AAD Forum 118:
Skin and Systemic Malignancy:
PARANEOPLASTIC DERMATOSES &
CUTANEOUS METASTASES

Vincent Liu, MD
University of Iowa

Monday, March 4, 2019
9:00 – 11:00 am
Skin & Systemic Malignancy

Systemic Malignancy

Skin
Skin & Systemic Malignancy

- Complementary Medicine
- Medications
- Drug rash
- Genodermatoses
- INTERNAL MALIGNANCY
- Paraneoplastic Dermatoses
- Cutaneous Metastases
Objectives

• To recognize the clinical and pathologic features of cutaneous metastases, with specific reference to how their cutaneous manifestation is influenced by primary tumor, gender, and anatomic location

• To understand how identification of skin metastases may impact prognosis & management

• To become familiar with the key clinical and pathologic features of the paraneoplastic dermatoses

• To identify the relationship between internal malignancies and cutaneous manifestations in paraneoplastic dermatoses
Q#1: What can cutaneous metastases mimic?

• A) Skin adnexal neoplasms
• B) Vascular neoplasms
• C) Cutaneous lymphomas
• D) Dermatitides
• E) All of the above
Q#1: What can cutaneous metastases mimic?

• A) Skin adnexal neoplasms
• B) Vascular neoplasms
• C) Cutaneous lymphomas
• D) Dermatitides
• E) All of the above
Malignant Melanoma
Metastatic to Skin

• **Overview**
  – Incidence: ~15-20% Stage I/II metastasize
  – Skin predilection: ~45% chance mets go to skin

• **Clinical**
  – Epidemiology:
    • #2-3 cutaneous met in Men (13-32% of all skin mets); #1 Men < 40 yo
    • #4 cutaneous met in Women (5-12% of all skin mets)
  – Morphology
    • Papulonodules (solitary, multiple)
    • Variably pigmented
  – Sites
    • Men: chest, arms, back
    • Women: lower extremities

• **Pathologic**
  – Epidermal sparing except in epidermotropic mets
  – Paucity of inflammation

• **Prognosis**
  – Distant skin metastasis => M1a
  – 5-y survival rate: 19%
Metastatic Renal Cell Carcinoma

• Overview
  – Hi frequency of metasasis
  – Skin 7th site

• Clinical
  – Morphology: red papulonodules
  – Sites: Trunk, scars, scalp

• Pathologic
  – Vascularized tumor
  – Clear cell adenocarcinoma
  – Papillary, acinar

• Prognosis
  – Little chance for cure
  – Death within 6-12 months
Q#2: What clinical clues help predict the primary tumor for a skin metastasis?

- A) Age of patient
- B) Gender of patient
- C) Anatomic location of skin metastasis
- D) Particular metastatic clinical patterns
- E) All of the above
Q#2: What clinical clues help predict the primary tumor for a skin metastasis?

- A) Age of patient
- B) Gender of patient
- C) Anatomic location of skin metastasis
- D) Particular metastatic clinical patterns
- E) All of the above
Tumor Metastasis

Intravasation & Lymphovascular travel

Detachment

Tumor

Extravasation

Implantation
Tumor Metastasis

Rate of Primary Malignancy to Metastasize

Incidence of Primary Malignancy:
- Age
- Gender

Rate of Metastasis to Localize to Skin

Intravasation & Lymphovascular travel

Detachment

Extravasation

Implantation
Relative Incidence of Cutaneous Metastasis by Primary Tumor

Likelihood metastasis involves skin

Skin mets = ~10%
Total mets

Incidence of primary tumor
Rate of metastasis
Incidence of Cutaneous Metastasis per Primary Cancer

G Ital dermatol Venereol 2018;153:77-94.

<table>
<thead>
<tr>
<th>Study</th>
<th>Cancer patients/ Autopsy cases</th>
<th>With skin metastasis</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gates (1937)</td>
<td>2298</td>
<td>64</td>
<td>2.3%</td>
</tr>
<tr>
<td>McDonald et al. (1950)</td>
<td>11,265</td>
<td>33</td>
<td>0.3%</td>
</tr>
<tr>
<td>Abrams et al. (1950)</td>
<td>1000</td>
<td>44</td>
<td>4.4%</td>
</tr>
<tr>
<td>Enticknap (1952)</td>
<td>1000</td>
<td>21</td>
<td>2.1%</td>
</tr>
<tr>
<td>Reingold (1966)</td>
<td>2300</td>
<td>36</td>
<td>1.6%</td>
</tr>
<tr>
<td>Held et al. (1972)</td>
<td>46,929</td>
<td>1046</td>
<td>2.2%</td>
</tr>
<tr>
<td>Brady et al. (1977)</td>
<td>2992</td>
<td>100</td>
<td>3.3%</td>
</tr>
<tr>
<td>Spencer et al. (1987)</td>
<td>7518</td>
<td>679</td>
<td>9%</td>
</tr>
<tr>
<td>Lookingbill et al. (1990)</td>
<td>7316</td>
<td>367</td>
<td>5%</td>
</tr>
<tr>
<td>Hu et al. (2009)</td>
<td>12,146</td>
<td>124</td>
<td>1.02%</td>
</tr>
<tr>
<td>Total</td>
<td>94,764</td>
<td>2514</td>
<td>2.65%</td>
</tr>
</tbody>
</table>
Frequency per Metastatic Tumor Type to Involve Skin*

<table>
<thead>
<tr>
<th>Malignancy</th>
<th>Rate of metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma (45%)</td>
<td></td>
</tr>
<tr>
<td>Breast (30%)</td>
<td></td>
</tr>
<tr>
<td>Nasal sinus (20%)</td>
<td></td>
</tr>
<tr>
<td>Larynx (16%)</td>
<td></td>
</tr>
<tr>
<td>Oral cavity (12%)</td>
<td></td>
</tr>
</tbody>
</table>

*Incidence data variable and evolving among different studies.
Relative Incidence of Cutaneous Metastasis by Primary Tumor

<table>
<thead>
<tr>
<th>Primary Tumor Type</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Lung</td>
<td>Breast</td>
</tr>
<tr>
<td>Breast</td>
<td>Lung</td>
<td>Breast</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Colon</td>
<td>Colon</td>
</tr>
<tr>
<td>SCC head/neck</td>
<td>Melanoma</td>
<td>Melanoma</td>
</tr>
<tr>
<td>Lung</td>
<td>SCC head/neck</td>
<td>Ovary</td>
</tr>
</tbody>
</table>

Likelihood metastasis involves skin
## Anatomic Involvement of Cutaneous Metastases by Primary Tumor

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Head/neck</th>
<th>Chest</th>
<th>Abd</th>
<th>Umbilicus</th>
<th>Back</th>
<th>Arms</th>
<th>Legs</th>
<th>Perineum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head/neck</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>+</td>
<td>++</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrocolic</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td></td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>++</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Proximity of skin metastatic site to primary tumor*
What’s in a zip code?

- Mapped all cutaneous mets at UCSF (1991-2014); n=1984
- Head/neck > trunk > UEs > LEs
- Using control samples for sites (n=140), measured local immunologic factors:
  - T regulatory cells
  - CD4+ effector cells
  - CD8+ cells
- Favored metastatic sites: Tregs CD8+ cells
Q#3: What would be the likely source of a skin metastasis to the fingers?

• A) Lung
• B) Genitourinary tract
• C) Melanoma
• D) Breast
• E) Oropharynx
Q#3: What would be the likely source of a skin metastasis to the fingers?

• A) Lung
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• C) Melanoma
• D) Breast
• E) Oropharynx
Breast Carcinoma Metastatic to Skin

- **Overview**
  - Skin predilection: Most common primary tumor

- **Clinical**
  - Epidemiology: ~70% skin mets in women
  - Morphology: *papulonodules*
    - Inflammatory (cellulitis-like)
    - Carcinoma erysipelaoides
    - Carcinoma telangiectoides
    - Carcinoma en cuirasse
    - Alopecia neoplastica
  - Sites: Anterior chest wall, abd, back,

- **Pathologic**
  - Single filing
  - Ductular differentiation
  - Stromal sclerosis
  - Lymphovascular invasion

- **Prognosis**
  - Incurable
  - Skin-only mets => Mean survival of 57 months
Q#4: What is the significance of cutaneous metastatic disease?

• A) May represent first observed sign of internal malignancy
• B) Associated symptoms may impair quality of life
• C) Influences stage and prognosis
• D) May influence management
• E) All of the above
Q#4: What is the significance of cutaneous metastatic disease?

- A) May represent first observed sign of internal malignancy
- B) Associated symptoms may impair quality of life
- C) Influences stage and prognosis
- D) May influence management
- E) All of the above
Impact of Recognition of Cutaneous Metastasis

• Diagnosis
  – Can precede internal CA diagnosis
  – Monitoring during therapy

• Prognosis
  – Generally upstage TNM
    • Generally adverse prognosis
    • Possible exceptions- breast
      – [JEADV 2008 Jun;22(6):735-40]

• Management
  – Palliative measures
    • Skin-directed therapy
      – Topical
        » Retinoids
        » Imiquimod
      – Excision
      – Intrallesional therapy
      – Radiotherapy
      – Cryotherapy
      – Laser
    • Systemic therapy
  – Molecular sampling of metastasis?
Q#5: What may cutaneous metastases mimic histopathologically?

- A) Primary cutaneous carcinomas
- B) Primary cutaneous adnexal tumors
- C) Primary cutaneous melanocytic lesions
- D) Primary cutaneous lymphomas
- E) All of the above
Q#5: What may cutaneous metastases mimic histopathologically?

- A) Primary cutaneous carcinomas
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Pathologic Differential Diagnosis of Cutaneous Metastases

- Primary Skin Tumor
  - Keratinocytic
  - Melanocytic
  - Adnexal- follicular
  - Adnexal- sweat gland
  - Merkel cell
  - Vascular
  - Smooth muscle
  - Neural
- Lymphoma
  - CTCL
  - CBCL
- Histiocytic
  - Histiocytoses
  - Granulomatous disorder
Cutaneous Metastatic Carcinoma: Pathologic Spectrum

Sinus

AdenoCA

Gastric

Bladder

Renal

Lung
## Immunohistochemical Distinction of Primary Tumors

<table>
<thead>
<tr>
<th>Primary</th>
<th>S100</th>
<th>CK5,6</th>
<th>CK7</th>
<th>CK20</th>
<th>ER, PR</th>
<th>EMA</th>
<th>PSA</th>
<th>CD45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanoma</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Breast</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+/-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lung</td>
<td>-</td>
<td>+ (SCC)</td>
<td>+ (aden)</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Colorectal</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Prostate</td>
<td>-</td>
<td>-</td>
<td>+/-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
</tbody>
</table>

*Others: p63, TTF-1, CAM 5.2, SOX10, MART-1, etc.*
Cutaneous Metastasis of Unknown Primary

• Incidence
  – All cancer risk of met to skin: ~0.7-9%
  – Metastatic cancer of unknown primary: ~5-10%
  – Fraction of cutaneous metastatic cancer with unknown primary: ~4.4%

• Significance
  – Unclear prognostic importance
  – Challenge of excluding primary skin source
Cutaneous Metastases: Conclusions

- Cutaneous metastases
  - Direct manifestations of internal malignancy
  - Usually **papulonodular**, but with a variety of skin variations
    => clinical ddx
  - Insight into pathogenesis, potential therapy
- Clinical clues to identifying primary:
  - Demographics: age, gender
  - Anatomic site: localize near primary
  - Statistical incidence: primary, likelihood of met to skin
- Pathologic differential diagnosis may be addressed with a battery of **immunohistochemical** studies
  - But thorough H&P and imaging frequently also required
  - Unknown primary
- **Poor** prognosis
Q#6: What defines a “paraneoplastic dermatosis”? 

- A) Primary tumor and dermatosis arise simultaneously, parallel courses 
- B) Specific tumor(s) associated with specific dermatosis 
- C) High frequency of association between primary tumor and dermatosis 
- D) Dermatosis is rare 
- E) All of the above
Q#6: What defines a “paraneoplastic dermatosis”?

• A) Primary tumor and dermatosis arise simultaneously, parallel courses
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• D) Dermatosis is rare
• E) All of the above
Paraneoplastic Dermatoses Overview

• Definition
  – Onset of tumor and skin disease occur approximately concurrently
  – Conditions follow parallel course

• Additional considerations
  – Onset & course are independent
  – Specific tumor=> specific skin manifestation
  – Dermatosis is uncommon
  – High rate of association
Paraneoplastic Dermatoses: Pathomechanism

- Depletion of specific substances
- Inanition
- Infections due to immunosuppression
- Generation of autoantibodies targeted to tumor antigens, cross-reacting to skin antigens
- Production of biologically active substances
- Immunologic response to newly exposed tumor epithelial antigens
Paraneoplastic Dermatoses: 
**Strength vs Frequency** of Association with Malignancy
Q#7: How may “paraneoplastic dermatosis” be conceptually organized?

- A) Clinical features of dermatosis
- B) Pathologic features of dermatosis
- C) Pathomechanisms
- D) Strength of associations
- E) All of the above
Q#7: How may “paraneoplastic dermatosis” be conceptually organized?

- A) Clinical features of dermatosis
- B) Pathologic features of dermatosis
- C) Pathomechanisms
- D) Strength of associations
- E) All of the above
Paraneoplastic Dermatoses: Classification

- Papulosquamous (epidermal proliferative) disorders
- Interface dermatitides
- Reactive erythemas
- Neutrophilic dermatoses
- Dermal proliferative disorders
- Deposition disorders
- Other dermatoses
## Paraneoplastic Dermatoses: Papulosquamous Disorders

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
<th>Histopathology</th>
<th>Systemic Neoplasm</th>
<th>Association</th>
<th>Epidemiology</th>
<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acanthosis Nigricans</td>
<td>Hyperpigmented, velvety papillomatosis: axillae</td>
<td>Hyperkeratosis, papillomatosis, acanthosis with elongated dermal projections</td>
<td>Most are Adeno CA: Intraabdominal: 70-90% Gastric: 50-60%</td>
<td>Commonly with insulin resistance</td>
<td>Age: &gt; 40</td>
<td>Before: 20% During: 60%</td>
<td>Closely parallel</td>
</tr>
<tr>
<td>Acquired Ichthyosis</td>
<td>Diffuse rhomboidal scales: trunk and extensor surfaces</td>
<td>Orthokeratosis, mild acanthosis, thin/absent granular layer</td>
<td>Hodgkin: 70-80%</td>
<td>NWE*</td>
<td>Gender: Both Age: Older</td>
<td>Usually after, but also before</td>
<td>Closely parallel</td>
</tr>
</tbody>
</table>

*NWE = Not well established

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
<th>Histopathology</th>
<th>Systemic Neoplasm</th>
<th>Association</th>
<th>Epidemiology</th>
<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Tripe Palms</strong></td>
<td>Rugose, velvety palms. May be associated with AN</td>
<td>Hyperkeratosis, acanthosis, papillomatosis</td>
<td>Lung CA #1 Gastric CA #2, esp. with AN</td>
<td>Over 90%</td>
<td>Gender: Both Age: Older</td>
<td>Before/During: 60%</td>
<td>NWE</td>
</tr>
<tr>
<td><strong>Sign of Leser-Trelat</strong></td>
<td>Increase in size and number of seborrheic keratoses. Pruritus. AN in 20% of cases.</td>
<td>Seborrheic keratoses. May resemble papilloma in AN</td>
<td>GI adeno CA: 1/3 Lymphoproliferative 1/5</td>
<td>NWE</td>
<td>Gender: Both Age: Older</td>
<td>Before and after</td>
<td>NWE</td>
</tr>
<tr>
<td><strong>Bazex</strong></td>
<td>Scaly erythematous plaques: acral areas</td>
<td>Hyperkeratosis, parakeratosis, mononuclear perivascular infiltrate</td>
<td>SCC of oropharynx, larynx, esophagus, lungs</td>
<td>Nearly every case</td>
<td>Mostly males Age: 60-70</td>
<td>Before: 60% During: 20% After: 15%</td>
<td>Closely parallel</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
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<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatomyositis</td>
<td>Heliotrope rash: periorbital. Flat topped papules over knuckles</td>
<td>Interface dermatitis with variable mucin deposition</td>
<td>Increased ovarian CA in females</td>
<td>25-30%</td>
<td>Gender: unclear</td>
<td>Before/during. Most within 1 year.</td>
<td>Closely parallel</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Age: 50’s, 60’s, Older than</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>non-CA assoc DM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paraneoplastic Pemphigus</td>
<td>Pruritic polymorphous lesions, bullae, papules/plaques: trunk, oral</td>
<td>Suprabasilar acantholysis, vacuolar interface degeneratio n</td>
<td>¾ hematolymp hoid: non-Hodgkin 42% CLL 29%</td>
<td>75%</td>
<td>Avg. age: 59</td>
<td>Before: 50%</td>
<td>Not parallel</td>
</tr>
</tbody>
</table>
# Paraneoplastic Dermatoses: Reactive Erythemas

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
<th>Histopathology</th>
<th>Systemic Neoplasm</th>
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<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema Gyratum Repens</td>
<td>Rapidly progressing erythematous rings: trunk, proximal extremities</td>
<td>Hyperkeratosis, superficial dermal perivascular lymphohistiocytic infiltrate</td>
<td>Bronchial CA #1 (32%)</td>
<td>82%</td>
<td>2 M: 1 F</td>
<td>Before: 80%</td>
<td>Closely parallel</td>
</tr>
<tr>
<td>Necrolytic Migratory Erythema</td>
<td>Erythematous macules/papules in annular configuration: face, abdomen, thighs, perianal/oral</td>
<td>Parakeratosis, keratinocytes with pyknotic nuclei</td>
<td>Pancreatic alpha cell tumor</td>
<td>Almost always</td>
<td>Gender: Both Age: 50’s, 60’s</td>
<td>Early or late</td>
<td>Not parallel</td>
</tr>
</tbody>
</table>
# Paraneoplastic Dermatoses: Neutrophilic Dermatoses

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
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<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sweet Syndrome</strong></td>
<td>Erythematous tender plaques/nodules in upper extremities. Fever, neutrophilia.</td>
<td>Dense and extensive neutrophilic infiltrate with vasculopathy</td>
<td>AML and Lymphoma: 85%</td>
<td>20%</td>
<td>Gender: NWE Median age: 52</td>
<td>Before: 2/3 Within 1 month: 40%</td>
<td>Closely parallel</td>
</tr>
<tr>
<td><strong>Pyoderma Gangrenosum</strong></td>
<td>Discrete ulcers with undermined borders. Pathergy.</td>
<td>Dense dermal neutrophilic infiltrate.</td>
<td><strong>AML # 1</strong> Multiple Myeloma #2 Solid Tumors: Rare</td>
<td>7%</td>
<td>F &gt; M Avg. age: 45-52</td>
<td>NWE</td>
<td>NWE</td>
</tr>
</tbody>
</table>

*NWE = Not well established*
NXG- Association with Internal Malignancy

- 80% have **monoclonal gammopathy** IgG-kappa
- 10% of these pts develop multiple myeloma
- Other lymphoproliferative associations
  - Hodgkin
  - Non-Hodgkin
Paraneoplastic Dermatoses: Dermal Proliferative

<table>
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<tr>
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<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multicentric Reticulohistiocytosis</td>
<td>Pink/brown papules/nodules: hands, face; symmetric athropathy</td>
<td>Nodular infiltrate of histiocytes and multicellular giant cells with eosinophilic ground glass cytoplasm</td>
<td>No predominant cancer type</td>
<td>20-30%</td>
<td>1 M : 1.85 F Avg. age: 50 80% Caucasian</td>
<td>Unknown</td>
<td>Not parallel</td>
</tr>
<tr>
<td>Dermatosis</td>
<td>Clinical</td>
<td>Histopathology</td>
<td>Systemic Neoplasm</td>
<td>Association</td>
<td>Epidemiology</td>
<td>Timing</td>
<td>Course</td>
</tr>
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<tr>
<td><strong>Necrobiotic Xanthogranuloma</strong></td>
<td>Red orange dermal nodules/plaques that ulcerate: periorbital, trunk</td>
<td>Mid dermis to panniculus. Palisading xanthogranuloma, Touton giant cells, necrobiosis</td>
<td>Hematologic and lymphoproliferative</td>
<td>80% with benign IgG</td>
<td>Gender: Both Avg. age: 54-56</td>
<td>NWE</td>
<td>NWE</td>
</tr>
<tr>
<td><strong>Scleromyxedema</strong></td>
<td>2-4 mm waxy papules: symmetrically on arms, hands, face (leonine facies)</td>
<td>Fibroblast proliferation. Mild perivascular lymphoplasmacytic infiltrate with mucin</td>
<td>No clear specific malignancy: MM, Hodgkin, non-Hodg.</td>
<td>80% have monoclonal gammopathy IgG-lambda</td>
<td>Gender: Both Age 30-50</td>
<td>NWE</td>
<td>NWE</td>
</tr>
</tbody>
</table>

*NWE = Not well established*
### Paraneoplastic Dermatoses: Deposition Disorders

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
<th>Histopathology</th>
<th>Systemic Neoplasm</th>
<th>Association</th>
<th>Epidemiology</th>
<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cutaneous Amyloidosis</td>
<td>Smooth, waxy, nonpruritic</td>
<td>Apple-green birefringence with Congo red when stained with purple and crystal violet</td>
<td>Multiple myeloma, Thyroid or MEN</td>
<td>13-16% have Multiple Myeloma</td>
<td>Systemic: M &gt; F</td>
<td>NWE</td>
<td>NWE</td>
</tr>
<tr>
<td></td>
<td>papules/plaques: “pinch purpura” on eyelids</td>
<td></td>
<td></td>
<td></td>
<td>Avg. Age: 65 Localized: NWE</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*NWE = Not well established*
## Paraneoplastic Dermatoses: Other

<table>
<thead>
<tr>
<th>Dermatosis</th>
<th>Clinical</th>
<th>Histopathology</th>
<th>Systemic Neoplasm</th>
<th>Association</th>
<th>Epidemiology</th>
<th>Timing</th>
<th>Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertrichosis Lanuginosa Acquisita</td>
<td>Soft, downy, nonpigmented lanugo hair: face, trunk, axillae</td>
<td>“Mantle hair” structures that extend parallel to epidermis</td>
<td>Men: Lung #1, Colorectal #2, Women: Colorectal #1, lung/breast #2</td>
<td>Nearly every case</td>
<td>3 F : 1 M Age: 40-70</td>
<td>Late in course of malignancy, but possible before</td>
<td>NWE</td>
</tr>
</tbody>
</table>

*NWE = Not well established*
Paraneoplastic Dermatoses associated with Hematolymphoid Malignancies

• Lymphoid
  – Paraneoplastic pemphigus
  – Exaggerated bite reactions

• Myeloid
  – Neutrophilic dermatoses

• Plasmacytoid
  – Necrobiotic xanthogranuloma
  – Scleromyxedema
  – Amyloidosis
  – Cryoglobulinemia
  – Subcorneal pustular dermatosis
Paraneoplastic Dermatoses: Conclusions

• Paraneoplastic dermatoses: heterogeneous group of dermatologic conditions associated with underlying internal neoplasms
• Paraneoplastic dermatoses useful
  – Allowing potential diagnosis of an underlying malignancy
  – Monitoring for tumor recurrence
  – Offering insight into pathogenesis.
• Association between internal malignancy and cutaneous manifestation vary
  – Strength
  – Timing
• Not always specific association, but clues for underlying malignancy
  – Sudden
  – Older
  – Rapid course
  – Atypical or more severe cutaneous lesions
Thank You!