Head and Neck Tumors at the Interface of Benign and Malignant

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The Interface of Benign and Malignant

- Keratinizing dysplasia
- Superficially invasive squamous cell carcinoma
- In situ and low grade salivary gland carcinomas

Keratinizing Squamous Lesions

- Keratin in mucosal surfaces = abnormal
  - Surface keratinization
  - Dyskeratosis
  - “Pink Cell” Change
Keratinizing Lesions

- Clinical terminology: “Leukoplakia”
- Pathology terminology: “Keratosis”
- Reaction to irritation
  - Denture rub
  - Bite lines
  - Tobacco
Diagnosing Keratosis with Dysplasia

- Keratosis with dysplasia
  - Early lesions may be reversible
  - Try to grade the dysplasia
    - But, recognize the inexactness
    - "Keratinizing dysplasia" is acceptable!

Dysplasia Continuum

- Normal
- Mild Dysplasia
- Moderate Dysplasia
- Severe Dysplasia

Keratosis without dysplasia (reactive atypia)

Keratosis with dysplasia
Keratosis with dysplasia
Keratosis without dysplasia (reactive atypia)
Keratosis with moderate to severe dysplasia
Keratosis with severe dysplasia
The Problem with Keratinizing Dysplasia

- “Drop-off” carcinoma: A carcinoma that does not go through the usual dysplasia pathway
  - Invasive carcinoma
  - No high grade dysplasia
  - But, often keratinizing dysplasia
The Interface of Benign and Malignant

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Superficial Invasion

- Nomenclature
  - Superficially invasive squamous cell carcinoma
  - Microinvasive squamous cell carcinoma

Superficial Invasion: Definition

<table>
<thead>
<tr>
<th>Miller</th>
<th>12-50 cells present just below the basement membrane</th>
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<tbody>
<tr>
<td>Friedman</td>
<td>Scattered tongues or discrete foci of invasion through the basement membrane</td>
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<tr>
<td>Padovan</td>
<td>2 mm or less of invasion</td>
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<tr>
<td>Crissman</td>
<td>1-2 mm of invasion (no angiolymphatic invasion)</td>
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<tr>
<td>Barnes</td>
<td>0.5 mm of invasion, measured from basement membrane (no angiolymphatic invasion)</td>
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</tbody>
</table>

Clues to Identifying Superficial Invasion

- Deep keratinization
- Keratin pearls
- Dyskeratosis
- Breach of basement membrane
- Single dropping off cells
- Islands of epithelium in the stroma
- Ragged borders & desmoplasia
- Reaction around stromal tumor cells
Deep dyskeratosis: Suspicious for superficial invasion

Deep keratin pearls: Superficial invasion

Islands and single cells in the stroma

Islands and single cells in the stroma
Tumors at the Interface

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Low Grade Cribriform Cystadenocarcinoma

- Other names that have been used
  - Low grade salivary duct carcinoma
  - Low grade cribriform cystadenocarcinoma
- Clinical
  - Excellent prognosis
  - Unknown relationship to salivary duct carcinoma
  - Rare tumor

Low Grade Cribriform Cystadenocarcinoma

- Histology
  - Smooth cysts with micropapillae
  - Cribriform, roman arches
  - Cytoplasmic microvacuoles
    - Refractile yellow pigment
  - Apocrine, with snouts
  - Intraductal pattern
    - Maintenance of myoepithelial cells
Low grade cribriform cystadenocarcinoma
Low Grade Cribriform Cystadenocarcinoma

- Immunohistochemistry
  - Cytokeratin positive
  - S100 positive
  - Her-2 and AR negative
  - Myoepithelial layer preserved

In Situ Salivary Duct Carcinoma

- Clinical
  - Extremely rare, poorly understood

- Histology
  - In situ or minimally invasive
  - High grade features
    - Necrosis, pleomorphism, mitotic figures
In Situ Salivary Duct Carcinoma

- Immunohistochemistry
  - Myoepithelial cells should be present
    - Invasive component loses myoepithelial cells
  - Androgen receptor and HER2/neu positive
Mammary Analogue Secretory Carcinoma

- Clinical
  - Rare tumor, but not well described yet
  - Mean age 46 (M:F approximately equal)
  - Parotid 13/16 cases
  - 3/15 developed recurrence, one died of disease

- Histology
  - Circumscribed, but not encapsulated
  - Lobulated mass divided by fibrous septae
  - Microcystic, tubular, solid structures
  - Low grade vesicular nuclei with nucleoli
  - Bubbly secretion in microcysts (PAS +)
Mammary Analogue Secretory Carcinoma

- Immunohistochemistry
  - Strong cytokeratin (7, 8, 18)
  - Strong diffuse S100
  - GCDFP (70%) and mammoglobin (100%)
- Molecular
  - ETV6-NTRK3
  - t(12;15)
Carcinoma Ex Pleomorphic Adenoma

- In situ carcinoma ex PA
- Intracapsular carcinoma ex PA
- Minimally invasive carcinoma ex PA
- Invasive (high grade) carcinoma ex PA

Carcinoma ex Pleomorphic Adenoma

- In situ carcinoma ex pleomorphic adenoma
- Histologically malignant
- Myoepithelial cells present
- No invasion

Di Palma, Histopath 46, 2005
Brandwein, Oral and Max Path, 81, 1996
Carcinoma ex Pleomorphic Adenoma

- *Intracapsular carcinoma ex pleomorphic adenoma*
  - Histologically malignant
  - No myoepithelial cells present
  - No invasion

Intracapsular carcinoma ex pleomorphic adenoma

Carcinoma ex Pleomorphic Adenoma

- Minimally invasive carcinoma ex pleomorphic adenoma
  - Histologically malignant
  - No myoepithelial cells present
  - Invasion is present, but is not extensive
    - <1.5 mm
    - <5 mm
    - <8 mm

Excellent prognosis
Carcinoma ex Pleomorphic Adenoma

- Invasive carcinoma ex PA
  - Relatively rare
  - Clinical
    - Long standing mass with recent rapid enlargement
    - History of PA
      - Resected incompletely
      - Recurrent

Invasive Carcinoma ex PA

- Histology
  - Residual pleomorphic adenoma
  - Carcinoma component
    - Specific salivary carcinoma (any type)
    - Adenocarcinoma, NOS
  - IHC
    - Specific to type of carcinoma
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