HIV Basics: Opportunistic Infection

Susan LeLacheur, DrPH, PA-C
Associate Professor of PA Studies
The George Washington University School of Medicine & Health Sciences
Learning Objectives
Upon completion of this presentation, learners should be better able to:

• Identify the symptoms and signs of common HIV-related opportunistic infections.
• Initiate the appropriate work-up and management of complications of an individual with HIV.

Faculty and Planning Committee Disclosures
Please consult your program book or the Conference App.

No potential conflicts to disclose

Off-Label Disclosure
There will be no off-label/investigational uses discussed in this presentation.
ACTHIV 2019: A State-of-the-Science Conference for Frontline Health Professionals

1.1 million
people living with HIV in the United States

85%
diagnosed
49%
virally suppressed


ACTHIV 2019: A State-of-the-Science Conference for Frontline Health Professionals

Buchacz Et al. JID 2016:214 NA-ACCORD data
Tracee R

- Tracee is a 36-year-old female, seen when in transitional phase of substance abuse recovery.
- No illicit drug use but continues tobacco use.
- HIV+2005 on ARV.
- She complains of persistent genital area itching and requests that her prescription for fluconazole be refilled. She has used the medication many times.

All That Itches is Not Yeast

Image courtesy of Deborah Smith, MD, MPH
The PAP screening recommendations for a woman age 21-29 newly diagnosed with HIV are:

A. Cervical cytology every 6 months
B. Cervical cytology with HR HPV co-testing every 6 months for one year then annually if both are normal
C. Cervical cytology every 6 months for one year then annually if normal
D. Cervical cytology every year then every 3 years if normal for 3 consecutive years

Tracee R

• **HPV Infection Screening vs Cervical Cancer Screening**
  • 2016: Pap LGSIL POS HR HPV
  • 2017: CIN 1-2
  • Went to long term residential drug treatment
  • 2018: Pap LGSIL POS HR HPV, Anal ASC-US
  • Missed her scheduled FU
  • 2019: CIN 2, VIN 2-3, AIN 1
Double Jeopardy

Images courtesy of Deborah Smith, MD, MPH

HPV-HIV Coinfection-Factor of 10

• Higher rates of HPV infection when compared with HIV uninfected women with similar risk factors
• HIV-infected women are more likely to be infected with multiple subtypes of HPV = higher rates of squamous intraepithelial lesion (SIL)
• Higher rates of oncogenic subtypes with lower CD4⁺ counts
• Higher rate of persistent infection & abnormal Pap smears
• Higher incidence of cervical cancer and precursors
• WIHS cohort VIN associated with abnormal Pap and high-risk HPV.
• High grade VIN not reduced by ART
• High grade AIN in 9% of HIV-infected women
• Anal cancer increasing in HIV-infection in the ART era
HPV-HIV Co-infection Management

- Vaccine prevention in adolescent and young women & men to age 26 (9 valent even if prior 2-4 valent)
- Consistent condom use
- Annual cervical cytology after normal Pap smear (+/- 6 mo first FU) start 1 yr post sexual debut no later than age 21
- May go to q 3 yr. after 3 consecutive nl
- ≥ 30 or ASC–US HPV co-testing
- ASC + HPV or >LSIL evaluated and followed every 6 month
- Post-treatment (excision) of high grade dysplasia q3-4 months x 1 year

Tobacco use cessation

HHS, Guide to the Clinical Care of Women with HIV-2013 Edition; DHHS, Guidelines for Prevention & Treatment of Opportunistic Infections in Adolescents & Adults

HPV-HIV Co-infection Management

- Visual inspection of vulva, vagina, perianal area
- Vaginal cytology hysterectomy and history of high grade dysplasia
- Screen for rectal symptoms/DRE
- Consider anal cytology in women with a history of abnormal cytology or other HPV disease

Tobacco use cessation

Guide to the Clinical Care of Women with HIV-2013 Edition
Thomas C

- Thomas is a 21-year-old male without any prior clinical diagnosis who presents to your ED with a 2 week history of gradually worsening shortness of breath, non-productive cough, intermittent fever with night sweats and chills last night
- Admits to some unintentional weight loss, 15 lb over the past 3 mo, and some oral irritation which he attributed to minimal dental care over his lifetime
- RR 20, T 36.4° C, Ox 96%, BP 155/85
- Mouth with areas of white plaque on an erythematous base
- Normal respiratory effort, resonant with vesicular breath sounds all fields, no adventitious sounds but with egophony scattered through bilateral lung fields
- Rapid HIV positive

Pulmonary infections

- Recurrent bacterial pneumonias: e.g., *Strep. pneumoniae, H. flu, S. aureus*, Gram-negative pneumonia
- Pneumocystis jiroveci (carinii) pneumonia (PJP)
- Other fungal pneumonias, e.g.: Aspergillus, Histoplasma, Cryptococcus
- Mycobacterial infections – MTB & MAI (MAC) though these often present atypically in HIV
Given his symptoms, you suspect PJP. The best diagnostic test

1. BAL and direct microscopy
2. Chest CT
3. Serum PCP antigen
4. Sputum PCR
PJP

- Insidious onset of fever, sweats, fatigue, non-productive cough
- Dyspnea is initially exertional, but progresses with impairment of gas exchange
- Blood gases reveal reduced oxygen levels and commonly low PCO$_2$ levels
- CXR most commonly reveal diffuse interstitial infiltrates (80%), but lobar, nodular, cavitary, asymmetric patterns can also occur
- Sputum, bronchoalveolar lavage or biopsy specimens are sent for staining (e.g., silver, Diff-Quik etc.) – PCR sensitive but not specific

Prevention

- Begin prophylaxis at CD4 counts < 200
- Trimethoprim-sulfamethoxazole (TMP-SMX) is the preferred regimen – 160 mg/800 mg one PO daily (also protects against Toxoplasma infections) Other options: dapsone, atovaquone

Treatment

- TMP-SMX 15-20 mg/kg/day TMP IV/PO divided q6-8h x21 days
Al G

• Al is a 54-year-old male with a long history of IDU and a recent relapse
• He has multiple HIV drug resistance mutations but his HIV was previously well controlled with TAF/FTC plus DRV/c
• He has suffered two prior hospitalizations with cryptococcal meningitis, most recently (4 years ago) for almost 3 months
• You get a call from ID at a nearby hospital to clarify his history and last HIV regimen...
• He had presented with severe headache and let them know of his prior meningitis episodes

In addition to Cryptococcus, which of the following might cause a headache in HIV

A. Cryptosporidiosis
B. JC Virus (PML)
C. Mycobacterium avium complex
D. Toxoplasmosis
CNS infections

- Cryptococcus
- Toxoplasma
- Cytomegalovirus
- Progressive Multifocal Leukoencephalopathy (PML), JC virus

CNS infections:

- Progressive Multifocal Leukoencephalopathy (PML):
  - Caused by a polyomavirus: JC virus
  - Rapidly progressive focal neurological deficits, most commonly hemiparesis, visual field defects, cognitive impairment
  - Diagnosis CSF JC virus PCR, MRI
  - Treatment: None – supportive and treat HIV with drugs that penetrate the CNS well
    - In IRIS associated PML consider corticosteroids
CNS Infections

- **Toxoplasmosis**
  - *Toxoplasma gondii* protozoal parasite
  - Headache, confusion, behavior/mood changes
  - Can also cause ocular disease
  - Ring enhancing lesion or lesions on CT or MRI
  - In HIV it is a reactivation – IgG will be positive for all, dx by CSF PCR
  - Prevention – if IgG positive & CD4 <100, PCP prophylaxis with TMP/SMX DS daily or atovaquone is sufficient, if not pyramethamine plus leucovorin
  - Treatment: Pyramethamine (alt. TMP/SMX) plus sulfadiazine OR clindamycin plus leukovorin

CNS Infections:

- **CMV:**
  - Polyradiculopathy: ascending weakness & loss of reflexes, as well as, meningoencephalitis
  - Can progress to flaccid paralysis
  - Diagnosis is made by CSF analysis, CSF CMV PCR, CT scan
  - Treatment: Ganciclovir (alt. foscarnet)
CNS Infections:

– Cryptococcal Meningitis:
  • *Cryptococcus neoformans* or *gotti* – an encapsulated fungus
  • Headache, altered mental status, seizure
  • Diagnosis is made by CSF analysis; cryptococcal antigen (serum or CSF); fungal culture
  • Treatment: induction therapy with liposomal AMB plus 5 flucytosine initially then fluconazole until CD4 recovery

Or…………..

• None of the above:
  – CSF CBC indicative of viral infection (DDx CMV, EBV, VZV etc.)
  – CSF HSV-2 DNA PCR positive, then the oral lesions appear
AI G

- CD4 2/mm³, VL 4900, CSF results indicate HSV
- After restarting his ARVs (TAF/FTC + DRV/c) along with his prophylactic meds (TMP/SMX & valacyclovir) his oral symptoms worsened, though his headache improved
- Valacyclovir dose was increased, though this was delayed for insurance pre-approval
- At 4 weeks he was doing well but his social situation remained worrisome, and valacyclovir dose reduced to maintenance
- At week 5 he returned with hx relapse, medication non-adherence and perianal HSV...
  - Nursing, case management, behavioral health and PA work to help with housing, drug treatment, adherence etc.

**In HIV, think about the zebras & horses**

As the CD4 count drops, more and rarer conditions become likely but common entities such as *Strep pneumonia, salmonella* & MTB remain common causes of OI

- Check the latest guidelines – DHSS or IAS-USA
  - [https://aidsinfo.nih.gov/guidelines](https://aidsinfo.nih.gov/guidelines)
  - [https://www.iasusa.org/resources/guidelines/](https://www.iasusa.org/resources/guidelines/)
- Get help when you need it – UCSF Clinician Consultation Center or your ID folks
  - [https://nccc.ucsf.edu/](https://nccc.ucsf.edu/)