Dermatologic Risks and Transplantation

Allison Hanlon, MD, PhD
Vanderbilt University School of Medicine
Department of Medicine
Division of Dermatology
I have no relevant conflicts of interest to disclose.
Dermatologic Risks and Transplantation

• Acne
• Folliculitis
• Sebaceous hyperplasia
• Overgrowth of hair
• Infections – warts, molluscum contagiosum
• Skin thinning and increased bruising
• Skin cancer
Folliculitis and Acne
Folliculitis
Sebaceous Hyperplasia
Overgrowth of Hair
Cyclosporine associated Gingival Hyperplasia
Molluscum Contagiosum
Verruca
Easy Bruising and Skin Thinning
Overview of Skin Cancer in SOTR

- Clinical appearance of most common skin cancers
- Risk factors for developing skin cancer
- Skin cancer prevention
- Multidisciplinary care
Basal Cell Carcinoma
Basal Cell Carcinoma
Nodular Basal Cell Carcinoma
Basal Cell Carcinoma
Squamous Cell Carcinoma
Squamous Cell Carcinoma
Field Cancerization
Immunocompromised patients at risk for metastasis
Melanoma
Nail Unit Melanoma
Nodular Melanoma
Benign Seborrheic Keratosis

Melanoma
Skin cancer is the most common malignancy in solid organ transplant recipients

- Skin cancer accounts for 40% of malignancies in solid organ transplant recipients (SOTR)
- 50% of Caucasian SOTR will develop skin cancer
- Non-melanoma skin cancer (NMSC) > melanoma

Skin Cancer in SOTR

- Squamous cell carcinoma (SCC) is the most common cutaneous malignancy in transplant patient
- Basal cell carcinoma (BCC) is second most common skin cancer in transplant patient
- Melanoma risk 3.6 times greater likelihood in SOTR than the general population

Lanov E et al. Int J Cancer. 2010;126:1724
Proposed Mechanisms Of Immunosuppression relationship to Skin Cancer Development

- Direct carcinogenic effects of immunosuppression medications
- Proliferation of oncogenic viruses
- Reduced immune surveillance within transplant skin cancers

Skin cancer in transplant patients can be life threatening

- Metastatic SCC 3 year disease specific survival of 56% in solid organ transplant recipients

- Melanoma specific mortality rate is threefold higher in transplant recipients compared with non-recipients

Sheil AG et al. Transplant Proc 1993; 25:1383
Buell JF et al. Transplant Proc 2003; 37:962-3
Older patients present earlier with skin cancer post transplant.

- Transplant at <50 years--delay in increase in relative risk of skin cancer (no skin cancers in initial 3 years) but by 8 years risk increased 200 fold as compared to age matched non-transplant controls.

- Transplant at 50+ years--increase in relative risk of skin cancer beginning in the first year, increased in years 2-6, then stabilize.

Risk is related to the organ transplanted

- Incidence of skin cancer greatest in thoracic transplant patients
- Pancreas-kidney transplant recipients have a greater incidence than kidney alone
- Lowest incidence of skin cancer is in liver transplant recipients

Wisgerhof et.al. J invest Dermatol 2009; 129:2886
Renal transplant recipients with skin cancer prior to transplant

76% developed additional skin cancers after transplant

Average of 16.5 cancers per patient

Pre-transplant history of NMSC increases risk of skin cancer following transplantation

Bouwes Bavinck, J.N. Transplantation, 1996; 61:715
Patients with a fair phenotype are at increased risk of developing skin cancer

- Light colored skin
- History of sunburns
- Red or blonde hair
- Blue or green eyes
Sun exposure associated with skin cancer in transplant patients

High cumulative sun exposure before the age of thirty

Two or more painful sunburns in childhood and adolescence increased risk of skin cancer

Moderate sun exposure vs. low exposure increased risk of skin cancer 2.4 times

High sun exposure vs. low exposure increased risk 47.6 times

Photo courtesy of Tom Stasko, MD
Post transplant sun protection decreases incidence of skin cancer

Daily sunscreen use for 24 months in SOTR significantly lowered the incidence of BCC and SCC

Incidence of a second NMSC after the first was significantly lower in SOTR who used sunblock regularly

HOW TO SELECT A SUNSCREEN

Choosing the right sunscreen can help reduce the risk of skin cancer and early skin aging caused by the sun.

SUNSCREEN IS AN IMPORTANT TOOL in the fight against skin cancer, including melanoma, the deadliest form of skin cancer.

1 in 5 Americans will develop skin cancer in their lifetime.

The American Academy of Dermatology recommends consumers choose a sunscreen that states on the label:

- **BROAD SPECTRUM**
  Means a sunscreen protects the skin from ultraviolet A (UVA) and ultraviolet B (UVB) rays, both of which can cause cancer.

- **SPF 30 OR HIGHER**
  How well a sunscreen protects you from sunburn.

- **WATER RESISTANT OR VERY WATER RESISTANT**
  For up to 40 or 80 minutes. Sunscreens are not waterproof or sweatproof and need to be reapplied.

ONE OUNCE OF SUNSCREEN, enough to fill a shot glass, is considered the amount needed to cover the exposed areas of the body.

© 2017 AMERICAN ACADEMY OF DERMATOLOGY (AAD). ALL RIGHTS RESERVED. NO PART OF THIS INFOGRAPHIC MAY BE REPRODUCED, TRANSLATED, STORED IN A RETRIEVAL SYSTEM, OR TRANSMITTED, IN ANY FORM OR BY ANY MEANS ELECTRONIC, MECHANICAL, PHOTOCOPYING, MICROFILMING, RECORDING, OR OTHERWISE, WITHOUT WRITTEN PERMISSION FROM THE AAD.
Everyday serious protection in casual denim.
Summary of Risk factors for skin cancer in SOTR

- Age at Transplantation
- History of Skin Cancer
- Fair complexion
- Proliferation of Oncogenic Viruses (MCC)
- Medications
- Sun Exposure
  - High UV exposure
Sirolimus and post transplant skin cancer development

• Systemic review and meta analysis of randomized trials comparing immunosuppressive regimens with and without sirolimus
• Sirolimus was associated with a 56 percent decrease in the risk of nonmelanoma skin cancer (HR 0.44, 95% CI 0.30-0.63)
• Patients converted to sirolimus from another immunosuppressive regimen with an overall decrease in nonmelanoma skin cancer (HR 0.32, 95% CI 0.24-0.42)
• Sirolimus was associated with an increased mortality risk in this meta analysis (HR 1.43, 95% CI 1.21-1.71) driven by cardiovascular and infection related deaths
• Additional studies will be useful for clarifying sirolimus role

Knoll et. Al. BMJ 2014; 349
Retinoids

- Modify keratinocyte turnover in the epidermis
- Preventative only when taking the medication
- Rebound when medication is stopped
- Plan on long-term/life-long therapy
Indications for Retinoids

- Numerous NMSCs per year (5-10/y)
- Innumerable actinic keratosis and multiple NMSCs
- Accelerating frequency of NMSCs
- Multiple NMSCs in high-risk locations (head and neck)
- Eruptive keratoacanthomas
- High-risk NMSC (>20% risk of metastasis)
- Metastatic NMSC
Side Effects of Retinoids

• Alopecia
• Chelitis and xerosis
• Transaminitis
• Hypertriglyceridemia
  – Monthly laboratory evaluations until stable dosage then labs at least every 3 months.
  – Elevated lipids may require statins
  – Co-ordinate with transplant team

Figure 58.9 Diffuse xerosis secondary to acitretin use. Dosage was decreased and side effect resolved.

© 2011 Elsevier Inc. Rigel et al: Cancer of the Skin, 2e.
Retinoids

- Acitretin--Double-blind study
  - 6 months--30mg per day
  - More than 10 keratotic skin lesions on the hands and forearms
- 2/19(11%) in treatment group developed 2 SCC’s
- 9/19(47%) in placebo group developed 18 SCC’s
- The effect was most pronounced in patients with a history of squamous cell carcinomas and basal cell carcinomas

Summary of Risk factors for skin cancer in SOTR

- Age at Transplantation: Younger patients
- History of Skin Cancer
- Fair complexion
- Proliferation of Oncogenic Viruses (MCC)
- Medications
- Sun Exposure
  - High UV exposure
Human Papilloma Virus (HPV) and Skin Cancer

- Genital SCC is associated with previous HPV infection
- Screen all transplant patients regarding their history of sexually transmitted diseases including HPV
Merkel Cell Carcinoma

- Merkel cells located in the basal layer of the epidermis
- Merkel cells are important for light touch sensation in the skin
- Second most common cause of non-melanoma skin cancer death
- 5-year relative mortality of 46%
- Metastasis to the nodal basin

Feng et al Science 2008; 319:1096-1100
Lemos BD et.al. doi:10.1016/j.jaad.2010.02.056
Merkel Cell Carcinoma (MCC)

2008 a polyomavirus (Merkel cell polyomaviruses MCPyV) was described as the causative agent for the majority (80%) of MCC.

Immunosuppression has been associated with the development of MCC.

Ratio of MCC and melanoma in the non-transplant population is 1:6; 65:1 in SOTR.

Intratumoral lymphocyte responses associated with improved MCC outcomes.

Summary of Risk factors for skin cancer in SOTR

- Age at Transplantation
  - Younger patients

- Medications

- Sun Exposure
  - High UV exposure

- History of Skin Cancer
  - Fair complexion

- Proliferation of Oncogenic Viruses (MCC)
- Medications

- Fair complexion
When do we send patients to the dermatologist?
## Skin Cancer Risk Post-Transplant

### Enter Recipient Characteristics

<table>
<thead>
<tr>
<th>Not Caucasian</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, less than 50 at Txp</td>
<td>Age, 50 or greater at Txp</td>
</tr>
<tr>
<td>No h/o pre-txp skin cancer</td>
<td>h/o pre-txp skin cancer</td>
</tr>
<tr>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Abdominal Txp</td>
<td>Thoracic Txp</td>
</tr>
</tbody>
</table>

### Cumulative Incidence of Skin Cancer

- Avg 5-Year Risk: 1.01%
- Avg 10-Year Risk: 2.33%

Low Risk: Screen within 10 yrs of Txp
### Skin Cancer Risk Post-Transplant

#### Enter Recipient Characteristics

<table>
<thead>
<tr>
<th>Not Caucasian</th>
<th>Caucasian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, less than 50 at Txp</td>
<td>Age, 50 or greater at Txp</td>
</tr>
<tr>
<td>No h/o pre-txp skin cancer</td>
<td>h/o pre-txp skin cancer</td>
</tr>
<tr>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Abdominal Txp</td>
<td>Thoracic Txp</td>
</tr>
</tbody>
</table>

#### Cumulative Incidence of Skin Cancer

Avg 5-Year Risk 44.75%
Avg 10-Year Risk 74.85%

*Very High Risk: Screen within 6 months of Txp or sooner as recommended by a dermatologist*
Resources

• International Transplant Skin Cancer Collaborative [www.itscc.org]
• At-risc – [www.at-risc.org]
• Skin Care in Organ Transplant Patients [www.scopenetwork.org]