Skin Chronic GVHD

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All therapeutics are off-label
How frequent is skin GVHD?

• The skin is involved in 40-80% of people with chronic GVHD

• Usually an early sign of chronic GVHD

• Relatively easy to detect and treat unless deep scarring occurs
How is the skin affected by chronic GVHD?

• Color change – too light, too dark
• Rash
• Thickening and scarring
  – Superficial type
  – “Bound down,” “wooden”
  – Fasciitis – tissue around muscles and fat
  – Slow to develop, slow to resolve, often permanent
• Fingernails and toenails – ridges, chips, fall off
• Hair thinning and loss
What are the symptoms of skin GVHD?

- Itching
- Thickness and tightness
- Restricted joint range of motion
- Usually not painful; rare person feels “burning”
Treatment Principles

• Control current symptoms
• Prevent additional organ damage
• Minimize treatment toxicity
• Avoid other late treatment effects
• Maintain an anti-cancer effect

Couriel et al, BBMT 2006; 12: 375-396
www.asbmt.org/GvHDForms
How do you treat skin GVHD?

• Rashes are usually easy to treat
• Skin color changes and scarring are difficult to treat
• Medications given by mouth or intravenously
• Symptomatic systemic medications
  – Anti-itch – benadryl, hydroxyzine, ranitidine
• Ancillary and supportive topical treatments
What topical treatments are helpful?

• Steroids
  – occlusion can increase potency
  – prolonged treatment can cause skin thinning
• Topical tacrolimus or pimecrolimus
• Moisturizers
  – ointments and creams are better than lotions
• Anti-itch treatments
• For ulcers: topical antibiotics, protective film, wound care, hyperbaric oxygen
What other treatments are there?

- PUVA – psoralen and UVA
  - Should not be used if a prior skin cancer
- UVB – light therapy
- ECP – extracorporeal photopheresis
Extracorporeal Photopheresis

Diagram showing the process:
- Patient
- Whole Blood
- Red Cells and Plasma
- Treated White Cells And Plasma
- Ultraviolet Energy
- Psoralen (Photo-sensitizing agent)
- White Cells And Plasma
Ancillary and Supportive Care

- Stretching
- Physical therapy
- Deep tissue massage
What precautions are needed?

• Know your skin
  – Notify your physician of any changes

• Sun protection:
  – avoidance, sunscreen, clothing
  – ↑ Skin cancer risk
  – ↑ Risk of worsening GVHD

• Moisturization

• Antibiotic/antiviral prophylaxis
Increased Risk of Skin Cancer

• Most common cancer in the US – more than 1 million people diagnosed annually
  – increased risk in immunosuppressed people
  – treatment with minor surgery, more extensive surgery (Moh’s), radiation, topical chemotherapy

• In transplanted people, after 20 years
  – 7% risk of basal cell cancer
    • radiation, if < 18 year old when treated; White; chronic GVHD
  – 3% risk of squamous cell cancer
    • acute and chronic GVHD

Leisenring et al, J Clin Oncol 2006; 24: 1119
Basal Cell Carcinoma

- “pearly,” “waxy,” “fleshy”
- raised edges
- any color
- “sore that does not heal”
- yellowish or white “scar tissue” but no injury
- blood vessels visible
- face and other sun exposed areas
- rarely spreads
Squamous Cell Carcinoma

- crusty, scaly bump or patch
- may grow rapidly
- often red, can see ulcerations and bleeding
- face and other sun exposed areas
- may occur in scars
- more likely to spread
Melanoma

- **A = Asymmetry**
- **B = Borders are uneven, “blurry”**
- **C = Colors not uniform, variety of colors – red, brown, blue, tan**
- **D = Diameter, larger than “pencil eraser”**
- **E = Evolution, growing and changing mole**
- most likely to spread
Procedures to avoid if you have skin GVHD

• Cosmetic surgery
• Skin pigmentation products
  – Tanning
  – Lightening – hydroquinone, tretinoin
• If you have skin thickening, avoid vigorous outdoor activities
  – marathons, long-distance bike rides
Does skin GVHD go away?

- Yes, but permanent problems may remain
- May take years to resolve
New treatments in development

• Anti-fibrotic agents – prevent or dissolve scars
• Medications that target the skin
Chronic GVHD Consortium

Clinical sites:
Fred Hutchinson
Stanford University
University of Minnesota
Dana-Farber Cancer Institute
Vanderbilt University
Medical College of Wisconsin
H. Lee Moffitt Cancer Center
Washington University
National Cancer Institute
Memorial Sloan Kettering
University of North Carolina
Weill Cornell Medical College
Mayo Clinics
Roswell Park Cancer Institute
Cleveland Clinic
Ohio State University

CA118953, CA163438
Consortium clinical trials

Randomized Phase III of Restasis vs. Placebo for Prevention of ocular GVHD (N=254) (Allergan providing drug)

Phase II of FAM for BOS (N=40) (GSK, Merck providing drug)

Steroid-refractory chronic GVHD
Nilotinib (N=41) – Novartis
IL-2 (N=31) – Prometheus
Tocilizumab (N=42) – Genentech
Carfilzomib - Onyx

Randomized Phase II of imatinib vs. rituximab for cutaneous sclerosis (N=74) (Novartis, Genentech providing drug)

Longitudinal study of Immune Mediated Disorders (N=1,118)

ORD CA163438
Summary

- Skin chronic GVHD is common
- Treat according to its severity
  - Local treatments if mild
  - Systemic treatments if more severe
- Some changes may be permanent