Corneal melts, perforations and worse: autoimmune diseases of the cornea

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How do you manage this?
Aims

– Differential diagnosis
– Pathogenesis
– Work-up
– Management
1. Systematic categorization of corneal melts

Easiest way to think about it is to construct a 2x2 grid:

<table>
<thead>
<tr>
<th>Local</th>
<th>Infective</th>
<th>Non-infective</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Local/Infective

- Microbial keratitis
  - Contact lenses
- HSV/VZV
  - Neurotrophic cornea
- Chlamydia
- Gonorrhoea
Local/Non-Infected

- Terrien's
- Pellucid
- Mooren's
- Rosacea
- Marginal keratitis
- VKC
- Exposure
- Drugs
  - NSAIDS, steroids, LA
- Trauma
Systemic/Infecctive

- TB
- Syphilis
- Leprosy
- HCV
- Lyme
- Onchocerciasis
Systemic/Non-Infective

- Connective Tissue Diseases
  - Rheumatoid arthritis
  - GPA/WG
  - SLE
  - Sjogrens
  - PAN
  - Relapsing polychondritis
  - Scleroderma
- Sarcoid
- Bechet’s
- IBD

Rheumatoid

With PED (use PED treatment algorithms)

Rheumatoid keratolysis – no ED

GPA/WG
<table>
<thead>
<tr>
<th>Local</th>
<th>Infective</th>
<th>Non-Infective</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Microbial keratitis</td>
<td>Terrien's</td>
</tr>
<tr>
<td></td>
<td>HSV/VZV (neurotrophic)</td>
<td>Pellucid</td>
</tr>
<tr>
<td></td>
<td>Chlamydia/gonorrhoea</td>
<td>Mooren's</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rosacea</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Marginal keratitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VKC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Exposure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Drugs (NSAIDS, steroids, LA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Trauma</td>
</tr>
<tr>
<td>Systemic</td>
<td>TB</td>
<td>Connective tissue diseases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Rheumatoid, GPA/WG, SLE, Sjogren's, PAN, Relapsing polychondritis, Scleroderma)</td>
</tr>
<tr>
<td></td>
<td>Syphilis</td>
<td>Sarcoid</td>
</tr>
<tr>
<td></td>
<td>Leprosy</td>
<td>Behcet</td>
</tr>
<tr>
<td></td>
<td>HCV</td>
<td>IBD</td>
</tr>
<tr>
<td></td>
<td>Lyme disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Onchocerciasis</td>
<td></td>
</tr>
</tbody>
</table>
2. Pathogenesis of corneal melts

- Peripheral HSV & bacterial infection
- Antibodies to corneal stroma
- Immune complexes in vasculitis

**Infection**
- Release of collagenases, proteases, MMP1
- Circulating immune complexes trapped in limbal vessels

**Disordered immunity**
- Auto-antibodies
- Activation of complement
- Chemotaxis of inflammatory cells (neutrophils/macrophages)
- Complexes in peripheral cornea

**Ocular surface disease**
- Dry eye
- Antibodies to bacteria
- Release of collagenases, proteases, MMP1
3. Clinical and laboratory work-up

- **AIM**: decide if systemic or local, infective or non-infective.
- **History**: 
  - CL wear, trauma (infection); previous HSV/VZV; known CTD/IBD; previous ocular surgery
- **Examination**: 
  - Scars of HSV/VZV; rosacea/SLE/GPA facial features; RA arthropathies; lid closure (exposure)
  - **Slit lamp**:
    - Ulcer (measure), infiltrate, AC inflammation, scleritis (**how bad is it**)
    - Dry eye (tear lake, PEEs), HSV scars, blepharitis (**what caused it**)
    - Dilated fundus exam (CWS, vitritis, SRF etc. c/ w posterior scleritis)
  - Examine both eyes!
Clinical and laboratory work-up

- Laboratory investigations:
  - Corneal scrape, incl HSV swab for PCR

- Systemic vasculitis screen
  - FBC, EUC, LFT, ESR, CRP
  - RF, anti-CCP Abs, ANCA, ANA, ENA, ACE
  - VDRL, TB-QG
  - CXR
  - Urine for blood and casts
4. Immediate management

- Depends on suspected aetiology

- **Local/Infective:**
  - Ofloxacin q1h d/n
  - Valtrex 500g tds (if suspect HSV)

- **Local/Non-infective:**
  - Ocular surface disease:
    - Ensure full lid closure
    - Reduce toxicity
    - Lubricate
    - Consider punctal occlusion (I wait until inflammation settles)
  - Local inflammatory disease (Marginal, mild Mooren’s or Terrien’s)
    - Topical steroids/cyclosporin

- **Systemic/Infective:**
  - treat underlying disease
Systemic/Non-infective (Vasculitis) - everyone

- Admit and tackle all three arms of pathogenesis
- Control of acute exacerbation:
  - Prednisolone 1mg/kg/day (can often get away with just 50mg/day)
  - Cyclosporin 5-7.5mg/kg (under 60 yrs)
  - Cyclophosphamide 1-2mg/kg (over 60 yrs; cumulative dose <20g safe)
  - +/- pulsed methylprednisolone
  - +/- rituximab
- No role for topical steroids
- Optimise ocular surface (lubricants, lid closure etc.)
- Decrease collagenase activity
  - Doxycycline 100mg/d
- Treat/prevent bacterial superinfection
  - Ofloxacin QID to q1h depending on clinical suspicion
## Rituximab for PUK

<table>
<thead>
<tr>
<th>Study</th>
<th>No. of pts</th>
<th>Ophth Disease</th>
<th>Systemic Disease</th>
<th>Previous Rx (+ Pred)</th>
<th>Number Rituximab Infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albert et al</td>
<td>2</td>
<td>PUK</td>
<td>RA</td>
<td>CSA/Inflix/Adalim</td>
<td>1 (but recurred at 8/12)</td>
</tr>
<tr>
<td>Huerva et al</td>
<td>1</td>
<td>PUK</td>
<td>Wegeners</td>
<td>MTX</td>
<td>2</td>
</tr>
<tr>
<td>Friedlin et al</td>
<td>1</td>
<td>PUK &amp; Scleritis</td>
<td>Wegeners</td>
<td>Cyclop</td>
<td>2</td>
</tr>
<tr>
<td>Cheung et al</td>
<td>1</td>
<td>Scleritis</td>
<td>Wegeners</td>
<td>MMF/Cyclop</td>
<td>2</td>
</tr>
<tr>
<td>Onal et al</td>
<td>1</td>
<td>Nec. Scleritis</td>
<td>Wegeners</td>
<td>Aza/Cyclop</td>
<td>2</td>
</tr>
<tr>
<td>Ahmadi-Simab et al</td>
<td>1</td>
<td>Scleritis</td>
<td>Sjogrens</td>
<td>MTX/CSA/Cyclop/Inflix</td>
<td>2</td>
</tr>
</tbody>
</table>


Courtesy R Stewart
Systemic/Non-infective (Vasculitis) – special cases

- **Topical protease inhibitors:**
  - Acetylcysteine
  - Aprotinin (Trasylol; no longer available for systemic use – increased risk of death when used for control of bleeding during heart surgery)

- **Therapeutic contact lenses:**
  - Occasionally useful

- **Maintenance therapy:**
  - Low dose prednisolone
  - Cyclosporin 1-5mg/kg (under 60 yrs)
  - Methotrexate (once finished cyclophosphamide) in older patients
Acute perforation - small

- Cyanoacrylate glue – buys time in small perforations
Acute perforation – not small

- Lamellar corneal patch grafts
- Almost eliminates the risk of rejection
- Reduces the risk of leak in the even of re-melt or dehiscence
- ? Replacement of conjunctiva post tectonic group
  - Yes
    - Re-establish epithelium
  - No
    - Not to re-establish blood supply (with immune complexes, cells, cytokines)
    - Conjunctiva = major reservoir of inflammatory cells, cytokines

Corneal patch technique – “copy and fix”
Special case – Mooren’s ulcers

- Conjunctival resection
- Superficial keratectomy
  - May be effective in some cases by removing antigen from the superficial cornea
Summary

- Peripheral melts occur in a heterogeneous group of ocular and systemic disorders
- Important to differentiate what the mechanism is
- Successful management often requires immunosuppression and is multi-disciplinary