A Cutaneous Facial Mass Identified as the New Entity ‘Mammary Analogue Secretory Carcinoma’ of Probable Salivary Gland Origin

Scott W. Binder, MD
Professor and Senior Vice Chair
Chief, Dermatopathology
Geffen/UCLA Healthcare
Case Presentation

A 50 year-old man presents with a 7 mm erythematous papule on the right face.

- Developed over a few months
- Asymptomatic
- No history of prior neoplasms including salivary gland tumors
Clinical Impression

“Rule out bug bite”
Differential Diagnoses

- Acinic cell carcinoma
- Apocrine or eccrine sweat duct tumor
- Mammary analogue secretory carcinoma
- Benign oncocyctic neoplasms
  - Oncocytoma, Oncocytic cystadenoma, Warthin tumor
- Mucoepidermoid carcinoma
- Salivary duct carcinoma
Diagnosis

Mammary Analogue Secretory Carcinoma (MASC)

? Primary salivary gland origin v. primary cutaneous tumor
Background

- MASC first described in 2010 by Skalova et al.
- Morphologic overlap between acinic cell carcinoma and secretory carcinoma of the breast
- Tumors affect all ages (range 14-77), slightly male-predominant
MASC

- Presents as slowly growing mass, often near parotid gland
- No evidence of primary cutaneous origin, as of yet
- Most treated with non-radical excision +/- radiotherapy
- Cases of lymph node metastases, local recurrences, low mortality

Chiosea et al, Histopathology 2012
Histology of MASC

- Unencapsulated, lobulated
- Intercalated duct cells in tubular, microcystic, papillary patterns
- Lumina with ample “bubbly” secretions (mucicarmine +)
- Absence of serous acinar granules
Immunohistochemistry of MASC

Staining

- Usually positive
  - S100
  - CK7
  - Vimentin
- Often positive
  - EMA
  - GCDFP
  - Mammoglobin
- Negative
  - CK5/6, CK20
  - P63, TTF-1, PSA, Thyroglobulin
### TABLE 3. Key Cytologic Differential Diagnoses of MASC

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Key Cytomorphologic Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign salivary gland</td>
<td>Acinar and ductal cells, low cellularity, more cohesive</td>
</tr>
<tr>
<td>Benign oncocytic neoplasms [oncocytoma, oncocytic cystadenoma, Warthin tumor]</td>
<td>Lack vacuolated cytoplasm, more cohesive</td>
</tr>
<tr>
<td>Acinic cell carcinoma</td>
<td>Usually lacks mucin</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>Epidermoid differentiation, High-grade nuclei and necrosis</td>
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<td>Salivary duct carcinoma</td>
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*Griffith et al, Cancer Cytopathology 2012*
Differentiating Features of MASC

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Key Ancillary Testing Features</th>
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<tr>
<td>Benign salivary gland</td>
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<tr>
<td>Benign oncocytic neoplasms</td>
<td>Antimitochondrial antibody positive, S-100 negative</td>
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<tr>
<td>[oncocytoma, oncocytic cystadenoma, Warthin tumor]</td>
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<tr>
<td>Acinic cell carcinoma</td>
<td>PASD-positive cytoplasmic granules, DOG-1 strong, S-100 weak, mammaglobin negative</td>
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<tr>
<td>Mucoepidermoid carcinoma</td>
<td>p63 positive, MAML2 translocation, S-100 negative Androgen receptor positive, S-100 negative</td>
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<td>Salivary duct carcinoma</td>
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Griffith et al, Cancer Cytopathology 2012
Fusion Gene

- Almost all MASC had fusion gene ETV6-NTRK3

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<tr>
<th>Telomere</th>
<th>12p13 Region</th>
<th>Chromosome</th>
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<tr>
<td>MLL1</td>
<td>ETV6</td>
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LSI ETV6 (TEL) Dual Color, Break Apart Rearrangement Probe

Normal Cells
No ETV6 Split Signals

Abnormal ETV6 split signals
Clinical Course

• Patient had neoplasm completely excised by the ENT service
• Work-up for primary underlying neoplasm is on-going and imaging studies are negative for primary salivary gland tumor
Summary

- MASC is likely an under-recognized diagnosis and can present a diagnostic pitfall, easily being confused with a primary adnexal tumor given that it is a newly-described entity and too bland to be immediately interpreted as a metastasis or recurrence. The origin of this particular tumor is still uncertain, as no salivary gland primary has been detected in this patient.

- Immunohistochemical stains for S100, CK7, p63, vimentin, mammaglobin, GCDFP, and identification of the ETV6-NTRK3 fusion gene would be required to completely evaluate tumors of this type.
Cutaneous Metastases v. Adnexal Primary Carcinoma: A Practical Approach
Cutaneous Metastases

- Clinical Considerations
  - Mean age at presentation is 62
  - Most common primary tumors
    - Lung  30%
    - Melanoma  18%
    - G.I. Tract  14%
    - Breast  5%
    - Lymphoma  5%
  - In approximately 10% of cases, the primary is unknown

- Histologic Types
  - Adenocarcinoma  40%
  - Melanoma  15%
  - Squamous carcinoma  15%
  - Other  30%
Cutaneous Metastases

- Relative frequencies of involvement of different skin sites
  - Face & Scalp  22%
  - Abdomen  18%
  - Back  12%
  - Chest  10%
Cutaneous Metastases v. Primary Adnexal Carcinoma

• **Histopathologic Characteristics of Metastases**
  • Tumor growth often concentrated in the deep dermis - “bottom heavy” appearance
  • Sparing of epidermis common
  • Ulceration and pagetoid spread rarely noted (colonic and melanoma)
  • Tumor necrosis sometimes present
  • Lymph/vascular invasion sometimes observed
  • High grade tumor cells with numerous mitoses
Cutaneous Metastases v. Primary Adnexal Carcinoma

- Immunohistochemical Considerations
  - Battery may include
    - Cytokeratin 7
    - Cytokeratin 20
    - S-100
    - MART-1/Melan-A/MITF or SOX-10
    - PSA
    - TTF-1
    - ER/PR/Her-2-neu
    - CDX-2
    - Cytokeratin 5/6, p63*
Cutaneous Metastases v. Primary Adnexal Carcinoma

• Most common patterns of staining:

• Lung adenocarcinoma:  CK7+/CK20-, S-100-, TTF-1+
• Melanoma:  CK7-/CK20-/S-100+/MART-1+/MITF
• Bladder (TCC):  CK7+/CK20+/S-100-
• Renal Cell CA:  CK7+/CK20-/S-100-/EMA+/CA-9+
• Breast:  CK7+/CK20-/ER/PR+/Her-2-neu+/-
• Prostate:  CK7-/CK20-/PSA+
Cutaneous Metastases v. Primary Adnexal Carcinoma

- Recent studies have shown that CK5/6 and p63 may help distinguish primary adnexal neoplasms (CK5/6+/p63+) from most metastatic carcinomas (CK5/6-/p63-)
- P63 especially helpful
- D2-40 not been especially helpful in my lab
Cutaneous Metastases v. Primary Adnexal Carcinoma

• Impossible to reliably distinguish primary or metastatic eccrine/apocrine tumors from cutaneous metastases of breast carcinomas, especially apocrine or mucinous types

• Immunohistochemical Staining of Breast v. Metastases
  • ER (estrogen receptor)
  • PR (progesterone receptor)
  • GCDFP-15 (gross cystic disease fluid protein)
  • CEA
  • Her-2-neu

• None of these may reliably separate primary sweat duct from breast metastases
Cutaneous Metastases v. Primary Adnexal Carcinoma

• Of these, the best combination:
  • Her-2-neu: more commonly positive in metastatic breast CA than adnexal/sweat duct primaries
  • Androgen receptor: more common in sebaceous tumors than breast metastases
Cutaneous Metastases v. Primary Adnexal Carcinoma

• Aberrant staining of metastases
  • Technical
    • Antibody
    • Technique
  • Therapeutic effect – chemo and/or radiation/immune modulators
  • Tumor metastases may have different immuno phenotypes than the primary
  • Tumors don’t always read the books
  • Another tumor/primary is responsible for the aberrant staining
Cutaneous Metastases v. Primary Adnexal Carcinoma

• **Take Home**
  
  • H&E considerations and clinical information most important for diagnostic purposes
  
  • Immunohistochemistry stains are useful ancillary studies, especially cytokeratin 5/6 and p63 but be careful as these may lead you astray
  
  • Be sure to eliminate the possibility of a basal cell carcinoma demonstrating unusual growth patterns
  
  • Always think of the possibility of a primary adnexal CA in the appropriate clinical and histologic context
  
  • Occasional inability to differentiate a primary adnexal CA from a visceral metastasis
References

References


