Assessment of chronic GVHD according to NIH criteria: Easily done in daily practice
Oral and other extra cutaneous manifestations

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Chronic GVHD NIH organ scores

Arai et al, Blood. 2011;118:4242
Assessment of chronic GVHD: Easily done in daily practice

- Establish diagnosis
  - 1. Not acute GVHD
  - 2. Diagnostic or distinctive
  - 3. Rule out other disease
  - “As is”
  - Based on symptoms, signs, function, therapy
  - May not score if other cause obvious

- Organ score

- Global score
  - Prognosis
  - Therapeutic decision
  - Quality of life and function
### Diagnosis of Oral cGVHD

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Distinctive*</th>
<th>Other</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen-type features</td>
<td>Xerostomia</td>
<td></td>
<td>Gingivitis</td>
</tr>
<tr>
<td>Hyperkeratotic plaques</td>
<td>Mucocele</td>
<td></td>
<td>Mucositis</td>
</tr>
<tr>
<td>Restriction of mouth opening from sclerosis</td>
<td>Mucosal atrophy</td>
<td></td>
<td>Erythema</td>
</tr>
<tr>
<td>Pseudomembranes</td>
<td>Ulcers</td>
<td></td>
<td>Pain</td>
</tr>
</tbody>
</table>

**Role of biopsy:** diagnostic or non-specific for cGVHD mostly done for differential diagnosis
Patient Positioning

- Sitting up or supine
- Comfortable for patient and examiner
- Direct visualization of all surfaces
- Move head to assure direct vision

Halogen Light Source

- Otoscope
- Ophthalmoscope
- Halogen flash light
Crenated tongue

Geographic tongue

Linea Alba

Fordyce Granules

Geographic tongue

Hairy tongue
Diagnostic: Lichen-type features

Erosive Lichenoid Lesion
Diagnostic: Hyperkeratotic plaques
Diagnostic: Restriction of mouth opening from sclerosis
## Organ scoring of oral chronic GVHD

<table>
<thead>
<tr>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No symptoms</strong></td>
<td><strong>Mild symptoms with disease signs but not limiting oral intake significantly</strong></td>
<td><strong>Moderate symptoms with signs with partial limitation of oral intake</strong></td>
<td><strong>Severe symptoms with disease signs on examination with major limitation of oral intake</strong></td>
</tr>
</tbody>
</table>

**Symptoms:**
- Oral pain or sensitivity
- Mouth Dryness
- Uncomfortable to eat
- Change of taste

**Limited oral intake:**
- Need to avoid certain foods
- Difficulty swallowing
- Need to interrupt meals
- Limited calories

**Differential diagnosis:** Cancer or precancerous lesion, infection, drug reaction, therapy-related mucositis
## Diagnosis of GI cGVHD

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Distinctive</th>
<th>Other</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esophageal web</td>
<td></td>
<td>Exocrine pancreatic Insufficiency</td>
<td>Anorexia, Nausea, Vomiting</td>
</tr>
<tr>
<td>Esophageal strictures or stenosis in the upper to mid third</td>
<td></td>
<td></td>
<td>Diarrhea Weight loss Failure to thrive (children)</td>
</tr>
</tbody>
</table>

Role of GI biopsy: non-specific for cGVHD used for isolated GI GVHD and differential diagnosis
Diagnostic Signs

Esophageal web

Esophageal stricture

post dilation
Organ scoring of GI chronic GVHD

| No symptoms | Symptoms such as dysphagia, anorexia, nausea, vomiting, abdominal pain or diarrhea without significant weight loss (<5%) | Symptoms associated with mild to moderate weight loss (5-15%) | Symptoms associated with significant weight loss >15%, requires nutritional supplement for most calorie needs OR esophageal dilation |

Differential diagnosis: Broad (infections, drug-induced, metabolic, functional)
### Diagnosis of Liver cGVHD

<table>
<thead>
<tr>
<th>Diagnostic</th>
<th>Distinctive</th>
<th>Other</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Total bilirubin, AP, AST, ALT</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>&gt;2xULN</td>
</tr>
</tbody>
</table>

Role of biopsy: non-specific for cGVHVD probably under utilized role in isolated liver GVHD and differential diagnosis isolated liver GVHD can’t be reliably classified as chronic
Pattern of liver enzyme elevation and differential diagnosis of GVHD

Transaminitis
- Viral hepatitis
- NASH
- Auto-immune hepatitis
- Hemochromatosis
- Wilson disease
- Celiac disease

Hepatitis pattern-GVHD

Cholestatic
- PSC
- PBC
- Chronic obstruction
- Infiltrative disease
- Granulomatous disease
- Sarcoidosis
- Tuberculosis
- Metastasis

Classic pattern of GVHD

Mixed
- Drug induced liver injury
- Acute on chronic liver disease
Organ scoring of liver chronic GVHD

<table>
<thead>
<tr>
<th>Normal LFT</th>
<th>Elevated Bilirubin, AP, AST or ALT &lt;2xULN</th>
<th>Bilirubin &gt;3mg/dl or AP, AST or ALT 2-5xULN</th>
<th>Bilirubin, AP, AST or ALT &gt;5xULN</th>
</tr>
</thead>
</table>

Differential diagnosis: Infection, drugs, metabolic, functional, extra-hepatic
## Diagnosis of Genital cGVHD

<table>
<thead>
<tr>
<th>Diagnostic</th>
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<th>Other</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lichen planus-like features</td>
<td>Erosions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal scarring</td>
<td>Fissures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaginal stenosis</td>
<td>Ulcers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Role of biopsy:** diagnostic or non-specific for cGVHD rarely done, mostly for differential diagnosis
Diagnostic: Reticulated leukokeratosis (lichen-planus like) of the right labia minora and posterior forchette
Diagnostic: sclerosis (scarring) of the labia; note tear/fissure at posterior commissure (distinctive)
Diagnostic: Lichen planus-like, violaceous papules which may coalesce into ring-like small plaques
## Organ scoring of genital (female) cGVHD

| No symptoms | Symptomatic with mild distinct signs on exam AND no effect on coitus and minimal discomfort with exam | Symptomatic with distinct signs on exam AND with mild dyspareunia or discomfort with exam | Symptomatic with advanced signs (stricture, labia agglutination or severe ulceration) AND severe pain with coitus or inability to insert vaginal speculum |

### Symptoms:
- Spontaneous vulvar pain
- Pain or burning on urination
- Vulvar pain with tight jeans
- Riding the bike
- During the foreplay
- Dyspareunia

### Differential Diagnosis:
- Infection
- Menopausal
- Malignancy
- Drugs effect
## Diagnosis of Lung cGVHD

<table>
<thead>
<tr>
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<th>Other</th>
<th>Common</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bronchiolitis obliterans (BO) diagnosed with lung biopsy</td>
<td>BO (BOS) diagnosed with PFTs and radiology (CT)</td>
<td></td>
<td>BOOP (COP)</td>
</tr>
</tbody>
</table>

Role of biopsy: diagnostic for cGVHHD (BO) risky rarely done, mostly for differential diagnosis
NIH cGVHD Criteria for Clinical Diagnosis of BO (BOS)

All of the following:

- FEV1/FVC < 0.7 and FEV1<75% predicted
- RV>120% and HR CT inspiratory and expiratory cuts (air trapping, small airway thickening or bronchiectasis)
- No evidence of active respiratory infection
- >1 distinctive cGVHD manifestation in a separate organ

Filipovich et al, BBMT;11:945; 2005
Organ Scoring for Lung cGVHD

Done only after cGVHHD is diagnosed in any organ
Lung Score >0 does not equal BO!!

<table>
<thead>
<tr>
<th>Score 0</th>
<th>Score 1</th>
<th>Score 2</th>
<th>Score 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lungs</strong>&lt;br&gt;No symptoms</td>
<td><strong>Mild symptoms</strong>&lt;br&gt;(shortness of breath after climbing one flight of steps)</td>
<td><strong>Moderate symptoms</strong>&lt;br&gt;(shortness of breath after walking on flat ground)</td>
<td><strong>Severe symptoms</strong>&lt;br&gt;(shortness of breath at rest; requiring O₂)</td>
</tr>
<tr>
<td><strong>FEV1</strong>&lt;br&gt;FEV1 &gt; 80%&lt;br&gt;OR LFS=2</td>
<td><strong>FEV1 60-79%</strong>&lt;br&gt;OR LFS 3-5</td>
<td><strong>FEV1 40-59%</strong>&lt;br&gt;OR LFS 6-9</td>
<td><strong>FEV1 &lt;39% OR LFS 10-12</strong></td>
</tr>
</tbody>
</table>

The LFS (Lung Function Score) = FEV1 score + DLCO score (range 2-12):
>80% = 1; 70-79% = 2; 60-69% = 3; 50-59% = 4; 40-49% = 5; <40% = 6

The final NIH lung score (0-3) is determined by maximum of individual components
FEV1 is scored only if DLCO is not available and therefore LFS can not be calculated
Special place of lungs in the NIH global severity scoring of cGVHD
Lungs are not part of mild cGVHD!

Mild
- 1-2 organs (no lungs)
- Maximum organ score 1

Moderate
- Three or more organs with max score 1
- One organ with max score 2
- Lung score of 1

Severe
- Score of 3 in any organ or site
- Lung score of 2

*Global severity is replacing “limited-extensive” nomenclature
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