Graft-versus-Host Disease: Eyes

Celebrating a Second Chance at Life
Survivorship Symposium

April 29 – May 5, 2023

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FINANCIAL DISCLOSURES

No relevant disclosures
INCIDENCE

- Incidence of ocular GVHD varies widely among studies (10-90%)  
- More recent study showed 40-60%  
- If patients already have other chronic graft-versus-host disease, 60-90% will have ocular GVHD  
  - Only 9% acute ocular GVHD  
- Ocular GVHD may be the first affected organ  
  - 22% of new onset dry eye patients after HSCT presented with dry eye and conjunctival inflammation without features of systemic GVHD


CLINICAL PRESENTATION: OCULAR SURFACE

- Lacrimal gland (tear-producing gland)  
- Lacrimal punctum  
- Canaliculi (tear ducts)  
- Nasolacrimal duct  
- Lacrimal sac
CLINICAL PRESENTATION: All layers of the eye

- **Eyelids**: Meibomian gland dysfunction, spontaneous punctal occlusion, cicatricial entropion or ectropion
- **Conjunctiva**: conjunctivitis, membranous or pseudomembranous
- **Cornea**: filamentary keratitis, epithelial defects, descemetocele, perforation
- **Lacrimal gland dysfunction**
- **Uvea**: uveitis, posterior synechiae

BURDEN OF DISEASE

- Impact of **severe** dry eye on a patient’s life:
- Comparable to moderate to severe chest pain
- For the **most severe** dry eye cases:
- Thought to be worse than a disabling hip fracture
EXAMINATION OF THE PATIENT

DRY EYE TESTING
ACUTE GVHD STAGING

The Eye in Bone Marrow Transplantation
III. Conjunctival Graft-vs-Host Disease

Table 4.—Proposed Clinical Staging of Conjunctival GVHD

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Conjunctival hyperemia</td>
</tr>
<tr>
<td>2</td>
<td>Conjunctival hyperemia with chemotic response or serosanguineous exudate</td>
</tr>
<tr>
<td>3</td>
<td>Pseudomembranous conjunctivitis</td>
</tr>
<tr>
<td>4</td>
<td>Pseudomembranous conjunctivitis plus corneal epithelial slough</td>
</tr>
</tbody>
</table>

*GVHD indicates graft-vs-host disease.*

CHRONIC GVHD STAGING

National Institutes of Health Consensus Development Project on Criteria for Clinical Trials in Chronic Graft-versus-Host Disease: I. The 2014 Diagnosis and Staging Working Group Report

<table>
<thead>
<tr>
<th>Eyes</th>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keratoconjunctivitis sicca (KCS) confirmed by opthalmologist: Yes</td>
<td>No symptoms</td>
<td>Mild dry eye symptoms not affecting ADL</td>
<td>Moderate dry eye symptoms partially affecting ADL</td>
<td>Severe dry eye symptoms significantly affecting ADL (special eyewear to relieve pain)</td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
<td></td>
<td>OR unable to work because of ocular symptoms</td>
</tr>
<tr>
<td>Not examined</td>
<td></td>
<td></td>
<td></td>
<td>OR loss of vision due to KCS</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>WITHOUT new vision impairment due to KCS</td>
</tr>
</tbody>
</table>

BMT infoNet.org
CHRONIC GVHD CONSENSUS: BACKGROUND

- International chronic ocular graft-vs-host disease consensus group held four working meetings in 2013
- Scored different variables to assign patients to three diagnostic categories: No, probable, and definite GVHD
- In 2022, there was a multicenter prospective validation study compared to NIH diagnostic criteria from 2014
- Good sensitivity, specificity, predictive value and correlation between the two studies

CHRONIC GVHD CONSENSUS: GRADING

<table>
<thead>
<tr>
<th>CORNEAL FLUORESCEIN STAINING</th>
<th>CONJUNCTIVAL INJECTION SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0</td>
<td>Grade 0</td>
</tr>
<tr>
<td>Grade 1</td>
<td>Grade 1</td>
</tr>
<tr>
<td>Grade 2</td>
<td>Grade 2</td>
</tr>
<tr>
<td>Grade 3</td>
<td>Grade 3</td>
</tr>
</tbody>
</table>

Scientific Reports May 2013
The Ocular Surface 2022
### CHRONIC GVHD CONSENSUS: QUESTIONNAIRE

**OSDI (Ocular Surface Disease Index)**

<table>
<thead>
<tr>
<th>Patient name:</th>
<th>Date of birth</th>
<th>Patient ID:</th>
</tr>
</thead>
</table>

**Have you experienced any of the following during the last week?**

- 1. Eyes that are sensitive to light?  
- 2. Eyes that feel gritty?  
- 3. Painful or sore eyes?  
- 4. Blurred vision?  
- 5. Poor vision?  

**Have you problems with your eyes limited your performance any of the following during the last week?**

- 6. Reading?  
- 7. Driving at night?  
- 8. Working with a computer or other machine (e.g., ATM)?  
- 9. Watching TV?  

**Have your eyes felt uncomfortable in any of the following situations during last week?**

- 10. Worn contact lenses?  
- 11. Places or areas with low humidity (e.g., dry room)?  
- 12. Areas that are air conditioned?  

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**CHRONIC GVHD CONSENSUS: SCALE**


**Table 1**: Severity scale in chronic ocular GVHD

<table>
<thead>
<tr>
<th>Severity scores</th>
<th>Schirmer’s test (mm)</th>
<th>CFS (points)</th>
<th>OSDI (points)</th>
<th>Conj. (points)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>&gt;15</td>
<td>&lt;13</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>1</td>
<td>11-15</td>
<td>13-22</td>
<td>Mild/Moderate</td>
<td>Conj.</td>
</tr>
<tr>
<td>2</td>
<td>6-10</td>
<td>2-3</td>
<td>23-32</td>
<td>Severe</td>
</tr>
<tr>
<td>3</td>
<td>≤5</td>
<td>≤4</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

**Table 2**: Diagnosis of chronic ocular GVHD

<table>
<thead>
<tr>
<th>Systemic GVHD(-)</th>
<th>0-5</th>
<th>6-7</th>
<th>≥8</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0-5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>4-5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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**Scientific Reports May 2013**
TEAR COMPOSITION

TREATMENT GOALS

• Ocular management:
  • First try organ specific treatments
  • Instead of just increasing systemic immunosuppression

• Three ocular goals:
  • Lubrication of the ocular surface
  • Control evaporation
  • Decrease ocular surface inflammation
### TREATMENTS

#### Lubrication
- Artificial Tears, gels, ointments
- Moisture Goggles
- Punctal occlusion (plug, cautery)
- Cyclosporine, lifitegrast
- Serum Tears
- Scleral lenses

#### Control evaporation
- Warm Compresses
- Lid Hygiene
- Topical antibiotic (Azithromycin)
- Oral antibiotic (Doxycycline)
- Lid procedures (Blephex, Lipiflow, IPL)

#### Decrease inflammation
- Corticosteroids
- Topical cyclosporine, lifitegrast

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### LUBRICATION
ARTIFICIAL TEARS

NIGHTTIME LUBRICATION
PUNCTAL PLUGS

CYCLOSPORINE & LIFITEGRAST

• Different formulations:
  • Restasis 0.05%
  • Cequa 0.09%
  • Xiidra 5%

• Can take time to reach peak efficacy

• Work to increase tear production and decrease inflammation
SERUM TEARS

Rigid gas permeable scleral prosthetic device
Fluid-ventilated with artificial tears
Liquid corneal bandage
Re-establishes a healthy stable ocular surface environment
Mitigates pain and photophobia
CONTROL EVAPORATION

BLEPHARITIS TREATMENT

• Warm compresses/heat masks
• Lid hygiene
• Topical antibiotics
• Oral antibiotics
EYELID PROCEDURES

DECREASE INFLAMMATION
TOPICAL CORTICOSTEROIDS

• Pulsed therapy
• Not a good long-term option
• Increases risk of both:
  • Cataracts
  • Glaucoma

SURGICAL OPTIONS
SURGICAL GOALS

• When conventional medical therapy fails
  • Surgical interventions should be considered
• Goals:
  • Increase lubrication
  • Assist epithelialization
  • Remove corneal opacities
  • Restore vision

TARSORRHAPHY
AMNIOTIC MEMBRANE

- Amniotic membrane is derived from inner layer of the placenta
  - Avascular connective tissue
- Promotes re-epithelialization
- Decreases inflammation and fibrosis
- Serves as biologic bandage

CORNEAL TRANSPLANTATION

- Need to optimize ocular surface prior to transplantation
- May need to combine with limbal stem cell transplant, amniotic membrane, bandage contact lens or tarsorrhaphy
  - Maximize tear function
  - Restore normal lid anatomy and function
TIMING OF TREATMENT

• Unclear
  • Pre-BMT initiation of topical cyclosporine may reduce the inflammatory response in the lacrimal glands and improve dry eye

• Mian et al 2010: 105 patient retrospective review
  • 81 patients received topical Cyclosporine 1 month prior to BMT
  • 24 patients did not receive Cyclosporine til at least 6 months after BMT
  • Dry eye symptoms were significantly more severe in control group at 3 months, 1 year and 2 years

SUMMARY

Ocular GVHD can lead to disabling pain and blindness

Early detection, diagnosis and treatment are key to prevent long-term complications

Evaluate all patients as early as possible, possibly even pre-transplant if feasible.
QUESTIONS?

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Let Us Know How We Can Help You!

Visit our website: bmtinonet.org
Email us: help@bmtinonet.org
Give us call: 888-597-7674