Corneal Infections

Carrie Lembach DO
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Objectives

• Identify differential diagnosis for corneal infections
• Identify most common organisms involved in corneal ulcers
• Describe method for performing corneal cultures
• List common antibiotics used to treat corneal ulcers
Outline

• Host defense mechanisms
• Normal ocular flora
• Risk factors for developing corneal ulcer
• Differential diagnosis
• Presentation of:
  • Bacterial ulcers
  • Fungal ulcers
  • Acanthamoeba
  • Herpes simplex keratitis
• How to perform cultures
• Treatment of most common infections
• 30,000-75,000
  • Estimate of corneal ulcers in United States yearly

• Rates more prevalent in southern states
Host defense mechanisms

• Bony orbit
  • Acts as cushion

• Blink response
  • Promotes tear turnover
  • Meibomian glands express lipid component
  • Wash away debris

• Tear turnover rate
  • Helps to reduce time with eye
    • Irritants
    • Microbes
• Lymphoid tissue
  • Tear lysozymes
  • Tear lactoferrin
  • Immunoglobulins (IgA)
  • Meibomian gland derived lipids
  • Globlet cell derived mucin
• Growth factors
  • Epidermal growth factor
  • Transforming growth factor beta
  • Hepatocyte growth factor
Natural defenses

- Tears contain lysozyme to break down bacterial cell walls
- Immunoglobulins in tear film
- Lipids from meibomian glands allow tears to stay on surface longer
  - Protects corneal epithelium from breakdown
• Mucin inhibits attachment of microbes to corneal epithelium
• Corneal epithelium acts as natural barrier
• Conjunctiva contains many immunologic mediators
• Vascular and lymphatic channels present in conjunctiva
Normal ocular flora

• Vary based on age and geography
• After birth
  • Staphylococcus aureus
  • S. epidermidis
  • Streptococci
  • E. coli
• First 2 decades
  • Streptococci
  • Pneumococci
• Increasing age
  • S. epidermidis
  • Coagulase negative staphylococci
  • S. aureus
  • Diptheroids
  • Increasing gram negative bacteria

• MRSA on the rise!!
- Other bugs
  - Propionibacterium acnes
  - Malassezia furfur
  - Candida

- Normal eyelid flora
  - Demodex folliculorum
  - Demodex brevis
Spread of infections

- Transplacental passage
- Direct contact in birth canal during delivery
- Fomites
- Fingers
- Airborne particles
- Sexual contact
- Hematogenous spread
- Upper respiratory tract
Bugs defense

- Virulence
- Adherence
- Evasion
- Invasion
- Replication and persistence
- Inoculum
Invasion

• Certain bacteria can invade an intact epithelium
  • Neisseria gonorrhoeae
  • Neisseria meningitidis
  • Cornebacterium diphtheriae
  • Shigella species
Risk factors

• Contact lens wear
• Trauma
• Ocular surface disease
  • Dry eye syndrome
  • History of chemical injury
• Use of topical steroid medication
• Neurotrophic cornea
• History of herpes simplex or shingles
• Poor eyelid closure
• Diabetes mellitus
Why contact lens wearers??

• Extended wear of lenses can block oxygen to cornea
• Bacteria on improperly cleaned lens can get trapped on undersurface of lens
• Scratches on edge of contact lens can scrape corneal surface
• Particles of dirt can be trapped underneath contact lens and scratch cornea
• Risk of developing ulcer increases with overnight wear
• Risk increases with number of consecutive days lenses are worn without removal
Not all ulcers look the same!
Common presentation

• Red eye
• Pain
• Foreign body sensation
• Tearing
• Discharge from eye
• Blurry vision
• Photophobia
• If ulcer is large patient may complain of white or gray round spot on cornea
• Detailed history
  • Is patient a contact lens wearer?
    • CL hygiene
      • What type of lens
      • Type of contact lens cleaning solution
      • Refill contact case after each use or top off bottle?
    • CL wearing schedule
    • Exposure to tap water
      • Did pain start while wearing contact lens?
  • When did pain/redness/irritation start?
  • Pain severity?
  • Recent exposure to vegetation or dirt
• Previous ocular surgery
• Previous episode of herpetic keratitis
• Use of any ocular medications
• History of recent trauma
• Dry eye syndrome
• History of diabetes mellitus
• History of rheumatologic disease
  • Rheumatoid arthritis
Differential diagnosis

• Bacteria
• Fungus
• Acanthamoeba
• Viral
  • Herpes simplex keratitis
• Non-infectious
  • Sterile infiltrate
  • Neurotrophic ulcer
  • Topical anesthetic abuse
BACTERIAL ULCERS
Bacterial ulcers

• Classic presentation
  • Painful
  • Diffuse injection
  • Decreased vision
  • Tearing
  • Photophobia
  • Discharge
  • Foreign body sensation
Bacterial ulcers

- Common exam findings
  - Eyelid swelling
  - Conjunctival hyperemia
  - Mucopurulent discharge
  - Stromal infiltrate
  - +/- surrounding epithelial defect

- Severe cases
  - Anterior chamber reaction
  - Hypopyon
Bacterial ulcers

• Common bugs
  • S. aureus
  • S. epidermidis
  • Streptococcus
  • Pseudomonas aeruginosa
    • Most common organism in CL wearers
  • Enterobacter

• Uncommon bugs
  • Neisseria
  • Moraxella
  • Mycobacterium
  • Nocardia
  • Corynebacterium
  • Anaerobes
Treatment bacterial ulcers

- NEED TO CULTURE!
- Start topical antibiotics
Corneal culturing

- Identify organism
- Allows for targeted treatment of organism
- Determine sensitivity of organism to treatment
  - Emerging resistance to multiple antibiotics
Treatment of bacterial ulcers

- Topical antibiotics
- Fluororoquinolones v. fortified antibiotics
  - Smaller, non-central ulcers may get topical fluoroquinolone
  - Larger, central ulcers fortified antibiotics
- Start every hour for the first 24-48 hours
- Loading dose of q 5 minutes for first 30 minutes
- After 24 hours of treatment can consider antibiotic ointment at night
- No steroids in early period
Topical fluoroquinolone

- Second generation
  - Ocuflox
  - Ciloxan
- Third generation
  - Iquix
- Fourth generation
  - Vigamox
  - Moxeza
  - Zymar
  - Zymaxid
- Fifth generation
  - Besivance
Fortified antibiotics

- Topical Fortified Vancomycin
  - 25 mg/ml
  - 50 mg/ml
- Topical Fortified Tobramycin
  - 9-14 mg/ml
- Topical Fortified Cefazolin
  - 50 mg/ml
Why fortified antibiotics?

• Developing resistance to fluoroquinolones
• Increasing amount of community acquired MRSA
• Ocular TRUST 2 trial found:
  • More than half of S. aureus isolates were MRSA
• Antibiotic resistance began to be evaluated in early 1990s
• MRSA rates
  • 1994
    • 4.4%
  • 2004
    • 42.9%
  • 2012
    • 54%

• Community acquired MRSA
  • 2000
    • 18.3%
  • 2005
    • 29.1%
Improvement in ulcer

- Decreasing area of stromal infiltrate
- Decreasing density of stromal infiltrate
- Decreasing stromal edema
- Decreasing endothelial inflammatory plaque
- Reduction anterior chamber inflammation
- Reepithelialization of cornea
- Cessation of corneal thinning
What is the role of topical steroids?

- Once infection under control steroids can be beneficial to help decrease scarring
- Don’t start steroids prior to initiation of antibiotics

- SCUT trial (Steroids for Corneal Ulcers Trial)
  - 500 patients
  - No overall difference in best corrected vision at 3 months
  - No increase in adverse events when using topical steroid along with antibiotic for bacterial corneal ulcer
FUNGAL ULCERS
Fungal ulcers

- Less common than bacterial ulcers
- Account for 5-10% ulcers in US
- Trauma to cornea with plant or vegetable matter is biggest risk factor
- Other risk factors
  - Contact lens wear
  - Topical steroid use
  - Immunocompromised
  - History of corneal surgery
  - Chronic keratitis
Outbreak of Fusaririum keratitis

• 2006 outbreak of Fusaririum keratitis in contact lens patients
• Found association with use of Renu with MoistureLoc solution (Bausch&Lomb)
• Removed from market
• Rapid decline in number of Fusaririum cases is US
Fungal ulcer

- Clinical presentation
  - May have symptoms for a longer duration until presentation
  - Pain
  - Infiltrate may appear grayish-white
  - Feathery borders
  - Satellite lesions
  - May not have associated epithelial defect
  - Endothelial plaque
  - Hypopyon
Fungal ulcer treatment

• Topical
  • Natamycin 5%
  • Amphotericin B 0.15-0.30%
  • Voriconazole 1%

• Systemic
  • Voriconazole 200-400 mg/day
  • Ketoconazole 200-600 mg/day
  • Fluconazole 200-400 mg/day
  • Itraconazole 200 mg/day

• Biopsy
• Debridement
ACANTHAMOEBA

Patient with Acanthamoeba keratitis. Note the ring-like stromal infiltrate and lack of bulbous dendrites. The latter are a symptom of herpes simplex.
Acanthamoeba

- Protozoa found in soil and freshwater
- Resistant to killing by freezing, desiccation, and chlorine used in hot tubs and pools
Acanthamoeba

- Clinical presentation
  - Pain out of proportion to exam findings
  - Photophobia
  - Early
    - Confined to epithelium, may resemble bacterial or viral keratitis
    - Frequently initially misdiagnosed
- Later in course disease
  - Stromal involvement
  - Ring infiltrate
  - Can develop radial perineuritis
    - Inflammation of corneal nerves
Acanthamoeba

- Hard to detect
- Yield is 35-50% on culture
- May need confocal microscopy
- Biopsy
Acanthamoeba

• Treatment may last up to 3-4 months
• Combination therapy is required
  • Chlorhexidine 0.02%
  • Polyhexamethylene biguanide (PHMB) 0.02%
  • Voriconazole

• May go on to require corneal transplant
  • poor prognosis
Herpes simplex keratitis

VIRAL INFECTIONS
Herpes simplex keratitis

- Clinical presentation
  - Photophobia
  - May not have as many complaints as exam findings
  - Corneal anesthesia
  - Can develop epithelial disease
    - Dendrite
  - Stromal disease
  - Endothelial disease
Herpes simplex keratitis

• Treatment
  • Oral antivirals
    • Acyclovir 400 mg po 5x day
    • Valtrex 1 g po tid
    • Famvir 500 mg po tid
  • Topical medication
    • Viroptic (Trifluridine) 1 drop 9x day
    • Zirgan (Gancyclovir) 5x day
  • Topical steroids
    • Use with caution
    • No epithelial defect
    • Active stromal inflammation
Sterile infiltrate, Neurotrophic ulcer, topical anesthetic abuse

NON-INFECTIOUS ULCERS
Sterile infiltrate

• Clinical presentation
  • Usually asymptomatic
  • Small, less than 1 mm lesions
  • Circumlimbal
  • Usually self limiting
  • Can be treated with topical steroids
    • May consider antibiotics when initiating treatment
Sterile infiltrate

• Common associations
  • Contact lens wear
  • Rosacea
  • Blepharitis
  • Entropion
  • Dry eye syndrome
Neurotrophic ulcer

• Clinical presentation
  • Minimal symptoms
  • Smooth, rolled edges to epithelium
  • Check corneal sensation!!

• Underlying conditions
  • Diabetes
  • HSV infection
  • Multiple ocular surgeries
  • Chemical burns
Topical anesthetic abuse

- Suspect in nonhealing epithelial defect
- No improvement despite adequate treatment
CASES
Case 1
Case 3
Case 4
Case 5
• Any questions??

• Thank you!