Graft-versus-Host Disease: How it Affects Skin, Nails and Hair

Celebrating a Second Chance at Life Survivorship Symposium

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Silvina Pugliese MD
Clinical Associate Professor of Dermatology, Stanford Cancer Institute
Learning Objectives

1. Identify skin symptoms of acute GVHD and treatment options for acute skin GVHD.
2. Recognize the many ways that chronic GVHD can appear on the skin and how it may affect the mouth, genital skin, hair, and nails.
3. Identify treatment options for various forms of chronic skin GVHD.
4. Review dry skin care and sun avoidance/protection in patients with chronic skin GVHD.
5. Emphasize the importance of monitoring for skin wounds and skin cancers.
What is Graft-Versus-Host-Disease (GVHD)?

• GVHD occurs when donor stem cells (graft) view the recipient cells (host) as foreign

• We’ll focus on skin GVHD

• We’ll discuss both acute skin GVHD and chronic skin GVHD
Time to Onset

Acute GVHD

• The incidence rate for acute GVHD affecting any organ varies widely and is up to 50%

• We classically viewed this as occurring during the first 100 days after transplant, but now know this is not always the case

• Skin + gut + liver

• Skin involvement can occur at the same time as gut involvement (diarrhea)

• Lab tests may show signs of liver injury
Acute Skin GVHD – what it looks like

• Pink, red, purple “measles-like” rash
• Can affect the hands and feet
• Can be itchy or have no symptoms
Acute Skin GVHD
Skin-directed treatment of acute GVHD

1. Topical steroids
2. Topical calcineurin inhibitors
3. Topical Janus kinase (JAK) inhibitors
4. Narrowband ultraviolet B (nbUVB)
5. Wound care if skin is open
6. Anti-itch medication if skin is itchy
Topical steroids

• Creams, ointments, solutions (liquids), oils, sprays
• Ointments absorb best into the skin
• Solutions and oils work better in areas with hair (scalp)
• Steroids vary in strength depending on the name, NOT the %
Topical steroid side effects

• Skin thinning
• Stretch marks
• Bruising
• Acne
• Rash (contact allergy)

dermnetnz.org/cme/dermatitis/corticosteroids
How to treat steroid side effects

- **Skin thinning**: stop topical steroids
- **Stretch marks**: stop topical steroids, consider creams (tretinoin, glycolic acid, L-ascorbic acid) and lasers (work best on red stretch marks)
- **Bruising**: stop topical steroids, moisturize, physically protect
- **Acne**: stop topical steroids, use acne washes like benzoyl peroxide, salicylic acid, glycolic acid, use topical or oral antibiotics
- **Rash (contact allergy)**: switch to another topical steroid class, consider non-steroidal topicalics (pimecrolimus, tacrolimus)
Chronic GVHD

• Occurs in 30-70% of transplant patients who receive donor cells
  • Of these patients, 60-80% will have skin involvement

• We classically viewed this as occurring 100 days after transplant, but now know this is not always the case

• Affects multiple organ systems

• Dermatologists are involved in diagnosis and treatment because it can affect the skin, mouth, genitals, nails, and hair
Chronic GVHD is polymorphous

- Polymorphous: occurring in different forms
- The appearance depends partly on which layers of the skin are affected
- It looks very different from acute GVHD
- It can also look like other skin conditions
Chronic GVHD affecting the outermost skin layer

Skin-directed treatment for this type of cGVHD

1. Topical steroids
2. Topical calcineurin inhibitors
3. Topical Janus-kinase (JAK) inhibitors
4. Narrowband ultraviolet B (nbUVB)
5. Wound care if skin is open
6. Anti-itch medication if skin is itchy
Other topicals

Topical calcineurin inhibitors

- Tacrolimus ointment, pimecrolimus cream
- Can have burning sensation upon application

Topical JAK inhibitors

- Ruxolitinib cream
- Best for very limited involvement, risk of systemic absorption and more serious side effects with widespread application
Narrowband UVB

• 311–312 nanometer (nm)
• 3x/week
• Sessions are short (few seconds to minutes)
• Treatment course is a few months
• https://find-a-derm.aad.org
  • “phototherapy”

dermnetnz.org/topics/uvb-phototherapy
Chronic GVHD affecting the middle layer of skin

Chronic GVHD affecting the deepest layer of skin

**Fig. 3** Rippling and groove sign on the inner arm of EF-like associated to skin sclerosis

**Fig. 4** Chronic GVHD-related EF: skin rippling on the anterior aspect of the thighs and on the abdomen. Skin is not involvement

Skin-directed treatment of “deeper” cGVHD

1. Topical medications “under occlusion”
2. Steroid injections into the skin
3. UVA (ultraviolet A)
4. Wound care if skin is open
5. Anti-itch medication if skin is itchy

dermnetnz.org/topics/intralesional-injection
UVA

• UVA1: 340-400nm
• Longer wavelength, penetrates deeper into the skin
• Reaches the dermis

Figure 2. UV penetration into the layers of the skin. The figure was created using Servier Medical Art [19], licensed under the Creative Commons Attribution 3.0 Unported License (www.creativecommons.org/licenses/by/3.0/).

Can develop in areas of pressure

Can develop in areas of skin injury

- In skin affected by shingles
- Where a line was
- After a blood draw
- In areas of prior radiation

Can affect movement

Fig. 1  Photographic range of motion: P-ROM scale. Series of images that captures ROM separately for shoulders, elbows, wrists/fingers, and ankles. Lower scores indicate more limited ROM. The P-ROM total score is the sum of scores in all 4 joints for a maximum of 25 points.
How Do We Diagnosis Chronic GVHD?

• There are some *diagnostic* skin findings
• A skin biopsy can be helpful in cases without diagnostic skin findings
• Many skin conditions can mimic chronic GVHD
  
  Some examples include:
  • Eczema
  • Psoriasis
  • Drug rashes
  • Lichen planus
  • Vitiligo
  • Keratosis pilaris
What is a skin biopsy?

- “Punch” biopsy for rashes
- In-office procedure
- Numbing medication is injected into the skin
- A small piece of skin is removed
- 1-3 stitches are placed
- Side effects: scar, bleeding, infection
Hints to diagnosis: triggers

• Decrease in immunosuppression
• Donor lymphocyte infusion
• CAR-T cell therapy
• Sunburn / UV exposure
• Infection (e.g. virus)
• New medication causing a drug rash
Chronic GVHD affecting the mouth

- Dry mouth, dry lips
- Sores
- White lines/streaks
- Puffy gums
- Pain
- Trouble eating
- Sensitivity to food
Treatment of cGVHD of the mouth

• Topical steroids (liquids/”swish & spit”, gels, dental paste)
• Topical calcineurin inhibitors (capsule contents in water)
• Topical lidocaine (to help with eating)
Chronic GVHD affecting the genitals

• Some patients may feel uncomfortable discussing genital symptoms with their doctors, but cGVHD of genital skin can have a significant impact on quality of life

• Symptoms include:
  • vaginal or penile pain
  • pain with sexual intercourse
  • pain/burning sensation when urinating

• Patients may see skin changes on their penis or vulva
Treatment of cGVHD of genital skin

• Topical steroids
• Topical calcineurin inhibitors
• Referral to gynecology or urology
• Pelvic floor physical therapy
• Some centers have dermatologists who specialize in genital skin
Chronic GVHD affecting the hair

• Can be **scarring** or **non-scarring**
  - Scarring: redness, flaking, scale, loss of hair follicles
  - Non-scarring: loss of hair throughout scalp

• Can affect hair from scalp, eyebrows, eyelashes, and anywhere on the body


Treatment of hair loss

• If itch, scale, or redness exist, certain topicals (such as topical steroids) can be used

• Steroids can also be injected into the scalp (intralesional)

• Topical minoxidil foam or solution

• Oral minoxidil

• Powders/lotions/sprays to mask thinning hair

• Hair/cranial prosthesis

• Hair transplant
Chronic GVHD affecting the nails

• Nail lifting
• Lines running throughout the nail
• Loss of nails
• Can be painful and significantly impact daily, routine activities
Treatment of cGVHD of the nails

• Topical steroids
• Injection of steroids into the nail
• Topical antifungals to prevent fungal infection
• Biotin (2500mcg) to make the nails stronger
• Avoid washing your hands with hot water
• Moisturize with cream-based moisturizer
• Petroleum jelly around the nail folds
General skin care for patients with chronic GVHD

• Dry skin care
  • Helps to prevent/treat: itch, rashes, bruising, open skin

• Sun protection
  • Helps to prevent/treat:
    • sun freckles
    • skin discoloration
    • skin aging
    • skin cancer
    • flares of chronic GVHD
Habits To Improve Dry Skin

• Shower/wash hands with lukewarm water (not hot!)
• Keep showers/baths short
• Wear gloves when washing dishes
• Avoid harsh soaps
• Avoid fragrances
• Moisturize daily
• Use cream-based moisturizers
• Use ointment moisturizers at night with white cotton gloves
Sun avoidance and protection

• Comprehensive approach
  • Avoidance: seek shade, avoid high UV index (10am-4pm)
  • Protection: UPF clothing + SPF sunscreen

• There are two main sunscreens: chemical blockers, physical blockers
  • The best sunscreen is the one you will wear
  • Broad-spectrum (blocks UVA + UVB)
  • At least SPF 30 (choose a bit higher to account for imperfect application)
  • Consider water-resistant depending on your activities
Monitor your skin for wounds

• The same factors that contribute to wound development can contribute to delayed wound healing
  • Status of chronic GVHD
  • Nutrition
  • Injury
  • Circulation
  • Infection

• Wounds that don’t heal as expected should be evaluated for skin cancer

Fig 5. Full-thickness ulcer on posterior scalp in a patient with chronic GVHD. GVHD, Graft-versus-host disease.

Identifying skin cancers

- Patients who have undergone bone marrow transplants have an increased risk of developing skin cancer.
- Chronic GVHD increases the risk of skin cancer development.
- Look for:
  - pink, red, purple, shiny or scaly bumps
  - spots that bleed or are painful
  - wounds that don’t heal
  - scars that open up

[Links to dermnetnz.org topics for cutaneous squamous cell carcinoma and basal cell carcinoma]
Find a dermatologist familiar with GVHD

BMT InfoNet Directory of GVHD Clinics and Specialists
bmtinfonet.org/gvhd-directory
Questions?

Silvina Pugliese MD
Clinical Associate Professor of Dermatology, Stanford Cancer Institute
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Email us: help@bmtinfonet.org

Phone: 888-597-7674 or 847-433-3313

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