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

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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
- Lesion located just lateral to nose
Clinical Impression

“Rule out bug bite”
Histopathology
Histopathology
Histopathology
Histopathology
Histopathology
Histopathology
Differential Diagnoses

- Acinic cell carcinoma
- Apocrine or eccrine sweat duct tumor
- Mammary analogue secretory carcinoma
- Benign oncocytic neoplasms
- Mucoepidermoid carcinoma
- Metastasis from a visceral primary
### Outside Special Stains

<table>
<thead>
<tr>
<th>Stain</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>S-100</td>
<td><img src="image" alt="S-100 Image" /></td>
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<tr>
<td>EMA</td>
<td><img src="image" alt="EMA Image" /></td>
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<tr>
<td>CK 7</td>
<td><img src="image" alt="CK 7 Image" /></td>
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<tr>
<td>CK 20</td>
<td><img src="image" alt="CK 20 Image" /></td>
</tr>
<tr>
<td>p63</td>
<td><img src="image" alt="p63 Image" /></td>
</tr>
<tr>
<td>Mucicarmine</td>
<td><img src="image" alt="Mucicarmine Image" /></td>
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</tbody>
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**UCLA Health System**
Additional Immunohistochemistry

Mammaglobin  CEA  CK 5/6  Thyroglobin

TTF-1  PSA  Ki67
Diagnosis

- Mammary Analogue Secretory Carcinoma (MASC)
  - ? Primary salivary gland origin v. primary cutaneous tumor
- Rule out metastasis
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
  - Mammaglobin
- Negative
  - CK5/6, CK20
  - P63, TTF-1, PSA, Thyroglobulin
Immunohistochemistry of most apocrine tumors

- Cytokeratin 5/6+, p63+
- S100+/-, cytokeratin 7+
- Mammaglobin +/-, EMA+ (patchy, highlights ducts)
- CEA+, GCDFP 15+/-
## Key Differential Diagnoses of MASC

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Key Cytomorphologic Features</th>
<th>Ancillary Testing Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benign oncocytic neoplasms (oncocytoma, oncocytic cystadenoma, Warthin tumor)</td>
<td>Lack vacuolated cytoplasm, more cohesive</td>
<td>S-100 negative, anti-mitochondrial antibody positive</td>
</tr>
<tr>
<td>Acinic cell carcinoma</td>
<td>Usually lacks mucin</td>
<td>PAS-D+ cytoplasmic granules, DOG-1 strongly positive, mammaglobin negative</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>Epidermoid differentiation</td>
<td>p63 positive, S100 negative, MAML2 translocation</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>High grade nuclei, many show necrosis</td>
<td>Staining variable</td>
</tr>
</tbody>
</table>
Fusion Gene

- Almost all MASC had fusion gene ETV6-NTRK3

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, cytokeratin 5/6, mammaglobin, and identification of the ETV6-NTRK3 fusion gene would be required to completely evaluate tumors of this type.

- Primary cutaneous/subcutis MASC v. unusual primary apocrine sweat duct tumor (solid and cystic hidradenoma)
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 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

- 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
46 yo F with history of breast cancer x7 years
Histopathology
Histopathology
Histopathology
IHC Results

CK7
IHC Results
IHC Results

HER2/neu
IHC Results

CK5/6
IHC Results

P63
68 yo M with paranasal mass present x 1 yr – rapid recent growth
Histopathology
Histopathology
Histopathology
IHC Results

CK5/6
IHC Results

p63
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 tumors from 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


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