Actinic Keratosis & Squamous Cell Carcinoma

Basic Dermatology Curriculum
Module Instructions

- The following module contains a number of underlined terms which are hyperlinked to the dermatology glossary, an illustrated interactive guide to clinical dermatology and dermatopathology.
- We encourage the learner to read all the hyperlinked information.
The purpose of this module is to help medical students develop a clinical approach to the evaluation and initial management of patients presenting with suspicious lesions.

By completing this module, the learner will be able to:

- Identify and describe the morphology of actinic keratoses
- Identify and describe the morphology of squamous cell carcinoma
- Initiate appropriate workup for suspicious lesions
- Recognize high risk factors for development of squamous cell carcinoma, including organ transplant and immunosuppression
- Refer patients with skin lesions suspicious for non-melanoma skin cancer to dermatology
Case One

Mr. Dominguez
Case One: History

- Mr. Dominguez is a 70-year-old man who presents to your office with a red, crusted bump on his right forearm.
- He first noticed the growth about 6 months ago. It has been increasing in size. It is sometimes itchy but never painful and has bled after minor traumas. The growth feels dry and rough, but applying lotion does not make it better.
Past Medical History:
- History of extensive sun exposure as a teen
- Burns minimally, always tans (Fitzpatrick skin type IV)
- No history of skin cancer
- No history of arsenic exposure or radiation

Medications:
- Vitamin D

Family History:
- No history of skin cancer

Social History:
Case One: Skin Exam

How would you describe Mr. Dominguez’s growth?
Case One: Skin Exam

Well-circumscribed, 2cm, erythematous nodule with central ulceration and crust. The lesion is firm with palpation.
What is your differential diagnosis?

After you have considered the differential diagnosis, click next for a list of possible diagnoses.
What is your differential diagnosis?

- Actinic keratosis
- Basal cell carcinoma
- Melanoma
- Seborrheic keratosis
- Squamous cell carcinoma
- Verruca vulgaris
What is your next step in management?

a. Liquid nitrogen cryotherapy
b. Reassurance with close follow-up
c. Incisional biopsy
d. Surgical excision
e. Topical antibiotics
Management

**Answer: c**

What is your next step in management?

a. **Liquid nitrogen cryotherapy** *(Would not treat the lesion with cryotherapy without knowing the diagnosis. This is a suspicious lesion that warrants a biopsy.)*

b. **Reassurance with close follow-up** *(A history of a new growing lesion with concerning characteristics warrants a biopsy.)*

c. **Incisional biopsy** *(Before treating this lesion, you must establish a diagnosis.)*

d. **Surgical excision** *(You must know the diagnosis before you can plan treatment with surgical excision and surgical margins)*

e. **Topical antibiotics** *(The lesion is not an infection)*
Incisional biopsy reveals...

Scanning magnification:
Normal epidermis

Dermal extension of well-differentiated ("keratinizing") keratinocytes
Incisional biopsy reveals...

High power view:
Variably-sized keratin pearls
Diagnosis

What is your diagnosis? Click on the correct answer.

- Actinic keratosis
- Basal cell carcinoma
- Melanoma
- Verruca vulgaris
- Seborrheic keratosis
- Squamous cell carcinoma
What is your diagnosis?

If your answer was incorrect, try again.

- Actinic keratosis
- Basal cell carcinoma
- Melanoma
- Verruca vulgaris
- Seborrheic keratosis
- Squamous cell carcinoma
Your diagnosis is correct!

- Actinic keratosis
- Basal cell carcinoma
- Melanoma
- Verruca vulgaris
- Seborrheic keratosis
- **Squamous cell carcinoma**
Squamous cell carcinoma (SCC)

- Most commonly occurs among people with white/fair skin
- Commonly located on the head, neck, forearms, and dorsal hands (sun-exposed areas)
- For African-Americans, incidence of SCC of sun-protected and sun-exposed skin presents equally; overall, 20-40% risk of metastases.
- Increased risk with tanning bed use
- Increased associated mortality compared to basal cell carcinoma, mostly due to a higher rate of metastasis
Squamous Cell Carcinoma

• Of the 3.5 million known new non-melanoma skin cancers diagnosed in 2.2 million Americans each year, about 20% of those are squamous cell

• Cases are underreported because non-melanoma skin cancers do not have to be recorded with cancer registries
SCC: Etiology

- Cell of origin: **keratinocyte**
- Cumulative UV exposure
  - Cause genetic alterations, which accumulate and provide selective growth advantage
- SCC arising in non-sun-exposed areas may be related to chemical carcinogen exposure (e.g. arsenic)
ULTRAVIOLET (UV) RADIATION and TANNING BEDS

• The International Agency for Research on Cancer, a World Health Organization affiliate, includes UV radiation and tanning beds in Group 1: the group ranked as the most dangerous cancer-causing entities/substances

• Other Group 1 members: cigarettes and plutonium
SCC: Clinical manifestations

- Various morphologies
  - Papule, plaque, or nodule
  - Pink, red, or skin-colored
  - Scale
  - Exophytic (grows outward)
  - Indurated (dermal thickening, lesion feels thick, firm)
  - May present as a cutaneous horn
- Friable – may bleed with minimal trauma and then crust
- Usually asymptomatic; may be pruritic/tender
More Examples of SCC
Squamous Cell Carcinoma

- History of recalcitrant wart of thumb
- Did not respond to liquid nitrogen therapy
- Biopsy showed in situ
- Excision revealed invasive squamous cell carcinoma
Well-Differentiated Squamous Cell

- Keratotic nodule in cardiac transplant patient
- Referral for Mohs surgery because of immunosuppression
- Follow with Dermatology for close monitoring
Multiple Squamous Cells

- Patient had received past total body radiation for cutaneous lymphoma
- This patient should be followed closely by Dermatology and the Oncology team
SCC \textit{in situ}

- Also known as Bowen’s Disease
- Circumscribed pink-to-red patch or thin plaque with scaly or rough surface
- Keratinocyte atypia is confined to the epidermis and does \textit{not} invade past the dermal-epidermal junction
Squamous cell in situ on the abdomen
Squamous cell in situ of distal nailbed, lateral nail fold, and fingertip
Squamous cell carcinoma of the nail unit

• Predominantly in males, ages 50-69 yo
• Common clinical signs of appearing warty, subungual hyperkeratosis, onycholyisis, oozing, and destruction of nail plate
• With in situ or invasive squamous cell, conservative excision utilizing Mohs micrographic surgery yields best results; otherwise, high recurrence.
Contrast with basal cell appearances

- Nodular basal cell
- Pigmented nodular basal cell
Superficial basal cell carcinomas
Morpheaform Basal Cell Carcinoma, pre and post Mohs
Mr. Dominguez was diagnosed with invasive SCC. What is your next step in management?

a. Liquid nitrogen cryotherapy
b. Reassurance with close follow-up
c. Incisional biopsy
d. Surgical removal
e. Topical antibiotics
What is your next step in management?

Answer: d

a. Liquid nitrogen cryotherapy (Liquid nitrogen is used to treat pre-cancerous actinic keratoses. It is not the treatment for invasive squamous cell carcinoma.)

b. Reassurance with close follow-up (Squamous cell carcinoma is a malignant lesion with potential for metastases. You must treat it!)

c. Incisional biopsy (You already know the diagnosis and there is no need for another biopsy.)

d. Surgical removal (The treatment of choice for squamous cell carcinoma is surgical excision. The specimen must be sent to dermpath/pathology to document clear margins (complete excision with appropriate margins).

e. Topical antibiotics (The lesion is not an infection.)
Pathology reports for SCC

- “Invasive squamous cell carcinoma”
  - Means there are SCC cells in the dermis
  - If there is no dermal involvement, it is squamous cell carcinoma *in situ*

- “Atypical squamous proliferation”
  - Description often used when biopsy is superficial
  - If dermis cannot be seen in the biopsy, invasive SCC cannot be excluded
  - Rebiopsy if necessary into reticular dermis or do narrow excision if feasible
There are several medical and surgical treatment options.

Suspicion of SCC should prompt referral to a dermatologist for evaluation and discussion of specific treatment approaches.

**Surgical Treatment Options**
- Surgical excision (standard of care for invasive SCCs)
  - Wide local excision with appropriate margins (based on high or low risk)
  - Mohs micrographic surgery if indicated (also for in situ nail unit)
- Curettage and Electrodesiccation or Cryosurgery (reserved for in situ SCC)

**Non-surgical Treatment Options**
- Radiation therapy for poor surgical candidates
- 5-Fluorouracil cream, imiquimod cream, diclofenac gel, ingenol mebutate, photodynamic therapy – typically reserved for in situ SCCs when excision is a suboptimal choice
5-Fluorouracil

- Antimetabolite, interfering with DNA synthesis
- Topical 0.5%, 1%, 2%, and 5% approved by FDA for actinic keratosis treatment
- 5% approved by FDA for superficial basal cell carcinoma treatment
Imiquimod

- Synthetic immune response modifier
- 2.5%, 3.75%, and 5% approved by FDA for actinic keratoses of scalp and face
- 5% approved by FDA for superficial basal cell carcinomas
- The greater the inflammatory response the better the cure rate
Diclofenac

- Downregulates cyclooxygenase enzymes and increases apoptosis
- 3% gel in 2.5% hyaluronic acid is approved by the FDA for actinic keratoses
- A potent nonsteroidal anti-inflammatory drug
Ingenol Mebutate

• Mode of action: causes cellular death followed by inflammatory response
• Approved by FDA for treatment of actinic keratoses:
  • 0.015% gel bid for 3 days for face and scalp
  • 0.05% gel daily for two days for trunk and extremities
For SCC arising in sun-exposed skin, the rate of metastasis to regional lymph nodes ~ 5%

Higher rates of metastasis if:

- Large (diameter > 2cm), deep (> 4mm), and recurrent tumors; poorly differentiated or undifferentiated path
- Tumor involvement of bone, muscle, and nerve
- Location on ears and non-hair bearing lip, scalp, and mask of face region
- Tumor arising in scars, chronic ulcers, burns, sinus tracts, or on the genitalia
- Immunosuppressed patients
- Tumors caused by arsenic ingestion
Patient Follow-up

- All patients treated for cutaneous SCC need surveillance for the early recognition and management of:
  - Treatment-related complications
  - Local or regional recurrences
  - Development of new skin cancers

- Patients with a history of non-metastatic SCC should have close follow-up: every 3-6 mos for 2 years; then every 6-12 months for 3 years; then annually for life
Case Two

Mr. Jenkins
Case Two: History

- Mr. Jenkins is a 66-year-old man with a history of SCC who presents to the dermatology clinic for his regularly scheduled follow-up visit. He reports that during a self skin exam, he noticed a few rough, red spots on the face. He asks if this could represent another cancer.

How would you describe the skin findings?
Case Two: Skin Exam

Rough, scaly, thin, red-pink plaques scattered on the forehead and right temple area
What is your diagnosis? Click on the correct answer.

- **Actinic keratosis**
- Basal cell carcinoma
- Melanoma
- Seborrheic keratosis
- Squamous cell carcinoma
- **Verruca vulgaris**
If your answer was incorrect, try again.

- **Actinic keratosis**
- Basal cell carcinoma
- Melanoma
- Seborrheic keratosis
- Squamous cell carcinoma
- **Verruca vulgaris**
- Actinic keratosis
- Basal cell carcinoma
- Melanoma
- Seborrheic keratosis
- Squamous cell carcinoma
- Verruca vulgaris
Actinic Keratosis (AK)

- AKs are premalignant lesions; they have the potential of transforming into a skin cancer. Virtually all AKs that transform into cancer will become **squamous cell carcinoma** (SCC). In studies, associated AKs have been found within or contiguous to an excised squamous cell in 60-100% of cases.

- Most AKs do not progress to invasive SCC
  - Risk of malignant transformation of an AK to SCC within one year is about 8% (range of 0.025%-20%)
  - Risk factors for malignant progression of AK to SCC include: persistence of the AK, cumulative ultraviolet exposure, history of skin cancer, genetic susceptibility, and immunosuppression.

- The keratinocyte is the cell of origin.
Actinic Keratosis

AKs may be considered as part of a disease spectrum:

- Photodamaged Skin
- Actinic Keratosis
- SCC in situ (Bowen’s disease)
- Invasive SCC
AK: Etiology

- Cumulative and prolonged **UV** exposure, resulting in:
  - UV-induced **p53** tumor suppressor gene mutations
- **Individual risk factors** can increase susceptibility:
  - Increasing age
  - Fair skin, light eyes/hair (Fitz skin types I,II)
  - Immunosuppression
  - Genetic syndromes, such as xeroderma pigmentosum and albinism
AK: Clinical manifestations

- May be symptomatic (tender)
- Located in sun-exposed areas
  - Head, neck, extensor forearms, and dorsal hands
- Typically on background of sun damaged skin
- Erythematous papule or thin plaque with a characteristic rough, gritty scale
- Often diagnosed by feel (like sandpaper)

*The diagnosis of AKs should be made cautiously in lesions > 6mm since these may represent SCC in situ or a superficial BCC.*
More Examples of AKs
Actinic keratoses with large central plaque of invasive squamous cell
Recognizing Sun-damaged Skin

- Skin features of chronic sun damage include:
  - Combination of atrophy and hypertrophy
  - Telangiectasia
  - Spotty depigmentation and hyperpigmentation
  - Wrinkles
  - Skin appears “leathery” and “prematurely aged”
Solar Lentigo (lentigines)

- Result from UV damage
- Sun-exposed areas
- One/many small brown macules
Effects of Sun Damage

Cutis rhomboidalis nuchae
(red neck with rhomboidal furrows)

Solar Elastosis
(fine nodularity, pebbly surface)
Actinic (senile) Purpura

- Easy bruising
- Extravasated erythrocytes and increased perivascular inflammation
Back to
Actinic Keratoses
Actinic cheilitis represents AKs on the lips, most often the lower lip

- Erythematous patch with rough gritty scale involving the lower lip
  - Persistent ulcerations or indurated areas should prompt a biopsy to rule out malignant transformation
How would you treat this AK?

Which of the following treatments would you recommend for this AK?

a. Liquid nitrogen cryotherapy
b. Surgical excision
c. Radiation therapy
d. Topical antibiotic
e. Topical corticosteroids
How would you treat this AK?

Answer: a

Which of the following treatments would you recommend for this AK?

a. Liquid nitrogen cryotherapy
b. Surgical excision
c. Radiation therapy
d. Topical antibiotic
e. Topical corticosteroids

Click here to view a video on cryotherapy
AK: Treatment

- There are several topical and procedural treatment options for AKs. The best option is chosen after consideration of the number of lesions, their location and thickness. Among other patient factors are an individual’s probable tolerance of treatment as well as the capability for compliance and ability to cover cost of medication.
- Therapies are considered local – treating the individual lesion, or field therapies – treating multiple AKs in one area
- Consultation with a dermatologist to guide therapy is useful

- Localized Therapies
  - Liquid nitrogen cryotherapy
  - Curettage +/- electrocautery

- Field Therapies
  - Topical 5-fluorouracil, imiquimod creams; ingenol mebutate gel
  - Photodynamic therapy
Patients with AKs are at increased risk of developing other non-melanoma and melanoma skin cancers.

- Therefore, these patients should have regular skin exams every 6-12 months
- Patients should be seen prior to their regularly scheduled follow-up if they notice a concerning lesion on a self-skin exam
Patient Education

- Educate patients about what squamous cell carcinoma looks like:
  - Skin Cancer Foundation:
    - Warning Signs of Squamous Cell Carcinoma
    - Skin Cancer Information
  - American Academy of Dermatology
    - Squamous cell carcinoma signs and symptoms
Patient Education

- There are multiple resources to educate patients about skin cancer prevention and early detection:
  - American Academy of Dermatology
    - Skin Cancer Prevention
    - How to Perform a Skin Exam video
    - Free resources (handouts, presentations, videos)
  - American Cancer Society:
    - Skin Cancer Prevention and Early Detection
Prevent skin cancer...
Prevent skin cancer...

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

- SPF 30 OR HIGHER
- BROAD SPECTRUM
  - Means a sunscreen protects the skin from ultraviolet A (UVA) and ultraviolet B (UVB) rays, both of which can cause cancer.
- WATER RESISTANT
  - For up to 40 or 80 minutes. Sunscreen can no longer claim to be waterproof or sweatproof.

ONE OUNCE OF SUNSCREEN, enough to fill a shot glass, is considered the amount needed to cover the exposed areas of the body.
Patient Education: Be Sun Smart®

- Generously apply a broad-spectrum, water-resistant sunscreen with a Sun Protection Factor (SPF) of 30 or more to all exposed skin.
  - “Broad-spectrum” provides protection from both UVA and UVB rays.
  - Reapply approximately every two hours, even on cloudy days, and after swimming or sweating.
- Wear protective clothing, such as a long-sleeved shirt, pants, a wide-brimmed hat, and sunglasses.
- Seek shade.
  - Remember that the sun's rays are strongest between 10 AM – 4PM.
  - If your shadow appears to be shorter than you are, seek shade.
Use extra caution near water, snow, and sand because they reflect and intensify the damaging rays of the sun, which can increase your chances of a sunburn.

Get vitamin D safely through a healthy diet that may include vitamin supplements. Don't seek the sun.

Avoid tanning beds. Ultraviolet light from the sun and tanning beds can cause skin cancer and wrinkling. If you want to look tan, consider using a self-tanning product, but continue to use sunscreen with it.

Check your birthday suit on your birthday. If you notice anything changing, growing, or bleeding on your skin, see a dermatologist.
How to perform a skin self-examination

Examine your body front and back in the mirror, then look at the right and left sides with your arms raised.

Bend elbows and look carefully at forearms, upper underarms, and palms.

Look at the backs of your legs and feet, the spaces between your toes, and the soles of your feet.

Examine the back of your neck and scalp with a hand mirror. Part hair for a closer look.
Take Home Points

- Indurated erythematous lesions with keratin are SCC until proven otherwise.
- The diagnosis of SCC is established via biopsy.
- The treatment of invasive SCC is surgical excision. Radiation therapy is a good choice in poor surgical candidates.
- Actinic keratoses are erythematous papules or thin plaques with scale. They feel rough on palpation but are not indurated.
- Actinic keratosis is a precancerous lesion that can evolve into squamous cell carcinoma.
- The treatment for actinic keratoses depends on the number of lesions and the patient’s preference.
- UV radiation and tanning beds: Group 1 cancer-causing entities
Take Home Points cont.

• Skin cancer as a group, including basal cell, squamous cell, and melanoma, is the most common type of cancer.

• P53 is the most altered tumor suppressor gene in squamous cell CA and is also found in AKs.

• The Human Papilloma Virus (HPV) is associated with ungual and periungual squamous cell carcinoma; viral genes affect growth-regulating proteins of infected cells.
• Skin cancer patients often require a team approach for quality care
• The primary care physician and dermatologist are the primary team
• With more involved localized disease, the Mohs surgeon is an added team member; as needed, Plastics and ENT join the care team.
• For metastatic disease, adding Oncology is essential, and if indicated, Radiation Oncology.
• For advanced disease and/or age, nutritional and social services are beneficial
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References


References cont

Resources

• Many thanks to The American Academy of Dermatology for permission to use their Library of Teaching Images.
Additional Resources


• Actually just the beginning 😊
• Do full body skin checks
• Collaborate with your area dermatologists
• Educate for sun protection and skin cancer prevention
• Educate for smoking cessation
To take the quiz, click on the following link: