BIOPSY DIAGNOSIS OF COLITIS
Common and Unusual Forms of Inflammatory Bowel disease

David A Owen
University of British Columbia

WHAT ARE THE MINIMAL CRITERIA REQUIRED TO DIAGNOSE COLITIS?
Cryptitis
Crypt abscess formation
Crypt atrophy
Epithelial reactive changes

THE FOLLOWING FEATURES ARE UNRELIABLE
Excess lymphocytes in lamina propria
Neutrophils in superficial epithelium
Apoptosis
Muciphages

Traditional Histologic Features for the Differential Diagnosis of IBD

ULCERATIVE COLITIS
• Diffuse continuous disease
• Rectal involvement
• Disease worse distally
• No fissuring ulcers
• No lymphoid aggregates
• Possible backwash ileitis
• No granulomas
• Mucosal based disease
• No upper GI involvement

CROHNS DISEASE
• Segmental disease
• Variable rectal disease
• Disease not worse distally
• Fissures sinuses fistulae
• Lymphoid aggregates
• TI involved in 80% of cases
• Epithelioid granulomas
• Transmural disease
• Upper GI involvement

UC WITH CD-LIKE FEATURES
• Treatment can result in rectal sparing
• Rectal sparing can occur de-novo in untreated children
• Appendiceal skip lesions mat occur in 85% of cases
• Rarely cecal or ascending colon patches may occur
• Backwash ileitis (mild lamina propria inflammation, focal cryptitis and crypt abscess formation, mild crypt atrophy) may occur in 17% of cases and is not confined to cases with total colitis
• Upper GI involvement may occur in UC
• Aphthoid ulcers may occur in up to 17% of otherwise typical UC cases

Rectal sparing in ulcerative colitis
Am J Surg Pathol 2010;34:689-696
• Absolute rectal sparing (normal mucosa), relative sparing (chronicity without active disease) and patchiness (normal plus active or chronic disease)
• Typically seen in children and adults post-treatment
• Post treatment biopsies may show rectal sparing in 30% and patchy disease in 25% of patients. However, resection specimens show absolute sparing in zero patients, relative sparing in 5% and patchy disease in 10%

CAUSES OF DIARRHEA

DIARRHEA
COLITIS PRESENT
• Infectious
• Non-infectious
COLITIS ABSENT
• Irritable Bowel
• Other Causes
Upper GI involvement in Ulcerative Colitis
J Pediatr Gastroenterol Nutr 2001;32:443-8

• Esophagitis 50%
• Gastritis 69%
• Duodenitis 23%
• Ulceration 8%
• Villus atrophy 15%
• Increased intraepithelial lymphocytes 31%

SUPERFICIAL CROHN’S DISEASE
• Disease is limited to the superficial mucosa without deep fissuring ulcers, transmural lymphoid aggregates, sinus tracks or fistulae
• Present in 14% of patients with CD and occurs equally in those with and without TI disease
• 50% of patients have disease limited to the left colon
• 44% have granulomas
• 40% have segmental disease
• 80% have submucosal fibrosis
• 40% have pyloric gland metaplasia

How to distinguish UC from CD in an endoscopic biopsy
Hardcore features of CD
Granulomas unassociated with crypt rupture
Chronic active ileitis

PRACTICAL HINT
When all else fails: Get the history
• Location of endoscopic and radiologic disease
• Strictures? Fistulae?
• Duration of disease (or symptoms)
• Previous or recent treatment
• Review any previous biopsies

Without a complete set of biopsies your task may be hopeless!!

NON IIBD CAUSES OF ILEO-COLONIC INFLAMMATION
• Infection
• Radiation
• Ischemia
• Drugs
• Microscopic colitis
• Diverticular disease related colitis
• Diversion colitis
• Pouchitis

INFECTIONOUS COLITIS
Campylobacter, Salmonella, Shigella
E. Coli O157
Clostridium difficile
Yersinia
Entameba histolytica
Neutropenic enterocolitis
**INFECTIOUS COLITIS**  
(acute self-limited colitis)  
- In many cases the pathogen is not isolated  
- Acute onset of bloody diarrhea - recovery in 10-14 days  
- Initially resembles UC but without crypt distortion, atrophy and basal plasmacytosis.  
- Resolving phase may show lamina propria neutrophils without cryptitis/crypt abscesses.  
- Resolution is patchy. Beware of focal active colitis misinterpreted as CD

**ENTEROHEMORRHAGIC E. coli O157:H7**  
- Afebrile patient with voluminous diarrhea  
- Hemolytic uremic syndrome/thrombocytopenia  
- Histology closely resembles acute ischemic colitis  
- Fibrin thrombi are often present  
- Disease is continuous rather than segmental and predominately right sided

**PSEUDOMEMBRANOUS COLITIS**  
Caused by overgrowth of *Clostridium difficile*  
Follows antibiotic therapy  
Mediated by exotoxins which bind to epithelial cells causing disaggregation  
Some *C. difficile* colitides are not pseudomembranous  
Some cases of PMC have causes other than *C. difficile* (*Klebsiella oxytoca*)

**PSEUDOMEMBRANOUS COLITIS**  
- Mainly affects the colon but can involve the small bowel.  
- Cream colored exudates are firmly adherent to mucosal surfaces.  
- Exudate starts in superficial inter cryptal mucosa then enlarges to involve dilated crypt mouths.  
- Membrane has a laminated appearance.  
- Differential dx is ischemic colitis

**YERSINIA ENTEROCOLITICA**  
Morphologic Features  
- Terminal ileitis and typhilitis  
- Aphthoid ulcers on Peyer’s patches  
- Edema, ulceration and lymphadenopathy  
- Hyperplastic lymphoid tissue  
- Slit shaped abscesses  
- Nodes matted together  
- Gram negative organisms with bluish colonies on mucosal surface

**ENTAMOEBA HISTOLYTICA**  
Morphology  
- Earliest lesion is pinpoint ulceration  
- Later expansion to form deep flask shaped serpiginous ulcers  
- Intervening mucosa may be normal  
- Ileal involvement is rare  
- Dirty necrosis in ulcers  
- Trophozoites are best found in surface slough – rarely in tissue  
- Eosinophils are rare
NEUTROPENIC ENTEROCOLITIS (TYPHLITIS)

- Neutropenia secondary to cancer chemotherapy
- Most patients have a hematologic malignancy
- Fever and right sided lower abdominal pain
- Severe rectal hemorrhage and shock
- Polymicrobial infection particularly C. septicum or C. perfringens type A
- Bowel wall thickening with deep ulceration
- Punched out hemorrhagic ulcers with bacteria growing in the attached slough

DRUG INDUCED COLITIS

NSAIDs
Potassium compounds
Antibiotics
Laxative
Mycophenolate
Taxanes

NSAIDs INDUCED COLITIS

- Proximal colonic ulcers and focal colitis
- Diaphragm disease
- Collagenous and lymphocytic colitis
- Increased apoptosis

POTASSIUM CHLORIDE

- Gastric, small bowel, large bowel erosions, ulcers and fibrous strictures

ANTIBIOTICS

- Pseudomembranous colitis
- Antibiotic associated hemorrhagic colitis (AAHC) (ampicillin, amoxicillin, macrolides, cephalosporin, chloramphenicol, fluoroquinolones, tetracycline)
- Histologically and clinically AAHC resembles acute colonic ischemia

DRUG MEDIATED ISCHEMIC COLITIS

- Antibiotics
- Phentermine
- Chemotherapeutic agents (Taxol, vinca alkaloids)
- Constipating agents (fecal impaction)
- Decongestants (pseudoephedrine)
- Digitalis, ergotamine, cocaine (vasoconstriction)
- Diuretics (lower blood volume)
- Steroid hormones (thrombosis)
**ENEMAS AND LAXATIVES**

- Melanosis coli
- Apoptotic colopathy

**MYCOPHENOLATE**

- Mycophenolate is used to prevent and suppress acute rejection
- Produces a colitis characterized by apoptosis, architectural distortion, crypt atrophy, IBD-like changes, GVHD-like changes and ischemia-like changes

**COLCHICINE AND TAXOL**

- Ischemic colitis
- Ring shaped mitotic figures may be seen in proliferation zones in all areas of the gastrointestinal tract

**MICROSCOPIC COLITIS**

- Lymphocytic colitis.
- Collagenous colitis.
- Others.

In North America microscopic colitis may account for 10% of all patients presenting with non-bloody diarrhea (20% in patients over age 65).

**LYMPHOCYTIC COLITIS**

- Incidence is 5.7 per 100,000, M:F
- Present in 25% of patients with celiac sprue
- Other causes include drugs and infectious agents
- Infiltration of surface and crypt epithelium by CD3+ and CD8+ lymphocytes with 20-30 lymphocytes per 100 epithelial cells (normal is <5)
- Non-specific inflammation (including eosinophils) in superficial lamina propria
- Surface epithelium is cuboidal rather than columnar and may show degenerative features

**COLLAGENOUS COLITIS**

- Incidence is 6 per 100,000, M:F = 1:7.
- 40% of patients have an associated "autoimmune" disease.
- Association with celiac disease is weak.
- The subepithelial collagen band generally exceeds 10µ and incorporates lymphocytes, fibroblasts and vessels. Thickening is patchy but is maximal in the right colon
- Non-specific lamina propria inflammation that is similar to lymphocytic colitis. Surface epithelial lymphocytosis is less than seen in LC
“VARIANTS” OF MICROSCOPIC COLITIS
(aka microscopic colitis-like)

- Cryptal lymphocytosis.
- Paucicellular lymphocytic colitis.
- Microscopic colitis with giant cells.
- Pseudomembranous lymphocytic colitis.
- Colitis with IBD features.
- Lymphocytic colitis with lymphocytic phlebitis.

ISCHEMIC COLITIS

- Acute
- Subacute
- Chronic