Corneal Infectious Disease

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Objectives

- List types of corneal infections
- Describe appearance of corneal infections
- Describe best treatment options available for each condition

First a little background

- Natural defenses of the ocular surface:
  - Bony orbit
  - Normal eyelid position and blinking
  - Tears: lysozyme, β‐lysin, lactoferrin
  - Immunoglobulins (antibodies)
  - Mucin and meibomian gland lipids
  - Corneal epithelium is a protective barrier

“Normal” ocular surface

- Some bacteria are found normally on the eye surface with cultures: *Staphylococcus epidermis*, *Staphylococcus aureus*, *corynebacterium spp*, *propionibacterium acnes*.
- Few bacteria can overcome in intact corneal epithelium: *Neisseria gonorrhoeae*, *Neisseria meningitidis*, and few others.
What can cause corneal infections?

- Viruses
- Bacteria
- Fungi
- Protozoa

Viruses

- Smallest of infectious agents. Viruses contain only a protein coat, and a core of genetic material (RNA or DNA) and cannot replicate on their own.
- Viruses attach to specific cells, enter cells and reprogram cells to make more viruses.
- Most common corneal virus infections: Herpes Simplex virus 1 or HSV (by far)
- Other corneal virus infections: HSV 2, VZV (shingles), Adenovirus, EBV, mumps, measles

HSV Keratitis

- Most common cause of corneal blindness in the US
- Acquired from direct contact with infectious lesions (usually lips) and spreads to trigeminal ganglion.
HSV keratitis

- Rarely is bilateral
- Usual presents with mild/moderate pain, redness and foreign body sensation
- Repeated episodes can lead to corneal scarring.
HSV can be tricky....

- Does not always appear like classic dendrite
- HSV can also cause:
  - Interstitial keratitis: Deep corneal vessels with haze
  - Disciform keratitis: Endothelitis in round shape with KP and edema
  - Necrotizing keratitis: Infiltrate with stromal vascularization (may look like bacterial or fungal infection)
  - Iritis

Treatment of HSV can be tricky too

- For active dendrite or epithelial disease: trifluridine, gancyclovir gel, acyclovir gel, oral antiviral, epithelial scrape
- NO steroids for active epithelial disease
- Steroids for stromal keratitis, or disciform keratitis
- Oral antiviral (ie acyclovir) to prevent recurrences and usually used in conjunction with steroids for disciform or stromal disease.
Adenovirus keratitis (EKC)

- A DNA virus with many subgroups. Group D associated with EKC (epidemic keratoconjunctivitis)
- Presents with severe follicular conjunctivitis
- May have chemosis, subconjunctival hemorrhages, punctate keratitis, preauricular adenopathy
- Diagnosis usually made by clinical appearance, but a new rapid test is available

Adenovirus (EKC)

- Very contagious
- Good Handwashing required!
- Be very careful to wipe down room after patient seen and clean tonometer tip
EKC

- Treatment is supportive: Artificial tears, cool compresses
- May use steroids if keratitis present

Bacteria

- Relatively complex single celled organisms which can reproduce on their own.
- Many different types of bacteria can infect the cornea
  - Most common: *Staph aureus*, *Staph epidermidis*, *Streptococcus pneumoniae* and other *Streptococcus* spp, *Pseudomonas aeruginosa* (associated with CLs)
Bacterial corneal ulcers

- Usually has rapid onset with pain, photophobia, redness and decreased vision
- Rate of progression depends on virulence
  - *Staph* epi. usually slow progression
  - *Pseudomonas* may have rapid progression
- May occur post trauma, associated with poor contact lens hygiene, impaired or poor ocular surface, post corneal transplant

Diagnostic tests

- Cultures: The only means of isolating and identifying the causative organism and determining sensitivity to antibiotics
- Cultures should be done if:
  - Sight threatening disease
  - There is a lack of response to treatment
  - There is a suspicion of fungal or acanthamoebal keratitis
Diagnostic tests

- Cornea scrapings for smear
  - Gram stain: best for bacteria, but may also visualize fungi. Rapid, and widely available.
  - Giemsa stain: May also visualize bacteria, fungi and chlamydia
  - KOH: rapid test for fungi
- Note that it is impossible to tell what type of corneal infection there is by appearance only – but appearance does give clues.
- Also it is possible to have a non-infectious ulcer (autoimmune)
Bacterial corneal ulcers

- *Pseudomonas*: May be found in contact lens related ulcers. Rapidly progressive and needs treatment emergently
- Staph. aureus: May be found in dry eyes or blepharitis. Not as rapidly progressive
- Mycobacteria: "Atypical" bacteria that grow like a fungus and important causes of infections after LASIK.

Treatment of bacterial corneal ulcers

- Small peripheral ulcers: May start treatment with a fluoroquinolone (available by prescription)
- Larger ulcers need to be cultured and started on fortified antibiotics (mixed by pharmacy or in office)
  - Cefazolin (covers some gram + and -)
  - Vancomycin (gram + coverage)
  - Tobramycin (gram – coverage)
- Treatment adjusted by culture results and course of ulcer

Treatment of bacterial corneal ulcers

- Steroid drops may be used to help decrease scarring (controversial)
- Corneal transplant may be needed if left with significant scar
Fungi

- Tiny microbes found worldwide. Many are harmless, but some can cause disease
- Fungal keratitis is less common than bacterial keratitis causing 5-10% of corneal infections in the US
- More common in warmer, humid locations
- Trauma to the cornea with vegetable matter is the greatest risk factor for fungal keratitis

Fungi vs Bacteria

Fungi
- Eukaryotic cells (have well defined nucleus)
- Multicellular, except for yeast
- Many different shapes
- Capable of sexual and asexual reproduction. Develop by branching and fragmentation while yeast through budding

Bacteria
- Prokaryotic cells (no nucleus)
- Single celled
- Three basic shapes: round, rod, or spiral
- Divide by binary fision

Fungi

- Moniliaceae (nonpigmented filamentary)
  - Fusarium
  - Aspergillus
- Dematiaceae (pigmented, filamentary)
  - Curvularia
  - Lasiodiplodia
- Yeasts
  - Candida
Fungal Ulcers

- Typically has history of trauma, steroid use, immune suppressed patient, or chronic keratitis
- Initial symptoms of pain and inflammation are usually not as bad as bacterial ulcers
- Infiltrate may be more grayish and have feathery edges with satellite lesions
- Occasionally fungi may penetrate into anterior chamber

Management of fungal ulcers

- If there is a suspicion for fungal infection – recommend diagnostic stains and culture
  - Stain with Gomori methamine silver or KOH
  - Culture with Sabarouds or blood agar at room temperature
Treatment of fungal ulcers

- Filamentous fungal keratitis: Natamycin 5% drops, and/or oral ketoconazole
- Yeast: amphotericin B (0.15-0.30%) drops, and/or oral fluconazole
- Oral voriconazole has great intraocular penetration and broad spectrum coverage (but expensive)
- If negative cultures and smear, may need to repeat cultures and consider corneal biopsy

Protozoa

- Single celled organisms with nuclei, but show two characteristics usually associated with animals
  - Mobility
  - Heterotroph: requires organic compounds for food (not sun or light)
Acanthamoeba keratitis

- Acanthamoeba are free-living protozoa found widely in freshwater and soil
- Resistant to killing by freezing, and typical chlorine levels used in pools
- May exist in mobile (trophozoites) or dormant cystic form
- Majority (70%) of cases in US have occurred with contact lens use
  - Homemade saline solution

Acanthamoeba keratitis

- Usually presents with severe pain, photophobia, and a prolonged course
- Has not responded to other antimicrobial drugs
- Often misdiagnosed as HSV
Acanthamoeba keratitis

- May present with “ring” ulcer
- Or “radial perineuritis” (inflammation around corneal nerves)
- Disproportionally severe pain

Diagnosis of Acanthamoeba keratitis

- Special stains: Giemsa, PAS, Calcofluor white, acridine orange
- Special culture: “Nonnutrient agar with E coli overlay”

Confocal microscopy
Confocal microscopy of Acanthamoeba keratitis

Treatment of Acanthamoeba

- Treatment is prolonged (possibly 6-12 mos) and eradication of organisms is difficult
- NO STEROIDS!
- Most drugs of these drugs are effective against trophozoites, but less effective against cysts:
  - Diamidines: Propamidine, hexamidine
  - Biguanides: polyhexamethylene biguanide (PHMB), chlorhexidine
  - Aminoglycosides: neomycin
  - Imidazoles/triazoles: voriconazole, miconazole, ketoconazole, itraconazole

Treatment of Acanthamoeba

- Corneal biopsy may be needed for diagnosis
- Penetrating keratoplasty may be required for cases that are progressing despite maximal medical therapy (prognosis is poor)
Any Questions?