Practical lessons from salivary gland cases: Application of the Milan System

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DISCLOSURE

FINANCIAL - NONE
I have not had any significant financial interest or other relationship with the manufacturers of the products or providers of the services that will be discussed in my presentation.

NONFINANCIAL - SOME
• I am one of the associate editors of the Milan System for reporting salivary gland cytopathology
• I am one of the authors of the Paris System for reporting urinary cytology
• I am the Vice President elect of the ASC Executive Board
• I am a member of the ABP Test Development Committee
Case History

• 59-year-old woman s/p thyroidectomy (years ago at another institution) for Hashimoto’s thyroiditis, presents for re-evaluation of a multiple bilateral neck lymph nodes.

• The patient has no complaints aside from tenderness in an enlarged left upper cervical lymph node
Left neck ultrasound

Morphologically suspicious left 2B lymph node with rounded contour measuring 1.1 x 1.0 x 1.8 cm

http://www.surgicalcore.org
Immunohistochemistry

Pancytokeratin

p63
Immunohistochemistry on the cell block

**POSITIVE**
- AE1/AE3
- SMA (patchy)
- p63 (patchy)

**NEGATIVE**
- S100
- GATA3
- PAX 8
- TTF1
- Thyroglobulin
- Synaptophysin
- CD 56
What is the best diagnostic category for this case?

A. Neoplastic, Benign
B. Atypical
C. Neoplasm of uncertain malignant potential
D. Suspicious for Malignancy
E. Positive for Malignancy
Differential Diagnosis - Clinical

- Benign salivary gland with lymphoepithelial sialadenitis
- Benign lymph node within the salivary gland or salivary gland inclusions in a lymph node?
- Metastatic thyroid carcinoma
- Metastatic basaloid squamous carcinoma
Differential Diagnosis - Cytomorphology

- Benign salivary gland with lymphoepithelial sialadenitis
- Benign lymph node within the salivary gland or salivary gland inclusions in a lymph node?
- Pleomorphic adenoma, cellular type
- Basaloid neoplasms
  - Basal cell adenoma/ carcinoma
  - Adenoid cystic carcinoma
  - Basaloid squamous carcinoma
- Neuroendocrine tumor
- Metastatic thyroid carcinoma
Differential Diagnoses?

Küttner Tumor

Case

Differential Diagnoses

Lymphoepithelial sialadenitis

Case

Atlas of Salivary Gland Cytopathology: with Histopathologic Correlations
VandenBussche, Ali, Faquin, Maleki, Bishop
Differential Diagnoses

Pleomorphic Adenoma

Case
Differential Diagnoses

Basal cell adenoma

Case

VandenBussche, Ali, Faquin, Maleki, Bishop
Differential Diagnoses

Basal cell adenocarcinoma

Case
Differential Diagnoses

Adenoid cystic carcinoma

Case
Differential Diagnosis

Adenoid Cystic carcinoma

Case
Differential Diagnoses

Basaloid squamous ca

Case
Lymph Node 2B, Left, Ultrasound Guided Fine Needle Aspiration:

Adequacy:
Satisfactory for evaluation.

Interpretation:
Cytological examination: SUSPICIOUS FOR BASALOID NEOPLASM. SEE COMMENT.

Comment: ...The morphology and immunostaining pattern do not support an origin from thyroid; rather they raise the possibility of basaloid tumor arising from the salivary gland (tail of parotid). Excisional biopsy is recommended for definitive diagnosis.

Dr. Swati Mehrotra
LYMPH NODE 2B, LEFT, ULTRASOUND GUIDED FINE NEEDLE ASPIRATION

-SPECIMEN ADEQUACY: Satisfactory for evaluation.

DIAGNOSIS:
Ductal epithelial groups with basaloid features and mild atypia in a background of blood and lymphocytes.

NOTE: ..There are basaloid groups of ductal salivary gland epithelium with mild atypia and admixed background lymphocytes. DDX: neoplasm, reactive changes of salivary gland in a background of chronic inflammation.
Left Parotidectomy
FINAL DIAGNOSIS

LEFT PAROTID TUMOR; PAROTIDECTOMY:
- BASAL CELL ADENOMA, 1.8 CM, COMPLETELY EXCISED
- TWO INTRAPAROTID REACTIVE LYMPH NODES
- SEE COMMENT

COMMENT: The tumor is likely arising from benign salivary gland inclusions in an intraparotid lymph node.
## Is there a helpful IHC panel?

<table>
<thead>
<tr>
<th>Tumor</th>
<th>PanK</th>
<th>LMWK</th>
<th>HMWK</th>
<th>p63</th>
<th>p40</th>
<th>S100</th>
<th>B-cat</th>
<th>CD117</th>
<th>PLAG1</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>v</td>
<td>+</td>
</tr>
<tr>
<td>BCA/BCAdC</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>v</td>
<td>v</td>
</tr>
<tr>
<td>AdCC</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+ (lum)</td>
<td>-</td>
</tr>
<tr>
<td>P(LG)A</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>v</td>
<td>v</td>
</tr>
</tbody>
</table>
# Molecular studies in salivary gland neoplasms

## Tumor Type

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Chromosomal Translocation</th>
<th>Gene Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pleomorphic Adenoma</td>
<td>Rearrangement of 8q12:</td>
<td><strong>PLAG1</strong></td>
</tr>
<tr>
<td></td>
<td>t(3;8)(p21;112)</td>
<td><strong>HMGA2</strong></td>
</tr>
<tr>
<td></td>
<td>t(5;8)(p13;q12)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Rearrangement of 12q13-15:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>t(3;12)(p14.2;q14-5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>ins(9;12)(p23;q12-15)</td>
<td></td>
</tr>
<tr>
<td>Adenoid Cystic Carcinoma</td>
<td>t(6;9)(q22-23;p23-24)</td>
<td><strong>MYB-NFIB</strong></td>
</tr>
<tr>
<td></td>
<td>rarely t(8;9)</td>
<td></td>
</tr>
<tr>
<td>CAMSG/PLGA Family**</td>
<td>t(1;14)(p36.11;q12)</td>
<td><strong>ARID1A-PRKD1</strong></td>
</tr>
<tr>
<td>CAMSG, “classic” type</td>
<td>t(1;14)(p36.11;q12)</td>
<td></td>
</tr>
<tr>
<td>PLGA, “classic” type</td>
<td>t(x;14)(p11.4;q12)</td>
<td><strong>DDX3X-PRKD1</strong></td>
</tr>
<tr>
<td></td>
<td>PRKD1 E710D mutation</td>
<td>Not known</td>
</tr>
</tbody>
</table>

Adenoid Cystic Carcinoma

• Most cases with MYB-NFIB show diffuse MYB nuclear reactivity (C), which can be seen in fusion-negative cases as well.
• This finding is specific to AdCC when strong and diffuse.
• A breakapart FISH assay can be used to show MYB gene rearrangement (D).

Pictures from Dr C. Moskaluk, University of Virginia
Nuclear β-catenin expression in basal cell adenomas of salivary gland

Akihiko Kawahara¹, Hiroshi Harada², Hideyuki Abe¹, Tomohiko Yamaguchi¹, Tomoki Taira¹, Kazutaka Nakashima¹, Hiroyuki Mihashi³, Jun Akiba⁴, Masayoshi Kage¹

• Nuclear β-catenin expression was examined in 22 basal cell adenomas; scores were
  – 2+ in 18 cases (81.8%),
  – 1+ in three cases (13.6%),
  – 0 in one case (4.5%).

• Expression was localized in the basaloid myoepithelial cells.

A comparative analysis of LEF-1 in odontogenic and salivary tumors

Elizabeth A. Bilodeau DMD, MD, Marie Acquafondata BS, E. Leon Barnes MD, Raja R. Seethala MD

Basal cell adenocarcinoma

Adenoid Cystic carcinoma

Human Pathology (2015) 46, 255–259
### The Milan System of Reporting of Salivary Gland Cytopathology

<table>
<thead>
<tr>
<th>Diagnostic Category</th>
<th>ROM*</th>
<th>Management*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. NON-DIAGNOSTIC</td>
<td>25%</td>
<td>Clinical and radiologic correlation/ repeat FNA</td>
</tr>
<tr>
<td>2. NON-NEOPLASTIC</td>
<td>10%</td>
<td>Clinical follow-up and radiologic correlation</td>
</tr>
<tr>
<td>3. ATYPIA OF UNDETERMINED SIGNIFICANCE (AUS)</td>
<td>20%</td>
<td>Repeat FNA or surgery</td>
</tr>
<tr>
<td>4. NEOPLASM</td>
<td></td>
<td>Conservative surgery or clinical follow-up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Conservative surgery</td>
</tr>
<tr>
<td>i) Benign</td>
<td>&lt;5%</td>
<td>Conservative surgery or clinical follow-up</td>
</tr>
<tr>
<td>i) Uncertain Malignant Potential (SUMP)*</td>
<td>35%</td>
<td>Conservative surgery</td>
</tr>
<tr>
<td>5. SUSPICIOUS FOR MALIGNANCY</td>
<td>60%</td>
<td>Surgery: Correlate LG vs HG</td>
</tr>
<tr>
<td>6. MALIGNANT</td>
<td>90%</td>
<td>Surgery: Correlate LG vs HG</td>
</tr>
</tbody>
</table>

*ROM = Range of Management

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**Drs. Diana Rossi and Bill Faquin**
What is the best diagnostic category for this case?

A. Neoplastic, Benign
B. Atypical
C. Salivary gland neoplasm of uncertain malignant potential
D. Suspicious for Malignancy
E. Positive for Malignancy
Salivary Gland Neoplasm of Uncertain Malignant Potential:

- Diagnostic of a neoplasm; however, a diagnosis of a specific entity cannot be made.
- A malignant neoplasm cannot be excluded.
Take home messages

• Reviewed morphological differential diagnosis of basaloid neoplasms in the salivary gland.
• Reviewed the available ancillary tests to differentiate between the “basaloid neoplasms” in the salivary gland.
• Introduced the “SUMP” category of the Milan System of reporting salivary gland cytopathology
Thank you!

Duomo di Milano  2015