Core Curriculum:

Impact of HIV on Gastroenterology/Hepatology

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Case

48 year old man presents with a history of :

- dysphagia
- odynophagia
- weight loss

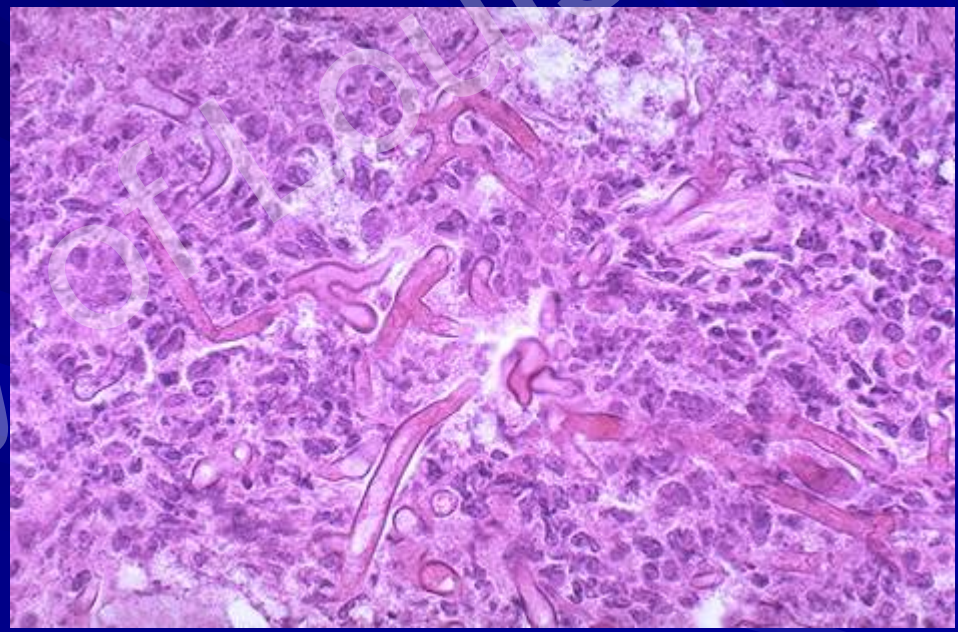
EGD was done to evaluate the problem

Case – EGD Report

Extensively scarred esophageal mucosa with mucosal bridging. Distal esophageal nodules with superficial ulceration

Case – Esophageal Nodule Biopsy

- Inflammatory lesion with ulcerated mucosa
- Special stains for fungi reveal non-septate branching hyphae consistent with **MUCOR**



Case

The patient was HIV positive !!

HAART

(Highly Active Anti Retroviral Therapy)

HIV/AIDS

Before HAART

After HAART

HIV/AIDS

Before HAART

- Immune dysfunction
- Opportunistic Infections
  - Prevention
  - Management
- Neoplasms
  - Management

After HAART

- Immune reconstitution
- Management of chronic diseases e.g. Hepatitis C Cirrhosis
- Management of drug side effects

General Considerations for GI symptoms in AIDS

- Clinical signs and symptoms seldom correlate with specific diagnosis
- If patient is on HAART – etiology is usually non-opportunistic or drug induced
- Likely diagnoses based in extent of immunocompromise → CD4 < 100 favors CMV, fungi, mycobacterium avium complex (MAC) while CD4 > 200 favors common bacteria and other non-opportunistic infections

General Considerations for GI symptoms in AIDS

- In AIDS, GI pathogens are a part of a systemic infections
- Early endoscopy is key in certain settings
- Multiple infections are common
- Evidence of tissue invasion → hallmark of pathogenicity

General Considerations for GI symptoms in AIDS

- Recurrence of opportunistic infections is common → maintenance antimicrobial may be needed unless HAART is initiated
- Treatment of all opportunistic disorders should include HAART

HIV/AIDS in Gastroenterology

- Odynophagia and Dysphagia
- Abdominal Pain
- Diarrhea
- Anorectal Disease
- Abnormal LFT
- Viral Hepatitides and HIV

Differential Diagnosis of Dysphagia and Odynophagia in AIDS

AIDS related esophageal disease

- Candida albicans*
- Cytomegalovirus*
- Idiopathic ulcerations*
- Herpes simplex
- Histoplasma capsulatum
- Mycobacterium avium complex
- Cryptosporidium spp.
- Neoplasm: Kaposi's sarcoma, lymphoma, squamous cell carcinoma, adenocarcinoma

Non-AIDS esophageal disease

- Gastroesophageal reflux
- Pill-induced esophagitis

* More common

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Candida albicans

- Most frequent esophageal infection in AIDS
- May occur during primary HIV infection (transient immunosupression)
- Oral thrush → PPV for esophagitis = 90%
  NPV for esophagitis = 82%
- Frequently coexists with other disorders

Candida albicans

Clinical presentation:

- Substernal dysphagia
- Odynophagia – usually not very severe

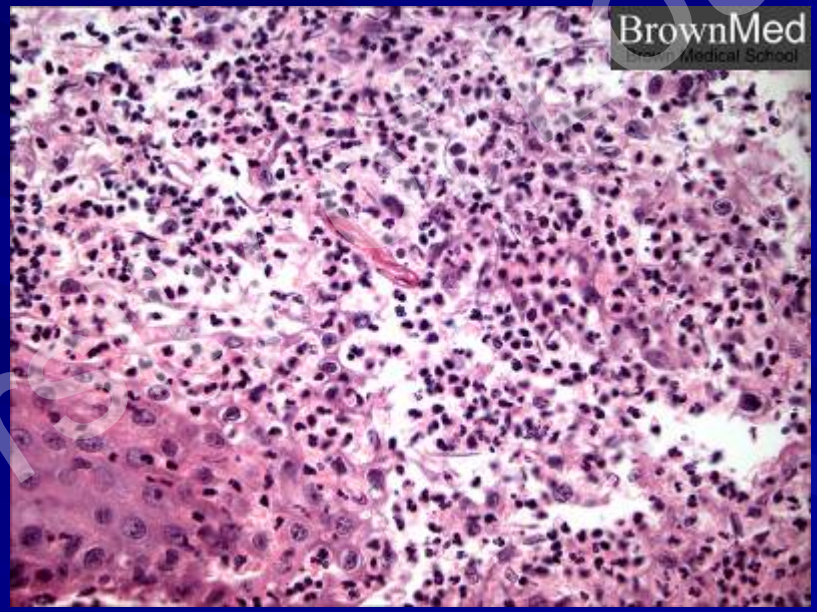
Diagnosis – by EGD

- Focal or diffuse plaques in association with mucosal hyperemia and friability

Candida esophagitis

Candida albicans

Histopathology: Desquamated epithelial cells with yeast forms present only in the superficial epithelium



Esophageal squamous mucosa with numerous pseudohyphae admixed within an acute inflammatory exudate

Candida albicans

Treatment:

- Fluconazole
  - 200 mg loading dose
  - 100 mg every day
- Narcotics for pain
- Caspofungin may be used in resistant cases
- Relapse can be prevented by HAART

CMV esophagitis

Clinical Presentation:

- Odynophagia or substernal chest pain – usually severe
- Dysphagia is less common compared to Candida
- Fever – reported occasionally
- Associated Candida infection - common

CMV esophagitis

Diagnosis – EGD:

- Extensive large and deep ulcers
- Biopsy – base of ulcer provides the highest yield
- Biopsy more sensitive than culture

CMV Esophagitis

Cytomegalovirus and herpes simplex virus esophagitis.

Multiple pathogens are frequently found in patients with AIDS.

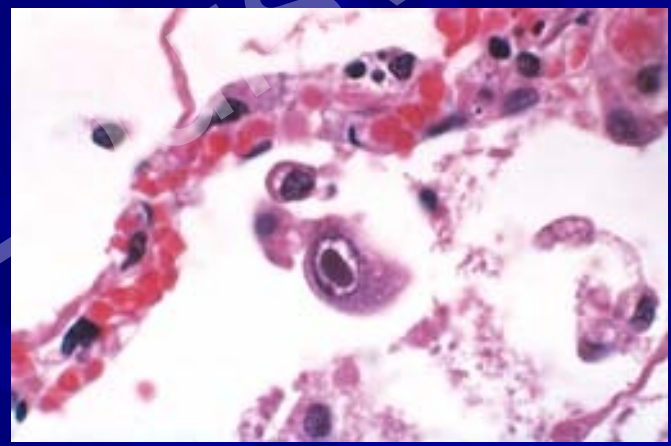
From Wilcox CM: Atlas of Clinical Gastrointestinal Endoscopy. Philadelphia, WB Saunders, 1995, p 28.

CMV esophagitis

Histopathology –

- Viral cytopathic effects in mesenchymal and/or endothelial cells in granulation tissue.
- Intranuclear inclusion bodies (Owls-eye) may be absent

  → confirmation by immunohistochemistry



CMV esophagitis

Treatment:

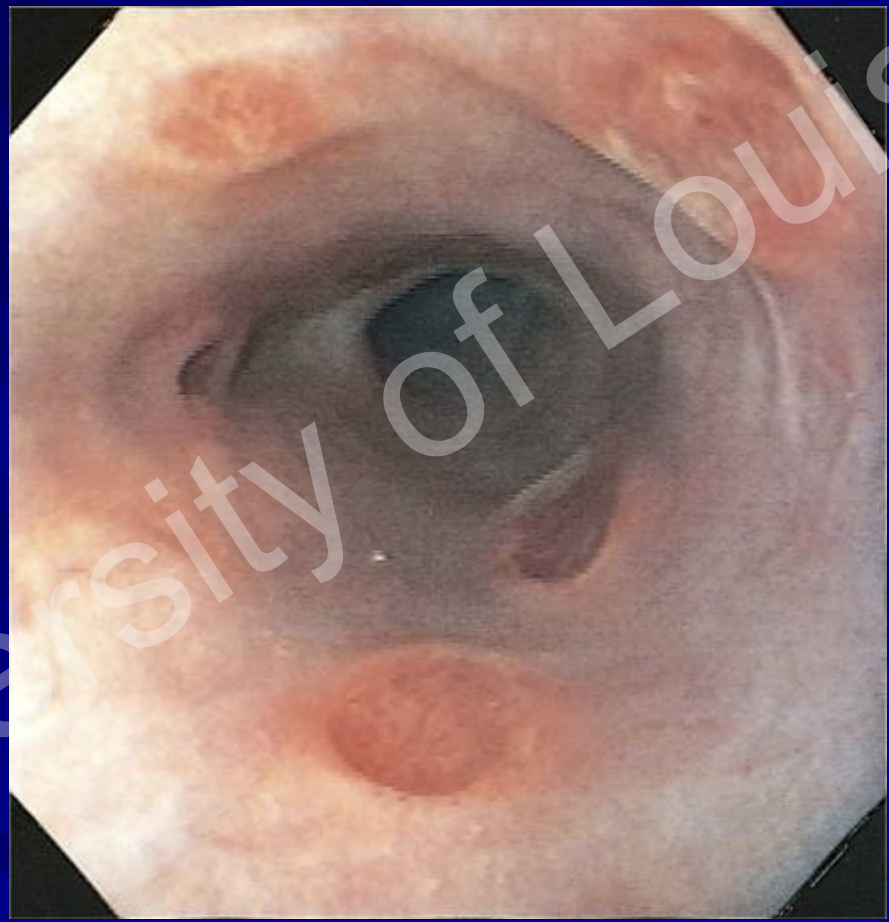
- Ganciclovir – 14-28 days
- Foscarnet – 14-28 days
- Cidofovir – 14-28 days
- HAART

HIV associated - Idiopathic ulcers

Clinical Presentation and EGD findings:

- Identical to CMV esophagitis
- Odynophagia worse than dysphagia
- Multiple large deep raised ulcers on endoscopy – punched-out appearance, normal intervening mucosa

HIV associated - Idiopathic ulcers



From Wilcox CM: Atlas of Clinical Gastrointestinal Endoscopy. Philadelphia, WB Saunders, 1995, p 75.

HIV associated - Idiopathic ulcers

Diagnostic criteria:

- Endoscopic and histopathologic ulcer
- No viral cytopathic effect, negative immunohistochemistry for CMV
- No clinical or endoscopic evidence of reflux disease or pill-induced esophagitis

HIV associated - Idiopathic ulcers

Treatment:

- Prednisone 40 mg/day tapered over 4 weeks is more than 90% effective
- Thalidomide
  - when Prednisone fails
  - also very highly effective

Herpes simplex esophagitis

- Not common in AIDS – also seen in immunocompetent patients
- HSV type I as well as HSV type II can cause
- Shallow ulcers as opposed to CMV
- Discrete vesicles → shallow ulcers → coalesce into regions of diffuse shallow ulcerations

Herpes simplex esophagitis

Shallow ulceration with islands of normal-appearing esophageal mucosa

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Herpes simplex esophagitis

Diagnosis:

- Biopsies are taken from ulcer edge
- Biopsies , cytologic brushings (also from ulcer edge) as well as culture of biopsy specimen are sensitive
- Histopathology – nuclear changes typical for Herpes virus infection in epithelial cells

Treatment:

- Acyclovir – 5-10 days

HIV/AIDS in Gastroenterology

- Odynophagia and Dysphagia
- Abdominal Pain
- Diarrhea
- Anorectal Disease
- Abnormal LFT
- Viral Hepatitides and HIV

Abdominal Pain

- In most patients with AIDS, abdominal pain when severe is related to HIV and its consequences
- However, also consider the most common causes of abdominal pain in the general population
- Use ultrasonography and CT scanning early in the assesment of abdominal pain

Abdominal Pain

- In patients with pancreatitis – consider drug induced disease
- Indications for surgical intervention are the same as general population
- All surgical specimens should be submitted for
  - Viral cultures
  - Fungal cultures
  - Histopathology
  - Mesentric nodes should be biopsied

Differential Diagnosis of Abdominal Pain in AIDS

Organ	Causes
Stomach	
Gastritis	CMV*, Cryptosporidium
Focal ulcer	CMV*, acid peptic disease
Outlet obstruction	Cryptosporidium, CMV, lymphoma
Mass	Lymphoma, KS, CMV
Small bowel	
Enteritis	Cryptosporidium*, CMV, MAC
Obstruction	Lymphoma*, KS
Perforation	CMV*, lymphoma

The differential diagnosis does not include non-AIDS specific conditions

* More frequent

(Adapted from Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.)

Differential Diagnosis of Abdominal Pain in AIDS

Organ	Causes
Colon	
Colitis	CMV, enteric bacteria*, HSV
Obstruction	Lymphoma*, KS, intussusception
Perforation	CMV*, lymphoma, HSV
Appendicitis	KS*, *Cryptosporidium*, CMV
Anorectum	
Proctitis	HSV*, bacteria, CMV
Tumor	KS, lymphoma, condyloma

dDI = didanosine; HSV = herpes simplex virus; KS = Kaposi's sarcoma; MAC = Mycobacterium avium complex

The differential diagnosis does not include non-AIDS specific conditions

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Differential Diagnosis of Abdominal Pain in AIDS

Organ	Causes
Liver, Spleen	
Infiltration	Lymphoma*, CMV, MAC
Biliary tract	
Cholecystitis	CMV*, Cryptosporidium,* Microsporidium
Papillary stenosis	CMV*, Cryptosporidium,* KS
Cholangitis	CMV*

dDI = didanosine; HSV = herpes simplex virus; KS = Kaposi's sarcoma; MAC = Mycobacterium avium complex

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Differential Diagnosis of Abdominal Pain in AIDS

Pancreas	
Inflammation	CMV*, KS, pentamidine, dDI
Tumor	Lymphoma, KS
Mesentery, peritoneum	
Infiltration	MAC*, Cryptococcus, KS, lymphoma, histoplasmosis, tuberculosis, coccidioidomycosis, toxoplasmosis

dDI = didanosine; HSV = herpes simplex virus; KS = Kaposi's sarcoma; MAC = Mycobacterium avium complex; CMV = cytomegalovirus

The differential diagnosis does not include non-AIDS specific conditions

* More frequent

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Evaluation of Abdominal Pain Syndromes in AIDS

Syndrome	Suspected diagnosis	Diagnostic approach
Dull pain, diarrhea, mild nausea, vomiting	Infectious enteritis	Stool culture, O&P, sigmoidoscopy
Acute, severe pain, with peritoneal irritation	Perforation, infectious peritonitis	Abdominal plain films, surgical consultation, ultrasound or CT, paracentesis if ascites is present, laparoscopy
Right upper quadrant pain, abnormal liver biochemistry	Cholecystitis, cholangitis, hepatic infiltrates, cholangiopathy	CT/ultrasound, ERCP, liver biopsy
Subacute pain, severe nausea and vomiting	Intestinal obstruction	Small bowel series, barium enema, endoscopy

(Adapted from Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.)

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HIV/AIDS in Gastroenterology

- Odynophagia and Dysphagia
- Abdominal Pain
- Diarrhea
- Anorectal Disease
- Abnormal LFT
- Viral Hepatitides and HIV

Diarrhea

- Before HAART seen in 90% of patients
- Remains common – etiology most often drug induced
- In AIDS:
  - alteration in mucosal immune system
  - untreatable chronic infection by usually benign organisms
  - more virulent course of common infections

Differential Diagnosis of Diarrhea in AIDS

Protozoa

- Microsporidium[*]
- Cryptosporidium[*]
- Isospora belli
- Toxoplasma
- Giardia lamblia
- Entamoeba histolytica
- Leishmania donovani
- Blastocystis hominis
- Cyclospora sp.
- Pneumocystis carinii

Bacteria

- Clostridium difficile
- Salmonella[*]
- Shigella[*]
- Campylobacter[*]
- MAC
- Mycobacterium tuberculosis
- Small bowel bacterial overgrowth
- Vibrio spp.

* More frequent. MAC = *Mycobacterium avium* complex.

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Differential Diagnosis of Diarrhea in AIDS

Viruses

- Cytomegalovirus[*]
- Herpes simplex
- Adenovirus
- Rotavirus
- Norovirus
- HIV?

Fungi

- Histoplasmosis
- Coccidioidomycosis
- Cryptococcosis
- Candidiasis

Neoplasms

- Lymphoma
- Kaposi's sarcoma

Idiopathic

- "AIDS enteropathy"

Drug-induced

- HIV protease inhibitors

Pancreatic disease

- Pancreatic insufficiency
- Chronic pancreatitis
- Infectious pancreatitis (CMV, MAC)
- Drug-induced pancreatitis (e.g., pentamidine)

* More frequent. MAC = *Mycobacterium avium* complex.

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Cryptosporidium

- Protozoa – most prevalent diarrheal pathogen
- Cryptosporidium – most frequent protozoa identified
- Small bowel most common site

Cryptosporidium

Clinical Presentation:

- Severe diarrhea – several liters/day stools
- Borborygmi
- Nausea
- Weight loss
- RUQ pain – suggests biliary tract involvement

Cryptosporidium

Diagnosis:

- Acid fast stain of stools – bright red spherules
- Small bowel or rectal biopsies – more sensitive

Treatment:

- Parmomycin
- HAART
- Nitazoxanide/Azithromycin → mixed results
- Symptomatic
  - Fluid support
  - Antidiarrheal – occasionally narcotic

Microsporidium

- Common in the US
- Two species implicated:
  - Enterocytozoon bienusi
  - Encephalitozoon intestinalis
- Infection associated with severe immunodeficiency – CD4 < 100

Microsporidium

Clinical Presentation:

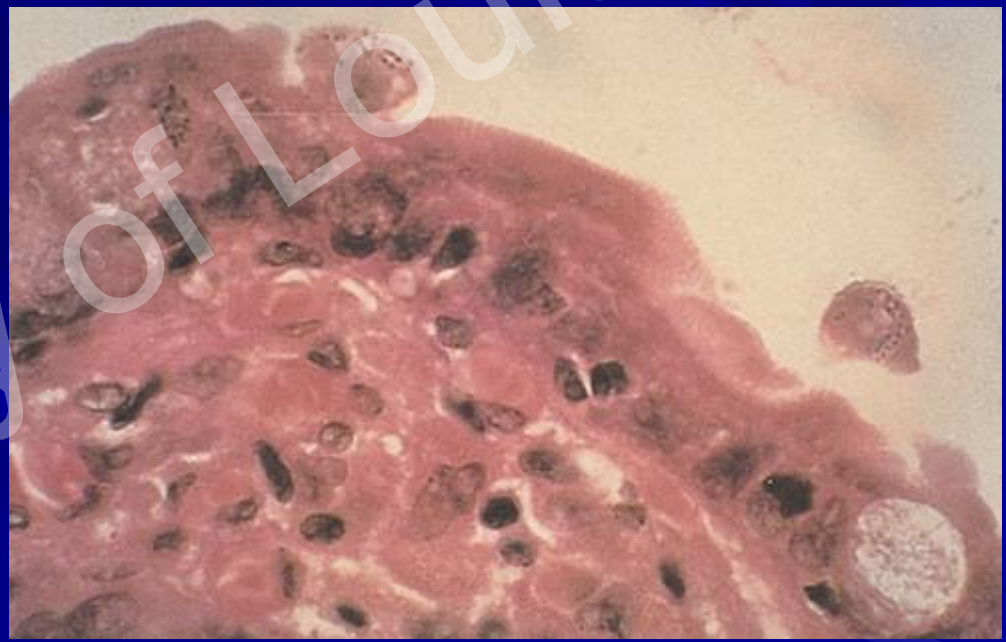
- Watery non-bloody diarrhea – mild to moderate
- Usually no abdominal cramping
- Weight loss (not as much as cryptosporidium)

Diagnosis:

- Stool stains – only moderately sensitive
- Small bowel biopsy → better – more sensitive with Brown-Brenn, Gram or Trichrome stain

Histopathology of Microsporidium/Cryptosporidium

- Pathogenesis is poorly defined
- Little tissue inflammation
- Rare villous atrophy or cell degeneration



Small bowel microsporidiosis – shedding epithelial cell containing microsporidial oocysts

From Gazzard BG: Diarrhea in human immunodeficiency virus antibody-positive patients. Semin Gastroenterol 2:3, 1991

Microsporidium

Treatment:

- Encephalitozoon intestinalis – albendazole
- Enterocytozoon bienusi – no effective treatment
- HAART – resolution of diarrhea and loss of pathogen from stool and small bowel biopsy

Isospora belli

- Endemic in Haiti
- Rare in US
- Diagnosis
  - Acid fast stain of stool, duodenal aspirate
  - Duodenal biopsy
- Treatment - effective
  - Sulfonamides
  - Pyrimethamine
  - Ciprofloxacin

CMV in small and large bowel

- CMV is the most commonly identified pathogen in AIDS
- It is the most common cause of viral diarrhea
- Most frequent cause of chronic diarrhea in AIDS with multiple negative stool studies
- CD4 count < 100
- Colon is most common site of infection (concomitant disease in esophagus, SB, stomach possible)

CMV in small and large bowel

Clinical Presentations:

- Asymptomatic carrier
- Weight loss and fever
- Abdominal pain without diarrhea (usually in SB infection)
- Watery non-bloody diarrhea
- Hematochezia
- Abdominal pain with chronic diarrhea (most common in colitis)

CMV in small and large bowel - Pathology

- Focal enteritis
- Focal colitis
- Appendicitis
- Diffuse ulcerating hemorrhagic inflammation
- Perforation
- Infection of vascular endothelial cells – possible role for mucosal ischemia

CMV Colitis

Diagnosis:

- Endoscopic biopsy
- Cultures – less sensitive than histopathology
- Histopathology
  - Viral cytopathic effect
  - Immunohistochemistry
- Disease vs. Colonization (few viral inclusions in macroscopically normal tissue)

CMV Colitis

Cytomegalovirus colitis
Edema and diffuse subepithelial hemorrhage in sigmoid colon

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

CMV Colitis

Treatment:

- Ganciclovir – IV daily
- Valganciclovir – oral, not well studied for GI
- Foscarnet – IV daily
- Cidofovir – IV weekly (less studied for GI)
- Duration – 14-28 days or more
- HAART
- Ophthalmologic evaluation must

Idiopathic AIDS Enteropathy

- Diarrhea with no identifiable pathogen in AIDS
- Indirect effect of HIV on enteric homeostasis
- HIV not demonstrated in epithelial cell
- Improved technology and ‘panendoscopy with biopsy’ → decreased reliance on this diagnosis
- Improves with protease inhibitors

Common Bacterial infections

- Salmonella, Shigella, Campylobacter – increased virulence, bacteremia, Abx resistance
- High fever, severe abdominal pain, diarrhea (possibly bloody)
- Diagnosis – stool cultures
- Treatment – empiric antibiotic while stool cultures pending – e.g. – ciprofloxacin

Clostridium difficile

- High prevalence due to high antibiotic use and frequent hospitalizations – not an OI
- **Clinical presentation, response to therapy and relapse rate – no different than in immunocompetent patient**
- Treatment – Metronidazole, vancomycin

  → generally effective

Mycobacterium avium complex

Clinical Presentation:

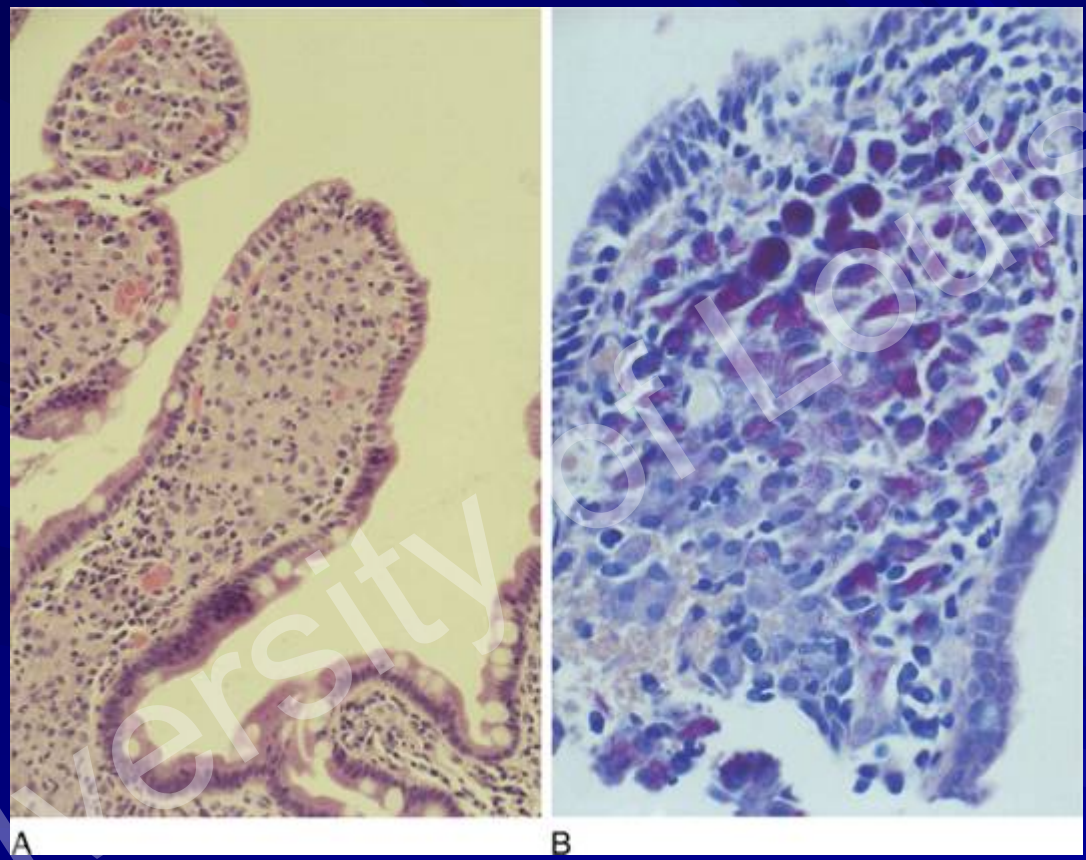
- Asymptomatic infection
- Diarrhea
- Abdominal pain
- Weight loss
- Malabsorption
- GI bleed (rare)
- Obstruction (rare)

Mycobacterium avium complex

Diagnosis:

- Endoscopy – yellow mucosal nodule in duodenum (duodenal involvement most common)
- Endoscopic biopsy – most sensitive
- Fecal acid fast smear – low sensitivity
- Blood culture

Mycobacterium avium complex



A = H&E stain – small bowel biopsy shows marked thickening of the villi with a cellular infiltrate.

B = High-power view with acid-fast staining shows numerous macrophages filled with mycobacteria

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Mycobacterium avium complex

Treatment:

- Multidrug therapy with combinations of:
  - Amikacin
  - Ethambutol
  - Rifampin
  - Clarithromycin
  - Ciprofloxacin
- HAART
  - Early resolution
  - No long term Abx therapy

GI - Mycobacterium tuberculosis

- Less common in US
- Ileo-cecal region, colon, rectum, peritoneal involvement
- Fistula, intususseption, perforation
- Responds to multidrug antituberculous therapy
- Immune reconstitution syndrome – exuberant inflammatory response to quiescent pathogen on institution of HAART (also MAC lymphadenitis, CMV uveitis, Hepatitis B)

GI - Histoplasmosis

- Usually with disseminated infection with hepatic and pulmonary involvement
- Diffuse, large ulceration with diarrhea /mass /serosal disease (peritonitis)
- High fever with marked elevation of LDH
- Diagnosis – fungal smear & culture of blood, urine, infected tissue
- IV amphotericin → suppressive therapy with itraconazole
- HAART

Evaluation of Diarrhea in AIDS

In all patients

- Stool for bacterial culture: Salmonella, Shigella, Campylobacter
- Stool for fecal leukocytes,
- Stool for O & P examination (at least 3-6 specimens) and acid-fast stain
- Clostridium difficile toxin in stool

If patient has rectal bleeding, tenesmus, or fecal leukocytes

- Flexible sigmoidoscopy or colonoscopy with biopsy of mucosa for pathology, viruses, protozoa
- Cultures of rectal tissue for bacteria (especially Campylobacter); viruses (optional)

If diarrhea and weight loss persist and above evaluation is negative

- Upper endoscopy with small bowel mucosal biopsy

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Specific Treatment of Diarrhea in AIDS

	Treatment	Duration (days)
Bacteria	* Duration of therapy dictated by immune reconstitution with highly active antiretroviral therapy	
Salmonella, Shigella, Campylobacter	Fluoroquinolone (e.g., ciprofloxacin)	10-14*
Clostridium difficile	Vancomycin, metronidazole	10-14
Small bowel bacterial overgrowth	Metronidazole, ciprofloxacin	10-14
Mycobacterium tuberculosis	Isoniazid, rifampin, pyrazinamide, ethambutol	9-12 mo
Mycobacterium avium complex	Multidrug regimens for symptomatic infection	9-12 mo

Adapted from Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Specific Treatment of Diarrhea in AIDS

	Treatment	Duration (days)
Viruses	* Duration of therapy dictated by immune reconstitution with highly active antiretroviral therapy	
Cytomegalovirus	Ganciclovir	14-28*
	Foscarnet	14-28*
	Cidofovir	14-28*
Herpes simplex	Acyclovir	5-10*
Fungi		
Histoplasmosis	Amphotericin B; then itraconazole	28
Coccidioidomycosis	Amphotericin B; then fluconazole	28
Cryptococcosis	Amphotericin B; then fluconazole	28

Adapted from Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Specific Treatment of Diarrhea in AIDS

	Treatment	Duration (days)
Protozoa		
Cryptosporidia	Paromomycin	14-28
Cyclospora	Trimethoprim-sulfamethoxazole or ciprofloxacin	14-28
Isopora belli	Trimethoprim-sulfamethoxazole or ciprofloxacin or pyrimethamine	14-28
Microsporidia	Albendazole (Encephalitozoon intestinalis)	14-28
	Metronidazole, atovaquone, fumagillin (not available in United States) (Enterocytozoon bienusi)	14-28

Adapted from Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

HIV/AIDS in Gastroenterology

- Odynophagia and Dysphagia
- Abdominal Pain
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- Anorectal Disease
- Abnormal LFT
- Viral Hepatitides and HIV

Anorectal Disease

- Frequent in AIDS patient
- Frequency in homosexual patients is higher than other AIDS patients
- Important to examine the anorectal region
- Common findings include:
  - Perirectal abscesses
  - Anal fistulas
  - Perianal HSV
  - Ulceration – idiopathic, CMV, tuberculosis, histoplasmosis
  - Infectious proctitis
  - Lymphoma

Differential Diagnosis of Anorectal Disease in AIDS Infections

Bacteria
- Chlamydia trachomatis*
- Lymphogranuloma venereum
- Neisseria gonorrhoeae*
- Shigella flexneri
- Mycobacterium tuberculosis

Protozoa
- Entamoeba histolytica
- Leishmania donovani

Viruses
- Herpes simplex*
- Cytomegalovirus*

Fungi
- Candida albicans
- Histoplasma capsulatum

Neoplasms
- Lymphoma*
- Kaposi's sarcoma
- Squamous cell carcinoma
- Cloacogenic carcinoma
- Condyloma acuminatum

Other
- Idiopathic ulcers*
- Perirectal abscess, fistula*

* More frequent

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

HIV/AIDS in Gastroenterology

- Odynophagia and Dysphagia
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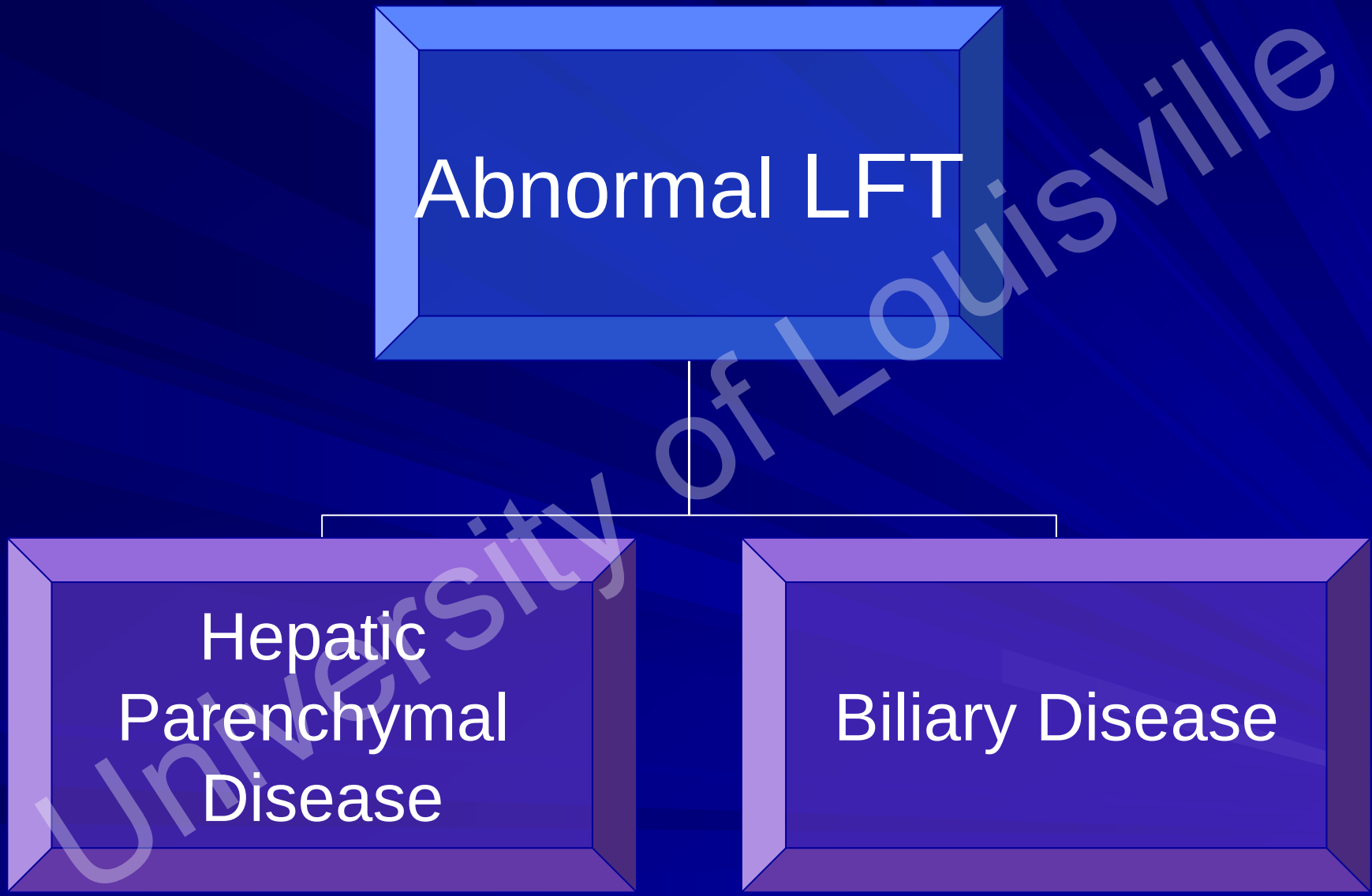
Liver Disease in HIV

- In the HAART era, liver disease has become a very important cause of morbidity and mortality in HIV patients
- Liver related complications are the most common reason for hospitalization in HIV patients
- End-stage liver disease is a leading cause of death in HIV patients
- There is a high prevalence of HIV and Hepatitis C/Hepatitis B co-infections



Differential Diagnosis of Abnormal Liver Tests/Hepatomegaly in AIDS

Hepatic parenchymal disease

- **Infection**
  - Mycobacterium avium complex
  - Cytomegalovirus
  - Hepatitis C
  - Bacillary peliosis hepatis
  - Mycobacterium tuberculosis
  - Cryptococcus
  - Hepatitis B, D
  - Pneumocystis carinii
  - Microsporidium
- **Drug-induced**[*]
  - Sulfonamides
  - Protease inhibitors
- **Neoplasm**
  - Lymphoma
  - Kaposi's sarcoma

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Differential Diagnosis of Abnormal Liver Tests/Hepatomegaly in AIDS

Biliary disease

- **Cholangitis**
  - Cytomegalovirus
  - Cryptosporidium
  - Microsporidium

- **Neoplasm**
  - Lymphoma
  - Kaposi's sarcoma.

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

Drug-induced liver injury in HIV

- Most prevalent cause of liver test abnormalities
- Etiology
  - Antiretroviral meds, other prescription and non-prescription meds, herbal remedies
  - Before HAART – sulfonamides (showed increased freq of DILI in AIDS)
  - HAART era – Protease inhibitors (#1 - ritonavir)

Drug-induced liver injury in HIV

- Mechanism
  - Allergic
  - Idiosyncratic
  - Exacerbation of underlying viral hepatitis
  - Immune reconstitution syndrome
  - Interaction with other agents of liver injury like NASH, alcohol abuse or other illicit drug abuse

Drug-induced liver injury in HIV

- Usually hepatocellular pattern of injury
- Increased transaminases
- Jaundice is uncommon except with indinavir

Lactic Acidosis Syndrome

- Marked hepatomegaly, steatosis, metabolic lactic acidosis and liver failure
- Etiology – nucleoside reverse transcriptase inhibitors (AZT, dDI, stavudine)
- Impaired mitochondrial DNA synthesis
- Associated – myopathy, peripheral neuropathy, pancreatitis
- Most patients – worsening disease → death
- Curative treatment – liver transplantation

Hepatitis B and HIV

- Higher rate of hepatitis B chronicity
- Higher level of HBV replication (higher viral load)
- Lower rate of spontaneous loss of HBeAg and seroconversion to antiHBe Ab
- Lower rate of spontaneous loss of HBsAg and spontaneous seroconversion to antiHBs Ab
- Reappearance of HepBsAg in HIV patients previously with antiHepBs Ab due to immunodeficiency (reinfection or reactivation)

Hepatitis B and HIV

- Contradictory data on activity of inflammation in HBV–HIV coinfections –
  - Initial studies in MSM show less severe necro-inflammation in HBV-HIV (less AST/ALT)
  - Some studies – no impact of HIV on Hep B progression
  - Other studies – more rapid progression to cirrhosis and higher rate of decompensation of cirrhosis in HIV-HBV coinfected
  - Recent study in MSM showed HIV-HBV coinfected at greater risk of liver related death compared to HIV or HBV alone

Hepatitis B and HIV - Treatment

- Patients who need anti-HBV but no anti-HIV therapy
  - Avoid HIV-active HBV agents (Lamivudine, Emtricitabine, Tenofovir)
  - Monotherapy with only HBV agents (Interferon α, Adefovir, Entecavir)
- Patients who need both HBV and HIV therapy
  - Agents with dual activity combining a nucleoside and nucleotide analog (Tenofovir + Lamivudine/Emtricitabine)

Hepatitis B and HIV - Treatment

- Patient who need anti-HIV but no HBV therapy
  - If HBV titer < 10^4 – can treat HIV alone and closely moniter ALT and HBV DNA
  - If HBV titer > 10^{4-5} – treat both to avoid HBV flare due to immune reconstitution
- Patient with cirrhosis
  - Combination HBV-HIV therapy
- Patients with Lamivudine resistant HBV
  - Tenofovir should be added to LAM

Hepatitis C and HIV

- Clinical course of Hepatitis C worsens as HIV immunocompromise advances
  - HCV RNA load increases
  - Transaminase increase
  - Accelerated course to cirrhosis and liver failure
  - Higher rate of active cirrhosis on biopsy
  - May cause lethal fibrosing cholestatic hepatitis
- Increases risk of HCV transmission
- HCV may act as co-factor in HIV disease progression

Hepatitis C and HIV- Treatment

- Favorable effect on liver histology and outcome in HCV-HIV coinfected who receive HAART
- Pegylated interferon + Ribavarin is the treatment of choice in HCV-HIV coinfections
- Control HIV disease with HAART before treating HCV

MAC in the Liver

- Most frequent hepatic pathogen in late-stage HIV disease
- Hallmark – poorly formed granulomas containing acid-fast bacilli in foamy histiocytes
- Marked elevation of alkaline phosphatase
- Diagnosis – liver histopathology, culture of mycobacterium avium complex from liver biopsy tissue,

Mycobacterium tuberculosis in Liver

- Occurs before profound immunocompromise
- May be part of miliary tuberculosis
- Tuberculous abscesses, bile duct tuberculomas
- Diagnosis - culture of mycobacterium tuberculosis from liver biopsy tissue, liver histopathology
- Multidrug therapy

CMV in the Liver

- Uncommon hepatic pathogen
- Can cause a hepatitis
- Diagnosis – typical viral inclusion bodies usually in Kupffer cells, sometimes in hepatocytes or sinusoidal endothelial cells
- Occasionally causes granulomatous disease

Lymphoma in the Liver

- May be the index manifestation of AIDS
- Lesions are focal, sometimes large
- Prognosis depends on extent of immunocompromise
- Improvement in survival in patients receiving HAART

AIDS Cholangiopathy

- Syndrome resembling sclerosing cholangitis with papillary stenosis
- Clinical presentation:
  - Upper abdominal pain
  - Marked alkaline phosphatase elevation
  - Minimal elevation of AST, ALT, bilirubin
  - CT/ultrasonography may or may not show ductal dilation

AIDS Cholangiopathy

- ERCP Findings
  - Papillary stenosis alone
  - Sclerosing cholangitis-like lesions alone
  - Combination of the two (most common)
  - Long extrahepatic strictures
- Etiology – in most cases due to infection of duodenal and biliary epithelium by
  - Cryptosporidium
  - CMV
  - Microsporidium

AIDS Cholangiopathy - ERCP

Arrow = Papillary stenosis

Feldman: Sleisenger & Fordtran's Gastrointestinal and Liver Disease, 8th ed.

AIDS Cholangiopathy

Treatment:

- Sphincterotomy for predominant papillary stenosis → symptomatic improvement
- Eradication of infecting pathogen
- HAART

Acalculous Cholecystits in AIDS

- Severe abdominal pain, occasional peritonitis
- Etiology –
  - Usually CMV infection
  - Sometimes microsporidia, cryptosporidia or isospora
- Treatment – Laparoscopic cholecystectomy