Non-Neoplastic Disorders of the Intestines
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Approach to Non-Neoplastic Biopsies
• Is it normal? (Many/most GI biopsies are normal)
• If inflamed, is it acute or chronic disease?
• If acute, can I make a specific diagnosis?
• If chronic, can I make a specific diagnosis?

Enema Effect
Acute Infectious-type Colitis

Clinical Presentation

• Acute onset bloody diarrhea
• Similar symptoms are seen in acute onset UC
• Colon biopsies may be required to distinguish between ASLC and new onset UC
  – provided the patient’s symptoms last long enough to get past their “gate keeper” and see a gastroenterologist

Histopathology

• At peak activity ASLC shows cryptitis, crypt abscesses, edema, and surface damage with erosions.

• ASLC does not have crypt distortion or basal plasma cells

• UC often has both crypt distortion and basal plasma cells even at first onset

Markers of Chronic Injury

• Forked or branched crypts
• Crypts shaped like animals, continents, or hebrew letters
• Paneth cells more distal than the right colon
• Basal plasma cells
• Lamina propria may be hypercellular with increased lymphs, eos, polys, and a few plasma cells - Don’t be fooled into calling this chronic colitis!
• There may be an increase in intraepithelial lymphocytes such that the changes mimic lymphocytic colitis - Don’t be fooled, as the clinical history is not right for this!

Acute Infectious-type Colitis
Histopathology - Resolving ASLC
Acute Infectious-type Colitis
Histopathology

• As ASLC resolves, there is mucus depletion with regenerative epithelial changes and a few residual foci of cryptitis or “focal active colitis”

Etiology of Focal Active Colitis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Adult #1</th>
<th>Adult #2</th>
<th>Children</th>
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<tbody>
<tr>
<td>Infectious</td>
<td>55%</td>
<td>48%</td>
<td>31%</td>
</tr>
<tr>
<td>Incidental</td>
<td>40%</td>
<td>29%</td>
<td>27.6%</td>
</tr>
<tr>
<td>Ischemia</td>
<td>5%</td>
<td>10%</td>
<td>0%</td>
</tr>
<tr>
<td>Crohn’s</td>
<td>0%</td>
<td>13%</td>
<td>27.6%</td>
</tr>
<tr>
<td>Allergic</td>
<td>0%</td>
<td>0%</td>
<td>6.9%</td>
</tr>
<tr>
<td>UC</td>
<td>0%</td>
<td>0%</td>
<td>3.45%</td>
</tr>
<tr>
<td>Hirschprung’s</td>
<td>0%</td>
<td>0%</td>
<td>3.45%</td>
</tr>
</tbody>
</table>

Etiology of Focal Active Colitis

• Oral sodium phosphate bowel preparation caused FAC as well as aphthous lesions of the colon.

• These lesions were not present when patients were re-endoscoped without the same bowel prep 1 to 8 weeks later.


Case 1

These rectal biopsies are from a 38 year-old man with Crohn’s disease who is status post resection of his terminal ileum and right colon. He has an ileostomy and a Hartmann’s pouch. The endoscopist described streaky erythema without ulcers in the Hartmann’s pouch. (1a and 1b)
Diversion Colitis

- Occurs in a diverted segment of colon
  - Usually Hartmann’s pouch
- Caused by lack of short chain fatty acids in fecal stream
  - Colonocyte malnutrition
- Symptoms: None, bloody or mucus discharge, pain
- Resolves if bowel hooked back up or with fatty acid enemas

Diversion Colitis Pathology

- Endoscopic: Erythema, friability, edema and nodularity +/- aphthous erosions.
- Histology: Large lymphoid aggregates with prominent germinal centers (so-called diversion reaction)

Diversion Colitis Pathology

- Cryptitis, Crypt abscesses, polyps in lamina propria.
- Aphthous lesions
- May have plasmacytosis and some crypt distortion (due to large lymphoid follicles)
Diversion Colitis
Differential Diagnosis

- Crohn’s Disease
  - Common problem in Crohn’s patients with a diverted segment. Is it Crohn’s or diversion?
- Ulcerative Colitis
- Infectious Colitis
- Pouchitis: Remember a Hartmann’s Pouch is diverted segment of colon - not a real pouch!
- History is paramount
It’s the Surgeon’s Fault!

Life in the Fecal Stream

Life without the Fecal Stream

Restoration of the Fecal Stream
(Life is good)

Case 2

These biopsies are from the sigmoid colon of a 67 year-old man with abdominal pain and occasional diarrhea. The endoscopist noted mild erythema in the sigmoid colon that seemed to spare the rectum. Scattered diverticula were also noted.
Diverticular Disease Associated Colitis

- IBD-like inflammatory disease that mimics UC
- Mild chronic colitis in distribution of diverticula
- Segmental colitis in sigmoid colon of sixty year olds (the 3 S’s)
- Spares the rectum (no tics here)
- This is not diverticulitis
- Pathogenesis is unknown


Diverticular Disease Associated Colitis

- Patients typically present with hematochezia
- Endoscopy shows hyperemia, granularity, and/or exudates - spares the rectum
- Therapy is varied: Some respond to fiber and antibiotics but UC-type therapy often needed.
- Some patients are refractory - need resection.
- Some patients develop full-blown UC

Diverticular Disease Associated Colitis

- Histology similar to mild UC
  - Increased plasma cells in lamina propria
  - Mild crypt distortion
  - Paneth cell metaplasia
  - Cryptitis and crypt abscesses
  - Can be more intense and look like severe UC
- Without endoscopic description of tics - tough DX to make!
**Diverticular Disease Associated Colitis**

- **Differential DX:**
  - UC with rectal sparing (seen in longstanding disease or with use of steroid enemas)
  - Crohn’s disease
- **Keys to DX:**
  - Distribution limited to that of tics
  - Age older than most de novo IBD patients

**Crohn’s-like Diverticulitis**

- A Crohn’s-like colitis found in diverticulitis specimens.
  - Patients without any history of IBD
  - Grossly fat wrapping and bear claw ulcers
  - Granulomas, sinus tracts and transmural inflammation
  - Lacks neural hypertrophy, pyloric gland metaplasia and viliform surface change.
  - Treatment is simple resection
- Pathologist must be careful not to label the patient as having Crohn’s disease


**CASE #3**

47 Year old woman had an eight month history of diarrhea, nausea, vomiting and peripheral eosinophilia of 11%. Patient underwent colonoscopy and mucosa was found to be normal.
COLLAGENOUS COLITIS

Clinical Features

- Chronic watery diarrhea
  Mean 5.3 years duration (Range 0.5-18)
- Crampy abdominal pain
- Arthritis (7%), other autoimmune (17 - 40%)
- Middle-aged patients (mean 59 years)
- Female predominance
- Normal colonoscopy and barium enema

Histopathology

- Mucosal inflammatory process
  Increased intraepithelial lymphocytes
  Surface epithelial damage
  Increased plasma cells and eos in LP
  Little crypt distortion or PMNs
- Subepithelial collagen band

A Chronic Inflammatory Disorder

- Two words in the name
- Recognition of inflammation
  Key to correct diagnosis
- Pathogenesis
- Distinctive from other chronic colitis
  CC - Increased intraepithelial lymphs
  UC & Crohn’s - Crypt distortion, PMNs
COLLAGENOUS COLITIS
Subepithelial Collagen Band
• Not a thick basement membrane
CIV, laminin negative
• Separate from and beneath BM
CIII, CVI, tenascin positive
COLLAGENOUS COLITIS
Subepithelial Collagen Band

- Quantification of thickness
  - Not necessary
  - Not adequate
  - Maybe misleading

- Qualitative changes
  - Tendrils extend into LP imparting “messy” edge to base - BM
  - Entraps superficial capillaries
  - Any increase in SCL in proper inflammatory context = CC
COLLAGENOUS COLITIS
Pitfalls in Diagnosis
• Rectum can be spared
• Subepithelial collagen can be patchy
  – Need multiple biopsies
• Do not focus exclusively on collagen band, inflammation necessary
• Tangential sections

COLLAGENOUS COLITIS
Pathogenesis
• Type of chronic idiopathic IBD
• ? Infectious agent or luminal toxin
  – Remission on diverting fecal stream
    (Swedish study of 9 patients, with rechallenge)
  – Improvement on bismuth
  – ↑ IELs suggests polarization to luminal agent
  – Luminal agent → cross reactivity to epith Ag
• ? Drug – NSAIDs, lansoprazole
• ? Autoimmune (17 – 40% other autoimmune)

COLLAGENOUS COLITIS
Differential Diagnosis
• Lymphocytic colitis
  – Similar in ↑IELS, increased CI,
    little crypt distortion or neutrophils
  – Lacks SCL, eosinophils
• Ulcerative colitis & Crohn’s disease
  – Similar increased CI in lamina propria
  – Differs in prominent crypt distortion & epithelial neutrophils
COLLAGENOUS COLITIS

Therapy

• Previously
  – Diet, ASA, Steroids
• Currently
  – Bismuth
  – Budesonide

ORIGIN OF THE TERM
“MICROSCOPIC COLITIS”

“A mild increase in the number of inflammatory cells on colonic or rectal biopsy was observed [without] crypt abscesses, pus on a rectal mucosal smear, abnormal sigmoidoscopic appearance, or abnormal barium enema…this mild inflammatory change…was designated ‘microscopic colitis’.”


CASE #4

54 Year old Jewish Physician underwent screening colonoscopy and was found to have several ulcers in the terminal ileum. Crohn’s disease had previously been diagnosed in a cousin.
DRUG INDUCED DAMAGE
Small Intestine

• Duodenum
  – Same meds that affect stomach but lesser incidence (NSAIDs)
  – Ulcers

• Ileum
  – NSAIDs, KCl
  – Ulcers, Strictures, Diaphragm disease

NSAID DAMAGE
Small Intestine

• Ulcers – aphthoid, bland
• Strictures
• Diaphragm disease
  - Multiple, concentric luminal protrusions of fibrotic mucosa & submucosa
  - Distal ileum >> prox colon > jejunum
  - Slow release NSAIDs, piroxicam
• NSAID enteropathy
NSAID DAMAGE
Ulcers in Small Bowel

- Endoscopic study of TI (Midwest)
  - Ulcers in 2% ileoscopies, screening
  - 84% Conventional NSAIDs, 16% COX2/other

- Autopsy study (Scotland)
  - Ulcers in 8.4% NSAID users, 0.6% non-users
  - Ulcers in 13.5% long term users
  - Ileum > jejunum

- High end users (RA) by push enteroscopy
  - Jejunal or ileal ulcers in 47%

Caution
Ulcers in TI
not always
Crohn’s
NSAID ENTEROPATHY

- Sensitive detection studies using radiolabelled PMN’s, RBC’s, other molecules, scintigraphy
- Changes in permeability
- Accumulation & fecal loss PMN’s
- Accumulation & fecal loss RBC’s
- Changes in bile acid & B12 absorption (ileal)
- Mild protein loss

CASE #5

74 year old man status post right lung lobectomy for carcinoma. Post-op day 4, patient developed an acute abdomen. He was taken to the operating room and grossly necrotic colon removed.
COLONIC NECROSIS DUE TO KAYEXALATE-SORBITOL ENEMAS

• Necrosis signaled by abrupt onset of severe abdominal pain within hours of enema administration
• Sorbitol likely culprit, Kayexalate marker
• Pathogenesis unclear - perhaps osmotic load leads to vascular shunting
• Renal disease pts particularly susceptible
**RESULTS AFTER ENEMAS IN UREMIC RATS**

<table>
<thead>
<tr>
<th>Experimental Group</th>
<th>Colonic Pathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>No enemas</td>
<td>Normal</td>
</tr>
<tr>
<td>Saline enemas</td>
<td>Normal</td>
</tr>
<tr>
<td>Kayexalate enemas</td>
<td>1/10 mucosal erythema</td>
</tr>
<tr>
<td>Sorbitol enemas</td>
<td>9/9 massive dilatation, extensive hemorrhagic transmural necrosis</td>
</tr>
<tr>
<td>Kayexalate-sorbitol enemas</td>
<td>10/10 massive dilatation, extensive hemorrhagic transmural necrosis</td>
</tr>
</tbody>
</table>

**Case #6**

- A 22 year old woman presented with diarrhea, occasionally alternating with constipation. She also had intermittent bright red blood per rectum.

**Case #6**

- The endoscopist noted a beefy, friable 1cm polyp in the rectum.

**Case #6**

- Low magnification view shows polyp with mushroom-like cap of fibrinopurulent exudate.
Case #6

• Architectural distortion, crypt abscesses, and reactive epithelial atypia are present, accompanied by marked hemosiderin deposition

Case #6

• Higher magnification shows congested capillaries within lamina propria, & hypertrophic muscularis mucosa with perpendicular extension into mucosa

Prolapse Polyps

• Any clinical scenario causing mucosal prolapse:
  – Diverticular disease
  – Solitary Rectal Ulcer Syndrome (SRUS)
  – Ostomy sites
  – Adjacent to mass lesions
• Pathology the same regardless of etiology

Prolapse Polyps

Solitary Rectal Ulcer Syndrome

• Name is largely misnomer
• Peak incidence in women in 30s-40s; can happen at any age and gender
• Rectal bleeding, mucus discharge, sense of prolapse, pain, straining at stool
• Can often induce prolapse clinically

Prolapse Polyps

Diverticula-Associated

• Prolapsing mucosal folds associated with diverticula
• Patients typically present with bleeding
• Polyps are often large, adjacent to diverticula
• Theory that diverticula are pulled out of their sacs by prolapse action

Prolapse Polyps

Inflammatory Cloacogenic Polyps

• Probably a very distal manifestation of SRUS
• Histology is the same as other prolapse polyps
• Differentiate from prolapsing hemorrhoid
Prolapse Polyps
Gross Pathologic Features

• Friable, +/- ulceration,
• Most common in distal GI tract
• Solitary or multiple

Prolapse Polyps
Gross Pathologic Features

• Hemosiderin may impart a beefy, red-brown appearance
• These were associated with a segment of diverticular disease

Prolapse Polyps
Gross Pathologic Features

• Some can be so large as to mimic a malignancy!

Prolapse Polyps
Gross Pathologic Features

• As polyps age, may have a more fibrotic appearance

Prolapse Polyps
Histologic Features

• Ulceration with superficial fibrin cap

Prolapse Polyps
Histologic Features

• Mucosa with crypt elongation, distortion, and associated inflammation
Prolapse Polyps
Histologic Features

• Lamina propria contains numerous small vessels and hemosiderin

• Hypertrophy and splaying of muscularis mucosae

Prolapse Polyps
Histologic Features

• Extensive fibrosis as lesion ages

Prolapse Polyps
Pathogenesis

• Prolapse of mucosa into the lumen
• Subsequent chronic intermittent ischemic damage
• Resultant mucosal injury, inflammation, and repair

Prolapse Polyps
Clinical/Management Issues

• Polyps are completely benign
• Patient outcome determined by underlying disorder
• If they bleed, can excise polyps
• Overall, patients respond best to nonsurgical management

• In lower GI tract, may be due to malfunction of pubo-rectalis muscle such that excessive straining upon defection results in initiation of prolapse
Prolapse Polyps

• DDX:
  – Juvenile polyps
  – Inflammatory polyps (e.g. in IBD)
  – Ischemia
  – Adenomas
  – Colorectal adenocarcinoma

Prolapse Polyps

Distinction from IBD

• Hemosiderin, perpendicular fibrosis, and capillaries in lamina propria help to distinguish from IBD. Clinical history of prolapse can be invaluable.

Prolapse Polyps

Distinction from Adenomas

• Reactive changes may mimic adenoma, but other features of prolapse and maturation of surface epithelium are helpful

Prolapse Polyps

Distinction from Adenocarcinoma

• Glands embedded in fibrous tissue can mimic invasive adenocarcinoma

Prolapse Polyps

Summary

• Fairly common polypoid lesion with similar pathologic features regardless of underlying etiology
• Often unrecognized clinically
• Important to differentiate from IBD, adenoma, carcinoma

Case 7

These colon biopsies are from a 38 year-old female who presented with hematochezia. At endoscopy, an edematous mass was seen at the splenic flexure and biopsied.
Ischemic Colitis
Etiology
- Low flow states such as sepsis, CHF, shock, etc.
- Thrombi/emboli - venous or arterial
- Mechanical - adhesions, volvulus, intussusception, strangulated hernia
- Drugs - Estrogen compounds (OCPs, replacement Tx), NSAIDs, Migraine meds, Cocaine
- Vasculitis

Ischemia
Differential Diagnosis
- Pseudomembranous Colitis
  - C.difficile
  - E. Coli O157:H7
- Radiation colitis
- Diffuse fibrosis of lamina propria:
  - SRUS/mucosal prolapse
  - IBD
  - Collagenous colitis

Pseudomembranous Colitis
Differential Diagnosis
- Clostridium difficile colitis
  - Toxin mediated necrosis
- Ischemia
- Enterohemorrhagic E. coli (O157:H7)
  - Probably through an ischemic process
  - Thrombi often seen in biopsies
Ischemia vs C. difficile
Histologic and Clinical predictors

- **Ischemia**
  - **Strong**: Hyalinized lamina propria, atrophic or withered crypts, localized process on endoscopy.
  - **Weak**: Mass or polyp seen on endoscopy, lamina propria hemorrhage, full-thickness mucosal necrosis, diffuse membranes in biopsy.

- **Clostridium difficile**
  - **Strong**: Pseudomembranes seen on endoscopy.
Case #8

- 8A. A 24 year old man presented with diarrhea and abdominal pain. The endoscopist saw a friable, nodular mass in the ileocecum.
- 8B. A 50 year old man presented with abdominal pain and fever. The endoscopist saw patchy areas of ulceration and mucosal nodularity in the ileum and right colon, with intervening normal mucosa.

**Yersinia-Case 8A**

- Low power: preservation of architecture, edematous mucosa
- High power: Prominent neutrophils, cryptitis
- ASLC pattern

**Yersinia-Case 8B**

- Sections of right colon show marked lymphoid hyperplasia and epithelioid granulomas, along with cryptitis, crypt abscesses, and mild architectural disarray

**Yersinia species**

Clinical Manifestations

- *Y. enterocolitica and pseudotuberculosis* pertinent to human GI disease
- Causes enteritis, colitis, appendicitis (granulomatous and suppurative), mesenteric adenitis
- Incidence rising in Europe and USA

**Yersinia species**

Clinical Manifestations

- Usually self-limited; may cause chronic and/or very serious disease
- Complications include perforation, peritonitis, toxic megacolon, hepatic abscess, generalized sepsis
- Immunocompromised and debilitated patients, those with iron overload at risk for serious disease from *Yersinia*
**Yersiniosis**

**Pathogenesis**
- Organisms invade mucosa of intestine
- Multiply within Peyer’s patches, and the regional nodes to which they drain
- Further spread is hematogenous
- Chronic infection may be due to harboring of organisms within MALT

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**Yersinia**

**Gross Pathology**
- Preferentially involves ileum, right colon, appendix
- Thickened, edematous gut wall
- Nodular masses centered on Peyer’s patches

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**Yersinia**

**Gross Pathology**
- Responsible for approximately 25% isolated granulomatous appendicitis
- May mimic suppurative non-granulomatous appendicitis grossly and clinically

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**Yersinia**

**Histologic Features**
- Variable inflammatory pattern
  – Ranges from ASLC pattern to epithelioid granulomas
- Histologic features of YE and YP overlap more than previously thought
- Mesenteric adenopathy variably present with either species

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**Yersinia**

**Histologic Features**
- Granulomas are often epithelioid, with a prominent lymphoid cuff; caseation sometimes seen
**Yersinia Biopsy Findings**

- Biopsy findings range from ASLC pattern to epithelioid granulomas

**Yersinia Histologic Features**

- Transmural inflammation, lymphoid hyperplasia, & lymphoid aggregates in linear array are frequently seen

**Yersinia Histologic Features**

- Extensive ulceration is common

**Yersinia Histologic Features**

- *Y. pseudotuberculosis* may show particularly striking ulceration and microabscess formation

**Yersinia Mesenteric Adenitis**

- Mesenteric lymph nodes may contain granulomas as well

**Yersinia Diagnostic Aids**

- Special stains—usually not helpful
- Culture
  - Fastidious
  - Need cold enrichment
  - Can’t tell virulent from nonvirulent strains
- Serologic studies
  - Many cross-reactive organisms
  - Need acute and convalescent titers
- PCR test excellent
**Yersiniosis**
Differential Diagnosis

- Other infectious processes
  - *M. tuberculosis*, atypical mycobacteria
  - *Salmonella*
- Crohn’s disease

**Yersinia vs. Mycobacteria**

- Acid-fast stains
- PCR

**Yersinia vs. Salmonella**

- Culture
- *Yersinia* typically has more neutrophils and/or frank granulomas than *Salmonella*, in which histiocyte is prominent inflammatory cell, neutrophils less prominent

**Yersinia vs. Crohn’s Disease**

- May have similar histologic and gross features
- *Yersinia* DNA found in some Crohn’s patients
- Usually have very different clinical courses

**Yersinia vs. Crohn’s Disease**

- Both can feature epithelioid granulomas with lymphoid cuffs and giant cells

**Yersinia vs. Crohn’s**

- Both can have mural microabscesses and mucosal ulceration
**Yersinia vs. Crohn’s Disease**

- Features favoring Crohn’s disease:
  - Cobblestoning of mucosa, skip lesions
  - Creeping fat
  - Fistulas
  - Changes of chronicity (architectural distortion, thickening of muscularis mucosa, neural hyperplasia)
- Sometimes indistinguishable on histologic grounds

**Yersinia Infection**

- **Summary**
  - *Yersinia* is commonly found in food, water, pets
  - May cause a wide variety of GI diseases, mostly self-limited
  - Can rarely cause chronic inflammatory conditions
  - Think of it in the Crohn’s differential

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**Case #9**

- 66 year old woman with CLL, undergoing chemotherapy. She presented with diarrhea and intermittent fever. The endoscopist saw mild erythema of colonic mucosa, and took random biopsies from left colon.

**Histoplasmosis**

- Dimorphic yeast initially described in 1905 by Dr. Samuel Darling
- Endemic (but not limited to) central United States (Ohio and Mississippi river valleys)
- Infection occurs by inhalation of airborne conidia

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**Histoplasmosis**

- Dimorphic yeast initially described in 1905 by Dr. Samuel Darling
- Endemic (but not limited to) central United States (Ohio and Mississippi river valleys)
- Infection occurs by inhalation of airborne conidia
**Histoplasmosis**

- Abundant in soil with bat or avian droppings
- Disseminated infection occurs primarily in elderly patients, young children, immunocompromised, well described in healthy patients too
- GI involvement in more than 80% of disseminated cases may be presenting symptom

**GI Fungal Infections**

- Increasing with numbers of patients with organ transplants, AIDS, other immune deficient states
- Signs and symptoms similar regardless of species of fungus:
  - Diarrhea, vomiting, melena, frank GI bleed, abdominal pain, fever
- GI manifestations are often presenting symptom/sign of disseminated infection

**GI Fungal Infections**

**Diagnosis**

- Can see on H&E in fulminant infection
- GMS, PAS, H&E/methenamine silver very helpful
- Culture remains gold standard
- PCR under development in many centers
- Immunohistochemistry available for some
- Therapy may vary depending on type of fungus identified

**Histoplasmosis**

**Gross Pathology**

- Ileum most common site
- Gross lesions range from ulcers to obstructive masses
- May be no gross findings in immunocompromised

**Histoplasmosis**

**Gross Pathology**

- Cecal ulcer in patient with no known immunocompromising condition; obstructive mass was presenting complaint in patient with AIDS

**Histoplasmosis**

**Microscopic Features**

- A common pattern is a lymphohistiocytic infiltrate or nodule, often with overlying ulceration
Histoplasmosis
Microscopic Features
• Discrete granulomas are rare

Histoplasmosis
Microscopic Features
• Often only a minimal inflammatory infiltrate is seen, especially in the immunocompromised

Histoplasmosis
Microscopic Features
• Gastrointestinal histoplasmosis may be found anywhere in the GI tract!

Histoplasmosis
Microscopic Features
• Organisms may sometimes be seen on H&E; there is a characteristic “halo” effect

Histoplasmosis
Microscopic Features
• Small, ovoid (2-5µm) yeast forms, usually intracellular, often with a small bud at the more pointed pole

Histoplasmosis
Pathogenesis
• Most primary human infections are asymptomatic pulmonary infections
• Once inhaled, yeasts are ingested by tissue macrophages
• Proliferate in macrophages until the development of cell mediated immunity
• Dissemination occurs through reticuloendothelial system
Fungal Infection of GI Tract
Differential Diagnosis

- Inflammatory lesions
  - IBD, sarcoidosis, occasionally tumors
- Fungal organisms
  - Other infectious agents such as P. carinii, C. glabrata, Cryptococcus, Leishmaniasis

GI Cryptococcus

- Mucicarmin positive capsule
- More pleomorphic

GI C. glabrata

- More frequent buds
- Larger
- More often extracellular

GI Fungal Infections
Summary

- Histoplasmosis occurs in all types of patients
- Gastrointestinal involvement is common
- Discrete granulomas are rare
- Numerous organisms may be present with minimal tissue reaction
- Tissue biopsy with special stains is an excellent diagnostic tool

Case 10

These duodenal biopsies are from a 20 year-old female who underwent a subtotal colectomy with ileostomy for ulcerative colitis three years earlier. Nine months after surgery, the patient became symptomatic again, prompting biopsies of the duodenum, stomach and ileum. At endoscopy the duodenum showed “diffuse enteritis”.
Variants of Ulcerative Colitis
(Things I used to call Crohn’s Disease)

• Patchy Distribution
  - Left sided UC with peri-appendiceal disease (The cecal red patch)
  - After therapy there is often uneven healing

• Rectal Sparing
  - Steroid enemas
  - Burnout in long-standing disease
  - Rare cases can present with a normal rectum
Ulcerative Colitis
Extra-Colonic Disease?

- Gastritis
  - Focally enhanced gastritis (FEG) thought to be typical of Crohn’s.
  - 2 recent studies found 12% and 50% of UC patients had FEG compared to 43% and 35% of CD patients.
- Duodenitis
  - Over the last 5 years many case reports have found diffuse duodenitis in patients with resection proven UC
  - Several of these patients also had gastritis
  - Pts tolerated endorectal pull-through procedures
Ulcerative Colitis
Histology in the new millennium

• Patchy distribution is often seen once the patient is on medical therapy.
• Rectal sparing can be seen in longstanding disease, in patients using steroid enemas, and rarely in de novo UC.
• Skip lesions (cecal patch) can be seen in UC.
• Focal gastritis and diffuse duodenitis can be seen in UC.