Graft-versus-Host Disease: Mouth

Celebrating a Second Chance at Life Survivorship Symposium

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Learning Objectives

Participants will learn about:

1. General oral care after transplant
2. Oral complications after transplant
3. How to recognize cGVHD in the mouth
4. Types of Oral cGVHD
5. Treatment for different types of oral cGVHD
Overview

• Take care of your mouth!
• Establish community dental care: Who, What, When
• Oral cancer screenings
• Non-GVHD post-transplant complications
• GVHD and your mouth
  • Symptoms
  • Appearance
  • Therapies

The Oral Cavity is the Gateway to the Body

- Gingiva
- Buccal Mucosa
- Tonsils
- Sublingual Immune Response
Take Care of Your Mouth - Brush

• Use toothpaste with fluoride

• Sensitive mouth?
  • Fruit-flavored or children’s toothpaste

• Sensitive teeth?
  • Fluoride rinse/gel or desensitizing toothpaste (Sensodyne, ProNamel, Colgate Sensitive, etc.)
  • Professional desensitizing treatment (several options in the dental office)

• Limited joint mobility?
  • Electric toothbrush (any kind from the drugstore)

Take Care of Your Mouth - Floss

• Floss picks

• Waterpic or other electric flosser

• See your Dentist 😊
Finding Community Dental Care (a dentist!)

- **Tell** your dentist that you are a transplant survivor
- **Show** your dentist anything unusual or new that you see or feel in your mouth
  - Mouth ulcers, lumps and bumps should heal within 3 weeks***
  - Teeth, gums, lips, tongue and cheeks
- **Do** ask for an oral cancer screening

***This time projection does not include GVHD, unfortunately

Finding Community Dental Care (a dentist!)

- Not every dentist appreciates your complex medical history and needs.
- If your dentist is not a good fit, interview other dental offices
- Ask, “Do you have experience treating medically complex patients?”
- University (dental school faculty or resident practice) or Medical Center Clinics are a good option
Get an Annual Oral Cancer Screening

- Highest risk in patients with oral cGVHD history
- 5-10+ years post-transplant
- Tongue is the most common site

Timing of Oral Post-Transplant Complications

<table>
<thead>
<tr>
<th>Early</th>
<th>Overlap</th>
<th>Late</th>
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</thead>
<tbody>
<tr>
<td>&lt;100 Days Post-Transplant</td>
<td>Mucositis</td>
<td>Drug-induced complications (MTX, sirolimus)</td>
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<tr>
<td></td>
<td>Dry Mouth</td>
<td>Viral infections (HSV, HPV)</td>
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<tr>
<td></td>
<td>Oral Thrush</td>
<td>cGVHD</td>
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<tr>
<td></td>
<td></td>
<td>Dry Mouth</td>
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<td>Perioral Fibrosis</td>
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<td>Oral ulcers</td>
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<td></td>
<td></td>
<td>Lichenoid lesions</td>
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<td></td>
<td></td>
<td>Hyperkeratosis</td>
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<td>Secondary oral cancer: squamous cell; HPV</td>
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</tbody>
</table>
Non-GVHD Post-Transplant Complications

- Loss or change in taste
- Radiation-induced dry mouth
- Medication-related oral ulcers or lesions
- Infections (thrush, bacterial or viral)
- Cold sores (herpes simplex virus recrudescence)

Herpes Simplex Virus (HSV) Recrudescence

- HSV reactivation is common: acute onset, exquisitely painful oral ulcers
- Diagnosis: swab ulcer for PCR lab test for HSV DNA
  Management: lidobenalox, systemic antivirals
Common Post-Transplant Complications: Oral Thrush (Candidiasis overgrowth)

- Pseudomembranous or erythematous
- Management: topical antifungals ( clotrimazole troches, etc) in addition to systemic antifungal prophylaxis

mTOR inhibitor/ Sirolimus-Induced Oral Stomatitis

- Excess circulating levels of mTOR (Mammalian target of rapamycin) inhibitors such as sirolimus may induce **painful** aphthous-like ulcers with well-demarcated borders and focal erythema
- Management: topical steroids, magic mouthwash, adjustment of sirolimus dose
Symptoms of Oral cGVHD

- Dry Mouth or temporary blisters on the roof of the mouth
- Red or White Patches in your mouth that you cannot scrape off
- Oral Sensitivity to spicy/citrus/acidic foods
- Mouth Ulcers
- White lines on the cheek lining or other mucosa
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Oral Manifestations of cGVHD

- Palatal hyperkeratosis
- Erythema
- Mucositis
- Lichenoid Lesion
- Ulcer
- Patchy tufted hyperkeratosis
- Sclerosing
Salivary Glands are a target of cGVHD

Immune cells infiltrate salivary glands:

Salivary glands can be targeted by cGVHD without oral mucosal involvement:

Dry mouth can lead to smooth surface cavities

Oral cGVHD is Three Distinct Diseases

- Oral mucosal disease
- Salivary Dysfunction
- Limited mouth opening
- Different types of oral cGVHD may need different treatment
- The underlying pathology is different
- The prognosis is different
**Oral cGVHD Diagnostic Criteria**

1) **Sufficient for diagnosis:** Lichen planus-like changes

2)  - or -

   The presence of at least 1 distinctive **manifestation** (xerostomia, mucoceles, mucosal atrophy, pseudomembranes, ulcerations) **confirmed by pertinent biopsy or other relevant tests**

3) **The exclusion of other possible diagnoses**
   - Oral infections
   - Drug reaction
   - New cancers

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**Diagnostic Features of Oral cGVHD: Lichenoid Lesion**
Distinctive Features of Oral cGVHD: Palate

- Palatal hyperkeratosis
- Mucoceles
- Erythema

Distinctive Features of Oral cGVHD: Tongue

- A. Atrophic glossitis
- B. Hyperkeratosis with patchy atrophy and associated erythema
- C. Patchy tufted hyperkeratosis
Distinctive Features of Oral cGVHD: Pseudomembranous Ulcerations

Salivary Gland cGVHD Diagnosis

- Is your mouth suddenly drier?
- Is your mouth progressively drier?
- Can you chew and swallow food without drinking water?
- Are you taking medications that can cause dry mouth?
- Did you have irradiation (total body irradiation or targeted to the head and neck) as part of your cancer therapy or transplant preparation?

* A biopsy of the minor salivary glands is needed for formal diagnosis.

Preventive Measures

– Stringent oral / dental hygiene
– Routine dental cleaning with possible endocarditis prophylaxis
– Surveillance for infection and malignancy

TOPICAL THERAPY FOR MUCOSITIS (EARLY POST-TRANSPLANT)

– Cryotherapy
– Supersaturated calcium phosphate rinses
– Pain control (opioid analgesics)
TOPICAL THERAPY FOR ORAL cGVHD

- First Line: Dexamethasone oral suspension (0.1mg/ml) - Expected ~29-58% patient response rate
- Second Line: Not well established


TOPICAL THERAPY FOR ORAL cGVHD: MOUTH SORES

- Lichen planus-like changes:
  - Steroid rinses
  - Calcineurin-inhibitor rinses

- Oral ulcers (isolated)
  - Topical steroid gel
  - Tacrolimus gel
  - Intra-lesional triamcinolone injection
Aids for Dry Mouth

• Sugar-free gum or candies
  • Xylitol is an alcohol-based sugar that can also reduce tooth decay – look for it in your sugar-free gum or candy
  • Lemon flavors can stimulate saliva
• Frequent sips of water
• Lubricating rinses such as biotene

Aids for Dry Mouth: Prescriptions

• Prescription medications can stimulate saliva production from intact salivary glands
  • Pilocarpine (Salagen)
  • Cevimeline (Evoxac)
  • May take a few weeks to show an effect
  • Only work if you have saliva-producing cells left in your glands
  • Not appropriate for everyone
Fluoride is Important

• Check your toothpaste: does it contain fluoride?
• Fluoride re-builds dental enamel that has mild damage
• Active Hydroxyapatite (nHA or Zn-HA) can also help rebuild tooth enamel
• Saliva washes food away from the teeth, buffers acids and bases in the mouth and returns calcium to damaged tooth enamel.
• Dry mouth = less saliva = less protection from decay! 😞

Aids for Reduced Opening

• Progressive gentle stretching can maintain or improve mouth opening
• Aids to help:
  • Stacked tongue depressors
  • Physical therapy
• In severe cases:
  • Perioral steroid injections
  • Surgical intervention
Key Points

• See your dentist regularly after your transplant has stabilized.
• Call your dentist if you notice any problem or change in your mouth.
• Take care of your mouth by brushing and flossing every day. A healthy mouth is less likely to develop problems (but cannot prevent every challenge!).

QUESTIONS?

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