Infectious Keratitis

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Case Presentation

ID: 35yo Female
CC: irritated, itching, discharge, tearing from the left eye
HPI: Several days of increasing irritation of the left eye. No recent injuries, although endorses rubbing for itching. Wears monthly contact lenses and takes them out “most nights.”

Case Presentation

POChx: Refractive error - contact lens wearer for 10 years
PMHx: none
SH: Smokes socially
FH: non-contributory

Exam

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual acuity (BCVA)</td>
<td>20/20</td>
<td>20/70</td>
</tr>
<tr>
<td>IOP</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Pupils</td>
<td>PERRLA</td>
<td>PERRLA</td>
</tr>
<tr>
<td>EOM</td>
<td>Full</td>
<td>Full</td>
</tr>
</tbody>
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Slit Lamp Exam

<table>
<thead>
<tr>
<th></th>
<th>OD</th>
<th>OS</th>
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</thead>
<tbody>
<tr>
<td>Lids/Lashes</td>
<td>normal</td>
<td>normal</td>
</tr>
<tr>
<td>Conjunctiva/Sclera</td>
<td>White and quiet</td>
<td>1+ injection</td>
</tr>
<tr>
<td>Cornea</td>
<td>Normal, contact lens in place</td>
<td>2mm x 3.5mm area of opacity with surrounding infiltrate just outside of visual axis inferiorly, underlying stromal edema, overlying 2mm area of epi defect</td>
</tr>
<tr>
<td>Anterior Chamber</td>
<td>Deep and quiet</td>
<td>1+ cell</td>
</tr>
<tr>
<td>Iris</td>
<td>Normal shape, size, morphology</td>
<td>Normal shape, size, morphology</td>
</tr>
<tr>
<td>Lens</td>
<td>clear</td>
<td>clear</td>
</tr>
<tr>
<td>Vitreous</td>
<td>clear</td>
<td>clear</td>
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</tbody>
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Diagnosis: **Infectious Keratitis**
(Corneal Ulcer)

Epidemiology

US based studies in 1950s-1980s: 11.0 per 100,000 people
Recent studies: 20.9 to 27.6 per 100,000 person-years
Contact lens wearers: 130.4 per 100,000 person-years
38.5 million contact lens wearers in the US

Contact lens wear is the single greatest risk factor for developing keratitis in the United States.

Healthy eyes do not develop spontaneous keratitis!

Need to have a compromised ocular surface:
- Direct injury (trauma, surgery)
- Any eye disease that leads to breakdown of the surface
  - Dry eye
  - Recurrent erosions
  - Corneal dystrophies
  - Corneal edema
  - Herpetic infections
- Patients who don’t heal well
  - Diabetics
  - Immunocompromised
  - Elderly
Why are contact lens wearers at higher risk?

What does contact lens wear do to the eye?
- Dry eye
- Micro-trauma
- Allergy
- Inflammation
- Brings microorganisms to the surface for prolonged periods of time

Infectious keratitis pathway

Corneal Injury → Infection → Tissue destruction → Inflammatory response → Scar

Bacterial Causative Agents

Often reflect the normal flora of the ocular surface (gram-positive)
- coagulase-negative Staphylococci
- Staphylococcus aureus
- Streptococcus sp.
- Corynebacterium

If gram-negative organisms are identified:
- Pseudomonas aeruginosa
- Serratia marcescens
- Moraxella sp.

Infectious keratitis pathway

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Infectious keratitis pathway

**Corneal Injury**

- Infection
- Tissue destruction
- Inflammatory response
- Scar

**History**

- Spontaneous keratitis in a healthy eye does not occur!
- Contact lens use?
- Trauma? (accidental or surgical)
- Underlying ocular history
  - Herpetic disease
  - ABDM/corneal erosions
  - Dry eye
  - Neurotrophic cornea
- Underlying medical history
  - Diabetes
  - Immune status
  - Recent illness
- Tempo of disease
  - Rapidly evolving vs indolent
  - Pain
  - Degree of vision loss

**Diagnostics**

**Empiric Treatment**

**Modify treatment**

**Minimize scar**
Infectious Keratitis Diagnosis and Treatment

**History**

**Diagnostics**

- Empiric Treatment
- Modify Treatment
- Minimize Scar

**To culture or not to culture…**

Many cases in the community are treated empirically without culture

**AAO guidelines:**
- Large ulcer
- Centrally located,
- Involving mid or deep stroma
- Infection that has not been responsive to initial treatment
- Atypical features which may indicate fungal, amoebic or mycobacterial keratitis


**Culture Options**

- Gram stain (slide)
- Aerobic culture: Tryptan soy broth, Blood agar, Chocolate: Neisseria, haemophilus
- Anaerobic culture: Thioglycolate broth
- Fungal: potato dextrose plate and smear
- Mycoplasma (TB): agar in a tube (Middlebrook/Lowenstein)
- Acanthomeba: e coli overlay plate on agar
- Viral culture: UTM (universal transport media)

Yield of cultures 40–60%

Delayed cultures does NOT decrease yields – may take longer to recover pathogens

**Culture Technique**

Use Kimura spatula or calcium alginate swab "exception viral = dacron"

**Tissue biopsy**

Advantages: tissue for culture and histopathology
Disadvantages: risk of procedure (perforation)

Yield of cultures 40–60%

Delayed cultures does NOT decrease yields – may take longer to recover pathogens

Causal agent was identified in 42% of cases either with culture or histopathologic examination

44% of patients had initial negative cultures from corneal scrapings

Complication rate: 3/53 perforation (6%)
Empiric Treatment

Don’t wait for culture data/gram stain

**Empiric treatment: BROAD SPECTRUM**

Fluoroquinolones: well tolerated, good ocular penetration

Currently use: FOURTH GENERATION (Vigamox)

Excellent gram-negative, including Pseudomonas

Good gram-positive

Initial treatment regimen is INTENSE:
every 30min-every 1 hour AROUND THE CLOCK

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Fortified antibiotics

**Gram negative coverage:**

- Tobramycin
- Gentamycin

**Gram-positive coverage:**

- Vancomycin
- Cefazolin

**Advantages:** Better coverage

**Disadvantages:** difficult to obtain, limited shelf life, ocular toxicity

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Infectious Keratitis Diagnosis and Treatment

**History**

**Diagnositcs**

**Empiric Treatment**

**Modify Treatment**

**Minimize Scar**

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Resistance

2008 Ocular Tracking Resistance in US Today (TRUST)
2009 Antibiotic Resistance Monitoring in ocular Microorganisms (ARMOR)

Across early fluoroquinolones:
Methicillin-sensitive S. aureus (MSSA) susceptibility 80%
Methicillin-resistant S. aureus (MRSA) susceptibility 15%

Alexandrakis, G., Haimovici, R., Miller, D. & Alfonso, E. C. Corneal biopsy in the management of progressive microbial keratitis.

Rational treatment strategies:

Double coverage? – using a multdrug approach similar to HIV or TB

Adding better gram+ coverage

Vigamox with fortified vancomycin/cefazolin

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Emerging Pseudomonas Resistance

Draft Genome Sequences of Two Drug-Resistant Isolates of Pseudomonas aeruginosa Obtained from Keratitis Patients in India

Rational treatment strategies:

Double coverage? – using a multdrug approach similar to HIV or TB

Adding better gram+ coverage

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Infectious Keratitis Diagnosis and Treatment

History
Diagnosis
Empiric Treatment
Modify Treatment
Minimize Scar

Steroids in Corneal Ulcers

Benefits: suppressing inflammation → reduce scarring

Disadvantages: increase in infection burden, increase risk of corneal melting, elevated IOP

Meta-analysis of existing trials (including SCUT):
- No benefit nor disadvantage with respect to:
  - Visual acuity
  - Re-epithelialization
  - Quality of life
  - Adverse affects


Sub-analysis of SCUT trial data:
3 month best spectacle-corrected acuity
Steroids: 3 days within diagnosis vs 4 or more days

Conclusions

- Corneal ulcers require prompt evaluation and treatment
- Obtain thorough history – remember healthy eyes do not develop keratitis
- Cultures and smears should be obtained, even if treatment has started
- Antibiotic resistance is prevalent – fortified antibiotics give the broadest coverage, particularly for gram positive organisms
- Steroids may provide some benefit with respect to scarring if initiated early

Severe ulcers:
- 3 line improvement if administered within 2-3 days (p=.02)
- 2 line improvement if administered after 4 days (p=.17)

Moderate ulcers:
- 1 line improvement if administered within 2-3 days (p=.09)
- 2 lines worse if administered after 4 days (p=.01)

Mild ulcers:
- No significant improvement compared to placebo
- 2 lines worse if administered after 4 days (p=.01)

Severe: CF vision
Moderate: 20/40-20/800
Mild: <20/40

Thank You