES OF SURGICAL THERAPY

- Gut-wide disease
- Ensure maximal medical therapy prior to surgical intervention
- Maximize nutritional state
- Control local sepsis
- Resection of least amount of bowel to re-establish satisfactory intestinal function
- Microscopic disease at resection margin does not influence recurrence
- No evidence that anastomotic technique affects recurrence
SURGICAL THERAPY

Indications

- Side effects of medical therapy
- Failure of medical therapy or steroid dependency
- Obstruction
- Symptomatic fistulas
- Abscess formation
- Hemorrhage
- Growth retardation
- Carcinoma or dysplasia
- Extraintestinal manifestations
OPERATIONS

• Resection with or without anastomosis
  – Ileocecal resection
  – Small bowel resection
  – Segmental colonic resection
  – Total abdominal colectomy with ileorectal anastomosis
  – Proctocolectomy with end ileostomy
  – Restorative proctocolectomy (IPAA) in carefully selected patients

• Strictureplasty
END