Glandular Lesions

Michael Thrall MD
Atypical Glandular Cells

- Glandular cells are one of the most problematic areas of cytology
- True lesions are rare, but reactive/metaplastic changes are common
- The interpretation of AGC is made in <1% of Paps in most series
- Of these, most are not true lesions, and the most common true lesion is HSIL involving glands
- Adenocarcinoma in situ and invasive cervical adenocarcinoma are rare and the sensitivity of Pap testing is low
- The identification of AIS/AGC is arguably harder on liquid-based Pap tests - probably the only disadvantage of liquid-based testing
• Air drying artifact accentuates the nuclear changes
• Feathering is more prominent
• Rosettes are more obvious
Conventional Pap test AIS
• Feathering and rosettes are less obvious
• Nuclei are better seen and nucleoli are more often apparent
• Short strips of tumor cells are seen – “Bird tails” or “fish tails”
• Individual tumor cells are more likely to be seen
• Large hyperchromatic crowded groups may also be prominent
• Single intact cells are more easily found
• Hyperchromatic crowded groups are smaller, denser, and more three-dimensional with smoother, sharper margins
• Pseudostratified strips of cells may be the most prominent architectural feature
• Architectural features of peripheral feathering, rosettes, and cell strips have a more subtle presentation
• Nuclear chromatin may be coarse or finely granular
• Nucleoli may be more readily visible
• All from p. 215 of 3rd Edition
Case #1 - bird tails
Case #1 - individual tumor cells
Case #2 - HCGs
Case #2 - feathering
Case #2 - histology
Case #3 - rosettes
Case #3 - nuclear atypia
• Invasive adenocarcinoma often resemble AIS
  – Greater nuclear atypia
  – More prominent nucleoli
  – Loss of polarity of nuclei and disorderly arrangement
  – Clinging diathesis
• Gastric type adenocarcinoma is a non-HPV-driven uncommon variant
  – Cytology is often more bland and difficult to recognize - “adenoma malignum”
• When poorly differentiated, cervical adenocarcinoma is difficult
to differentiate from endometrial adenocarcinoma or metastasis
• Cell groups tend to be denser, spherical, and three-dimensional; nuclei within the central portions may be completely obscured
• Isolated abnormal cells are more frequently seen
• Chromatin is more vesicular with irregular chromatin distribution and chromatin clearing
• Nucleoli are more prominent
• Tumor diathesis is less apparent, consisting of aggregates of proteinaceous and inflammatory debris clinging to the surface of individual cells or cell clusters; SurePath specimens have a finer “cotton candy” diathesis
• All from p. 225 of 3rd Edition
Case #4 - diathesis
Case #4 - feathering
Case #4 - rosettes
Case #4 - bird tails and strips
Case #4 - histology
Adenocarcinoma

• Adenocarcinoma:
  – Endocervical
  – Endometrial
  – Extra-uterine
  – Not otherwise specified (NOS)
Endocervical Adenocarcinoma

- High N:C Ratio
- Syncytial
- Clumpy Chromatin
- Nuclear enlargement
- Nuclear Pleomorphism
Endocervical Adenocarcinoma

Clinging Diathesis

Complex 2D and 3D Architecture
Endometrial Adenocarcinoma

- Watery Diathesis
- Large Pleomorphic Nuclei with Nucleoli
- Tight Clusters
- Engulfed Neutrophils
Serous carcinoma

Low Grade Serous - Psammoma Body
# Endocervical vs. endometrial

## Cytologic Distinction Between Endocervical and Endometrial Primaries

<table>
<thead>
<tr>
<th>Features</th>
<th>Endocervical Carcinoma</th>
<th>Endometrial Carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellularity</td>
<td>Hypercellular</td>
<td>Low cellularity</td>
</tr>
<tr>
<td>Pattern</td>
<td>Strips, rosettes, large abnormal sheets, peripheral feathering, single malignant cells</td>
<td>Small clusters, rarely papillae or single cells</td>
</tr>
<tr>
<td>Diathesis</td>
<td>Visible, type varies by preparation</td>
<td>Watery, absent or subtle</td>
</tr>
<tr>
<td>Cell shapes</td>
<td>Oval, columnar, pleomorphic</td>
<td>Round, irregular, smaller</td>
</tr>
<tr>
<td>Nuclei</td>
<td>Oval, elongated, pleomorphic</td>
<td>Round, irregular in higher grade</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Mucin (+)</td>
<td>Degenerate vacuoles, mucin (-)</td>
</tr>
<tr>
<td>Squamous intraspinillar lesion or SQCA</td>
<td>Usually present</td>
<td>Absent</td>
</tr>
<tr>
<td>High-risk HPV</td>
<td>Positive</td>
<td>Negative</td>
</tr>
</tbody>
</table>

SQCA = squamous cell carcinoma; HPV = human papillomavirus.
Atypical Glandular Cells (AGC)

• Atypical glandular cells
  – NOS (not otherwise specified)
  – Favor neoplastic

• Atypical endocervical cells
  – NOS (not otherwise specified)
  – Favor neoplastic

• Atypical endometrial cells
Atypical Endocervical Cells

Resembles AIS

Hyperchromatic Crowded Group
Contrast Atypical vs. Normal
Atypical Endometrial Cells

Engulfed Neutrophils

Relatively Large Nuclei

Vacuolated

Irregular Architecture