

MECHANISMS OF HUMAN DISEASE: LABORATORY SESSION
PATHOLOGY OF THE SKIN LAB

Friday, February 12, 2012
9:30 am – 11:00 am

FACULTY COPY

GOALS:

Describe the basic clinical and morphologic features of various diseases of the skin.

OBJECTIVES:

- 1. Describe the clinical and morphologic features of common premalignant and epidermal disease of the skin.**
- 2. Describe the clinical and morphologic features of malignant melanoma.**
- 3. Describe the clinical and morphologic features of common inflammatory dermatoses of the skin.**

CASE 1

HISTORY:

A 55 year-old female with a past medical history significant for a renal transplant and multiple cutaneous squamous cell carcinomas presents to her dermatologist for a routine “follow-up” skin exam.

PHYSICAL EXAMINATION:

Examination of the skin reveals several scattered, 1 mm-reddish brown ill-defined papules with adherent scale over the forehead and cheek.

1. What is your clinical differential diagnosis?

Actinic keratosis/hyperplastic actinic keratosis, squamous cell carcinoma, basal cell carcinoma, inflamed seborrheic keratosis,

2. Describe the characteristic changes in the specimen.

Sections of the skin show small proliferative buds of cytologically atypical keratinocytes with overlying parakeratosis and loss of the granular layer. The proliferation spares adnexal structures. The dermis contains solar elastosis.

3. What is your diagnosis?

Actinic keratosis

4. Discuss the significance of the patient's history of renal transplant?

- **A series of progressively dysplastic changes (actinic changes) occur in the epidermis prior to the development of overt malignancy (squamous cell carcinoma).**
- **The dysplasia is usually the result of chronic exposure to sunlight.**
 - **Exposure to ionizing radiation, hydrocarbons, and arsenicals may induce similar lesions.**
- **Whether all actinic keratosis will eventuate in carcinoma given time is subject to debate.**
- **Immunosuppressed patients, particularly renal transplant patients, have a high rate of cancers of the skin, particularly squamous cell carcinoma and precursor lesions such as actinic keratosis.**
 - **Such findings suggest a dysregulation of the local immune system in the skin, which allows these tumors to develop.**

CASE 2

CHIEF COMPLAINT:

“I’ve noticed this bump near my eye; it sometimes bleeds. I had skin cancer before – the doctor said it was the “good” kind.”

HISTORY:

69 year-old male who worked as a roofer and house painter in the past. He is retired and spends half the year in Florida.

PHYSICAL EXAMINATION:

Examination of the skin reveals chronic sun damage with coarsening and yellow discoloration of the skin and deep furrows, particularly around the mouth. A pearly papule is present near the left eye. The surface is focally ulcerated and prominent subepidermal blood vessels (telangiectasias) are present on the surface of the papule.

1. Describe the changes in the specimen.

Sections show nests of basaloid cells (resembling the basal layer of the epidermis) attached to the undersurface of the epidermis and within the dermis. The nests exhibit peripheral palisading and stromal retraction artifact.

2. What is your diagnosis?

Basal cell carcinoma; basal cell carcinomas tend to occur at sites subject to chronic sun exposure and patients with immune suppression such as transplant patients and in patients with inherited defects in DNA replication or repair (xeroderma pigmentosum).

3. What genetic mutation has been described/associated with this process?

- **Basal cell carcinoma has been associated with dysregulation of sonic hedgehog, or PTCH, pathway**
- **PTCH functions as a tumor suppressor**
- **Inherited defects in PTCH gene with loss of heterozygosity in numerous individual tumor foci cause familial basal cell carcinoma syndrome (Gorlin syndrome)**
- **Some component of the PTCH pathway is usually mutated in the majority of sporadic BCC**

CASE 3

CHIEF COMPLAINT:

“My husband says I have this funny mole on my back. I’m really worried about it. He says it looks like it’s changing and it itches sometimes.”

HISTORY/PHYSICAL EXAMINATION:

40 year-old female with no significant past medical history presents with a 1 cm pigmented lesion on the back. The borders are irregular and the color is variegated.

1. What is the clinical problem?

**Changing pigmented lesion;
discuss ABCD’S of melanoma – a = asymmetry, b = border, c = color change, d = diameter; most important clinical sign of the disease is change in color in a pigmented lesion.**

2. Describe histologic changes in the specimen.

Sections show an asymmetric proliferation of cytologically atypical melanocytes with haphazardly placed junctional nests and upward pagetoid scatter. The melanocytes fail to mature with increasing dermal depth and mitotic figures are identified.

3. What are clinical warning signs in pigmented lesions?

Clinical warning signs include enlargement of a pre-existing mole, itching or pain in a pre-existing mole, development of a new pigmented lesion during adult life, irregularity of the borders of a pigmented lesion and variegation of color within a pigmented lesion.

4. Describe some prognostic factors for this lesion.

A number of clinical and pathologic features are used to gauge the probability of metastatic spread and prognosis: These include:

- **Tumor depth (Breslow thickness)**
 - Depth of <1.7mm more favorable prognosis
- **Number of mitoses**
 - No or few mitoses more favorable prognosis
- **Evidence of tumor regression (host immune response)**
 - Absence of regression more favorable prognosis
- **Presence and number of tumor infiltrating lymphocytes**
 - Brisk more favorable prognosis
- **Gender**
 - Female more favorable prognosis
- **Location (central body vs extremity)**
 - Extremity more favorable prognosis

CASE 4

HISTORY/PHYSICAL EXAMINATION:

A 25 year-old male presents to his dermatologist with well-demarcated, scaly, pink to salmon colored plaques over the elbows. Areas of “pin-point” bleeding are noted when the scales are lifted off the surface of the plaque.

1. What is your diagnosis?

Psoriasis; sections show marked psoriasiform hyperplasia, parakeratotic scale, neutrophils in the stratum corneum and thinning of the suprapapillary plates.

2. Why does the patient have “pin-point bleeding?”

The thinning of the suprapapillary plates leads to dilated, tortuous blood vessels in the dermal papillae (characteristic of this process) to come close to the skin surface. Lifting the parakeratotic scale leads to bleeding spots (Auspitz sign).

3. What are some systemic manifestations associated with this process?

Psoriasis is a common chronic inflammatory dermatosis affecting as many as 1 to 2% of people in the United States. Any age may be affected. Psoriasis is sometimes associated with arthritis, myopathy, enteropathy, spondylitic heart disease, or the acquired immune deficiency syndrome. Psoriatic arthritis may be mild or may produce severe deformities resembling the joint changes seen in rheumatoid arthritis.