A Pot-Pourri of Pitfalls in Non-GYN Cytopathology

Cady Zeman-Pocrnich
October 26, 2019

Conflict of Interest Disclosure

- Member of the IQMH Cytopathology Scientific Committee

Objectives

- After this session on Non-GYN pitfalls, participants should be able to:
  - Appropriately classify lesions from a variety of Non-GYN sites by correctly applying morphological criteria, ancillary study criteria, and clues from the clinical history;
  - Reflect on diagnostic misses and near misses in Non-GYN cytopathology

Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

- Neuroendocrine Lesions
- Salivary Gland Tumours
- Thyroid Nodules

Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

- Neuroendocrine Lesions
- Salivary Gland Tumours
- Thyroid Nodules
Pitfalls in the Cytopathological Dx of Neuroendocrine Lesions

False Negative
Missing Small Cell CA

- Especially on BrBrush/BrWash/BAL
  - Relatively few malignant cells, single cells > clusters
  - Malignant cells misinterpreted as lymphocytes
  - Usually LBC

Small Cell CA on CS vs LBC

<table>
<thead>
<tr>
<th>Small Cell CA on CS</th>
<th>Small Cell CA on LBC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single cells &amp; large tight clusters</td>
<td>Single cells &amp; small loose clusters</td>
</tr>
<tr>
<td>Tight nuclear molding</td>
<td>Loose nuclear molding</td>
</tr>
<tr>
<td>Long strands of nuclear material</td>
<td>Nuclear elongation &amp; few tangles</td>
</tr>
<tr>
<td>Scant cytoplasm</td>
<td>Thin rims of cytoplasm</td>
</tr>
<tr>
<td>Necrosis = obvious</td>
<td>Necrosis = subtle</td>
</tr>
</tbody>
</table>

Small Cell CA on CS
Single Cells & Large Tight Clusters

Small Cell CA on LBC
Single Cells & Small Loose Clusters
Pay attention to clusters
Before dismissing as a “lymphocyte,” consider size & shape
Be aware that the classical cytomorphological features of small cell CA as seen on CS are not as well developed on LBC preps

How can this pitfall be avoided?

Pitfalls in the Cytopathological Dx of Neuroendocrine Lesions

False Negative
Missing Small Cell CA

False Positive
Overcalling Carcinoïd Tumour as Small Cell CA
Pitfalls in the Cytopathological Dx of Neuroendocrine Lesions

False Negative

Missing Small Cell CA

False Positive

Overcalling Carcinoid Tumour as Small Cell CA

Distinguishing Carcinoid Tumor From Small Cell Carcinoma of the Lung

Correlating Cytologic Features and Performance in the College of American Pathologists Non-Gynecologic Cytology Program


Single cells & cells at edges of clusters appear bland and have ample cytoplasm
- Absence of necrosis, apoptotic bodies, and mitotic figures
- Clinical information
- Cell block & Ki67

How can this pitfall be avoided?

Pitfalls in the Cytopathological Dx of Neuroendocrine Lesions

False Negative  →  False Positive  →  Misclassification

- HGNECa ↔ PDAC
- HGNECa ↔ PDSqCC
- HGNECa ↔ Lymphoma
- HGNECa ↔ Sarcoma
How can this pitfall be avoided?

- If you are going to call small cell CA based on cytomorphological features alone, the cytomorphological features must be absolutely perfect
- Immunostudies
- Second opinion for any case where the Ddx is small cell vs other
- Clinical information

Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

- Neuroendocrine Lesions
- Salivary Gland Tumours
- Thyroid Nodules
Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

- Neuroendocrine Lesions
- **Salivary Gland Tumours**
- Thyroid Nodules

Diagnosis? Pitfall?
Pitfalls in the Cytopathological Dx of Salivary Gland Tumours

False Negative
- Calling something WT when it’s not
  - Mucoepidermoid CA
  - Acinic cell CA
  - CC + Lymphocytes + “oncocyes”

False Positive
- Calling something PA when it’s not
  - AdCyCa & other basloid neoplasms

Misclassification
- Oncocytes in WT
- “Oncocytes” in MucoEpCa
- “Oncocytes” in Acinic Cell CA
Pitfalls in the Cytopathological Dx of Salivary Gland Tumours

**False Negative**
- Not common (in our lab) due to use of diagnostic categories
- Beware acceptable atypia in a PA – stay at LP
- Beware of metaplasias (squamous, mucinous)
- Beware of repair

**False Positive**
- BN ↔ LPN
- BN ↔ Metastatic CA
Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

• Neuroendocrine Lesions
• Salivary Gland Tumours
  • Thyroid Nodules

Special Acknowledgement: Dr. M. Weir

Pitfalls in the Cytopathological Dx of Thyroid Nodules

- Architecture Pitfalls
  - Undercalling Small Follicle Pattern
  - Overcalling Small Follicle Pattern
- Atypia Pitfalls
  - Undercalling Atypia
  - Overcalling Atypia

Pitfalls in the Cytopathological Dx of Thyroid Nodules

- Architecture Pitfalls
  - Undercalling Small Follicle Pattern
  - Overcalling Small Follicle Pattern
- Atypia Pitfalls
  - Undercalling Atypia
  - Overcalling Atypia
Before classifying as FN/HCN...

1. Is there chronic thyroiditis?
2. Is there fragmentation?
3. Is evaluation of architecture limited due to blood clot?
4. Could this be parathyroid?

Chronic thyroiditis is **easy** to recognize when it looks like this...

Chronic thyroiditis is **harder** to recognize when it looks like this...

Or this...

Or this...

- Lymphoid tangles & fibrosis
- Lymphoid aggregates
- "Sticky follicles"
- Not true microfollicles
Before classifying as FN/HCN...

1. Is there chronic thyroiditis?
2. Is there fragmentation?
3. Is evaluation of architecture limited due to blood clot?
4. Could this be parathyroid?

What to do if fragmented groups are the predominant finding?
- If very low cellularity → insufficient
- If cellularity meets adequacy criteria → FLUS/HCL
Before classifying as FN/HC...

1. Is there chronic thyroiditis?
2. Is there fragmentation?
3. Is evaluation of architecture limited due to blood clot?
4. Could this be parathyroid?

- Microfollicles
- +/- Colloid-like material
- Tiny cuboidal cells, very uniform
- Lateral/unusual location
- Prior thyroidectomy
- Hypercalcemia

Parathyroid Hormone IHC

Pitfalls in the Cytopathological Dx of Thyroid Nodules

- Architecture Pitfalls
  - Undercalling Small Follicle Pattern
  - Overcalling Small Follicle Pattern
- Atypia Pitfalls
  - Undercalling Atypia
  - Overcalling Atypia

Increase atypia threshold if...

1. Chronic thyroiditis
2. Cyst repair
3. Hurthle cells

Respect atypia, but...

1. Chronic thyroiditis
2. Cyst repair
3. Hurthle cells
Increase atypia threshold if...

1. Chronic thyroiditis
2. Cyst repair
3. Hurthle cells

Respect atypia, but...

Image: Dr. M. Weir
Pitfalls in the Cytopathological Dx of Thyroid Nodules

Outline

Pitfalls I have encountered in the cytopathological diagnosis of:

- Neuroendocrine Lesions
- Salivary Gland Tumours
- Thyroid Nodules

Conclusions

- Neuroendocrine Pitfalls
  - Small cell CA can be easily missed → be aware of morphological criteria on LBC preparations
  - Carcinoid tumour can be misdiagnosed as small cell → awareness of morphological criteria, clinical parameters, use of Ki67
  - Small cell CA is a morphological diagnosis, BUT → beware of mimics, use ancillary studies & 2nd opinions as necessary
- Salivary Gland Pitfalls
  - Avoid FN → strict criteria for a definitive diagnosis of WT or PA
  - Avoid FP → diagnostic categories
  - Misclassification → lymphomas, small cell CA, metastatic CA may mimic BNs
- Thyroid Pitfalls
  - Before ascribing a microfollicular architecture, consider → CT, fragmentation, blood clot, PT
  - Before flagging nuclear atypia, consider → CT, cyst repair, Hurthle cell changes

Don’t carry your mistakes around with you. Instead, place them under your feet and use them as stepping stones.