Paracentral Corneal Melting in Four Patients With Chronic Graft-Versus-Host Disease

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The authors have no financial interest in the subject matter of this poster

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Study

• Background
  • Graft-versus-host disease (GVHD) is classically divided into acute and chronic entities.
  • The incidence of chronic GVHD is 50-70% among patients who receive hematopoietic stem cell transplants.\textsuperscript{1-3}
  • GVHD may involve skin, oral mucosa, eyes, GI, genitalia, liver, lung, muscles and joints.\textsuperscript{4}
  • Ocular symptoms manifest as features of aqueous deficiency dry-eye (foreign-body sensation, pain, dryness).

• Purpose
  • To identify the symptomatology and clinical course of patients with chronic GVHD who developed sterile corneal melting

• Materials and Methods
  • Retrospective case review with approval from the University of Wisconsin-Madison (UW-Madison) Institutional Review Board.
  • Inclusion criteria: Patients seen at the UW-Madison Cornea clinic between 2008 and 2012 with a diagnosis of GVHD complicated by corneal thinning or perforation
# Results

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>26</td>
<td>49</td>
<td>54</td>
<td>66</td>
</tr>
<tr>
<td><strong>Malignancy</strong></td>
<td>ALL</td>
<td>AML</td>
<td>CML</td>
<td>AML</td>
</tr>
<tr>
<td><strong>Time from transplant to melt</strong></td>
<td>40 months</td>
<td>23 years</td>
<td>16 months</td>
<td>25 months</td>
</tr>
<tr>
<td><strong>Other systemic involvement</strong></td>
<td>Skin, mouth, lungs</td>
<td>Mouth</td>
<td>Skin, mouth, liver</td>
<td>None</td>
</tr>
</tbody>
</table>

ALL = acute leukocytic leukemia; AML = acute myelogenous leukemia; CML = chronic myelogenous leukemia
Two patients (A, B) had complete corneal melts. One (A) required penetrating keratoplasty that later melted in a similar inferior paracentral location within the graft. The second (B) was glued and did not require surgical intervention. Two patients (C, D) had paracentral areas of thinning that were addressed successfully with conservative measures.
# Melt characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Melt type</strong></td>
<td>Full thickness</td>
<td>Full thickness</td>
<td>Partial</td>
<td>Partial</td>
</tr>
<tr>
<td><strong>Melt location</strong></td>
<td>6 o’clock paracentral with recurrence in same location</td>
<td>5:30 o’clock paracentral</td>
<td>4 o’clock paracentral</td>
<td>3:30 o’clock paracentral</td>
</tr>
<tr>
<td><strong>Culture</strong></td>
<td>Pathology of corneal button without organisms</td>
<td>Rare Strep. viridans</td>
<td>Negative</td>
<td>Not performed (no infiltrate)</td>
</tr>
<tr>
<td><strong>Initial treatment</strong></td>
<td>Glue + BCL</td>
<td>Glue + BCL</td>
<td>Lubricating and antibiotic drops, acyclovir, punctal plugs</td>
<td>Lubricating and antibiotic drops, punctal plugs</td>
</tr>
<tr>
<td><strong>Vision before and after treatment</strong></td>
<td>LP 20/60</td>
<td>20/60 2 ‘/200</td>
<td>20/300</td>
<td>20/80</td>
</tr>
</tbody>
</table>

BCL = bandage contact lens
LP = light perception
# Treatments

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Punctal plugs</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Artificial tears (PF)</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Autologous tears</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>(tried previously</td>
<td></td>
<td>(tried previously without relief)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic drops</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Surgery</td>
<td>PKP x 2</td>
<td>PKP x 1</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Other</td>
<td>Vitamin C, PKP x 2</td>
<td>Doxycycline, Restasis</td>
<td>Acyclovir</td>
<td>Vitamin C</td>
</tr>
</tbody>
</table>

PF = preservative free
PKP = penetrating keratoplasty
Discussion

• Corneal perforation is a rare but vision threatening complication of GVHD that can vary both in severity and response to treatment.

• Thus far, perforation has been described only in individual case reports and small series. 5-11

• Both the non-infectious etiology in 3 cases and paracentral location appear to be shared features among the cases presented here as well as those described elsewhere. 5, 7-11
Etiology of melting in GVHD

• Does corneal melting result from a direct immunologic process or indirectly as a complication from sicca syndrome?
• One study found histologic evidence of a direct cytotoxic etiology consistent with immune dysregulation.¹⁰
• Apoptotic epithelial cells and keratocytes have also been noted in perforated GVHD corneas,¹² which could result from a cytotoxic reaction though keratocyte apoptosis may also be seen in dry eye disease unrelated to GVHD.¹³
Does eye disease parallel severity of GVHD?

- Patient 1 had recurrent melt in a similar location as the initial site of perforation.
- This patient was the youngest patient in our series with multi-system involvement of GVHD including bronchiolitis obliterans.
- Currently, it remains unclear if the level of ocular disease parallels the overall severity of GVHD.
Timing of GVHD Onset

- Flares of dry eye symptoms that coincide with the tapering of immunosuppressants have been described. ¹⁴
- It has been hypothesized that the symptoms of chronic GVHD manifest at about three months post-transplant because of the coincident changes made to immunosuppressive medications at that time. ¹⁵
- Some graft-versus-tumor effect is desirable and therefore complete suppression of GVHD is generally not favored.
Conclusions

• Dry eye is a significant source of morbidity in patients with chronic GVHD.
• Close follow-up is necessary to control symptoms and monitor for sight-threatening complications including corneal thinning, ulceration, and perforation.
• The link between immunologic dysfunction and corneal disease remains unclear at this time.
References