Disclosures

• Actelion: speaker, advisory board, investigator
• Elorac: investigator
• Kyowa: investigator, advisory board
• Seattle genetics: advisory board
• Soligenix: investigator

• Some of the therapies reviewed in this presentation involve off-label use of medications.
Overview

• Introduction to transplants

• Morbilliform eruptions in the post transplant period

• Fungal infections

• Surprise Case
Case
Definition – aka Names

• Names:
  • Hematopoietic transplant
  • Bone marrow transplant
  • Stem cell transplant

• Types:
  • Autologous
    • Patient’s own cells
  • Allogeneic
    • Donor cells
Reasons for Transplant

Indications for Hematopoietic Cell Transplant in the US, 2016
Donor Types

• Matched donor
  • Siblings (1 in 4 match)

• Matched unrelated donor
  • Registry

• Other relatives
  • Parent = haploidentical

• Umbilical cord blood
Conditioning Regimens

• **Myeloablative**
  • Intense chemotherapy
  • Total body irradiation
  • Destroys bone marrow function
  • Generally used when disease control is need.
  • Ie: AML

• **Non-myeloablative**
  • Aka: reduced intensity
  • Relies on the Graft vs Tumor effect
  • Ie: Lymphoma
Engraftment

• Definition: Judged based on neutrophils (myeloid engraftment)
  • ANC 500 x 3 days
  • ~15-20 days for BM and PBSC
  • ~21-35 days for cord blood

• Important as we look at complications in the post transplant period.
What is Our Roll as Dermatologist?

• **Transplant related mortality**
  - Death due to causes unrelated to the disease
  - Contrasted with disease related mortality

• Estimated at 20-50%

• Can we help improve mortality?

![Pie charts showing causes of death after unrelated donor HCT done in 2014-2015](chart.png)

*Data reflects 3-year mortality*
When Does Myeloid Engraftment Occur?

1. Days 0-5 post transplant
2. Days 5-10 post transplant
3. Days 14-20 post transplant
4. Anytime post transplant
When Does Myeloid Engraftment Occur?

1. Days 0-5 post transplant
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3. Days 14-20 post transplant
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Case
What is the Diagnosis?

1. Acute graft versus host disease
2. Morbilliform drug eruption
3. Engraftment syndrome (hyperacute GVHD)
4. Viral exanthema
5. Eruption of lymphocyte recovery
What is the Diagnosis?

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Acute Graft Versus Host Disease

• Clinical:
  • Starts: palms, soles, ears, neck
  • Progresses to trunk and legs
• Appears follicular
  • Tracks down follicles on histopathology, also
• Occurs **2-4 weeks** after transplant
• **Engraftment must have occurred**
• Can recur after donor lymphocyte infusions
Case
What is the Diagnosis?

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Morbilliform Drug Eruptions

• Start on trunk and arms, gradually enlarge and become confluent, purpuric on LE, likes sites of pressure

• Occur 7-14 days after exposure (10 days)
  • Time frame often complicated by prior antibiotic exposure

• Associated symptoms: Pruritus, low-grade fever, mild eosinophilia
Why Do We Need to Differentiate?

• Diagnosis guides subsequent therapies.
  • Possible systemic corticosteroids vs observation

• Risk of mortality for GVHD is high, so observation without treatment is often not an option.
Drug Hypersensitivity Versus Acute GVHD

FIGURE 2. Cutoff criteria of ave. eos/10 HPFs in distinguishing DHR from aGVHD.

Quantitative Analysis of Eosinophils in Acute Graft-Versus-Host Disease Compared With Drug Hypersensitivity Reactions.
Weaver, Joshua; Bergfeld, Wilma
DOI: 10.1097/DAD.0b013e3181a85293
Should We Biopsy?

• Do not put the patient through an unnecessary procedure if it is not going to change treatment.

Versus

• A biopsy may provide additional information on this patient or guide future patients.
Morbilliform Drug Eruption vs Acute GVHD

**Morbilliform Drug Eruption**
- Truck and arm with distal spread
- 10-14 days after starting the offending agent
  - 1-2 days if previously exposed
- May appear purpuric, particularly on LE
  - Tx: Observation or removal of offending agent

**Acute GVHD**
- Face/ear with palms/soles
- Diarrhea and hyperbilirubinemia
- Follicular appearance both clinically and histopathologically
  - Tx: Immunosuppression

Morbilliform Eruption in the First 30 Days

• Acute graft versus host disease
• Morbilliform drug eruption
• Engraftment syndrome
  • <14 day – at neutrophil engraftment
  • Rash, fever, weight gain, pulmonary edema
• Viral exanthem
  • Uncommon (CMV/HHV6)
• Eruption of lymphocyte recovery
  • 1\textsuperscript{st} lymphocytes after chemo nadir
  • 2-3 weeks
  • Self limited
Case
What is the diagnosis?

1. Leukemia cutis

2. Neutrophilic dermatosis

3. Invasive fungal infection
What is the diagnosis?

1. Leukemia cutis
2. Neutrophilic dermatosis
3. Invasive fungal infection
Common Fungal Infections

- Aspergillosis
- Invasive candidiasis
  - Candida glabrata
  - Candida albicans
- Zygomycosis
- Other molds (Alternaria)
- Fusariosis
- Pneumocystosis
- Cryptococcosis

Kontoyiannia et al. TRANSNET. Clinical Infectious Disease. 2010:50
Invasive Fungal Infections

• Mortality ~ 30%
  • Greatest with Fusarium infections
  • Lowest with Candidiasis

• Increase risk with...
  • Antibiotic use
  • Neutropenia
  • Exposer to corticosteroids
  • Parental nutrition
## Antifungal Therapy

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Nett JE, Andes DR. Antifungal Agents. Infectious Disease Clinics of N. America. 2010, 30:1
Fungal Key Points

• Lesions appear necrotic or targetoid

• Organisms may be influence by the antifungal prophylaxis used

• Fungal coverage should be changed if a mold is suspected
Case
Solid organ GVHD

• Rare
• Often poor outcomes
• Donor lymphoid chimerism of >20% at 1 week is specific
• Typical symptoms
  • Rash
  • Fever
  • Pancytopenia
  • LFT
  • Diarrhea
Solid Organ GVHD - Liver
Solid Organ GVHD - Lung
Solid Organ GVHD - Liver
Solid Organ GVHD - Key Points

• High clinical suspicion

• May mimic drug rash

• Symptoms similar to patients with aGVHD from a SCT

• Histopathology similar to aGVHD, but it maybe more inflammatory
Questions?