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## HIV (Human Immunodeficiency Virus)

### Overview

- Retrovirus that infects CD4<sup>+</sup> T lymphocyte (cell-mediated immunity)
- Severe immunodeficiency permits the development of opportunistic infections and malignancies
- Transmission
  - Sexual contact
  - Blood: Intravenous Drug Use (IVDU), blood products
  - Mother to child
- Highly active antiretroviral therapy (HAART) has led to dramatic improvement in the prognosis of HIV infection

### Ocular Manifestations of HIV Infection

- Most common
  - Ocular manifestation of human immunodeficiency virus, acquired immunodeficiency syndrome (HIV-AIDS): HIV retinopathy
  - Retinal opportunistic infection: Cytomegalovirus (CMV) retinitis
- Multifocal choroiditis
  - Tuberculosis (TB), mycobacterium avium complex, histoplasmosis, cryptococcosis, pneumocystosis, other fungi, lymphoma
  - Look for disseminated systemic infection

## HIV Retinopathy

### Overview

- Definition
  - Retinal microvasculopathy
  - Most common ocular manifestation of HIV-AIDS
- Symptoms
  - Asymptomatic
  - Blurring with macular involvement
- Laterality: Mostly bilateral
- Course: Spontaneously resolved within weeks or months
- Age of onset: any
- Gender/race: no gender or racial predilection
- Systemic association: Usually found in HIV patients with low CD4 count

### Exam: Ocular

#### Anterior Segment

- No inflammation

#### Posterior Segment

- Cotton-wool spots
  - Posterior pole, often adjacent to retinal vessels
  - Large or progressive lesions should cause suspicion of early CMV retinitis
- Scattered dot blot or flame-shaped hemorrhages
- Microaneurysms
- Isolated perivascular sheathing without opportunistic infections
  - Common in African patients (especially children)

### Exam: Systemic

- Variable depending on opportunistic infections
- Acute systemic infection (HIV prodrome)
  - Occurs days to weeks after inoculation
  - Fever, lymphadenopathy, pharyngitis, rash, myalgia, malaise, headache, nausea, weight loss, diarrhea, night sweats, neurologic symptoms
  - Patients are more infectious during acute primary infection
- Latent stage
  - Occurs weeks to years after inoculation
  - Lymphadenopathy

- Acquired immune deficiency syndrome (AIDS)
  - Less common in the setting of HAART
  - Designated as AIDS with the onset of opportunistic infections or malignancies that are uncommon in the general population

## Imaging

- FA: hyperfluorescent microaneurysms; microvasculopathy, occlusive disease; blocking defects with hemorrhages

## Laboratory and Radiographic Testing

- HIV 1/2 Ag Ab immunoassay
- CD4 count/%
- Viral load
- Complete Blood Count (CBC) with differential
- Comprehensive Metabolic Panel (CMP)
- $\beta$ hCG
- Serologic screening for various infectious comorbidities

## Differential Diagnosis

- Early CMV retinopathy
- Diabetes/hypertensive retinopathy

## Treatment

- No treatment for HIV retinopathy
- HAART for systemic infection

## Referral/Co-management

- Infectious Disease
- Primary Care

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## CMV Retinitis

See Chap. 35 Herpesviruses

## Immune Recovery Uveitis (IRU)

### Overview

- Definition
  - An ocular form of immune reconstitution inflammatory syndrome (IRIS) involving increased ocular inflammation in previously opportunistic infected eyes, after improvement of immune function from HAART therapy
    - CMV (most common)
    - TB
    - Toxoplasma*
  - Typically manifests 2–16 weeks after CD4 count increases above 100 cells/ $\mu$ L following the initiation of HAART
- Symptoms
  - Asymptomatic
  - Blurring
  - Floaters
- Laterality: unilateral or bilateral
- Course: subacute
- Age of onset: any
- Gender/race: no gender or racial predilection; any exposed individual
- Systemic association
  - Diseases associated
    - CMV retinitis: most common
    - Inactive toxoplasmosis
    - Tuberculous retinochoroiditis
    - Cryptococcal infection
  - Risk factors
    - Inactive CMV retinitis involving more than 30% of retinal area
    - Patients initially treated with cidofovir
    - Low CD4<sup>+</sup> cell before starting HAART

### Exam: Ocular

#### Anterior Segment

- Anterior uveitis
- Cataract

#### Posterior Segment

- Vitritis
- Cystoid macular edema (CME)
- Epiretinal membrane
- Retinal and optic disc neovascularization
- Glaucoma

## Exam: Systemic

- Variable depending on opportunistic infections
- Same as HIV retinopathy, but expect systemic course to be improved with immune recovery

## Imaging

- OCT: CME, ERM

## Laboratory and Radiographic Testing

- CD4 count elevated above 100 cells/ $\mu$ L
- Serologic testing to evaluate for/rule out other forms of inflammation

## Differential Diagnosis

- Relapse of the previous infection
- New opportunistic infection

## Treatment

- Can be self-limiting
- Appropriate antimicrobial therapy
- Topical corticosteroid for anterior segment inflammation
- Mild vitritis without CME with good vision can be observed
- Intravitreal, periocular, or short-course systemic corticosteroids for vitritis and CME

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## Pneumocystis carinii Choroidopathy

### Overview

- Definition
  - Caused by fungus *Pneumocystis jirovecii* (former name *Pneumocystis carinii*)
  - Choroidal involvement is a sign of disseminated life-threatening fungal infection
- Symptoms
  - Loss of central vision or no visual disturbance
- Laterality: mostly bilateral

- Course: subacute
- Age of onset: any
- Gender/race: no predilection; any exposed individual
- Systemic association
  - CD4 count below 50 cells/ $\mu$ L (in contrast to CD4 200 cells/ $\mu$ L in pneumonia patient)
  - Pulmonary infection
  - Extrapulmonary: lymph nodes, spleen, liver, bone marrow

## **Exam: Ocular**

### **Anterior Segment**

- No anterior chamber reaction

### **Posterior Segment**

- Plaque-like, deep, yellow-white, round or multilobular foci at the posterior pole
- No vitritis or vasculitis

## **Exam: Systemic**

- Full physical examination may reveal findings, especially in lung, lymph nodes, and GI

## **Imaging**

- FA: early hypofluorescence and late staining

## **Laboratory and Radiographic Testing**

- Diagnosis is based on clinical and FA findings
- Systemic workup for disseminated disease: Chest X-ray, sputum culture, CBC, liver function test

## **Differential Diagnosis**

- Fungus: candidiasis, cryptococcosis, histoplasmosis
- Syphilis
- Tuberculosis, mycobacterium avium complex
- Primary intraocular lymphoma

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## Treatment

- Systemic trimethoprim (15 mg/kg/day)–sulfamethoxazole (75 mg/kg/day) in 3 divided doses, for 21 days
- Followed by secondary prophylaxis until immune reconstitution (CD4 >200 cells/ $\mu$ L)

## Referral/Co-management

- Infectious Disease
- Pulmonologist

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## Mycobacterium Avium Complex (MAC)

### Overview

- Definition
  - MAC disease typically is a disseminated, multi-organ infection in AIDS patients who are not on HAART.
  - The mode of transmission: inhalation, ingestion, or inoculation via the respiratory or gastrointestinal tract.
- Symptoms
  - Blurring
  - Floaters
- Laterality: unilateral, but bilateral can occur
- Course: subacute
- Age of onset: any
- Gender/race: no gender or racial predilection; any exposed individual
- Systemic association
  - CD4 T cells <50 cells/ $\mu$ L
  - Fever, night sweats, weight loss, diarrhea, anemia, and abdominal pain

### Exam: Ocular

#### Anterior Segment

- Granulomatous anterior uveitis
- Iris nodules

#### Posterior Segment

- Multifocal choroiditis with panuveitis
- Unifocal choroidal infiltrate
- Endophthalmitis

**Exam: Systemic**

- Hepatomegaly, splenomegaly, lymphadenopathy, and skin lesion

**Laboratory and Radiographic Testing**

- Ocular fluid or tissue
  - Gram, modified Acid fast bacilli (AFB), AFB staining
  - Culture and PCR for mycobacterium
- CBC, liver function test, chest X-ray

**Differential Diagnosis**

- Fungus: candidiasis, cryptococcosis, histoplasmosis, pneumocystosis
- Syphilis
- TB
- Intraocular lymphoma

**Treatment**

- At least two antimycobacterial drugs to prevent or delay the emergence of resistance
  - Azithromycin (500 mg daily) or clarithromycin (500 mg PO twice daily) and ethambutol (15 mg/kg PO daily)
- Alternative therapy: rifabutin (300 mg PO daily), levofloxacin (500 mg PO daily), moxifloxacin (400 mg PO daily), amikacin, streptomycin
- Followed by secondary prophylaxis until immune reconstitution (CD4 >100 cells/ $\mu$ L) and disease controlled

**Referral/Co-management**

- Infectious disease