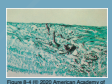
9.8.2. Endophthalmitis (II): Fungal Endophthalmitis (I)

Aspergillus endophthalmitis

- Aspergillus fumigatus/Aspergillus flavus
  - found in soil and decaying vegetation
  - depends on the virulence of the fungal pathogen and immunocompetence of the host
  - infection is rare
  - human exposure is very common
  - hematogenous dissemination to the choroid
  - seed the lungs and paranasal sinuses of humans
  - become airborne
  - spores
- predisposing conditions
  - severe chronic pulmonary diseases
  - cancer
  - endocarditis
  - severe immunocompromise
  - intravenous drug abuse
  - orthotopic liver transplantation
  - rare
  - may occur in immunocompetent patients
- lung
- eye
  - second most common site of infection
- associated with disseminated aspergillosis
- clinical presentation
  - rapid onset of pain and loss of vision
  - confluent yellowish infiltrate is often present in the macula
    - commonly invades the retinal and choroidal vessels
      - retinal hemorrhages
      - retinal vascular occlusions
        - broad areas of ischemic infarction
          - full-thickness retinal necrosis
            - forms central atrophic scar when healed
    - choroid and subretinal space
      - ± hypopyon in the subretinal or subhyaloidal space
      -
        Figure 8-5 (© 2020 American Academy of Ophthalmology)
    - in contrast to Candida chorioretinitis, Aspergillus lesions are larger and more likely to be hemorrhagic
  - dense vitritis
  - variable degrees of cells, flare, and hypopyon in the anterior chamber
- diagnosis
  - culture
    - pars plana vitreous biopsy
  - Gram and Giemsa stains
    - septate, dichotomously branching hyphae
  - difficult to culture from the blood
  - coexisting systemic aspergillosis can be a strong clue, especially among high-risk patients
- pathology
  - angiocentric
    - hemorrhage in all retinal layers
  - branching fungal hyphae spreading on the surface of the Bruch membrane without penetrating it
    - form small vitreous abscesses
    - surrounded by macrophages and lymphocytes
  - mixed acute (polymorphonuclear leukocytes) and chronic (lymphocytes and plasma cells) inflammation
    - granulomas contain rare giant cells
    - polymorphonuclear leukocytes in the vitreous
  - primary focus of infection
    - Candida endophthalmitis
      - vitreous
    - Aspergillus endophthalmitis
      - retinal and choroidal vessels
      - subretinal/subretinal pigment epithelial space
- differential diagnosis
  - Candida endophthalmitis
  - cytomegalovirus retinitis
  - Toxoplasma retinochoroiditis
  - coccidioidomycotic choroiditis
  - bacterial endophthalmitis
- treatment
  - pars plana vitrectomy
    - ± intravitreal corticosteroids
    - intravitreal amphotericin B or voriconazole
  - systemic treatment
    - infectious diseases specialist
    - oral voriconazole
    - intravenous amphotericin B
    - caspofungin
      - activity against Candida and Aspergillus
    - other systemic antifungal drugs, such as itraconazole, miconazole, fluconazole, and ketoconazole
  - VA<20/200
    - visual prognosis is poor because of frequent macular involvement

Candida endophthalmitis

- General
  - focal or multifocal areas of chorioretinitis
    - begins in the choroid
      - yellow-white lesions with indistinct borders
      - from small cotton-wool spots to several disc diameters
    - can subsequently break through into the vitreous
      - localized cellular and fungal aggregates overlying the original site(s)
  - etiology
    - Candida (the most common cause)
    - Aspergillus
    - Coccidioides
    - Histoplasma capsulatum
    - Cryptococcus neoformans
    - Sporothrix schenkii
    - Blastomyces dermatitidis
    - less common
  - granulomatous or nongranulomatous inflammation
    - keratic precipitates
    - hypopyon
    - vitritis with cellular aggregates
  - ± iris nodules
  - ± rubeosis
  - nonneoplastic masquerade syndrome
    - mistaken for noninfectious uveitis
      - Candida (the most common cause)
      - Aspergillus
      - Coccidioides
    - corticosteroids alone usually worsen the disease
  - requires aggressive systemic and local antifungal therapy as well as surgical intervention
- etiology
  - Candida species are the most common cause of endogenous fungal endophthalmitis
    - in both pediatric and adult populations
  - organisms
    - Candida albicans
      - the most common pathogen
    - non-albicans species (eg, C glabrata)
  - budding yeast
    - characteristic pseudohyphate appearance
      - 
        Figure 8-4 (© 2020 American Academy of Ophthalmology)
  - reach the choroid hematogenously
    - break through the Bruch membrane
      - form subretinal abscesses
      - involve the retina and vitreous
- epidemiology
  - prevalence of intraocular candidiasis in patients with candidemia
    - 9%–78%
    - <37% if not receiving antifungal therapy
    - 3% if receiving antifungal therapy
  - patients with ocular lesions are more likely to have infection involving a greater number of organ systems
  - predisposing conditions
    - recent major gastrointestinal surgery
    - bacterial sepsis
    - systemic antibiotic use
    - use of indwelling catheters
    - hyperalimentation
    - debilitating diseases
      - diabetes mellitus
    - immunomodulatory therapy
    - prolonged neutropenia
    - organ transplantation
    - hospitalized neonates
    - intravenous drug users
    - immunodeficiency per se does not appear to be a prominent predisposing factor
      - paucity of Candida chorioretinitis/endophthalmitis among patients with HIV/AIDS
- clinical presentation
  - symptoms
    - blurred or decreased vision
    - pain
  - multiple, bilateral, white, well-circumscribed lesions
    - <1 mm
    - postequatorial fundus
      -
        Figure 8-3 (© 2020 American Academy of Ophthalmology)
  - overlying vitreous cellular inflammation
    - string-of-pearls appearance
  - vascular sheathing
  - intraretinal hemorrhages
- diagnostic workup
  - all patients with candidemia should undergo baseline dilated funduscopic examination
    - monitoring for ≥2 weeks after an initial eye examination
    - earlier treatment of candidal endophthalmitis has been associated with better visual outcomes
  - blood culture
  - diagnostic and therapeutic vitrectomy
    - in presence of vitreous snowballs and endophthalmitis
    - undiluted vitreous sample
    - vitreous culture
    - Giemsa stain
    - PCR for Candida species
- differential diagnosis
  - toxoplasmic retinochoroiditis
  - pars planitis
- consultation with a specialist in infectious diseases is essential
- treatment
  - chorioretinal lesions not yet involving the vitreous
    - oral antifungal drugs (triazoles)
      - voriconazole (200 mg, twice daily)
      - fluconazole
      - x 2–4 weeks
      - good oral bioavailability
      - broad spectrum of antifungal activity
      - good vitreous penetration
  - vitreous body is involved
    - intravenous + intravitreal antifungal drugs
    - intravitreal injection of antifungal drugs
      - usually in conjunction with pars plana vitrectomy
        - debulking the pathogen load
      - amphotericin B, 5–10 μg/0.1 mL
        - OR
        - voriconazole, 100 μg/0.1 mL
      - ± dexamethasone, 0.4 mg/0.1 mL
    - intravenous amphotericin B ± flucytosine
      - more severe infections
      - dose-limiting toxicities
        - renal, cardiac, and neurologic
      - liposomal lipid complex formulations
        - less toxicity
    - intravenous caspofungin
      - activity against Candida and Aspergillus
      - echinocandin class
        - inhibit synthesis of glucan in the cell wall
    - intravenous micafungin
      - echinocandin class
    - oral voriconazole, flucytosine, fluconazole, or rifampin
      - may be administered in addition to intravenous treatment
  - treatment of both peripherally located lesions/lesions not involving the macular center may salvage useful vision.

Ophthalmology Mind Maps/Arman Mashayekhi, MD