Pathology
Unknown Case:
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Kyle Muir
MS4
Pathology Elective
Clinical History

A 71yo healthy male presented with progressive fatigue and was found to be pancytopenic. Bone marrow biopsy was consistent with myelodysplastic syndrome. He received a CMV- BMT and was admitted 5 weeks post-transplant with vomiting and diarrhea.
EGD Findings (Stomach/Duodenum)

Erythema, edema, erosions.
Microscopic Findings
GASTRIC MUCOSA
DUODENAL MUCOSA
Microscopic Description

Gastric and duodenal mucosa with epithelial apoptosis and dropout without significant inflammatory cell infiltration.
What is the diagnosis?

A. Ischemia
B. Infectious gastroenteritis
C. Graft-versus-host disease
D. Autoimmune enteropathy
C. Graft-versus-host disease
Clinical Question

• Which of the following etiologies can most closely resemble the pathology of this condition?
  
  a. CMV reactivation
  b. Acute colitis
  c. C. Difficile infection
  d. Ischemic bowel
a. CMV reactivation

CMV infection of the GI tract can present with a wide variety of pathologic features including the typical GVHD findings of crypt dropout and epithelial apoptosis. Therefore, it is crucial to look for inclusions (unfortunately can be rare or even absent in these cases) and perform appropriate IHC testing if there is any doubt.
Overall Pathologic Impression

• Further IHC testing was negative for CMV, herpes and adenovirus.

• Overall pathology consistent with a diagnosis of graft-versus-host disease (GVHD).
Acute GVHD Clinical Staging

- Most commonly affected organs in acute GVHD are skin, liver and GI tract.
- Below is the clinical grading scheme for acute GVHD

<table>
<thead>
<tr>
<th>Clinical Stage</th>
<th>Skin</th>
<th>Liver—Bilirubin, μmol/L (mg/dL)</th>
<th>Gut</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rash &lt;25% body surface</td>
<td>34–51 (2–3)</td>
<td>Diarrhea 500–1000 mL/d</td>
</tr>
<tr>
<td>2</td>
<td>Rash 25–50% body surface</td>
<td>51–103 (3–6)</td>
<td>Diarrhea 1000–1500 mL/d</td>
</tr>
<tr>
<td>3</td>
<td>Generalized erythroderma</td>
<td>103–257 (6–15)</td>
<td>Diarrhea &gt;1500 mL/d</td>
</tr>
<tr>
<td>4</td>
<td>Desquamation and bullae</td>
<td>&gt;257 (&gt;15)</td>
<td>Ileus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Overall Clinical Grade</th>
<th>Skin Stage</th>
<th>Liver Stage</th>
<th>Gut Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1–2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>II</td>
<td>1–3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>III</td>
<td>1–3</td>
<td>2–3</td>
<td>2–3</td>
</tr>
<tr>
<td>IV</td>
<td>2–4</td>
<td>2–4</td>
<td>2–4</td>
</tr>
</tbody>
</table>
Acute GVHD of the GI tract

- **Definition:** attack by engrafted hematopoietic cells on host GI tissues in first 100 days post-transplant

- **Diagnostic Criteria (Grade I-IV)**
  - Increased crypt apoptosis progressing to crypt destruction and mucosal necrosis in higher grades

<table>
<thead>
<tr>
<th>Grade 1</th>
<th>isolated apoptotic epithelial cells, without crypt loss</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2</td>
<td>individual crypt loss</td>
</tr>
<tr>
<td>Grade 3</td>
<td>contiguous area of multiple crypt loss</td>
</tr>
<tr>
<td>Grade 4</td>
<td>extensive crypt dropout with denudation of epithelium.</td>
</tr>
</tbody>
</table>

- **Potential Pitfalls**
  - Consider infection if presence of acute or chronic inflammation or neutrophilic abscesses/ulceration. Also keep in mind the possibility of a diminished inflammatory cell response in these immunocompromised patients.
  - Use IHC to check for CMV/herpes
  - Be vigilant as infection can often coexist with GVHD and has a profound impact on management
References

• Modern Pathology (2011) 24, 117–125; doi:10.1038/modpathol.2010.163; published online 15 October 2010