MELANOMA AND NON-MELANOMA SKIN CANCER: WHAT YOU NEED TO KNOW

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- Applies to adults without history of malignancy or premalignant conditions
- Clinicians should remain alert for skin lesions with malignant features noted in the context of the physical exam performed for other purposes
  - LOOK! for ABCDs, rapidly changing lesions, do a biopsy when indicated

Clinical Guidelines

Screening for Skin Cancer: U.S. Preventive Services Task Force Recommendation Statement

Applies to adults without history of malignancy or premalignant conditions

Clinicians should remain alert for skin lesions with malignant features noted in the context of the physical exam performed for other purposes

- LOOK! for ABCDs, rapidly changing lesions, do a biopsy when indicated

Know who is at risk:
- Fair skin patients >65yrs
- Atypical nevi
- > 50 nevi
- Positive family history of skin cancer
- History of significant sun exposure and sunburns

Recommendation: The USPSTF concludes that the current evidence is insufficient to assess the balance of benefits and harms of screening for skin cancer by primary care clinicians or by patient skin self-examination.
**Derm Speak**

- **Pigmented Lesions:**
  - Moles, Seborrheic Keratoses, Melanoma
- **Non-Pigmented Lesions:**
  - Actinic Keratoses, Basal Cell Carcinoma, Squamous Cell Carcinoma

**Nonmelanoma Skin Cancer (NMSC)**

- **Actinic Keratosis**
- **Basal Cell Carcinoma**
- **Squamous Cell Carcinoma**

- Caused primarily by ultraviolet radiation
- SCC and Actinic Keratoses
  - P53 tumor suppression gene mutated by UV
- BCC
  - PTCH gene

**Diagnosis of Skin Cancer**

- Recognize the suspicious lesion
- **BIOPSY TO CONFIRM YOUR DX**

**Actinic Keratosis**

- In-situ dysplasia from ultraviolet exposure.
- Sign of sufficient sun injury to develop NMSC.
- Precancerous (low rate <1%)
- Prevented by sun screen use, even in adults.
**Actinic Keratosis**
- **Diagnosis - Clinical inspection**
  - Red, scaly patch < 6mm.
  - Tender to touch.
  - Sandpaper consistency.
- **Location - Scalp, face, dorsal hands, lower legs (women)**
- **When very thick, suspect hypertrophic AK or SCC**

**Actinic Keratoses and SCC**

**Actinic Keratoses - Treatment**
- **Liquid nitrogen (single freeze-thaw cycle)**
- **Topical treatment**
  - 5-fluorouracil (0.5-5%)
    - 5% qd or BID for 2-4 weeks
  - Imiquimod 5% cream (Aldara)
    - TIW x 4 weeks, with repeated cycles PRN
    - BIW or TIW x 16 weeks
    - QW x 24 weeks
  - Diclofenac
    - Long term treatment (>120 days), moderately effective, side effects
- **Photodynamic therapy**
Actinic Keratoses- Treatment
- Always biopsy if an AK is not responding to appropriate therapy
  - r/o SCC, superficial BCC

Basal Cell Carcinoma
- Most common of all cancers
  - > 1,000,000 diagnosed annually in USA
  - Lifetime risk for Caucasians: up to 50%
- Intermittent intense sun exposure and overexposure (sunburns)
- Locally aggressive, very rarely metastasize

Basal Cell Carcinoma- Clinical Subtypes
- Nodular (classic)
- Superficial
- Pigmented
- Morpheaform (scar-like)
- Clinical subtypes have different biologic behavior
- Histologic subtypes also influence behavior

Basal Cell Carcinoma- Nodular
Basal Cell Carcinoma - Superficial

- Clinically pink, slightly scaly, slightly shiny patch
- Looks like an actinic keratosis
- May be treated with imiquimod, ED+C
Basal Cell Carcinoma - Pigmented

- May be entirely pigmented or there may be specks of pigment within what otherwise looks like a nodular or superficial BCC
- Melanoma is on the differential!!
Basal Cell Carcinoma - Morpheaform

- Clinically scar-like
- Difficult to determine clinically where lesion begins and ends
- Treat with excision (have pathologist check margins) or Mohs micrographic surgery
  - DO NOT ED+C

Basal Cell Carcinoma - Treatment Location, Size, and Subtype Guide Therapy

- Superficial
  - Imiquimod
  - Electrodesiccation and curettage (ED+C)
- Nodular or pigmented
  - ED+C
  - Excision (4mm margins)
  - Mohs micrographic surgery
  - Radiation - comorbidities, tumor size and location
- Morpheaform, infiltrative, micronodular
  - Excision (4mm margins)
  - Mohs micrographic surgery

Topical Treatment of Skin Cancer

- Nonsurgical approaches for managing some skin cancers are available
- Patient selection is the key
- Topical treatments work for superficial cancers (not invasive ones)
  - Superficial BCC, SCC in situ
- Long courses of treatment (months) may be required
- **Biopsy to confirm diagnosis before treating**
Topical Treatment of Skin Cancer
- Imiquimod 5% cream can effectively treat superficial BCC’s and SCC in situ
- Treatment regimen is 5X per week for 6-10 weeks depending on the host reaction
- Efficacy is relatively high (75%-85%)
- Scarring may be reduced compared to surgery

Basal Cell Carcinoma - Treatment Mohs micrographic surgery
- Recurrent or incompletely excised tumors
- Aggressive histologic subtype (infiltrative, morpheaform, micronodular)
- Poorly defined clinical margins
- High risk location (face, ears, eyes)
- Large (>1.0 cm face, >2.0 cm trunk, extrem)
- Tissue sparing location (face, hands, genitalia)
- Immunosuppressed patients
- Tumors in previously irradiated skin or scar
- Tumors arising in setting of genetic diseases

Squamous Cell Carcinoma
- Presents as red plaque, ulceration, or wart like lesion
- Risk factors:
  - Fair skin
  - Inability to tan
  - Chronic sun exposure
- Special situations:
  - Organ transplant recipients
Keratoacanthoma

- Rapidly growing (1 month)
- Dome-shaped nodule with central core of keratin
- May spontaneously regress, but treat as an SCC

Squamous Cell Carcinoma Treatment

- SCC in situ
  - 5FU, imiquimod, liquid nitrogen, electrodesiccation and curettage
- Invasive SCC
  - Excision with 4 mm margins
  - Mohs micrographic surgery
Squamous Cell Carcinoma- Treatment Mohs micrographic surgery

- Recurrent or incompletely excised tumors
- Aggressive histologic subtype (perivascular, perineural)
- Poorly defined clinical margins
- High risk location (face, ears, eyes)
- Large (>1.0 cm face, >2.0 cm trunk, extrem)
- Tissue sparing location (face, hands, genitalia)
- Immunosuppressed patients
- Tumors in previously irradiated skin or scar
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Skin Cancers on the Lower Legs

- BCC and SCC in situ is common on the lower legs, especially in women
- They present as a fixed, red, scaly patch(es)
- It looks very much like a spot of eczema
- Think of skin cancer when red patches on the lower legs don’t clear with moisturizing.

Case

- 64 year old man with psoriasis, hypertension, s/p renal transplant
- 3 months of ulceration of medial aspect of left lower leg, thought to be due to venous insufficiency
- 3 months of topical treatment fails to improve ulceration
Skin Biopsy = Squamous Cell Carcinoma
Chronic phototherapy and immunosuppressive treatments have led to skin cancer
If leg ulcer doesn’t heal with appropriate treatment—refer or biopsy

Question: Which of the following is FALSE about skin cancer in organ transplant recipients

1. Basal cell cancers are more common than squamous cell cancers
2. Voriconazole use is associated with skin cancer in transplant patients
3. The skin cancers are more aggressive
4. The skin cancers are potentially fatal
5. Skin cancers are the most common type of malignancy in this group

Skin Cancer in Organ Transplant Recipients
- Skin cancer is the most common malignancy in sold organ transplant patients
- Incidence increases with survival time post transplant
- Ongoing debate as to whether one or another immunosuppressive is more associated with skin cancer risk
- 90% are nonmelanoma skin cancer
  - Squamous cell carcinoma (SCC)
    - 65X the incidence in the general population
  - Basal cell carcinoma (BCC)
    - 65X the incidence in the general population
- Biologic behavior much more aggressive than in the general population
  - SCC
    - Presents at a younger age
    - Presents 3-5 years after transplantation
    - High frequency of local recurrence in first 6 mo after excision (13.4%)
    - 7% LN metastasis during second year after excision
    - Grow rapidly
    - Aggressive histologic growth pattern

Derm Surg 2004. 30: 642-50
Skin Cancer in Organ Transplant Recipients

- Risk Factors
  - Increased age
  - Increased exposure to UV radiation
  - Increased amount of immunosuppression (SCC)
  - Fair skin (Fitzpatrick skin types I, II, III)
  - Personal history of AK, NMSC, melanoma
  - Heart > kidney > liver transplants
  - HPV infection

To reduce skin cancer risk in transplants:
- Reduce total immunosuppressive dose to minimum required
- Absolute sun protection
- Oral acitretin (25 mg daily) may reduce rate of SCC development
- Please refer your organ transplant patients to a dermatologist for regular skin checks

Seborrheic Keratoses

- BENIGN
  - Appear beginning at age 40, earlier in sunny regions
  - Stuck-on morphology (above the skin)
  - Greasy/waxy/warty texture, horn cysts
  - Face, under breasts, trunk
  - 0.1 to 2.0 cm in diameter
  - Treatment: Reassure, cryotherapy
Acquired Nevi (Moles)

- Almost universal
- In areas of sun exposure
- Change throughout life, appearing at preschool age, growing during young adulthood, and involuting in old age
- 5mm in diameter or less (size of pencil eraser)
- Size (>6mm), number (more than 50) and pattern (not in sun exposed sites) predicts melanoma

Atypical Moles

- Not in sun exposed sites
- Larger than 6 mm in diameter
- Greater than 50
Question: The most important prognostic indicator in melanoma is:

1. Duration of lesion before diagnosis
2. Depth of lesion
3. Presence of ulceration
4. Size of radial growth phase
5. Location of lesion

Malignant Melanoma
- Most frequent cause of death from skin cancer
- Frequently occurs in young adults
  - #1 cause of cancer death in women age 30-35
- Intermittent, intense sun exposure (sunburns)
- Certain genetic mutations explain melanoma in non sun-exposed sites

Lifetime Risk of Melanoma
- 1935: 1 in 1,500
- 1980: 1 in 250
- 1991: 1 in 105
- 2000: 1 in 75
Malignant Melanoma

- Current lifetime risk of melanoma in US
  - 1.94% males, 1.30% females
- Current lifetime risk of dying of melanoma in US
  - 0.35% males, 0.20% females
- 2/3 of melanomas diagnosed bet 1988-99 <1mm in depth (thin)
- Proportion of thick melanomas (≥ 2mm) stayed the same (14.4-15.5%)
- KEY: know who is at risk and what to look for and diagnose early

Ann Int Med. 2009; 150: 188-93

Diagnosis of Melanoma

- The prognosis is DEPENDENT on the depth of lesion (Breslow’s classification) and lymph node status
- Melanoma of < 1mm in thickness is low risk
- Sentinel lymph node biopsy is recommended for melanoma > 1mm (controversial)
- If melanoma is on the differential, complete excision or full thickness incisional biopsy is indicated

Risk factors for melanoma

- **M**oles - atypical
- **M**oles - typical > 50
- **R**ed hair and freckling
- **I**nability to tan – skin types 1 and 2
- **S**evere childhood sunburns
- **K**indred - first degree relatives with melanoma; genetic mutations: CDKN2A, CDK4, others
Melanoma and Sunscreen Use

- Sunscreen use does decrease the risk of melanoma
  - 1621 patients
    - Regular sunscreen vs. "discretionary sunscreen" use
    - 11 melanomas in sunscreen group vs 22 in discretionary group
    - Fewer invasive melanomas in sunscreen group

Acral Melanoma

- Suspect in African American, Latino, Asian patients
Malignant Melanoma

- Asymmetry
- Border
- Color
- Diameter
- Evolution

Malignant Melanoma

- Asymmetry – Two halves of lesion not the same
- Border
- Color
- Diameter
- Evolution

Malignant Melanoma

- Asymmetry
- Border – Irregular, notched, vague
- Color
- Diameter
- Evolution
Malignant Melanoma

- Asymmetry
- Border
- Color - Variations in color: red, white and blue
- Diameter
- Evolution

Malignant Melanoma

- Asymmetry
- Border
- Color
- Diameter - Approximately 6mm (pencil eraser)
- Evolution
Malignant Melanoma

- Asymmetry
- Border
- Color
- Diameter
- Evolution - Changing

Amelanotic Melanoma

- Form of melanoma that lacks pigment
- Must THINK about it in order to make the diagnosis
Melanoma and Imiquimod

- Lentigo maligna (LM) = in situ melanoma in sun exposed areas
- Lentigo maligna melanoma (LMM) - when LM becomes invasive melanoma

Reports in literature supporting treatment of LM with imiquimod CONTROVERSIAL, more studies needed, I don’t recommend

Melanoma and Pregnancy

- In pregnant patients
  - Biopsy suspicious lesions
  - Localized melanoma does not change prognosis
  - Treatment with wide local excision is safe
  - SLN mapping/ biopsy controversial in pregnancy
- Pregnancy before or after melanoma does not change prognosis
- No absolute contraindication to OCPs or HRT in patient with history of melanoma with no reasonable alternative

NEW Therapies in the Treatment of Skin Cancer

- Vismodegib (Erivedge)
  - Hedgehog signaling pathway inhibitor
  - Indicated for metastatic, relapsed, inoperable BCC or BCC not amenable to radiation
- Vemurafenib (Zelboraf)
  - BRAF inhibitor (V600E mutation)
  - Melanoma (late stage)
- Ipilimumab (Yervoy)
  - Inhibits CTLA4
  - Melanoma (late stage)
What to Biopsy/ Refer to Dermatology

- ANY suspicious pigmented lesion
- Any bleeding skin lesion
- Any red spot that doesn’t clear in 6-8 weeks
- Any non-healing erosion or ulceration
- Persons with greater than 50 moles, atypical moles, or family history of melanoma
- Fair-skinned OTR’s with prior sun exposure

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