

Pre- Cancerous Lesions of the Skin & Mucosa

ACTINIC KERATOSES

- Aka solar keratosis, or senile keratosis
- Precursor lesions of cutaneous squamous cell carcinoma (SCC).
- Consists of proliferations of atypical epidermal keratinocytes ,that may progress to invasive SCC
- The overall risk of progression to invasive SCC is (5 -10)%.

ACTINIC KERATOSES

- Risk factors
 - cumulative UV radiation exposure (most important)- outdoor work/hobby
 - fair skin, red or blond hair, blue eyes (Fitzpatrick type 1).
 - age,
 - immunosuppression,
 - prior history of non-melanoma skin cancer.
 - certain genetic syndromes, namely albinism, xeroderma pigmentosum,

ACTINIC KERATOSES

- Site: sun-exposed areas,
 - balding scalp, head, neck, forearms, dorsal hands, dorsal legs in women
- asymptomatic, pruritus, burning or stinging pain, bleeding.
- 2- to 6-mm, erythematous, flat, rough, gritty or scaly papule
- more easily felt than seen.
- against a background of photodamaged skin



ACTINIC KERATOSES

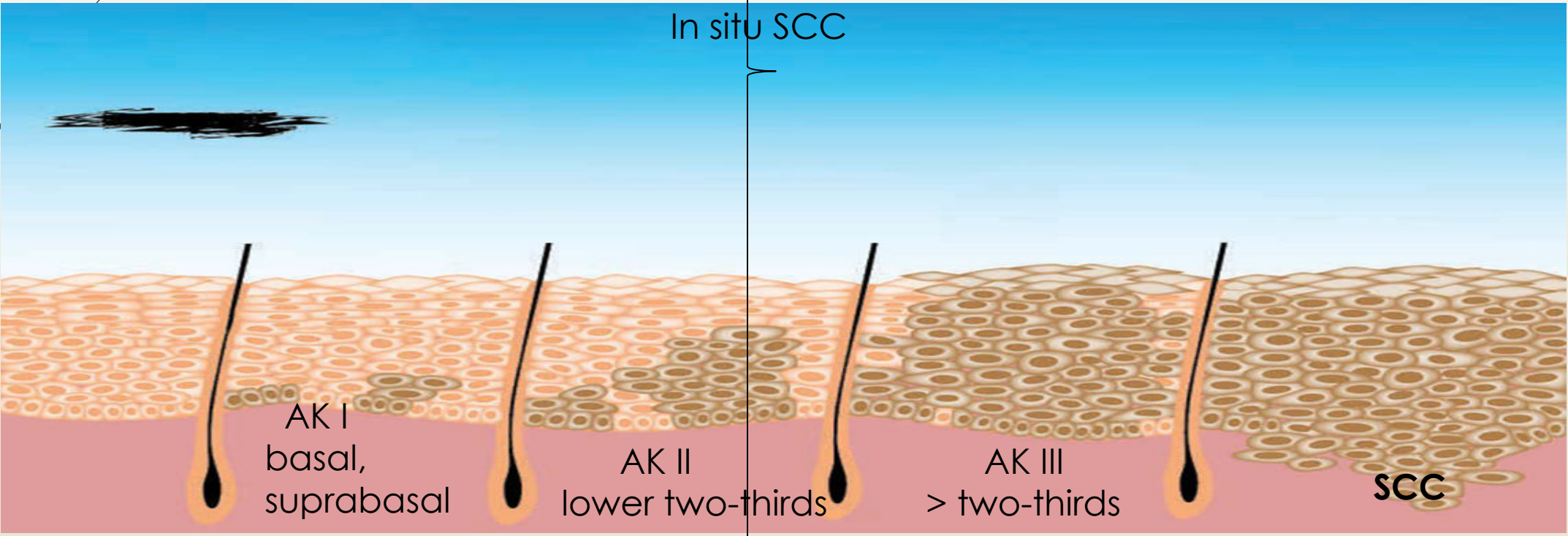
- A punch biopsy with depth upto mid-reticular dermis
- Common indications for a biopsy
 1. Rapidly enlarging lesions,
 2. bleeding or ulceration,
 3. Evidence of inflammation,
 4. strong induration,
 5. lesions extending beyond 1 cm of size,
 6. resistance to treatment.

ACTINIC KERATOSES

- DD
 - seborrheic keratosis, arsenical keratosis
 - melanocytic nevi, Senile lentigo,
 - cutaneous lupus erythematosus
- Established AKs chronic course
- lesions persist, spontaneously regress, or progress to invasive SCCs.
- Spontaneous resolution range from 20% to 30%
- limiting sun exposure, use of sunscreen promote regression.

PROGRESSION TO INVASIVE SCC

- each AK : potential to progress into SCC (5-10% in reality)
- Direct cancerous invasive transformation of basaloid atypical keratinocytes is the most common mechanism of disease progression



ACTINIC KERATOSES Treatment

Lesion-Targeted Therapies

Liquid nitrogen cryosurgery

Surgical approaches (conventional excision, shave excision with/without electrodesiccation)

Ablative lasers

Topical therapy (5-fluorouracil plus salicylic acid)

Lesion-directed photodynamic therapy (PDT) ("patch" PDT)

Field-Targeted Therapies

treat entire actinically damaged areas

Topical/Medical

5-fluorouracil

Imiquimod

Diclofenac-Na

Ingenol mebutate

Procedural

Conventional PDT (with blue light or red light)

Natural daylight PDT

Topical Treatments for Actinic Keratoses		
DRUG	PREPARATION	DOSAGE/APPLICATION
Diclofenac-Na	3% gel	Twice daily for 90 days
5-Fluorouracil (5-FU)	0.5% cream	Once daily for up to 4 weeks
	1% cream	Twice daily for 2-6 weeks
	4% cream	Once daily for 4 weeks
	5% cream	Twice daily for 2-4 weeks
	2% solution	Twice daily for 2-4 weeks
	5% solution	Twice daily for 2-4 weeks
5-FU plus salicylic acid (SA)	0.5% (5-FU) and 10% (SA) solution	Once daily up to 12 weeks
Imiquimod	5% cream	Three times per week for 4 weeks
	3.75% cream	Once daily for 2 weeks
	2.5% cream	Once daily for 2 weeks
Ingenol mebutate	0.015% gel	Once daily for 3 days
	0.05% gel	Once daily for 2 days

PREVENTION of AK

- SUNSCREENS : Broad-spectrum against UVB and UVA, minimum SPF 30
- RETINOIDS:
 - Systemic retinoids in preventing nonmelanoma skin cancer, Ak
 - only effective while taking them; limited by systemic toxicities
- Oral nicotinamide: doubtful

BOWEN DISEASE

- squamous cell carcinoma (SCC) in situ.
- Progress to Bowen carcinoma (invasive SCC) - 5% of cases.
- Etiologic factors include
 1. UV radiation,
 2. arsenic,
 3. previous therapy with psoralen and UVA radiation (PUVA),
 4. immunosuppression,
 5. exposure to ionizing radiation,
 6. infection with HPV(16, 18, 31, 34, 35, 54, 58, 61, 62, and 73)

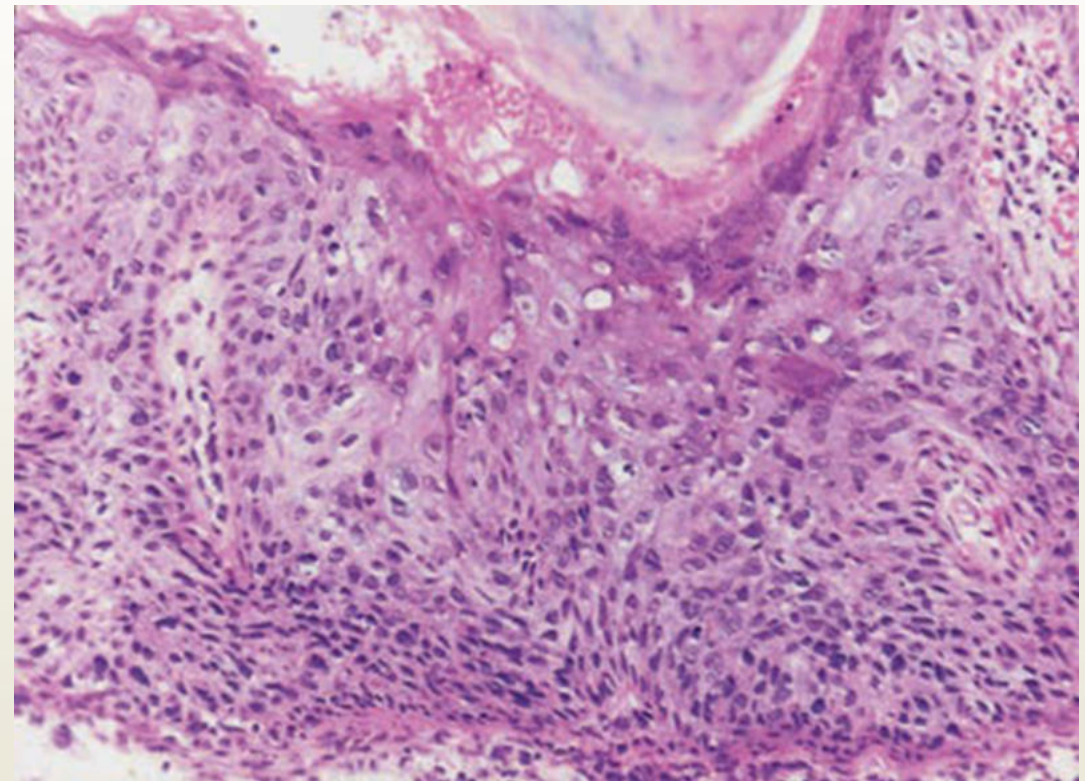
BOWEN DISEASE

- Slow growing, usually asymptomatic.
- erythematous plaques with irregular, clearly demarcated borders.
- Surface scaly, crusted, hyperkeratotic. measure up to several centimeters.



Bowen Disease

- Clinical variants
 - pigmented, intertriginous, periungual, and subungual BD.
- HPE
 - full-thickness epidermal atypia with large, round cells and possible adnexal involvement.



Differential Diagnosis of Bowen Disease

- Erythematous Bowen disease
 - Superficial basal cell carcinoma
 - Dermatitis, eczema
 - Psoriasis
 - Seborrheic dermatitis
 - Lichen planus
 - Benign lichenoid keratosis
 - Irritated or inflamed seborrheic keratosis
 - Actinic keratosis
 - Squamous cell carcinoma
 - Amelanotic melanoma
- Hyperkeratotic Bowen disease
 - Verruca vulgaris
 - Seborrheic keratosis
 - Discoid lupus erythematosus
 - Hypertrophic lichen planus
 - Squamous cell carcinoma

- Pigmented Bowen disease
 - Melanoma
 - Bowenoid papulosis
- Intertriginous Bowen disease
 - Inverse psoriasis
 - Seborrheic dermatitis
 - Candidiasis
 - Paget disease
 - Hailey-Hailey disease
- Subungual or periungual Bowen disease
 - Nail dystrophy
 - Onychomycosis
 - Squamous cell carcinoma
 - Amelanotic melanoma

Treatment of Bowen Disease

➤ Surgical & Destructive therapies

1. Excision
2. Mohs micrographic surgery
3. Curettage with or without
4. Electrosurgery
5. Cryosurgery

➤ Topical Therapies

1. 5-Fluorouracil

➤ Nonsurgical Ablative Therapies

1. Photodynamic (PDT)
2. Laser ablation
3. Chemoablation :TCA
4. Radiation therapy

ARSENICAL KERATOSES

- result from chronic exposure to arsenic
- potential to become squamous cell carcinoma (SCC)
- punctuate, keratotic, yellow papules overlying pressure points
- Palms and soles.



HPV ASSOCIATED EPITHELIAL PRECANCEROUS LESIONS

PRECANCEROUS LESION	ASSOCIATED HUMAN PAPILLOMAVIRUS TYPES ^a
Bowenoid papulosis (BP)	16, 18, 31-35, 39, 42, 48, 51-54
Epidermodysplasia verruciformis (EV)	2, 3, 5, 8, 9, 12, 14, 15, 17, 19, 25, 26, 38, 47, 50
Anal and perianal intraepithelial lesions (AIN, PaIN)	16, 18, 31, 33
Vulvar intraepithelial lesions (VIN)	16, 18, 31, 33
Penile intraepithelial lesions (PIN)	16, 18, 31, 33
Digital/periungual Bowen disease	16

BOWENOID PAPULOSIS

- BP is a precancerous condition of the genitalia
- infection with high-risk HPV, (16, 18, and 33)
- young to middle-aged sexually active, M>F
- multiple red to brownish flat papules on the penis or vulva.



BOWENOID PAPULOSIS

- location
 - on the glans penis, prepuce, and penis in males,
 - around the labia minora and majora in females.
- BP : transitional state between genital warts and in situ SCC.
- Benign, clinical course: spontaneous regression, persistence, rarely transformation into BD and invasive SCC (1% to 2.6%).
- DD
- lichen planus, condylomata acuminata, erythroplasia, molluscum contagiosum, and seborrheic keratoses.

Treatment of Bowenoid Papulosis

- | | |
|---|---------------|
| ➤ Local destructive | ➤ Topical |
| 1. curettage with or without electrosurgery | 1. Tretinoin, |
| 2. CO2-laser | 2. 5-FU, |
| 3. neodymium:YAG laser, | 3. Cidofovir |
| 4. cryosurgery | 4. Imiquimod |
| 5. excision. | |

HPV-specific vaccination for types 6, 11, 16, and 18 in prevention: ????

EPIDERMODYSPLASIA VERRUCIFORMIS

- inherited skin condition
- Loss-of-function mutations of the genes EVER1 and EVER2
- High local susceptibility to infection with HPV, commonly types 5 and 8.
- Factors contributing to pathogenesis
 1. host genetic background
 2. HPV infection,
 3. UV exposure
 4. immunosuppression

EPIDERMODYSPLASIA VERRUCIFORMIS

- develop skin lesions early in life
- clinical presentation
 1. numerous thin, pink, flat-topped papules and plaques that resemble verrucae planae ; knees, elbows, and trunk.
 2. widespread scaly, erythematous, or hypopigmented macules and flat papules resemble tinea versicolor
- High risk to develop AK, BD, invasive SCC in future
- Sun avoidance, sun-protective measures, regular follow up, screening of family members
- topical 5% imiquimod cream and retinoids – mixed results

EPIDERMODYSPLASIA VERRUCIFORMIS



POTENTIALLY MALIGNANT DISORDERS OF THE ORAL CAVITY

LEUKOPLAKIA

- ▶ white lesion of the oral mucosa that cannot be rubbed off or characterized by any other definable lesion or known disease.
- ▶ most common potentially malignant lesion of the oral mucosa
- ▶ potential to become oral SCC is 0.2% to 3.4%.



LEUKOPLAKIA

➡ Etiologic factors for leukoplakia

1. Chronic chemotoxic exposure,
Tobacco is the strongest risk factor: either as smoke or by chewing
2. mechanical trauma with poor oral hygiene
ill-fitting prosthesis, chronic cheek biting,
3. HPV (16 and 18)
4. alcohol consumption

Differential Diagnosis of Oral Leukoplakia

- | | |
|------------------------------|-----------------------------|
| 1. Tobacco-associated lesion | 7. Frictional lesion |
| 2. Candida-associated lesion | 8. Oral white sponge nevus |
| 3. Leukoedema | 9. Oral hairy leukoplakia |
| 4. Lichen planus | 10. Verrucous carcinoma |
| 5. Lupus erythematosus | 11. Squamous cell carcinoma |
| 6. Habitual cheek biting | |

LEUKOPLAKIA treatment

- OMMISSION
 1. consumption of tobacco products, alcohol, bethel nuts,
 2. chronic mechanical trauma
- Surgical excision is the first treatment of choice.
- recurrence after surgical excision : cryotherapy or CO2-laser
- the patient should be followed closely

ERYTHROPLAKIA

- a red macule or patch on a mucosal surface that cannot be categorized as any other known disease entity caused by inflammatory, vascular, or traumatic factors.
- commonly seen with leukoplakia
- least common of all oral potentially malignant lesions
- greatest potential to become oral squamous cell carcinoma
- Males
- Risk factors tobacco products, alcohol consumption.

ERYTHROPLAKIA

- ▶ asymptomatic,
- ▶ solitary, erythematous macule or patch.
- ▶ sharply demarcated from the surrounding pink mucosa,
- ▶ surface is smooth and homogeneous in color



ERYTHROPLAKIA - DD

- ▶ Erythematous candidiasis
 - ▶ Atrophic lichen planus
 - ▶ Lupus erythematosus
 - ▶ Pemphigus
 - ▶ Cicatricial pemphigoid
 - ▶ Kaposi sarcoma
 - ▶ Chronic allergic contact dermatitis
 - ▶ Chronic mechanical trauma
 - ▶ Thermal or mechanical injury
 - ▶ Squamous cell carcinoma
- High potential for malignant transformation : early treatment.
 - Surgery or excision with CO2- laser: treatment of choice

THANK YOU

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