Marginal Ulcers or Peripheral Ulcerative Keratitis

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W Bruce Jackson
In this interactive module, peripheral ulcerative keratitis will be reviewed. This will be in the context of a diagnostic classification, management algorithm and case presentations.

Learning Objectives

- To better understand the various etiologies of corneal ulcers including Infectious vs. Non-Infectious and Systemic vs Local
- Discuss the approach to diagnosis including dry eye testing, review of systems, cultures and systemic testing
- Review management principles including wound healing, prevention of perforation and addressing the underlying condition
Peripheral Ulcerative Keratitis (PUK)

- Crescent shaped, destructive inflammatory lesion affecting the juxtalimbal corneal tissue
- Often associated with systemic disease
- May signify “vasculitis” and thus, be potentially life-threatening
These are all PUK – How do you manage them?
MARGINAL INFILTRATIVE / ULCERATIVE KERATITIS

Etiology

Sterile
- Systemic Autoimmune/Inflammatory
- Local Toxic

Infectious
- Bacteria and Fungi
- Viruses
- Acanthamoeba
What would you use?

- No therapy
- Antibiotics
- Steroids
- Antifungals
- Antihistamines
- Systemic drugs
TWO CASES TO CONSIDER
What would you do?
KNOW MORE ABOUT...

• History
• The patient
• Previous therapies
What would you do?
MANAGEMENT PRINCIPLES

- Enhance wound healing
- Prevent perforation
- Address the underlying condition
## Etiologic Considerations

<table>
<thead>
<tr>
<th>Local</th>
<th>Systemic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Infectious</td>
<td>Non-Infectious</td>
</tr>
<tr>
<td>Infectious</td>
<td>Infectious</td>
</tr>
</tbody>
</table>
Which is which?

LOCAL
NON-INFECTIONOUS

LOCAL INFECTIONOUS
Which is which?

- SYSTEMIC NON-INFECTIONOUS
- LOCAL INFECTIONOUS
NON INFECTIOUS PERIPHERAL INFILTRATIVE KERATITIS

Microulcerative

Macroulcerative
NON INFECTIOUS PERIPHERAL INFILTRATIVE KERATITIS

Microulcerative

• Punctate marginal keratitis
• Peripheral keratitis associated with blepharitis

Macroulcerative

• Generally manifestation of systemic, immune-mediated disease
• Most common: Rheumatoid arthritis, Wegener’s granulomatosis and polyarteritis nodosa
NON INFECTIOUS PERIPHERAL INFILTRATIVE KERATITIS

Microulcerative

• Punctate marginal keratitis
  – Staphylococci, Streptococci, Haemophilus, hypersensitivity to medications

• Peripheral keratitis associated with blepharitis
  – Catarrhal ulceration
  – Phlyctenulosis
  – Peripheral rosacea keratitis
Are There Any Distinguishing Features?

- Size
- Number
- Location
- Intervening space
- …not really, although:
  - Catarrhal may have intervening space, and be located at the 2, 4, 8 and 10 o’clock positions
<table>
<thead>
<tr>
<th></th>
<th>Infectious</th>
<th>Immunologic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Epithelium</strong></td>
<td>Usually epithelial defect</td>
<td>Usually intact initially</td>
</tr>
<tr>
<td><strong>Discharge</strong></td>
<td>Usually</td>
<td>Unlikely</td>
</tr>
<tr>
<td><strong>Infiltrates</strong></td>
<td>Spread centrally</td>
<td>Spread concentrically</td>
</tr>
<tr>
<td><strong>Hypoppyon</strong></td>
<td>Common</td>
<td>Uncommon</td>
</tr>
</tbody>
</table>
Which Ones Need to Be Worked Up?

- Treat without testing?
- Treat, but testing required?

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<th>LOCAL NON-INFECTIOUS</th>
<th>SYSTEMIC NON-INFECTIOUS</th>
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<td>LOCAL INFECTIOUS</td>
<td>SYSTEMIC INFECTIOUS</td>
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</table>
HERPETIC ULCERS (HSV)

• Avoid treating with topical steroids
CONSIDER THE ROLE OF:

<table>
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<tr>
<th>DRY EYE TESTING</th>
<th>REVIEW OF SYSTEMS</th>
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<tr>
<td>CULTURES</td>
<td>SYSTEMIC TESTING</td>
</tr>
</tbody>
</table>
DRY EYE TESTING

- Dry Eye Questionnaire
- Assessment of lid margins
- Tear film breakup time
- Corneal and conjunctival staining
- Tear osmolarity
- Schirmer test
- Serology: SSA, SSB, Rheumatoid Factor, ANA
CULTURES

• Bacterial
• Viral
• Fungal
• Acanthamoeba
• Chalmydia
• Rule out those conditions associated with peripheral ulcerative keratitis
SYSTEMIC TESTING

- Complete blood count
- Erythrocyte sedimentation rate
- C reactive protein
- Urinalysis
- Chest X-ray
- Renal function tests
- Syphilis, Hepatitis C
SYSTEMIC TESTING

- Rheumatoid factor
- Antinuclear antibodies
- Antineutrophil cytoplasmic antibodies (ANCA)
- Tissue biopsy
  - Lung, kidney
MARGINAL INFILTRATE

- When to culture?
- When to use antibiotics?
- When to add steroids?
ETIOLOGIC CONSIDERATIONS

LOCAL NON-INFECTIONOUS
ETIOLOGIC CONSIDERATIONS

LOCAL NON-INFECTIONOUS

- Catarrhal infiltrates
- Phlyctenulosis
- Acne rosacea
- Psoriasis
- Contact lenses
- Topical anesthetic abuse
- Toxic
- Food allergies
- Mooren’s ulcer (??)
ETIOLOGIC CONSIDERATIONS

LOCAL INFECTIOUS
ETIOLOGIC CONSIDERATIONS

LOCAL INFECTIOUS

- Bacterial
- Viral
- Fungal
- Acanthamoeba
1-2-3 RULE

- One infiltrate
- Larger than 2mm in diameter
- Less than 3mm from the visual axis

ALWAYS CULTURE
ALSO...

- History of contact lens wear or trauma
- Non resolving
- Ring infiltrate

ALWAYS CULTURE

CONSIDER CORNEAL BIOPSY
ETIOLOGIC CONSIDERATIONS

SYSTEMIC INFECTIOUS
ETIOLOGIC CONSIDERATIONS

- Herpes virus
- Chlamydia

SYSTEMIC INFECTIOUS
ETIOLOGIC CONSIDERATIONS

SYSTEMIC NON-INFECTIOUS
ETIOLOGIC CONSIDERATIONS

SYSTEMIC NON-INFECTIONOUS

- Rheumatoid arthritis
- SLE
- Discoid lupus
- Scleroderma
- Relapsing polychondritis
- Crohn’s
- Ulcerative colitis
- Polyarteritis nodosa
- Wegener’s granulomatosis
- Churg-Strauss
- Benign hypergammaglobulinemic purpura
- Temporal arteritis
MANAGEMENT PRINCIPLES

- Enhance wound healing
- Prevent perforation
- Address the underlying condition
ENHANCE WOUND HEALING
ENHANCE WOUND HEALING

- Lid Hygiene
- Antibiotic coverage
- Lubrication: Preservative-free
- Autologous serum drops
PREVENT PERFORATION

- Collagenase or collagenase synthetase inhibitors
  - 1% Medroxyprogesterone
  - 10-20% Acetylcysteine
- Cyclosporine 0.05%
- Doxycycline
- Tissue adhesive, bandage CL, lamellar and tectonic grafts, amniotic membrane transplant
- CAUTION: topical steroids
ADDRESS THE UNDERLYING CONDITION
ADDRESS THE UNDERLYING CONDITION

• Glucocorticoids
  – IV pulse initially
  – Oral

• Systemic immunomodulators
  – Antimetabolites
  – Alkylating agents
  – T cell inhibitors
  – Biologics
ADDRESS THE UNDERLYING CONDITION

• Glucocorticoids
  – IV pulse initially: 1g per day, for 3 consecutive days
  – Oral: 1mg/kg/day, not to exceed 60-80 mg/day
ADDRESS THE UNDERLYING CONDITION

• Systemic immunomodulators
  – Antimetabolites:
    • MTX, AZT, Mycophenolate mofetil, Leflunomide
  – Alkylating agents:
    • Cyclophosphamide
  – T cell inhibitors:
    • Cyclosporin A
  – Biologics:
    • Infliximab, etanercept, rituximab
Back to Our Two Cases to Consider
What would you do?
KNOW MORE ABOUT...

- History
- The patient
- Previous therapies
CASE HISTORY SH

• 62yoM

• Original presentation: conj cyst OD - marsupialization

• MGD = full Lid Hygiene, tea tree oil facewash, Doxycycline

• Possible history of CRVO? Amblyopia?

• 5 mo later: PUK
CASE HISTORY SH
CASE HISTORY SH
CASE HISTORY SH
What would you do?

• Do you think this is Dry Eye/Ocular Surface related?
• Do you think this is a local infection?
• Do you think this is related to a systemic condition?
• Do you think systemic testing is warranted?
CASE HISTORY SH

• 62yoM
• Original presentation: conj cyst OD - marsupialization
• MGD = full Lid Hyg, TTO, Doxy
• Possible history of CRVO? Amblyopia?
• 5 mo later: PUK
• Prednisolone acetate 1% tid – better 3 wks later
• Tests: all negative, except atypical ANCA
CASE HISTORY SH: 3 WEEKS LATER
ONE MONTH LATER…

- Worse again: 20/60
- New lesions superiorly and inferiorly
- What would you do?
MANAGEMENT HISTORY

• Enhance wound healing
  – Lid hygiene
  – Fucidic acid to lids

• Prevent perforation
  – Prednisolone acetate 1%
  – Doxycycline 100mg PO qhs

• Address the underlying condition
  – Systemic testing: Atypical ANCA (+)
  – Referral to Internal Medicine
IMPROVED AND STABLE
IMPROVED AND STABLE
WHAT ABOUT ANCA?

ANCA Testing

New Developments and Clinical Implications

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2Research Unit of Autoimmune Diseases, Dept. of Medicine,
Sheba Medical Center, Tel-Hashomer Israel,
Affiliated to Sackler Faculty of Medicine, Tel-Aviv University, Israel
ANCA

• Antineutrophil cytoplasmic antibodies are specific and sensitive markers for different forms of vasculitides
<table>
<thead>
<tr>
<th>ANCA-Associated diseases</th>
<th>ANCA pattern</th>
<th>Autoantigens</th>
<th>Incidence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wegener's granulomatosis</td>
<td>C</td>
<td>PR-3, BPI</td>
<td>85</td>
</tr>
<tr>
<td>Microscopic polyarteritis (MPA)</td>
<td>C</td>
<td>PR-3, MPO</td>
<td>85</td>
</tr>
<tr>
<td>Churg-Strauss syndrome</td>
<td>C, P</td>
<td>PR-3, MPO, BPI</td>
<td>50</td>
</tr>
<tr>
<td>Classic polyarteritis nodosa</td>
<td>C, P</td>
<td>PR-3, MPO</td>
<td>20</td>
</tr>
<tr>
<td>Renal vasculitis (MPA with renal involvement)</td>
<td>P, X</td>
<td>MPO, elastase, lysosome, lactoferrin, cathepsin G</td>
<td>40</td>
</tr>
<tr>
<td>Rapidly progressive glomerular nephritis</td>
<td>P, X</td>
<td>MPO, elastase, cathepsin G, lysosome, h-lamp-2, lactoferrin</td>
<td>80</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>X</td>
<td>Lactoferrin, BPI, lysosome, cathepsin G, β-glucuronidase</td>
<td>70</td>
</tr>
<tr>
<td>Autoimmune hepatitis</td>
<td>X</td>
<td>Lactoferrin, lysosome, cathepsin G, β-glucuronidase</td>
<td>70</td>
</tr>
<tr>
<td>Primary sclerosing cholangitis</td>
<td>X</td>
<td>Lactoferrin, BPI, lysosome, cathepsin G, β-glucuronidase</td>
<td>70</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>X</td>
<td>Lactoferrin, BPI, lysosome, cathepsin G, β-glucuronidase</td>
<td>30</td>
</tr>
<tr>
<td>SLE</td>
<td>X</td>
<td>Lactoferrin, elastase, cathepsin G</td>
<td>20</td>
</tr>
<tr>
<td>Primary biliary cirrhosis</td>
<td>P, X</td>
<td>MPO, lactoferrin, BPI, lysosome, elastase</td>
<td>40</td>
</tr>
<tr>
<td>Giant cell arteritis</td>
<td>P</td>
<td>MPO</td>
<td>14</td>
</tr>
<tr>
<td>Kawasaki disease</td>
<td>P, C</td>
<td>MPO, PR-3</td>
<td>40-80</td>
</tr>
<tr>
<td>Cutaneous leukocytoclastic angiitis</td>
<td>P</td>
<td>Unknown</td>
<td>?</td>
</tr>
<tr>
<td>Henoch-Schönlein purpura</td>
<td>C</td>
<td>Unknown</td>
<td>79</td>
</tr>
<tr>
<td>HIV infection</td>
<td>X</td>
<td>Lactoferrin, elastase, lysozyme, cathepsin G</td>
<td>50</td>
</tr>
<tr>
<td>Drug-induced glomerulonephritis</td>
<td>P</td>
<td>MPO</td>
<td>100</td>
</tr>
<tr>
<td>Antiglomerular basement membrane disease</td>
<td>P, C</td>
<td>MPO, PR-3</td>
<td>20</td>
</tr>
<tr>
<td>Crescentic nephritis (without immune deposits)</td>
<td>P, C</td>
<td>MPO, PR-3</td>
<td>80</td>
</tr>
<tr>
<td>Rheumatoid arthritis (uncomplicated)</td>
<td>X</td>
<td>Elastase, lactoferrin, cathepsin G, β-glucuronidase</td>
<td>25</td>
</tr>
<tr>
<td>Rheumatoid arthritis (complicated by Felty’s syndrome)</td>
<td>X</td>
<td>Lactoferrin, cathepsin G</td>
<td>100</td>
</tr>
<tr>
<td>Rheumatoid arthritis (complicated by vasculitis)</td>
<td>P</td>
<td>MPO</td>
<td>75</td>
</tr>
<tr>
<td>Drug-induced vasculitis</td>
<td>P, X</td>
<td>MPO, elastase</td>
<td>?</td>
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CASE HISTORY FW

- 51yoF
- Glaucoma on multiple meds
- Chronic red eye OS 1-2 yrs
- Is this toxic? Stopped everything
- Some improvement, but…
- 4-5mo later, worse, gooey, leaky, on Pataday
- Now with PUK
- OD perfectly fine
CASE HISTORY FW: 5MO
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CASE HISTORY FW: 8MO
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What would you do?

- Do you think this is Dry Eye/Ocular Surface related?
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- Do you think systemic testing is warranted?
CASE HISTORY FW

- 51yoF
- Glaucoma on multiple meds
- Chronic red eye OS 1-2 yrs
- Toxic? Stopped everything
- 4-5mo later, worse, gooey, leaky, on Pataday
- PUK
- Cultures:
  - Dx Strep Anginosus, Eikenella corrodens
  - Sensitive to Ciprofloxacin –Improved!
CASE HISTORY FW:
Follow Up –on Ciprofloxacin gtt/ung
CASE HISTORY FW:
Follow Up – on Ciprofloxacin gtt/ung
CASE HISTORY FW:
Follow Up –on Ciprofloxacin gtt/ung
CASE HISTORY FW:
Follow Up – on Ciprofloxacin gtt/ung
BUT... 2 MO LATER

- Worse again!
- Marked inflammation, PUK, discharge, corneal thinning and vascularization
- Extreme photophobia
- NO intraocular inflammation
What would you do?
MANAGEMENT HISTORY

• Enhance wound healing
  – Lid hygiene
  – Continue with topical ciprofloxacin

• Prevent perforation
  – IV Methylprednisolone 1g daily for 3 days
  – Continue with oral Prednisone

• Address the underlying condition
  – Referral to Internal Medicine: IMT

• Improved at last visit
LATEST FOLLOW-UP
LATEST FOLLOW-UP

- Well controlled on oral Prednisone and Methotrexate
ETIOLOGIC CONSIDERATIONS

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## Diagnostic Considerations:

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<tr>
<td>ADDRESS UNDERLYING CONDITION</td>
<td>REFER AS NEEDED</td>
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