Dr Kamal G Ishak (1928-2004)

- b. Atbara Sudan to Syrian and Turkish parents.
- English Mission College Cairo
- Cairo Univ - MB BCh 1951
- Fulbright Scholar to US Naval Base - Schisto & Brucellosis
- To USA 1957 San Antonio, Baylor Dallas,
- AFIP 1963, Chief Hepatic branch in 1965
- 1967 DD Hepatoblastoma HCC
- DID disease, Knodell score with the “Gnomes” - Ishak score
- Co-editor MacSween - endless book chapters
➢ Wife Betty 2 daughters (Leila and Magenta)
➢ Cook
➢ Photographer
➢ Tennis fan
➢ The humble facilitator
➢ The small giant
What’s on the menu?
Problems in Colitis

- Is it IBD?
  - (Usual DD is ac inf colitis (ASLC)
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn's disease
- Mimics of Crohn's disease
- When pathology can't help (so don't try)
- Microscopic colitis
Typical infectious colitis

- No architectural changes during active phase
- No (minimal) basal plasmacytosis
- Neutrophils in lamina propria
  - If scant - consider preparation effect
  - If purulent think AIC/ASLC
- If pseudomembranes consider
  - PMC, Verotoxin E.coli, culturable infections
- If crypt destruction can resolve with architectural distortion
Typical infectious colitis

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Supposition

- Ulcerative colitis typically
  - involves the rectum
  - extends proximally for a variable extend
  - often is a transition to a normal mucosa
    - abrupt or gradual.

- Crohn's colitis
  - can involve the ano-rectal region
  - is usually discontinuous grossly & histologically
  - apthoid ulcers typical
  - can involve SB (TI, more proximal SB, UGI)

- In biopsies - need to demonstrate extent /focality
- So what are the pitfalls?
Issues - Is it IBD?

1. Architectural distortion
2. Paneth cell metaplasia distal to HF (CI) - CC
3. Deep plasma cells excluding ICV region (CI)
   - Chronic infection (amoebiasis, resistant PMC), CC/LC
4. Duplication of muscularis mucosae (Ulceration)
   - useful in areas where architecture has reverted to normal
Issues

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn’s disease
- Mimics of Crohn’s disease
- “Hot” colitis
- When pathology can’t help
- Microscopic colitis
Pitfalls in the diagnosis of UC -
Atypical distribution of disease.

- Presence of a cecal or periappendiceal patch.
- Real rectal sparing
  - Ab initio (think diverticular colitis as well as CD)
- Apparent rectal sparing
  - Longterm reversion to normal
    - Implication - is it ever possible to exclude IBD?
  - Normal grossly but abnormal histologically
- Bowel preparation effect - Oral Fleets-associated changes
Pathology 201

- Recognize that a cecal patch is part of UC with distal disease and NOT call it CD

Pathology 301

- Recognize that a cecal patch can be part of CD - but needs other evidence of CD - e.g.
  - Focal inflammation / architectural distortion within & between Bx
  - Typical Bx of aphthoid ulcers
  - Granulomata (not mucin)
  - Terminal ileal (or other proximal) disease
Ulcers and sparing at both ends; healed longitudinal ulcers
Issues

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn’s disease
  - Mimics of Crohn’s disease
  - “Hot” colitis
- When pathology *can’t* help
- Microscopic colitis
Pathology Consultation

Lab number: S
Date: 07/10/17
Room: 1411
Referring Physician: Dr. Mac Rae

Past History and Current Treatment:
Crohn's

Nature and Site of Specimen:
0 Colon, rectum, anus.

Operative Consultation: (Do not write in this space)

Pathologist: M.D.
Pitfalls - other diseases (mimics or exacerbators)

- Superimposed infection in IBD
  - Bacterial
  - Viral CMV
- Drugs / medications
  - NSAIDs
  - Rx causing marked focality
- Pediatric disease
  - Chronic eosinophilic infiltrates (kids)
    - Churg-Straus
    - Chronic allergic colitis
  - Atypical CD-like (young +/- severe UGI disease)
- Diversion
- Pouchitis
Upper GI disease

Established in CD

- Focal chronic active Hp neg gastritis
- Hp neg erosions
- Granulomas
- ? Mild superficial chronic gastritis

- Severe UC - esp children (??adults)
  - Active duodenitis (bulb)
  - ? Chronic (active) Hp neg gastritis

- Resolves post Rx / Colectomy
Why are there problems?

- The pathologist does not know or understanding the reasons why the biopsies were taken
  - question or reason biopsies taken not stated. (Can’t answer a question if there isn’t one)
- Pathologist is unaware of criteria (“NSp inflammation”)
  - CME courses, web, call a friend
- The endoscopist is unaware of what biopsies are needed to answer the questions that has been specifically asked
  - know the criteria used to make the diagnoses
  - take the appropriate biopsies to answer the Qu
- The question being asked cannot be answered at all using biopsies
  - know when pathology cannot answer the question
Abnormal endo - Looks like CD. Is it?

- Have to demonstrate the *distribution* and *focality*
- Erosions / Aphthoid ulcers / Edges of ulcers
  - Usually on background of
    - focal inflammation
    - Crypt sparing
    - <5% CD is really diffuse
    - Rare in UC (highly asymmetric healing)
Crohn’s disease - pitfalls

- Other causes of focal disease:
  - Biopsy of inflammatory polyps
  - Biopsy of granulation tissue at anastomotic lines
  - Cecal patch (normal, UC as well as CD)
  - Overcalling normal terminal ileal lymphoid aggregates as inflamed
  - Fulminant colitis of any cause - including UC (aphthoid ulcers, rectal sparing)

- Diffuse disease
Differential Diagnosis of CD

- Other cause of endoscopic aphthoid ulcers
  - Diversion proctitis / colitis, Pouchitis, Ischemia
  - Drugs / medications - NSAIDs, BCPs, isotretanoin
  - Fulminant colitis of any cause including UC
  - Oral Fleet’s (phosphasoda) preparation
  - Diverticular-associated colitis
  - Reactive arthropathy / Behcets (subclinical/clinical CD)

- Infections including
  - Yersinia, TB, Salmonella, Herpes
  - Immunosuppression / AIDS (including lymphomas &KS)
  - Immunological mimicry
    - Behcets, GVHD, Chronic granulomatous disease, Immunodeficiency, Glycogen Storage Disease 1b
Pitfalls

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn’s disease
- Mimics of Crohn’s disease
- When pathology can’t help (so don’t try)
- Microscopic colitis
Rectal stump post colectomy

Is it Crohn’s?

- Diversion disease / diversion proctitis
  - Classically mucosal lymphoid hyperplasia
    - BUT
  - Can look focal with aphthoid ulcers or diffuse
  - Can have granulomas
  - Can be diffuse with crypt abscesses
  - If resected can have Crohn’s like transmural lymphoid hyperplasia
- Therefore Can mimic CD or UC
Pouchitis + Fistula. Is it CD?

- **Pouchitis**
  - Classically is Crohn’s-like
  - Can look focal with aphthoid ulcers
  - Can have granulomas
  - If resected can have Crohn’s like transmural lymphoid hyperplasia
  - Therefore *Can mimic UC or CD*
  - Therefore *DON’T ASK!!! We can't tell you.*
  - *It is always Pouchitis*

- Possible exception – *pre-pouch ileitis with skip*
  - Can mimic CD and may respond to Remicade
  - Does that make it CD?
Issues

- Is it IBD?
- Pitfalls in the diagnosis of ulcerative colitis
- Pitfalls in the diagnosis of Crohn’s disease
- Mimics of Crohn’s disease
- “Hot” colitis
- When pathology can’t help
- Microscopic colitis
Descriptive colitides
Can be based on endoscopic or morphologic descriptors

- **Pseudomembranous**  
  Cl. difficile, Ischemia, Heavy metals -Hg

- **Hemorrhagic**  
  Verotoxin-producing bugs, Ischemia

- **Collagenous**  
  NSAIDs, ? ischemia, ? Inf, IBD-related, with Pseudo membranes

- **Microscopic**  
  ? Infections, CD, ? Bile salts, Celiac, lymphocytic/CC
  drugs ? NSAIDs, Cyclofort3, Zantac, ticlopidine

- **Granulomatous**  
  CD, Infections, foreign antigens, drugs

- **Eosinophilic**  
  Allergies, parasites, occ IBD

- **Follicular**  
  Diversion, UC, CD, Chlamydia (LGV)
Diarrhea with normal endoscopy, but abnormal biopsy

- Microscopic colitides
  - Collagenous colitis, Lymphocytic colitis
  - Granulomas (Crohn’s esp.)
  - Microscopic colitis NOS variants
- Drugs / medications (apoptotic colopathy)
  - Laxatives, NSAIDs
- Infections (any may be endoscopically normal)
  - MAI, Cryptosporidium, ? Spirochetosis, Post-inf IBS
  - Eosinophilic infiltration – allergy, mast cell disease
- Amyloid
- Quiescent IBD
- Diabetic changes (E.M.)
The Microscopic Colitides, Collagenous and Lymphocytic Colitis

- A group of syndromes characterized by
- Clinically – MC often used to encompass LC and CC
  - Watery diarrhea
  - Often middle-aged to elderly females
- Endoscopically by a normal appearance
- Histologically by
  - An unequivocal colitis – MUST be present – microscopic
  - With increased intraepithelial lymphocytes – lymphocytic
  - With increased PMNs and/or eosinophils – collagenous
  - With a thickened subepithelial collagen band – collagenous
- Must distinguish between non-inflammatory but microscopic causes of diarrhea – e.g. cryptosporidia, ? spirochetosis, amyloid, melanosis
Criteria for microscopic colitis

- There are no agreed upon histological criteria for “MC”
  - Most fit into lymphocytic or collagenous colitis
  - Therefore largely institutionally driven
  - “Mild NSp CI” IS MC - Good communication essential
- Suggested criteria
  - Normal crypt architecture (may be pushed apart)
  - Excess plasma cells – must be a colitis (often to musc. muc)
    - Normal in cecum in some individuals
    - Multiple Bx preferable - ↑ confidence
  - Look for IELs, - from c.5 / 10 (N) epithelial cells to 15-25+ in LC
  - Collagen band (may be very focal) - > 10µ abnormal
    - Use lympho/plasma cell nucleus - well oriented
Lymphocytic colitis

Drug-related
   NSAIDs, ticlopidine, zantac, cyclofor, PPIs
Celiac disease-related
Microscopic colitis with giant cells (behave as LC)
Microscopic colitis with granulomas (behave as LC)
Pauci-IEL lymphocytic colitis
Colonic epithelial lymphocytosis associated with an epidemic diarrhea (Brainerd-type)
Idiopathic
Associations of MC/LC/CC

- **In the GI tract**
  - Small bowel disease – celiac disease / PVA (note – celiac disease also associated with intraepithelial lymphocytosis [IELs] in the stomach and proximal large bowel)
  - Collagenous “itides” in other organs

- **Extra-intestinal – upregulated immune system**
  - Thyroid disease
  - ? Seronegative spondyloarthropathy
Algorithm for Colitis

1. architectural abnormality
   - yes: deep plasma cells
     - yes: infectious type colitis
       - yes: LC(CD)
         - no: MC (IBD)
     - no: no normal biopsy
   - no: superficial chronic inflammation
     - yes: official chronic inflammation

Yes = IBD
No = MC (IBD)

Dr. Kamal G. Ishak