Intestinal Infectious Pathology and its Differentiation from IBD

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Overview

- Histological features of ulcerative colitis
- Classical infective colitis.
  - Typical histological features of infective colitis.
  - Microscopic features IBD versus infective colitis.
- Atypical infective colitis.
- Infection complicating ulcerative colitis.
- Infective intestinal pathology in the immunocompromised patient.
- Parasitic infections
Histological features of ulcerative colitis.
Microscopic appearances

- Villiform mucosal surface.
- Crypt architectural distortion with crypt shortening.
- Paneth cell metaplasia
- Basal lymphoid aggregates.
- Diffuse mucosal chronic inflammation.
- Cryptitis and crypt abscess formation
• Diffuse chronic inflammation limited to mucosa
• Villiform mucosal surface.
• Crypt distortion.
• Crypt shortening.
• Basally located lymphoid aggregates.
- Paneth cell metaplasia
• Diffuse chronic inflammation
• Cryptitis
• Crypt abscess formation
Classical infective colitis
(Acute infective colitis)
Typical histological features of infective colitis.
Typical acute infective colitis

- Preserved crypt architecture
- Increased inflammatory cell infiltrate in the superficial lamina propria
- Cryptitis with withered crypts and ‘beaded’ crypt abscesses
- Patchy inflammation.
Typical acute infective colitis

- Preserved crypt architecture
- Increased inflammatory cell infiltrate in the superficial lamina propria
- Cryptitis with withered crypts and ‘beaded’ crypt abscesses
- Patchy inflammation.
Microscopic features IBD versus infective colitis.
• Distorted crypt architecture
• Crypt atrophy
• Villous surface epithelium
• Epithelioid granulomas
• Basally located individual giant cells
• Basal lymphoid aggregates
• Lamina propria acute and chronic inflammatory cell infiltrate

• Distorted crypt architecture.
• Increase in lymphocyte/plasma cell infiltrate
• Basal lymphoid aggregates.

- Villous mucosal surface
- Paneth cell metaplasia
- Distorted crypt architecture
- Basal lymphoid aggregates
- Plasma cell infiltration in lamina propria

• Villous mucosal surface
• Paneth cell metaplasia
• Crypt architectural abnormalities
• Basal plasmacytosis with severe inflammation
• Distal Paneth cell metaplasia

“Consensus” criteria favouring UC over infective colitis.

- **Architectural changes**
  - Distorted crypt architecture
  - Crypt atrophy
  - Villous surface epithelium

- **Cellular changes**
  - Paneth cell metaplasia

- **Inflammatory changes:**
  - Increased plasma cell/lymphocyte infiltrate
  - Basal lymphoid aggregates
“Consensus” criteria favouring UC over infective colitis.

- **Architectural changes**
  - Distorted crypt architecture
  - Crypt atrophy
  - Villous surface epithelium

- **Cellular changes**
  - Paneth cell metaplasia

- **Inflammatory changes:**
  - Increased plasma cell/lymphocyte infiltrate
  - Basal lymphoid aggregates

**Using such criteria:**

**Sensitivity** 97%

**Specificity** 97%

Amoebic colitis
"Consensus" criteria favouring UC over infective colitis.

- Architectural changes
  - Distorted crypt architecture
  - Crypt atrophy
  - Villous surface epithelium

- Cellular changes
  - Paneth cell metaplasia

- Inflammatory changes:
  - Increased plasma cell/lymphocyte infiltrate
  - Basal lymphoid aggregates

Associated with chronicity of inflammation
Crypt architectural abnormalities

- Take 6 weeks to develop.

- May not be present in early UC, particularly in children.
Atypical infective colitis.
Atypical infective colitis.

• Enteric pathogens
  – Shigella
  – Salmonella
  – Aeromonas (occasionally)
  – *Entamoeba histolytica*

• Granulomatous colitis
  – Tuberculosis
  – Yersiniosis

• Sexually transmitted diseases
  – Syphilis
  – Lymphogranuloma venereum
### Table 1. Classification of selected gastrointestinal infections by histological pattern

<table>
<thead>
<tr>
<th>Minimal or no inflammatory changes</th>
<th>Acute infectious-type colitis pattern</th>
<th>Architectural distortion</th>
<th>Prominent necrosis and ulceration</th>
<th>Ischaemic-type pattern</th>
<th>Pseudomembranes</th>
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</thead>
<tbody>
<tr>
<td>Vibrio cholera</td>
<td>Shigella species</td>
<td>S. typhi</td>
<td>Enterohaemorrhagic E. coli</td>
<td>Enterohaemorrhagic E. coli</td>
<td>Enterohaemorrhagic E. coli</td>
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<tr>
<td>Enteropathogenic and enteroadherent E. coli</td>
<td>Campylobacter species</td>
<td>Shigella species</td>
<td>C. perfringens</td>
<td>C. perfringens</td>
<td>Shigella species</td>
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<tr>
<td>S. aureus</td>
<td>Aeromonas species</td>
<td>Aeromonas (occasionally)</td>
<td>Tularemia</td>
<td>CMV</td>
<td>C. difficile</td>
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<td>Enteric viruses</td>
<td>Non-typhoid Salmonella</td>
<td>Amoebiasis</td>
<td>Listeria Anthrax</td>
<td>Vasotrophic fungi</td>
<td></td>
</tr>
</tbody>
</table>
Morphological appearances in Shigella and Salmonella colitis

- Non-specific histological appearances
- Mild crypt distortion 26%
- Crypt branching 21%
- Increased chronic inflammatory cells +/- acute 62%

Rectal biopsies - ? Microscopic colitis
Salmonella mbandaka
Intestinal tuberculosis
Yersiniosis.
Sexually transmitted diseases.
Historical increases in STDs in male homosexual population (MSM)

• Introduction of highly active antiretroviral therapies (HAART) 1996.

• Serosorting (sexual partners chosen on basis of HIV serostatus).
Figure 1  Trends in rates* of diagnoses of HIV and other sexually transmitted infections in men who have sex with men. England and Wales 1997-2002 by year and region of diagnosis.
Syphilis
Gonorrhoea
Basal lymphoid aggregates
Mild to moderate crypt architectural distortion with crypt shortening.
Areas of superficial mucosal ulceration.
Syphilis serology:

TPHA - +ve
RPR - 1/16 +ve → Consistent with active infection.
FTA - +ve
32 year old male presented bloody diarrhoea

? IBD
Same patient 8 weeks later
Same patient 8 weeks later

→ Lymphogranuloma Venereum
<table>
<thead>
<tr>
<th>Case no.</th>
<th>Time between biopsy &amp; LGV diagnosis (months)</th>
<th>Mucosal ulcers</th>
<th>Cryptitis</th>
<th>Crypt abscess</th>
<th>Crypt distortion</th>
<th>Granuloma</th>
<th>Plasma cell infiltrate</th>
<th>Giant cells present</th>
<th>Initial histological diagnoses/suggestions</th>
<th>Mode of initial LGV diagnosis</th>
<th>LGV DNA results from biopsy (date of biopsy)</th>
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<tr>
<td>1</td>
<td>23</td>
<td>□</td>
<td>■</td>
<td>■</td>
<td>mild</td>
<td>■</td>
<td>■</td>
<td></td>
<td>Uncertain aetiology Possible IBD</td>
<td>Rectal swab LGV Positive</td>
<td>LGV Positive (September 2004) lgv negative (December 2002 &amp; June 2003)</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>?IBD ?infective</td>
<td>Rectal swab LGV Positive</td>
<td>LGV Positive (May 03)</td>
</tr>
<tr>
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<td>□</td>
<td>□</td>
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<td>□</td>
<td>□</td>
<td>?Due to prolapse ?IBD</td>
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<td>Negative</td>
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<tr>
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<td>□</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>Uncertain aetiology</td>
<td>Clinical &amp; Serology WIF titre = 1:4000</td>
<td>lgv negative (September 2004) inhibitory (December 2003)</td>
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<td>?Infective ?Crohn's</td>
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<td>Positive</td>
</tr>
<tr>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>Exclude LGV</td>
<td>Clinical Rectal swab CT detected, not sent for LGV testing</td>
<td>lgv positive</td>
</tr>
<tr>
<td>7</td>
<td>9</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>Favours infective aetiology</td>
<td>Rectal swab LGV Positive</td>
<td>lgv negative (September 2004 and January 2005)</td>
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<tr>
<td>8</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>?IBD. Exclude CT/LGV</td>
<td>Clinical &amp; Serology CFT titre = 1:512 WIF titre = 1:4000</td>
<td>lgv positive (March 2005) lgv negative (June 2005)</td>
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<td>10</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>Diagnosed Crohn's 1999, thought to be recurrence</td>
<td>Rectal swab LGV Positive</td>
<td>lgv negative (November 2005) lgv negative (November 2005)</td>
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<tr>
<td>11</td>
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<td>□</td>
<td>□</td>
<td>?IBD. Exclude LGV Concurrent Anal SCC present</td>
<td>Rectal swab LGV Positive</td>
<td>lgv negative (November 2005) lgv negative (November 2005)</td>
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<tr>
<td>12</td>
<td>6</td>
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<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>?Early ulcerative colitis</td>
<td>Rectal swab LGV Positive</td>
<td>lgv negative</td>
</tr>
</tbody>
</table>

Lymphogranuloma Venereum

- Classically – penile lesion with suppurative inflammatory reaction in inguinal nodes.

- Rectum and colon:
  - Presents with tenesmus and constipation.
  - Distal proctocolitis.
  - Perianal abscesses and fistulae.
  - Anorectal scarring and stenosis.

- Histology – May mimic Crohn’s (granulomas)

- Diagnosis – serology, PCR from anal swab.
Lymphogranuloma Venereum

- *Chlamydia trachomatis.*
- Previously largely disease of tropics.
- Netherlands MSM population
  - 2001 5 cases
  - 2003 30 cases
  - 2004 62 cases
- Minor epidemic in western world
Ongoing epidemic of lymphogranuloma venereum in HIV-positive men who have sex with men: how symptoms should guide treatment

Mohrmann, Gerrit¹; Noah, Christian¹; Sabranski, Michael²; Sahly, Hany¹ and Stellbrink, Hans-Jürgen²

Abstracts of the HIV Drug Therapy Glasgow Congress 2014
Infection complicating ulcerative colitis.
Infection complicating pre-existing ulcerative colitis

- UC patients often immunocompromised → same/increased risk of infectious colitis as general population.

- Organisms thought to complicate/exacerbate UC:
  - Salmonella
  - Clostridium difficile
  - CMV
Indeterminate colitis
Summit lesion

Eruptive/volcano lesion
Pseudomembranous colitis exacerbating chronic ulcerative colitis
Acute exacerbation of ulcerative colitis - refractory to medical therapy
• Inclusions predominantly in endothelial cells.
• Immunostaining greater sensitivity than H&E alone.
CMV inclusions are often present in a very patchy distribution

→ Carefully examine all levels
CMV reactivation in UC

- Looked at resection specimens from UC patients (H&E and CMV immuno)
  - Severe UC 25%
  - Refractory 8.3%
  - Dysplasia (control) 0%

CMV reactivation in UC

- Looked at resection specimens from UC patients (H&E and CMV immuno)
  - Severe UC 25%
  - Refractory 8.3%
  - Dysplasia (control) 0%

→ Association of CMV with active disease.

Infective intestinal pathology in the immunocompromised patient.
Diarrhoea post BMT
CMV re-activation in an immunocompromised patient
Appendicitis
CMV appendicitis – AIDS patient
BMT patient colonic biopsies - ?GVHD
Adenovirus colitis in immunocompromised patient
EBV-associated ulceration
Fungal colitis

- Typically neutropaenic patients (chemotherapy for haematological malignancies).
- Mucor and aspergillus species
UK HIV/AIDS population

- Men who have sex with men (MSM).
- Intravenous drug abusers.
- Migrants from high risk countries.
- Blood transfusion / blood product recipients.
UK HIV/AIDs population

- Men who have sex with men (MSM).
- Intravenous drug abusers.
- Migrants from high risk countries.
- Blood transfusion / blood product recipients.

- Most HIV+ve cases will be stable on treatment but some patients still get AIDs:
  - Health migrants.
  - Unknown HIV infection.
  - HIV patients who have failed HAART.
CD4 count and opportunistic infections

- >500 cells/mm³: Not considered at risk.
- 500 – 200 cells/mm³:
  - Candidiasis
  - Kaposi sarcoma
- 200 – 100 cells/mm³:
  - Pneumocystis, Histoplasmosis and coccidiodomycosis.
  - Progressive Multifocal Leukoencephalopathy (PML)
- 100 – 50 cells/mm³:
  - Toxoplasmosis, Cryptococcosis and Cryptosporidiosis.

Patient’s with AIDS often have a CD4 count ≈50 cells per mm³
Mycobacterium avium complex
Visceral Leishmaniasis

- *Leishmania donovani*
- Amastigotes 1.5 – 3μm
Leishmaniasis
Leishmaniasis
Histoplasmosis

- *Histoplasma capsulatum*
- 2-4μm yeast form
- Immunocompromised and immunocompetent.
Histoplasmosis

Risk factor: exposure to bird or bat droppings
Cryptococcosis

- *Cryptococcus neoformans*
- 4 – 7μm (+ capsule 3-5μm)
Cryptosporidiosis

- *Cryptosporidia parvum*
- 2 – 5 μm
- Immunocompromised and immunocompetent
Cryptosporidiosis
Cryptosporidia in colon
AIDS-associated cholangiopathy

• Inflammation leading to fibrous stricturing.

• Causative organisms
  – Cryptosporidium ++
  – CMV++
  – Microsporidialia

• Can get similar picture non-HIV immunocompromised patient.
Cryptosporidial cholangitis
Microsporidiosis

- Now considered to be fungi
- *Enterocytozoon bieneusi* + others.
- Difficult to see on H&E
- In enterocytes - not basophilic blobs in goblet cells!
- Warthin-Starry staining +/- polarized light (spores polarize).
- PCR-based stool assay.

ANDREW S. FIELD. Pathology (2002) 34, pp. 21–35
Kaposi sarcoma

- Effacement of muscularis mucosa.
- Red cell extravasation
- Haemosiderin deposition
- Lymphoplasmocytic infiltrate
Kaposi sarcoma
What is the most frequent GI infection in western HIV patients?
What is the most frequent GI infection in western HIV patients?

Helicobacter-associated gastritis
Parasitic infections
Giardiasis
Giardiasis
Amoebiasis
*(Entamoeba histolytica)*
Schistosomiasis (S. Mansoni)
Schistosomiasis (S. Haematobium)
Intestinal schistosomiasis associated with colorectal carcinoma
\( (S. \textit{mansoni}, S. \textit{japonicum}) \)
Strongyloides stercoralis

- Nematode
- Predominantly infects patients in tropical and subtropical areas.
- May get fatal systemic dissemination in AIDs
Pinworm
Enterobious Vermicularis
Diphyllobothrium latum
Diphyllolobothrium latum

- Fish tapeworm.
- Longest human tapeworm.
- Mature worm 3 - 7 feet (up to 30 feet!).
- Produce up to 1,000,000 eggs/day.
- Live up to 20 years.
- Infected eating raw or lightly cooked fish.
Conclusions

• Most cases of infective colitis can be differentiated from IBD on routine H&E sections.

• Atypical infective colitis can mimic IBD.

• Consider STDs in the differential diagnosis of proctitis in MSM patients.

• In refractory UC exclude a superimposed infective colitis.

• In the immunocompromised patient there may be little in the way of an inflammatory response.

• In known HIV +ve patients check the CD4 count.