HIV/AIDS and the Eye: Epidemics, Endemics, and Syndemics

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http://www.hivguidelines.org/clinical-guidelines/adults/ophthalmologic-complications-of-hiv-infection/
What is HIV?

• The Human Immunodeficiency Virus (HIV-1) causes the disease AIDS (Acquired Immunodeficiency Syndrome)

• This retrovirus (that converts RNA to DNA) specifically attacks T cells (CD4+ cells)

http://ipaki.com/content/html/34/102.html
HIV Close Up

http://en.wikipedia.org/wiki/HIV

http://www.niaid.nih.gov/topics/hivaids/understanding/biology/Pages/structure.aspx

HIV/AIDS in Cities Worldwide

- 33.4 million people living with HIV/AIDS in 2008 (down from 40.3 in 2005)
- 2.7 million people newly infected with HIV (down from 4.9 million in 2005)
- 60% of infections are in sub-Saharan Africa
- Women ~50% of all infections worldwide

HIV/AIDS in America (2010)

• As many as 1,000,000 people infected
  – 20% are unaware
  – 56,300 new infections per year
  – Over 18,000 die of AIDS each year in the US alone

HIV/AIDS by County in US (2011)

- Leading killer of African-American males, age 25-44
  - 7x more than whites
  - 2/3 of AIDS cases in both women and children were among African-Americans

[Map of HIV/AIDS rates by county in the US, 2011]

http://weblogs.baltimoresun.com/health/hivaids/
HIV Transmission

http://www.nckansil.com/transmission-of-hiv-1021746.html
Acute HIV Manifestations

- Lymphadenopathy
- Fever
- Chills
- Night sweats
- Weight loss
- Diarrhea
  - weeks or months duration

Main symptoms of Acute HIV infection

Systemic:
- Fever
- Weight loss

Central:
- Malaise
- Headache
- Neuropathy

Pharyngitis
- Sores
- Thrush

Mouth:
- Sores

Esophagus:
- Sores

Muscles:
- Myalgia

Liver and spleen:
- Enlargement

Skin:
- Rash

Gastric:
- Nausea
- Vomiting

Maculopapular Rash (left) and Cryptococcal Infection (right)
Molluscum Contagiosum (left) and Eosinophillic Folliculitis (right)
Oral Hairy Leukoplakia (left) and Esophageal Candidiasis (right)
Chronic AIDS Manifestations: Dementia

- Characterized early by difficulty concentrating
- Decreased short-term memory, slowed mentation and movement disorders are seen
- Without treatment, expect progression to severe global dementia

AIDS Toxoplasmosis: Retinitis and Dementia
AIDS and Kaposi’s Sarcoma
AIDS and CMV Retinitis
Symptoms of Ocular Infection in AIDS Patients

- Painless decrease in vision in one or both eyes
- Hazy vision
- Floaters/flashes
- Metamorphopsia (left; use Amsler Grid)
- VF defect
- May be asymptomatic

http://www.myvisiontest.com/about.php
Early Signs of HIV/AIDS Retinopathy

- Cotton wool spots (CWS) may be initial ocular manifestation of AIDS
- While CWS are present in 2/3 of patients, they are nonspecific for AIDS
- DDX: Diabetic retinopathy, hypertension, severe anemia, lupus, leukemia
- The presumed cause is CMV (cytomegalovirus) infection

Source: Salisa Williams, OD
Retina of AIDS Patient #1
November, 1985
Retina of AIDS Patient #1
January, 1986

Source: Salisa Williams, OD
Retina of AIDS Patient #2
September, 1986

Source: Salisa Williams, OD
Retina of AIDS Patient #2
October, 1986

Source: Salisa Williams, OD
AIDS-Related Cytomegalovirus (CMV) Retinitis

- CMV is infectious for patients of all ages
- Latent infections are common, as between 50 -80% of US adults are CMV seropositive
- CMV infection in AIDS patients is common, especially in those without treatment
CMV Retinopathy in AIDS

- CMV infection occurs most commonly through reactivation of latent virus
- Prior to treatment of AIDS, CMV was the most common ocular opportunistic infection (12%-46%), as well as the leading cause of blindness in AIDS

http://imagebank.asrs.org/file/3352/hiv-retinopathy-re
Signs of CMV Ocular Infection in AIDS Patients

- Necrotizing retinitis with or without hemorrhages is usual presentation
- Patchy yellow-white areas with secondary hemorrhage along the edges
- This is often described as brushfire retinitis

http://www.pacificu.edu/library/DigitalCollections.cfm
Centrifugal Retinitis

- Occurs most frequently along the major vascular arcades or near the optic nerve head
- ALL retinal layers affected → full thickness retinal destruction, spreading directly from diseased to healthy retina

http://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/CMV-Retinitis/index.htm
Sequelae of CMV Retinitis

- Vessel attenuation
- Calcifications in atrophic retina
- Capillary nonperfusion
- Chorioretinal scarring
- Loss of VA (site specific)
- Optic atrophy
- Retinal detachment (24-50%)

Complications of CMV Retinitis

- HIV retinopathy (CWS and/or intraretinal hemorrhages)
- HZV and HSV retinitis
- Toxo retinochoroiditis
- Infectious multifocal choroiditis
- PORN (progressive outer retinal necrosis, shown here)

http://www.lookfordiagnosis.com
Other CMV Ocular Complications

- Papillitis, macular edema, vasculitis, and uveitis are all possible
- Uveitis can result from CMV alone
- Immune recovery uveitis (IRU) – may occur when patient’s immune system recognizes and reacts to viral antigens in the retina after successful HIV therapy

Anterior Segment Manifestations of AIDS

• Molluscum contagiosum
  – Umbilicated center; shed viral particles

• Conjunctival vascular changes (75%)

• Dry eye (10-15%)

• SPK
  – Microsporidia (parasitic protozoan) is cause
  – Mild conjunctivitis
  – CD4 below 50 cells/ml3

• Herpes Zoster Ophthalmicus
Herpes Zoster Ophthalmicus and HIV/AIDS
Kaposi’s Sarcoma

• Rare dermatologic neoplasm in immunocompromised patients
• Endemic in Africa
• One of the more common cancers in AIDS
• Sites:
  – Lymph nodes 80%
  – GI tract 80%
  – Pulmonary involvement 10%
  – Conjunctival and/or lid involvement in 17%-24% of AIDS patients
Kaposi's Sarcoma in a 70-Year-Old Male Immunocompetent Patient

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3128134/
Kaposi’s Sarcoma Treatment

- Radiation (brachytherapy, beam irradiation)
- Chemotherapy (antineoplastic drugs)
- Excision/destruction (cryo/thermal)

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3128134/
HIV Tests

- Enzyme-Linked Immunosorbent Assay (ELISA)
- Western Blot
- Rapid Antibody Tests
- OraQuick® In-Home HIV Test
  - OraSure Technologies
  - FDA approved July 3, 2012; no Rx needed
  - Tests fluid sample from mouth
  - 20-40 minute results
- Medical consult/testing still encouraged due to potential for false positives/negatives
Bloodwork and HIV/AIDS

• Always ask about Helper T cell (CD₄) count and HIV viral load when managing these patients
• These monitor the progression of HIV infection
• Normal CD4 = 1,000 cells/mm³
• Average decline of 85 cells/year
• Retinitis develops at ~ 50-75 cells/mm³
• Return to clinic based on CD₄ count
• CD₄ > 400: RTC q 1 year
  – Solitary IRH and/or CWS
Bloodwork and HIV/AIDS

• There is no viral load in non-infected patients
• Zero virus copies are in all non-infected patients
• Infected patients could have ‘undetectable’ (i.e. 40-75 copies, depending on lab) viral load
• Can number in the millions in one blood sample
• The trend of viral load over time is important
• CD4 count is more important than viral load
• US Federal guidelines recommends treatment when CD4 count drops below 350 cells/mm3

Source: http://aids.gov
Untreated HIV Time Course

http://en.wikipedia.org/wiki/HIV
HIV Treatment

1. Nucleoside Reverse Transcriptase Inhibitors (NRTIs)
2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)
3. Protease Inhibitors (PIs)
4. Antiretroviral Fusion Inhibitor
5. Three or more drugs used concurrently for best outcomes (usually from two or more classes) – HAART
HIV Tx #1. Nucleoside Reverse Transcriptase Inhibitors

Zidovudine (ZDV, AZT)

• Thymidine analog; first approved for HIV
• Incorporate into cell and viral DNA
• Useful for AIDS dementia
• Can reduce mother-to-infant HIV transmission from 25% to 8%
• Myelosuppression can occur
Other Nucleoside Reverse Transcriptase Inhibitors

- Didanosine
  - Pancreatitis
  - Peripheral neuropathy can occur

- Zalcitabine
  - Peripheral neuropathy can occur

- Stavudine
  - Peripheral neuropathy can occur

- Lamivudine
  - No dose-limiting toxic effects
HIV Tx #2: Non-Nucleoside Reverse Transcriptase Inhibitors

• Binds/inactivates reverse transcriptase
• Inhibits HIV-1 (but not HIV-2 or other retroviruses)

Nevirapine
  – Can reduce mother-infant transmission by 40%

Delavirdine

Efavirenz
  – Unique neurotoxic effects (abnormal dreams)

Tenofovir
  – Newer drug
HIV Tx #3: Protease Inhibitors

- Binds to viral proteases, preventing viral assembly; do not need intracellular activation

Saquinavir
  - First protease inhibitor (1995); not used much now

Ritonavir

Indinavir

Amprenavir

Nelfinavir

Ganciclovir (not available)
  - Intravitreal pellet used for CMV retinitis
HIV Tx #4: Antiretroviral Fusion Inhibitor

- Prevents fusion of HIV with host cell outer membrane, preventing infection of cells
- Recently introduced

Enfuviritide (T20)
- Subcutaneous injection
- Trade name: Fuzeon
HIV Tx #5: Combination Anti-HIV Therapy

- Combination of NRTI with two NNRTIs
- Called “Triple Therapy”, or “Highly Active Antiretroviral Therapy” (HAART), better known as “the cocktail”
- Not often well-tolerated, expensive, can lead to multi-drug resistance if not used correctly
- Drugs targeting HIV integrase in the works
## Combination HIV/AIDS Medications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Drug Names (INN)</th>
<th>Date of FDA Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Combivir</td>
<td>zidovudine + lamivudine</td>
<td>September 26, 1997</td>
</tr>
<tr>
<td>Triziv</td>
<td>abacavir + zidovudine + lamivudine</td>
<td>November 15, 2000</td>
</tr>
<tr>
<td>Kaletra</td>
<td>lopinavir + ritonavir</td>
<td>September 15, 2000</td>
</tr>
<tr>
<td>Epozicomp (in USA)</td>
<td>abacavir + lamivudine</td>
<td>August 2, 2004</td>
</tr>
<tr>
<td>Kivexa (in Europe)</td>
<td>abacavir + lamivudine</td>
<td>August 2, 2004</td>
</tr>
<tr>
<td>Truvada</td>
<td>tenofovir/emtricitabine</td>
<td>August 2, 2004</td>
</tr>
<tr>
<td>Atripla</td>
<td>efavirenz + tenofovir/emtricitabine</td>
<td>July 12, 2006</td>
</tr>
<tr>
<td>Complera</td>
<td>rilpivirine + tenofovir/emtricitabine</td>
<td>August 10, 2011</td>
</tr>
<tr>
<td>Stribild</td>
<td>el-tuviravir + cobicistat + tenofovir/emtricitabine</td>
<td>August 27, 2012</td>
</tr>
</tbody>
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HIV/AIDS Pre- and Post-Care with HAART

- Medical care with HAART Suppress viral replication, increases CD4 count

- Pre-HAART (1995-98)
  - CMV retinitis in 20-40%
  - Survival 1985 → 12 months

- HAART (1998-00)
  - CMV retinitis decreased by 80%
  - Survival 2005 → 30 months

http://www.natap.org/2006/CROI/CROI_32.htm
CMV Retinitis Pre-HAART

http://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/CMV-Retinitis/index.htm
CMV Retinitis Post-HAART

http://webeye.ophth.uiowa.edu/eyeforum/atlas/pages/CMV-Retinitis/index.htm
Bottom Lines: Comanagement of Patients with HIV/AIDS

• Early diagnosis
• Screening exam every few months:
  – With retinal specialist
  – With primary care physician
  – With infectious disease specialist
  – With immunologist
• Low vision devices

• Testing to determine HIV infection
• Consultation/referral to medical physician skilled in treating HIV-infected patients
• No separate treatment of the eyes may be necessary
Thank you!

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The authors have no financial interest in products herein
References


• For more on HAART, see Retina. Jul-Aug 2005; 25(5):633-49