Scleral and Corneal Inflammatory Disorders

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Vijayawada
India
Poll question

Please indicate your position?

a. Ophthalmologist in practice
b. Resident/Fellow
c. Optometry
d. Ophthalmic Nurse/paramedic
Poll question

Do you have rheumatology support services for your practice?

a. Yes
b. No
c. Limited
d. Administer systemic immunosuppressants under your own care
Why scleritis is important?

» Scleritis is serious vision threatening inflammatory eye disease

» Incidence - 3.4 per 100,000 person-years. Honik et al

» Associated systemic disease is present in 40-57%

• Necrotizing scleritis with RA:
  • 27% mortality in 5 years Watson et al
  • 45% mortality in 3 years Mc Gavin et al
Episcleritis

- Diffuse
- Nodular
Episcleritis - Clinical features

- Association with systemic diseases
- Transient mild pain or ocular discomfort
- Raised nodular or diffuse elevated mass
- Blanches with 10% phenylephrine
Episcleritis Systemic associations

- **Autoimmune diseases**- RA, IBD, SLE, myositis, RP, erythema nodosum, GPA, Cogan syndrome
- **Bisphosphonate Drug reactions** (pamidronate, alendronate, risedronate)
- **Miscellaneous** Atopy, rosacea, gout, herpes zoster, herpes simplex, syphilis, psoriasis,
Episcleritis - Treatment

• Transient, self limiting
• Treatment with lubricants and NSAIDs
• Short course of topical corticosteroids in non-responsive cases
When?

Which of the following is least commonly associated with Episcleritis?

a. Decreased vision
b. Uveitis
c. Peripheral ulcerative keratitis
d. Systemic associations
Episcleritis - case study

- 45 F
- RE Recurrent attacks of redness - 4-5 years
- Mantoux strongly positive
- Raised ESR
- RA factor negative
- CBC WNL
Episcleritis
Episcleritis

• Management-
• Lubricants
• Oral NSAIDs
• Physician consult for Koch’s
Scleritis - Classification

- Anterior
  - Diffuse
  - Nodular
  - Necrotizing
    - With inflammation
    - Without Inflammation

- Posterior

Watson and Hayreh BJO 1976
Poll question

How to clinically detect scleritis?

a. Diffuse illumination
b. Yellow light
c. Natural light
d. Green light
Scleritis - Clinical features

- Deep boring nocturnal pain
- Violaceous hue
- Examine under natural light
- Capillary drop out
- Scleral thinning and uveal show
- Congestion in the deep episcleral plexus
Scleritis with peripheral ulcerative keratitis

» Increased chances of associated systemic disease association

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>GPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scleritis Alone</td>
<td>11%</td>
<td>3%</td>
</tr>
<tr>
<td>Scleritis with PUK</td>
<td>38.3%</td>
<td>29.2%</td>
</tr>
</tbody>
</table>
Case Study

34 Years/Female

Diagnosed with BE Scleritis

Laboratory Investigations - negative

Rheumatologist consult-

Oral Azathioprine

Oral Prednisolone
Clinical Pearls:

1) Initial investigations for all scleritis patient may be RA factor, C-ANCA, P-ANCA.

2) Mantoux test may be advised in later visits before starting immunosuppressants.
Case Study

41/F
RE watering pain and redness 3 months
LE -WNL
RE Diffuse Scleritis, C-ANCA and RA positive
Advised Rheumatologist consultation

Started on Tab Azathioprine 50 mg and IVMP given

Rheumatologist pulsed IV Cyclophosphamide 4 cycles
Could not initiated because of low HB%
Clinical course:

Patient stopped oral corticosteroids

Presented with pain in RE

Oral and topical steroids started

Lab investigation CBC, Hb% and LFT and followed by oral Methotrexate
Clinical Pearls

1. All scleritis patients eyelid elevation and examination of sclera for nodules is important.

2. Red free light to look for capillary drop out

3. CBC, LFT, RFT, Mantoux and R.B.S should be done before starting immunosuppressants.

4. Mantoux positivity at the start of treatment need not necessarily mean Koch’s focus in high endemic areas
Persistent or recurrent episcleritis

All scleritis versus bilateral scleritis

Unilateral necrotising

Suspected infection
Laboratory Investigations

• All scleritis need to be investigated
• Diffuse anterior, unilateral scleritis: commonest
• Necrotising scleritis: may have seropositivity for ANCA, ANA, RA

• Interpretation:
  • Raised ESR, CRP
  • S. ANCA levels
  • Other tests: Anti CCCP
  • HLAs
  • Positive Mantoux
  • In case of viral suspicion
Laboratory Investigations

- **Management:**
  - CBC, RBS,
  - Mantoux,
  - S. HIV, S. VDRL

- **Etiological:**
  - RA, ANA
  - C & P ANCA,
  - Ds DNA, Anti-Rho, Anti-LA

- **Local:**
  - Ant. FA
  - UBM, B-scan
  - Scrapings
  - Impression cyto
  - Biopsy
Scleritis Therapy

1. NSAIDS
2. SYSTEMIC STEROIDS
   Therapeutic failure
   Remission Maintain on NSAIDS
3. IMMUNOSUPRESSIVES
   Methotrexate
   Cyclophosphamide
   Cyclosporine
   Azathioprine
4. Biologics
   Infliximab
   Eternecept
   Rituximab

Therapeutic failure
An Analysis of Therapeutic Decision for Scleritis

Ophthalmology 1993;100:1372–1376
Maite Sainz de la Maza, MD, PhD, Nada S. Jabbur, MD, C. Stephen Foster, MD, FACS

<table>
<thead>
<tr>
<th></th>
<th>Diffuse</th>
<th>Nodular</th>
<th>Necrotizing</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>27</td>
<td>11</td>
<td>4</td>
<td>42</td>
</tr>
<tr>
<td>SAIDs</td>
<td>19</td>
<td>18</td>
<td>11</td>
<td>48</td>
</tr>
<tr>
<td>IMM</td>
<td>15</td>
<td>4</td>
<td>23</td>
<td>42</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>61</strong></td>
<td><strong>33</strong></td>
<td><strong>38</strong></td>
<td><strong>132</strong></td>
</tr>
</tbody>
</table>

NSAIDs = systemic nonsteroidal anti-inflammatory drugs; SAIDs = systemic steroidal anti-inflammatory drugs with or without NSAIDs; IMM = systemic immunosuppressive drugs with or without SAIDs.
## An Analysis of Therapeutic Decision for Scleritis

*Ophthalmology 1993;100:1372–1376*

Maite Sainz de la Maza, MD, PhD, Nada S. Jabbour, MD, C. Stephen Foster, MD, FACS

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Diffuse</th>
<th>Nodular</th>
<th>Necrotizing</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs</td>
<td>2 (7%)</td>
<td>1 (9%)</td>
<td>4 (100%)</td>
<td>7 (17%)</td>
</tr>
<tr>
<td>SAIDs</td>
<td>3 (16%)</td>
<td>5 (28%)</td>
<td>10 (91%)</td>
<td>18 (37.5%)</td>
</tr>
<tr>
<td>IMM</td>
<td>4 (27%)</td>
<td>1 (25%)</td>
<td>6 (26%)</td>
<td>11 (26%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>9 (15%)</td>
<td>7 (21%)</td>
<td>20 (53%)</td>
<td>36 (27%)</td>
</tr>
</tbody>
</table>

NSAIDs = systemic nonsteroidal anti-inflammatory drugs; SAIDs = systemic steroidal anti-inflammatory drugs with or without NSAIDs; IMM = systemic immunosuppressive drugs with or without SAIDs.
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Table 3. Second-line Therapy for Scleritis

<table>
<thead>
<tr>
<th>Category</th>
<th>No.</th>
<th>Therapeutic Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAIDs → SAIDs</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>NSAIDs → IMM</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>SAIDs → IMM</td>
<td>18</td>
<td>6</td>
</tr>
<tr>
<td>IMM → IMM</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>13 (10%)</td>
</tr>
</tbody>
</table>

NSAIDs = systemic nonsteroidal anti-inflammatory drugs; SAIDs = systemic steroidal anti-inflammatory drugs with or without NSAIDs; IMM = systemic immunosuppressive drugs with or without SAIDs.
## An update on the cause and treatment of scleritis

Aleksandra Rachitskaya, Efrem D. Mandelcorn and Thomas A. Albini

### Current Opinion in Ophthalmology 2010,

21:463–467

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**Table 1** Assembled noncomparative data derived from multiple retrospective series in the Systemic Immunosuppressive Therapy for Eye Diseases cohort study

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of scleritis patients</th>
<th>Treatment success within 6 months, %</th>
<th>Treatment success within 12 months, %</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>≤10 mg prednisone/day</td>
<td>≤5 mg prednisone/day</td>
<td>No systemic steroids</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>56</td>
<td>37.3</td>
<td>26.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>16</td>
<td>22.2</td>
<td>18.2</td>
<td>0.0</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>33</td>
<td>25.5</td>
<td>20.5</td>
<td>7.1</td>
</tr>
<tr>
<td>Cyclosporine A</td>
<td>15</td>
<td>52.8</td>
<td>40.8</td>
<td>16.7</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>48</td>
<td>30.2</td>
<td>17.9</td>
<td>0.0</td>
</tr>
</tbody>
</table>

GI, gastrointestinal; IOP, intraocular pressure. Reproduced from [8, 9*, 13*].
Scleritis with SLE

• Case study
• 53/F
• LE Recurrent attacks of redness- 4 years
• ANA and Anti SM Positive
• Raised ESR
• RA factor positive
Scleritis with SLE

Presentation & Progression
Scleritis with SLE

- Oral steroids
- IV Cyclophosphamide
- Oral HCQ, Azathioprine
- Systemic tests CBC/LFT/Blood sugar are WNL
- Raised ESR
Scleritis with cataract

Case Study

- 65 F
- LE redness - 2 months
- Labs negative
- CBC WNL
Presentation
Post treatment of scleritis
Management

- Oral corticosteroids
- Methotrexate maintenance dose
- Planned for LE Phaco + Foldable
- Disease quiescent with adequate visual rehabilitation- BCVA 20/30
Infectious vs Non - infectious

- Symptomatic
- Pus pointing
- Sometimes concomitant involvement of adjacent area
- Cellularity and infiltrate
- Anterior chamber reaction/Hypopyon
Unusual scleritis: masquerade
Peripheral ulcerative keratitis

- Crescent-shaped stromal inflammation
- Involving juxtalimbal cornea
- Overlying epithelial defect
- Progressive loss of the corneal stroma
- Adjacent conjunctival, episcleral and scleral inflammation
Poll question

PUK with scleritis is most commonly seen in which condition?

a. Rheumatoid arthritis
b. Granulomatosis with polyangitis
c. SLE
d. PAN
• **Case Study**

• 50 year, Female

• C/o pain watering and redness

• Diagnosed as RE Peripheral ulcerative keratitis

• Investigations – c – ANCA was positive

• Advised rheumatology opinion
• Rheumatology opinion- lack of access
• Started on oral steroids with Tab Azathioprine BD
• Continued deterioration
• RE Scleral patch graft was planned
Peripheral ulcerative keratitis

- Case Study
- 36 F
- RE redness - 5 days
- LE Loss of vision 2 years ago, anterior staphyloma
- RS S/P TA BCL elsewhere ~ 3 months ago
- Labs - p ANCA weakly positive
- Rest WNL
- Oral corticosteroids and Azathioprine
MOOREN’S ULCER

- Pain disproportionate to lesion
- Overhanging edge
- Vascularization upto bed of cornea
- No associated scleritis
- No associated systemic disease
Terrien’s Marginal degeneration

- Superior
- Fine yellow–white stromal opacities
- Peripheral gutter separated from the limbus by a clear zone
- Band of lipid - at the central edge
<table>
<thead>
<tr>
<th>Non–infectious</th>
<th>Infectious</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Systemic</strong></td>
<td><strong>Systemic</strong></td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Herpes simplex keratitis</td>
</tr>
<tr>
<td>Wegener’s granulomatosis</td>
<td>Varicella-zoster keratitis</td>
</tr>
<tr>
<td>Relapsing polychondritis</td>
<td>Bacterial keratitis,</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>Fungal keratitis,</td>
</tr>
<tr>
<td>Polyarteritis nodosa and variants</td>
<td>Acanthamoeba species</td>
</tr>
<tr>
<td>Sjögren’s syndrome</td>
<td></td>
</tr>
<tr>
<td>Dermatological disorders</td>
<td></td>
</tr>
<tr>
<td>Inflammatory Bowel disease</td>
<td></td>
</tr>
<tr>
<td><strong>Local</strong></td>
<td><strong>Local</strong></td>
</tr>
<tr>
<td>Mooren ulcer</td>
<td><em>Shigella</em> species</td>
</tr>
<tr>
<td>Marginal keratitis</td>
<td>Tuberculosis</td>
</tr>
<tr>
<td>blepharitis</td>
<td>Syphilis</td>
</tr>
<tr>
<td>contact lens use</td>
<td>Hepatitis</td>
</tr>
<tr>
<td>chemical injury to the eyes</td>
<td>HIV</td>
</tr>
<tr>
<td>Trauma</td>
<td>Gonococcus</td>
</tr>
<tr>
<td>neurotrophic and neuroparalytic causes Terrien marginal degeneration</td>
<td><em>Salmonella</em> species</td>
</tr>
<tr>
<td>Pellucid marginal degeneration</td>
<td>Bacillary dysentery</td>
</tr>
</tbody>
</table>

*Yagci et al. 2012*
Mooren’s Ulcer

- Painful, progressive, chronic ulcerative keratitis
- Begins peripherally and progresses circumferentially and centrally
- Adjoining sclera and the underlying Descemet membrane are uninvolved
<table>
<thead>
<tr>
<th>Type</th>
<th>Clinical picture</th>
<th>Anterior FA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral Mooren’s ulceration</td>
<td>Painful progressive corneal ulceration elderly patients</td>
<td>Non-perfusion of the superficial vascular plexus of the anterior segment</td>
</tr>
<tr>
<td>Bilateral aggressive Mooren’s ulceration</td>
<td>Young patients, progressing circumferentially then centrally.</td>
<td>Vascular leakage and new vessel formation into base of ulcer</td>
</tr>
<tr>
<td>Bilateral indolent Mooren’s ulceration</td>
<td>Middle-aged patients presenting with progressive peripheral corneal guttering in both eyes, with little inflammatory response</td>
<td>No change from normal vascular architecture</td>
</tr>
</tbody>
</table>
Laboratory tests

- Complete blood counts
- Erythrocyte sedimentation rate
- Rheumatoid factor
- Antinuclear antibody
- Antineutrophil cytoplasmic antibodies
- X-ray examination of chest and sacroiliac joint
- Liver enzymes
- Fluorescent treponemal antibody absorption test
- Hepatitis C antigen
- Urine and stool examination
Conjunctival resection Glue + BCL

Conjunctival Resection
(2mm from each end 4mm from limbus)

Dr Aravind Roy
Clinical Pearls

- Early Mooren’s: role of conjunctival resection and TA+BCL
- Role of systemic immuno suppression
- Advanced Mooren's
- Patch graft
Surgical management of Mooren’s Ulcer

- Conjunctival resection + Glue + BCL
- Lamellar keratoplasty
- Lamellar keratectomy
- Keratoepithelioplasty
- Tectonic grafts - patch graft/penetrating graft
- Cataract surgery
Poll question

What is the cause for decreased vision in Mooren’s ulcer?

a. Iritis
b. Irregular astigmatism
c. Corneal scar
d. All of the above
Step ladder approach for treatment of Mooren’s Ulcer

<table>
<thead>
<tr>
<th>Features</th>
<th>Immunosuppression</th>
<th>Follow-up schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unilateral cases, less than 2 quadrants of peripheral corneal involvement, less than 50% stromal loss</td>
<td>Topical steroids</td>
<td>Every 3 days follow-up till healing in acute phase; 3-monthly thereafter for 6 months; As and when thereafter</td>
</tr>
<tr>
<td>Bilateral cases, more than 2 quadrants of peripheral corneal involvement, more than 50% stromal loss</td>
<td>Oral steroids</td>
<td>Alternate day follow-up in acute phase till healing; monthly follow-up for 6 months; 3-monthly thereafter</td>
</tr>
<tr>
<td>Steroid intolerance, young patients &lt;40 years, bilateral disease, single eyed</td>
<td>Oral methotrexate</td>
<td>Daily follow-up in acute phase till healing; monthly follow-up thereafter for 6 months; 3-monthly thereafter</td>
</tr>
<tr>
<td>Bilateral, single eyed, more than 3 quadrants of peripheral corneal involvement, &gt;50% stromal loss, impending perforation</td>
<td>IVMP</td>
<td>In patient care if possible in conjunction with an internist; daily monitoring for healing in acute phase; 1–2 weekly follow-up till 3 months; monthly follow-up till 6 months; 3-monthly thereafter</td>
</tr>
<tr>
<td>Bilateral, single eyed, more than 3 quadrants of peripheral corneal involvement, perforation, early postoperative period after keratoplasty</td>
<td>IVMP+IV cyclophosphamide</td>
<td>In patient care if possible in conjunction with an internist; daily monitoring for healing in acute phase; 1–2 weekly follow-up till 3 months; monthly follow-up till 6 months; 3-monthly thereafter</td>
</tr>
</tbody>
</table>

IV, intravenous; IVMP, intravenous methyl prednisolone.

Step ladder approach for treatment of Mooren’s Ulcer

<table>
<thead>
<tr>
<th>Immunosuppression</th>
<th>Number of cases receiving the therapy</th>
<th>Overall final success rate*</th>
<th>Keratoplasty needed†</th>
<th>Time to success</th>
<th>Duration of follow-up</th>
<th>Number of recurrences during the therapy</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topical steroids</td>
<td>145</td>
<td>76% (47)</td>
<td>3</td>
<td>34.33 ± 52.23 (1–432)</td>
<td>51.88 ± 81.90 (1–521)</td>
<td>41</td>
<td>Infection-5</td>
</tr>
<tr>
<td>Topical steroids alone</td>
<td>62</td>
<td>76% (47)</td>
<td>3</td>
<td>36.28±55.31 (1–432)</td>
<td>51.88±86.72 (1–521)</td>
<td>26</td>
<td>Infection-3</td>
</tr>
<tr>
<td>Oral steroids</td>
<td>66</td>
<td>86% (57)</td>
<td>12</td>
<td>28.68±38.21 (12–158)</td>
<td>50.38±57.35 (1–217)</td>
<td>11</td>
<td>Infection-3</td>
</tr>
<tr>
<td>Oral methotrexate</td>
<td>14</td>
<td>78.5% (11)</td>
<td>3</td>
<td>32.1±57.33 (3–131)</td>
<td>47.5±70.86 (1–260)</td>
<td>5</td>
<td>Infection-3</td>
</tr>
<tr>
<td>IVMP</td>
<td>7</td>
<td>71.4% (5)</td>
<td>2</td>
<td>24.31±28.33 (2–54)</td>
<td>38.2±32.29 (2–78)</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>IVMP+IV</td>
<td>15</td>
<td>73.3% (11)</td>
<td>3</td>
<td>33.33±34.2 (5–100)</td>
<td>46.61±64.78 (1–217)</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

*Success defined as resolution of disease.
†Indicator of worsening of disease leading to perforation or severe thinning threatening the tectonic stability of cornea.
IV, intravenous; IVMP, intravenous methyl prednisolone.

Rituximab - a new therapeutic option in refractory Mooren’s ulcers

Management of severe and refractory Mooren’s ulcers with rituximab

Table 1 Patients’ characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30</td>
<td>45</td>
<td>49</td>
<td>39</td>
<td>36</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td>Female</td>
<td>Male</td>
<td>Y</td>
</tr>
<tr>
<td>Origin</td>
<td>African</td>
<td>African</td>
<td>Caucasian</td>
<td>African</td>
<td>N</td>
</tr>
<tr>
<td>Affected eye</td>
<td>RE</td>
<td>RE</td>
<td>RE</td>
<td>RE</td>
<td>RE</td>
</tr>
<tr>
<td>Corneal perforation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cyclosporamine treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total follow-up after the first visit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Period before between the first and the second visit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to withdrawal of systemic therapy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCVA at the end of the follow-up (Snellen)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RE</td>
<td>20/25*</td>
<td>20/400</td>
<td>20/400</td>
<td>20/60</td>
<td>20/60</td>
</tr>
<tr>
<td>LE</td>
<td>20/32*</td>
<td>20/32</td>
<td>20/32</td>
<td>20/32</td>
<td>20/32</td>
</tr>
</tbody>
</table>

*With scleral lens.

BCVA, best-corrected visual acuity; BE, bilateral; LE, left eye; N, no; RE, right eye; Y, yes.

Conclusions

1. Surface inflammations are chronic ocular disorders
2. Sight threatening and life threatening
3. Ocular manifestations may be the first clinical sign
4. Multidisciplinary approach to management
Acknowledgements

Somasheila I Murthy (Mentor) Dr Sushank Bhalerao (colleague) and fellows- Phaneendra, Priyanka, Samruddhi
Thank you!

L V Prasad Eye Institute
www.lvpei.org

Excellence  •  Equity  •  Efficiency