Clinical Decision-making in Infectious Keratitis

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Clinical Decision-making in Infectious Keratitis

• 46 year old woman with a history of non-hodgkins lymphoma
• Soft contact lens wear
• Red eye, mild decrease in vision (20/30)
• Decreased corneal sensation
Clinical Decision-making in Infectious Keratitis

- Management?
  - Scraping for stains, microbial culture?
  - Samples for PCR?
  - Empirical treatment?

- Initial treatment?
  - Antivirals
  - Antibiotics
  - Corticosteroids?
Clinical Decision-making in Infectious Keratitis

• Role of samples for stains, culture, diagnostics
  – Culture techniques

• Empirical treatment
  – Antimicrobial choices

• Corticosteroids

Clinical Decision-making in Infectious Keratitis

• Why culture?
  – 90% of bacterial ulcers will respond favorably to fourth generation fluoroquinolone
  – Culture results are not consulted unless initial (empirical) treatment fails
  – Culture plates expensive to maintain, limited lifespan
  – Most practitioners see a small volume of infectious cases
Clinical Decision-making in Infectious Keratitis

- Empirical therapy without culture
  - Requires high probability of first antibiotic being successful
  - Low probability of atypical, non-bacterial organisms
  - High diagnostic accuracy
  - Fusarium outbreak: many cases identified late!

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To save time and money, consider alternatives to universal culture with direct inoculation of media:

1. Selective culture of particularly suspicious, severe or atypical lesions

2. Use of swab-based transport media rather than direct inoculation of plates and broth
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• When to culture?
• Risk for empiric treatment failure
  – Referral practice
  – History that suggests risk
    • Trauma involving vegetative material
    • Home-made saline for contact lenses
    • Interface infiltrate following LASIK
  – Atypical or suspect clinical presentation
  – Atypical or suspect clinical course


Clinical Decision-making in Infectious Keratitis

• Can experienced clinicians distinguish bacterial vs fungal keratitis based on appearance?
  – 80 photos of proven bacterial and fungal keratitis
  – Experts from Proctor and Aravind
  – Correct 66%. Higher error rate for fungal infection

Clinical Decision-making in Infectious Keratitis


Clinical Decision-making in Infectious Keratitis

A. Strep pneumo

Clinical Decision-making in Infectious Keratitis

A. Strep pneumo
B. Pseudomonas


Clinical Decision-making in Infectious Keratitis

A. Strep pneumo
B. Pseudomonas
C. Aspergillus

Clinical Decision-making in Infectious Keratitis

A. Strep pneumo  
B. Pseudomonas  
C. Aspergillus  
D. Fusarium


Clinical Decision-making in Infectious Keratitis

• If we do decide to culture, how should it be done?
• Alternative to scrapings and direct inoculation of culture plates: Amies transport medium without charcoal
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• Rather than maintain plates with rapid expiration, a supply of transport medium tubes and swabs is kept on hand.

• Samples obtained with preplaced swab, placed in carrier tube and delivered to lab within 24 hours (end of that work day, beginning of the next)

Clinical Decision-making in Infectious Keratitis

• Steroids in Infectious Disease
  – Important role in limiting damage associated with immune response to infection in pediatric meningitis, tuberculous meningitis and tuberculous pericarditis
  – Ophthalmology: used to control inflammation in bacterial endophthalmitis
  – Is there a role in infectious keratitis?
“To combine the corticosteroids with an antibiotic as is a common practice, is to convert two useful agents into one bad compound and to indulge in blunderbuss therapy of a particularly objectionable type.” ~A. Sorsby, Br. Med J 1960

“The ideal therapeusis is the control of the deleterious aspects of the inflammatory response until such time as the infective or other causal agent is eliminated by other means.” ~Duke Elder, BJO 1951

- Randomized, double-masked, placebo-controlled trial to determine whether there is a benefit to the use of topical corticosteroids.
- Culture (+) bacterial ulcers treated with topical steroids 48 hours after antibiotics
- Primary outcome BSCVA 3 months

Arch Ophthalmol 2012;130:143-150.
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- 500 patients Aravind, UCSF and Dartmouth
- At 3 months, all comers: **no difference** between steroids vs. placebo
  - BSCVA (controlling for enrollment VA) \( (p=0.82) \)
  - Infiltrate/scar size \( (p=0.40) \)
  - Time to re-epithelialization \( (p=0.44) \)
  - Corneal perforation \( (p>0.99) \)

Early treatment

*Early = Steroid/Placebo administered after 2 or 3 days of antibiotic treatment*

<table>
<thead>
<tr>
<th>Early Groups</th>
<th>N</th>
<th>Steroid vs. Placebo (Snellen lines)</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients treated Early</td>
<td>311</td>
<td>1.1-lines</td>
<td>0.01</td>
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Early treatment

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<td>311</td>
<td>1.1-lines</td>
<td>0.01</td>
</tr>
<tr>
<td>Severe Ulcers</td>
<td>85</td>
<td>2.7-lines</td>
<td>0.02</td>
</tr>
<tr>
<td>Moderate Ulcers</td>
<td>165</td>
<td>0.9-lines</td>
<td>0.09</td>
</tr>
<tr>
<td>Mild Ulcers</td>
<td>61</td>
<td>No difference</td>
<td>0.70</td>
</tr>
</tbody>
</table>

Severe Ulcers at 3 months

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>N</th>
<th>Steroid vs. Placebo (Snellen lines)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSCVA CF or worse</td>
<td>117</td>
<td>1.7 lines</td>
<td>0.03</td>
</tr>
<tr>
<td>Compete fill of central 4mm</td>
<td>97</td>
<td>2 lines</td>
<td>0.02</td>
</tr>
<tr>
<td>Depth &gt; 2/3</td>
<td>100</td>
<td>1.5 lines</td>
<td>0.07</td>
</tr>
</tbody>
</table>
The *Nocardia* confounder

Baseline
LogMAR 0.28

3 Months
LogMAR 1.8

12 Months
LogMAR 1.8

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**Nocardia**

3 month primary end point:

- Better vision at presentation (20/45 vs 20/145; p<0.001)
- Similar vision at 3 months (20/25 vs 20/40)
- Translates into less improvement
- Steroids associated with greater scar size at 3 months (p=0.03)

12 month follow up:

- No significant differences between placebo and steroid treated group as a whole
- *Exclude* Nocardia: mean one line improvement at 12 months (p 0.02)
- Larger scar size in Nocardia maintained (p=0.02)
SCUT Lessons

- Taking all comers, no difference between steroids and placebo
  - No increased risk of perforation or complications noted
- Nocardia should not be treated with steroids
  - Larger scar size

However

- Steroids may improve outcomes across the board if Nocardia infections are excluded
- Steroids may improve outcomes in more severe ulcers
- Steroids may improve outcomes with early treatment

Fungal Keratitis

1. Rough textured surface
2. Elevated stuck-on plaque
3. Feathery edges
4. Satellite lesions
5. Epithelium intact over infiltrate
6. Endothelial plaque
7. Ring infiltrate
8. Waxing and waning hypopyon
9. Purulent discharge
10. Pigmented anterior plaque
Fungal Keratitis Treatment

• Which is the best agent for the treatment of filamentous fungal keratitis?
  – Survey of 14 corneal experts in the US
  – “Which is the best agent for treatment of filamentous keratitis: natamycin, voriconazole, no difference?
  – 11 respondents, 10/11 cornea specialists
    • 64% no difference
    • 27% voriconazole better
    • 9% natamycin better

• Double masked, multicenter trial of smear positive filamentous fungal ulcers
• 323 patient enrolled
• Well matched baseline demographics and clinical characteristics

• Natamycin
  • Superior BSCVA at 3 months
• Voriconazole
  • Greater corneal perforation
  • Increased frequency of therapeutic PKP
• Is oral voriconazole beneficial when added to topical antifungals in the treatment of fungal keratitis?
  • Prospective, randomized, multicenter clinical trial
  • 240 patients in India and Nepal
  • “severe” filamentous keratitis (baseline acuity less than 20/400 presumably due to corneal infiltration)
  • Randomized to oral voriconazole vs placebo, in addition to standard topical treatment (200mg BID for 20 days)
  • Outcome: perforation or need for therapeutic PKP within 3 months

• 240 patients enrolled
• No difference in rate of corneal perforation or need for TPK between oral voriconazole vs placebo

• Pre-specified question: is there a difference between species?
• Suggestion that Fusarium might have slightly reduced perforation rate or TPK when treated with oral voriconazole
• Smaller infiltrate and scar size at 3 weeks and 3 months
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• CDC Case #001 of contact lens associated Fusarium keratitis
  
  – Initially treated with valacyclovir
  – Changed to natamycin, amphotericin and voriconazole q1 hour.
  – Increasing density and infiltration followed by resolution and re-epithelialization
  – 20/30 pinhole vision