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

Celebrating a Second Chance at Life Survivorship Symposium

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Chronic Graft-versus-Host Disease of the Skin and Connective Tissue

2022 Celebrating a Second Chance at Life Survivorship Symposium

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No Disclosures

Learning Objectives

• Define GVHD as it relates to the skin
• Recognize the skin changes of chronic graft-vs-host disease (cGVHD)
• Understand how the diagnosis is made
• Review skin directed management of cGHVD
• Be familiar with other skin problems post transplant
What is GVHD?

- Multi-organ disorder
- Immunocompetent donor T cells “graft” are given to immunocompromised “host”
- Major cause of morbidity and mortality
- Skin changes are very common
- Often resembles autoimmune or connective tissue disease

What is Chronic Skin GVHD?

Traditional definition

- Skin findings that look inflammatory (lichen planus) or fibrotic/scar-like (scleroderma) that occur 100 or more days post transplant

Current definition

- Long term complication of allogeneic stem cell transplantation characterized by inflammatory or fibrotic skin problems that are not defined by time after transplant
- Most of these changes are diagnosed on clinical examination
- There may be no preceding acute GVHD
Chronic Cutaneous (skin) GVHD

- What does it look like?
- How do we grade and document these changes?

NIH Consensus Criteria....

NIH Consensus Criteria

Attempt to categorize features of cGVHD for clinical trials:

- **Diagnostic** features (sufficient to establish diagnosis)
- **Distinctive** features (insufficient alone to establish diagnosis)
- Other features

Biol Blood Marrow Transplant 2015, 21: 389
**Morphology:** cGVHD involving the epidermis, dermis, collagen and fascia

- **Body Surface Area**
- **Morphology**
  - (Description of what the skin lesions look like)
- **Sclerosis**
- **Other skin, nail, and hair findings**
cGVHD changes of the epidermis

- Symptomatic pruritis (itching) even without rash
- Dry “fish-scale” like skin called ichthyosis
cGVHD of the epidermis

Change of pigmentation (hypo or hyperpigmentation, loss of pigment):

- Pigment cells (melanocytes) are located at the dermal-epidermal junction
- Anything that affects these cells may cause pigment disturbances.

GVHD of the epidermis and dermis

Purple polygonal papules are a diagnostic feature of lichen planus-like cGVHD
Body Surface Area

Localized

versus

Widespread

GVHD of the epidermis and dermis

Scaly thick plaques and papules
GVHD of the epidermis and dermis

- May present with skin thinning
- Poikiloderma:
  - atrophy
  - hypo and hyperpigmentation
  - telangiectasia

GVHD of the hair follicles
GVHD of the hair follicles may cause hair loss

Changes in Nails

Over 50% patients with cGVHD develop nail changes:

**Dystrophy**
- Thickening and thinning
- Ridging
- Pterygium (scarring at nail bed)
- Nail destruction

These may be treatable early on
- Systemic agents
- Injected corticosteroids
Sclerotic (scar-like) changes

**Sclerotic (scar-like, fibrotic, scleroderma-like):**

- Occurs in the dermis but may extend deeper
  - Superficial morphea (sclerosis) is often "pinchable", localized and moveable
  - May occur in areas of trauma
Deep sclerosis

- "Hidebound" skin
- Sclerosis may extend through the dermis and to deeper layers
- May have epidermal changes characterized by erosions and scaling
- Skin is fragile and prone to injury

Deep sclerosis without epidermal change

Cellulite-like changes
**Fasciitis**

Inflammation of the layer of the skin overlying the muscles and tendons

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**Fasciitis**

Painful edema  
Positive prayer sign  
Fasciitis + Sclerosis
Diagnosing skin cGVHD

- Clinical impression +/- skin biopsy
- Characterize the morphology & extent of involvement
- Determine other organs that are involved
- Identify secondary skin problems

Chronic skin GVHD: It takes a village....
Topical Treatment

- GVHD affecting the **epidermis and superficial dermis** may be amenable to topical therapy
- Topical corticosteroids and topical calcineurin inhibitors (tacrolimus and pimecrolimus) are useful for short-term treatment of localized disease
- Phototherapy

Topical Therapies

**Steroids**
- Many different formulations and many different strengths
- Common measures of potency:
  - Anti-inflammatory properties.
  - Vasoconstriction assay
  - Atrophogenicity (thinning of the skin)

**Calcineurin Inhibitors**
- Use in areas of high risk for atrophy
- Poorly tolerated on erosions
- Possibility of significant systemic drug levels in children
Ultraviolet radiation (UVR) for cGVHD

Types of UVR
- PUVA (330-400nm)
- NBUVB (311-313nm)
- UVA1(340-400nm)

Mechanism of action
- modify inflammatory response
- modifies cells in the epidermis which help regulate the immune system
- modifies circulating cells
Light Therapy for Cutaneous GVHD: NB UVB

Fasciitis

- Topical therapy not effective
- Consider systemic therapy
- Physical and occupational therapy
Fasciitis: Importance of supportive care

Other skin problems related to transplant and GVHD

- Tumors of the skin (benign and malignant)
- Skin infections
- Hard to heal wounds
Malignant Tumors of the Skin

Related to:
• Long term immune suppression or chemotherapy
• Persistent inflammation
• Preceding sun damage
• Ionizing radiation

Leads to:
• Increased risk of squamous cell carcinoma, basal cell carcinoma and melanoma
• Curable when found early

How to protect your skin

Early recognition is important
• Get undressed for a full skin examination
• Tell your provider about any skin concerns
• Check your range of motion
• Protect your skin from trauma
• Treat skin cuts and scrapes early
• Use photoprotection:
  – protective clothing
  – sunscreen
Review Objectives

Define GVHD as it relates to the skin:
• long term complication of allogeneic stem cell transplantation characterized by inflammatory or fibrotic skin problems

Recognize the skin changes of cGVHD
• Epidermal, dermal, subcutaneous & fascial inflammatory or fibrotic changes

Understand how the diagnosis is made
• Clinical, biopsy and correlation with other organ systems

Review Objectives

Skin directed management of cGHVD
• Topical therapy and UVR

Other skin problems post transplant
• Infection, wounds and skin cancers
Questions?

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