A practical approach to the diagnosis of cutaneous carcinomas and their mimics

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Goal of this Presentation

• To review common non-melanoma skin cancers and some of their mimics
• To discuss their histopathologic features
• To examine diagnostic strategies and ancillary studies that aid in rendering the correct diagnosis in difficult cases

Skin Cancer Prevalence

• Approximately 1,000,000 non-melanoma skin cancers are diagnosed each year in the United States
• Of these roughly 80% are basal cell carcinomas
• 20% are squamous cell carcinomas
• Small percentage of rare carcinomas
• High likelihood of encountering skin carcinomas in daily practice

Basal cell carcinoma

• The most common non-melanoma skin cancer
• Associated with sun-exposure
• Most commonly seen on the head and neck
• May be seen in children associated with genetic disorders: Basal cell nevus (Gorlin) and xeroderma pigmentosum

Basal cell carcinoma

• Accurate diagnosis unusually not a problem
• “Classic” criteria
• Basaloid cells
• Peripheral palisading
• Clefting from the surrounding stroma
• Mitotic figures and individually necrotic tumor cells

BCC reporting

• Histologic subtype (to guide further therapy i.e. “aggressive” subtypes area treated with surgery, topical treatment an option for superficial variants)
• Involvement of margins (biopsy and excision)
• Stromal involvement of margin is considered positive
BCC reporting
• Other notable features such as perineural infiltration
• Other associated lesions (i.e. nevus sebaceus)

Diagnostic difficulties in BCC
• Unusual subtypes that mimic other carcinomas and benign adnexal neoplasms
• Small biopsies from the head and neck (sampling error)
• Carcinoma may detached from its stroma while in formalin
• Squamous metaplasia in ulcerated BCC's

Strategies
• Small biopsies may require many level sections to find tumor and often only a small portion of tumor is present (rendering accurate sub-typing impossible)
• May never find tumor (ask for a deeper biopsy)

Strategies
• "Spin the bottle" to help visualize all tissue (grossly basal cell carcinomas are translucent and may be hard to see at the time of grossing)

Immunostaining
• Ber-EP4 helpful to visualize aggregates of basal cell carcinoma that are subtle or obscured by inflammation
• BCC is positive for androgen receptor
• Cytokeratin 20
• Stains resident Merkel cells
• Merkel cells are typically lost in basal cell carcinomas

Benign basaloid proliferations
• Trichoepitheliomas
• Trichoblastomas
• Follicular hamartomas
• Follicular induction above dermatofibromas
Benign basaloid

- Typically show a more organized growth pattern
- 50/50 rule of thumb
- Stroma/stroma clefting
- Different immunophenotype
- Retain CK20 positive Merkel cells
- Androgen receptor negative
- Stroma is CD10 positive

BCC vs B9 basaloid neoplasm

<table>
<thead>
<tr>
<th>Basal Cell CA</th>
<th>Basaloid neoplasm</th>
</tr>
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<tbody>
<tr>
<td>AR positive</td>
<td>AR negative</td>
</tr>
<tr>
<td>CK 20 negative</td>
<td>CK20 positive (Merkel cells)</td>
</tr>
<tr>
<td>CD10 positive tumor cells</td>
<td>CD10 positive stromal cells</td>
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Squamous cell carcinoma

- Second most common non-melanoma skin cancer
- Great variety of clinical and histopathologic presentations

Squamous cell carcinoma risk

- Sun exposure
- Viral
- Toxins
- Radiation
- Ulcers
- Transplant patients (know the population you serve)

SCC

- Diagnosis usually straightforward
- Full thickness keratinocytic atypia of the epidermis with parakeratosis (implying disordered maturation)
- Extension of irregular aggregates of tumor cells into the dermis
- Increased mitoses, often atypical
- Keratin “pearls”

SCC

- Most squamous cell carcinomas arise in association with solar keratoses
- Gray areas between AK and SCC
- Look for presence of a granular layer and adnexal sparing in AK
Difficulties

- Small biopsies
- Tremendous heterogeneity of histopathology
- Poorly differentiated lesions and subtle variants
- Wide variety of reactive conditions that mimic SCC

Ancillary studies

- Levels of small biopsies
- Keratin, p16, p53, p63, ki-67 stains

Mimics of SCC

- Reactive
- Primary inflammatory
- Infectious
- Benign neoplastic

Pseudoepitheliomatous Hyperplasia

- Irregular squamous epithelial hyperplasia that may involve the epidermis, follicles, and acrosyringia
- It simulates the architecture of invasive carcinoma but fails to demonstrate significant cytologic atypia and increased mitotic activity

Pseudoepitheliomatous hyperplasia

- Result of trauma, chronic inflammation, or infection with a wide range of agents
- Recognition of the histopathology in context of the appropriate clinical setting is important

Wound healing

- One of the most common places to see this type is reaction is adjacent to a biopsy site
- The question is whether or not carcinoma remains
- When in doubt comparison to the prior biopsy can be helpful
Chondrodermatitis
• Occurs on the sun-damaged ears of older individuals
• Clinical impression is frequently carcinoma
• Characterized by marked epidermal hyperplasia, hypergranulosis, and an underlying proliferation of small blood vessels
• May also see epidermal ulceration, and underlying degenerated cartilage

P.E.H Infectious
• Classically seen above deep fungal and mycobacterial infections
• Very often see a “suppurative and granulomatous” infiltrate underlying PEH
• May also see neutrophilic microabsecces in keratoacanthomas
• Special stains/culture study vital

Infectious causes
• May also see P.E.H. at the edge of chronic ulcers
• In AIDS patients HSV and syphilis may lead to chronic ulcers that can be misdiagnosed as carcinoma
• Know your patient population

PEH and other neoplasia
• May be seen in association with lymphoproliferative disorders

Hypertrophic Lichen Planus
• Commonly seen on the shins of older individuals
• We commonly see squamous and basal cell carcinomas on the shin
• May present at a hyperkeratotic plaque and clinically masquerade as squamous cell carcinoma

Benign Keratoses
• Many benign squamous lesions can mimic squamous cell carcinoma in the right setting
• Often these lesions present clinically as a carcinoma and are located on sun-damaged skin
<table>
<thead>
<tr>
<th>Desmoplastic Trichilemmoma</th>
<th>Inverted follicular keratosis</th>
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</thead>
<tbody>
<tr>
<td>• First described in 1990 by Santa Cruz et al and thought to be a secondary change in a pre-existing trichilemmoma</td>
<td>• A benign keratosis thought to arise from either hair follicles or represent a traumatized seborrheic keratosis or verruca</td>
</tr>
<tr>
<td>• Characterized by thin cords of epithelial cells that infiltrate through a sclerotic stroma thereby simulating a carcinoma</td>
<td>• May be seen anywhere on the body</td>
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<tr>
<td>• Most commonly seen on the face of older individuals</td>
<td>• Characterized by an endophytic lesion with acanthosis, hypergranulosis and squamous eddies that can mimic invasive squamous cell carcinoma</td>
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