Chronic Graft-versus-Host Disease of Skin and Connective Tissues

Celebrating a Second Chance at Life Survivorship Symposium

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City of Hope

Your Skin and Chronic Graft-versus-Host Disease

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Financial Disclosures

I have received honoraria as a consultant and/or speaker in the past from the following:

• Sanofi Genzyme – unrelated to GVHD
• Regeneron – unrelated to GVHD
• Kadmon – I participated in an advisory board to discuss a medication in development for chronic graft versus host disease

Learning Objectives

• Risk factors for developing cGvHD of skin
• Review the various manifestations of cGvHD on skin
• Review the therapies available to manage cGvHD of skin
• Skin cancer after bone marrow transplantation
Chronic Graft-versus-Host Disease

- Major barrier to an otherwise successful HSCT
- 30-70% of patients who have undergone allogeneic HSCT develop cGvHD
- Patients with cGvHD have reduced quality of life and increased risk of morbidity and mortality
- Resembles autoimmune disease

Risk Factors for Developing Chronic GVHD

<table>
<thead>
<tr>
<th>Risk factors for development of cGVHD</th>
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<tr>
<td>Prior acute GVHD</td>
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<tr>
<td>Older age of recipient</td>
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<tr>
<td>Peripheral blood stem cell graft</td>
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<tr>
<td>Diagnosis of chronic myeloid leukemia</td>
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<td>Female donor to male host</td>
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<td>HLA disparity between recipient and donor</td>
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Patient experience with cGvHD

- **1377** completed patient surveys about quality of life, symptoms, health status, comorbid conditions and medications
- **Patients reported disease severity:**
  - Mild: 18.7%
  - Moderate: 8%
  - Severe: 1.8%
  - Never had cGvHD: 27.4%
  - Had cGvHD, but has since resolved: 20.3%
  - Excluded for not completing surveys: 23.8%

More likely to report:
- Worse quality of life
- Lower performance status
- More likely to take prescription meds for pain, anxiety and depression

Self-reported measures were similar between those who had resolved cGvHD and those who never had it

**What is Graft-versus-Host Disease?**

- Graft (donor) versus host (recipient) disease
- New immune system cells attack tissues that appear foreign
- Skin is the most commonly involved organ

![Graph showing tissue involvement in Graft-versus-Host Disease](image)


**Sections of Skin Affected by cGVHD**

- Epidermis
- Dermis
- Subcutaneous fat
- Fascia

Donor immune cells recognize host skin as foreign, thereby triggering inflammation, injury, and repair

**Symptoms of Skin GVHD**

- Rash
- Itching
- Changes in skin color
- Sweat gland and hair follicle damage
- Skin sores and ulcerations
- Tightening of the skin
  - Mouth and around joints
  - Pseudo-cellulite
  - Difficulty with taking deep breath

**Morphologies of Skin cGvHD**

Historically, skin cGvHD has been described as either scleroderma or lichen planus

- Sclerotic
- Morphea-like
- Lichen planus
- Lichen sclerosus et atrophicus-like
- Dyspigmentation
- Vitiligo
- Eczema like
- Papulosquamous-like
Sclerotic

Fascial damage resulting in dry river bed sign & dimpling or cellulite appearance

Reduced “pinch-ability”

**Morphea-Like**

Localized areas of sclerosis


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**Lichen sclerosus**

**Lichen sclerosus**

Thinning and fibrosis of the superficial skin that leads to a “cigarette-paper” like wrinkled appearance

Easily breaks down

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**Lichen Planus**

Lichen Planus

- Violaceous papules that may have thin scale
- “5 P’s”: purple, polygonal, planar, pruritus, papule

Papulosquamous

Pigmentary changes

Nail Changes
TREATMENT OF SKIN CHRONIC GVHD

Optimize skin-directed therapy → Systemic therapy

Optimize Skin Directed Therapies

- **Topical anti-inflammatory medications**
  - Steroids
  - Non-steroids (calcineurin inhibitors)

- **Phototherapy**
  - Psoralen + UVA
  - UVA alone
  - UVB

Higher efficacy for superficial subtypes of chronic GvHD including lichen planus, lichenoid, psoriasiform, eczematous.

Sclerotic subtypes are less likely to improve with skin-directed therapy, although there are reports.
Topical Therapies

- **Considerations for steroids**
  - Potency: mild to super-potent
  - Vehicle: ointment, cream, solution
  - Site specific
  - Side effects from overuse: skin thinning, atrophy

- **Calcineurin inhibitors (tacrolimus, pimecrolimus)**
  - Safe alternative to topical steroids
  - Expensive

Dry Skin Care

- Helpful for itch and hyperkeratotic skin lesions (heaped up skin)
- By “exfoliating” the excess skin in these lesions, you make it less likely to tear and leave behind a sore
**Phototherapy**

- **Psoralen + UVA**
  - Penetrates into the dermis
  - Limited availability due to shortage of facilities that have UVA machine

- **UVB**
  - More superficial penetration into the skin

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**Systemic Therapies**

- **Systemic corticosteroids**
- **Other immune modulating options**
  - Ruxolitinib
  - Ibrutinib
  - Imatinib
  - TNF-inhibitors
  - Rituximab
  - Sirolimus
  - Tacrolimus
  - Mycophenolate mofetil
  - Cyclosporine
  - Photopheresis
Watch Out for Skin Cancer

- Nonmelanoma and melanoma skin cancers occur at a higher rate in patients who undergo bone marrow transplantation than the general population
- Self monitor every 1-2 months
- At least annual screening with a dermatologist
- Practice sun safety – UV exposure is only modifiable risk factor
- No tanning booths!

Skin cancer after bone marrow transplant

- Basal cell carcinoma
- Squamous cell carcinoma
- Melanoma

Clinical images courtesy of www.dermnetnz.org
Skin cancer prevention

Common sunscreen mistakes
- Forgetting to re-apply
- Missing areas

Summary
- Chronic GvHD is common after transplant and a major barrier to health
- The skin is the most-likely involved organ, with symptoms manifesting in one of several morphologies
- Treatment:
  - Skin directed
  - Systemic
- Chronic syndrome – improvement of symptoms and quality of life can be achieved
Questions?

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