Approach to Glandular Atypia on Paps

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Objectives

After this session on glandular lesions in Pap tests, should be able to:

1. Design an approach to glandular lesions in your practice
2. Distinguish benign mimics from abnormal glandular cells
3. Apply criteria for diagnostic categories
Background

- Pap test screening for SIL
- Reduction of cervical squamous cell ca
- Pap test: not great for glandular especially endometrial
- Increase in cervical adenocarcinoma

1 ATYPICAL GLANDULAR LESIONS ON PAP
Relevance Glandular Lesions

- Although only < 2% of cases
- Results in 80% headaches!
- Significant management difference
  - not a repeat Pap
  - referral – colp/gyn

Bethesda Classification

<table>
<thead>
<tr>
<th>GLANDULAR ABNORMALITIES</th>
<th>NOS</th>
<th>Neoplastic</th>
<th>AIS</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocervical</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Endometrial</td>
<td>+</td>
<td>*</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Glandular Cells</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

* For Ontario Guidelines, not Bethesda

CASE 1

- 34 year old female
- Follow-up Pap test
- Post cone biopsy for HSIL
- LMP: day 10
Your diagnosis

- a) HSIL
- b) AIS
- c) Adenocarcinoma, endometrial
- d) LUS sampling
- e) Atypical endocervical cells, neoplastic

Approach to Atypia

- Atypical Glandular Cells
  - Benign mimic
  - True glandular atypia
  - Squamous lesions
    - NOS Neoplastic Malignant
Approach to Atypia

Benign mimic:
- Tubal metaplasia
- Endometrial
  - LUS sampling
- Endocervical
  - polyp, repair, XRT, MSH, Arias Stella

Is There Glandular Atypia?

- 3 IMPORTANT CRITERIA benign vs. neoplastic
  1. Irregular nuclear outline
  2. Atypical single cells
  3. Reduced cytoplasm amount (increased N/C)

Diagnostic Criteria

<table>
<thead>
<tr>
<th>LUS SAMPLING</th>
<th>AIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Honeycomb, overlapping</td>
<td>Crowding, overlapping</td>
</tr>
<tr>
<td>Sheets, glands</td>
<td>Strips</td>
</tr>
<tr>
<td>- uniform, tightly packed</td>
<td>Feathering</td>
</tr>
<tr>
<td>Pseudostratification</td>
<td>Rosettes</td>
</tr>
<tr>
<td>Nuclear atypia</td>
<td>Pseudostratification</td>
</tr>
<tr>
<td>Small cells, scant cytoplasm</td>
<td>Nuclear atypia (carrots)</td>
</tr>
<tr>
<td>Biphasic - stroma</td>
<td></td>
</tr>
</tbody>
</table>

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LUS SAMPLING
Cohesive
No feathering
Polarized
Stroma

WHICH ONE IS LUS vs AIS?

Now you try

LUS
Spindled stroma
Organized gland
No feathering

AIS
Disorganized
Feathering, carrots
Nuclear atypia, variation

WHICH ONE IS LUS vs AIS?
Now you try
a) HSIL
b) AIS
c) Tubal metaplasia
d) LUS sampling
e) Atypical endocervical cells, NOS

Diagnostic Criteria

**TUBAL METAPLASIA**
- Crowding, overlapping
- Strips, groups
- Cilia, terminal bars
- Pseudostratification
- Nuclear atypia (rounder)

**AIS**
- Crowding, overlapping
- Strips
- Feathering
- Rosettes
- Pseudostratification
- Nuclear atypia (carrots)
Management

- LUS sampling
- Tubal metaplasia

RULE IN A BENIGN MIMIC

Remember
LUS sampling
Tubal metaplasia
CASE 2

- 31 year old female
- Colposcopy Pap test
- Referred for abN Pap
- LMP: now day 15

Your diagnosis

a) HSIL
b) AIS
c) Adenocarcinoma, endometrial
d) LUS sampling
e) Atypical endocervical cells, neoplastic
Approach to Atypia

Atypical Glandular Cells

Benign mimic

Squamous lesions

True glandular atypia

NOS Neoplastic NOS

Squamous Lesions

- Atypical glandular cells on Pap
  - 10-40% are HSIL on investigation

- HSIL involves endocervical glands

- Mix – squamous & glandular in group

Diagnostic Criteria

<table>
<thead>
<tr>
<th>HSIL in glands</th>
<th>AIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sheets, depth of focus&lt;br&gt;- Focal feathering&lt;br&gt;- Loss of central polarity&lt;br&gt;- Hard edge, dense cytoplasm&lt;br&gt;- Central nuclei&lt;br&gt;- Single HSIL background&lt;br&gt;- Beware: nucleoli</td>
<td>- Strips, rosettes&lt;br&gt;- Diffuse feathering&lt;br&gt;- Maintain central polarity&lt;br&gt;- Crowded columnar cells&lt;br&gt;- Basal carrot nuclei&lt;br&gt;- Nucleoli possible</td>
</tr>
</tbody>
</table>

HSIL in glands

AIS

Now you try
Which one is HSIL, AIS?
Management

- LUS sampling
- Tubal metaplasia
- HSIL

Routine screening

Colposcopy
- biopsy/ECC
- ablation/resection

THINK SQUAMOUS

CASE 3

- 42 year old female
- Routine Pap test
- LMP: now day 20
WHAT IS YOUR DIAGNOSIS?

Negative F/U Endocervical Repair

% DIAGNOSES

- NILM
- ASCUS
- ASC-H
- LSIL
- HSIL
- SQCC
- A EC
- A EM
- AIS
- ADENOCA

Atypical Endocervicals

NOS
- Atypia exceeds reactive or reparative changes
- Lack unequivocal features of AIS, adenoca
- Crowding, overlapping
- Increased N/C ratio
- Nuclear atypia

NEOPLASTIC
- Atypia like AIS, adenoca
- Falls short
  - quantity (too few)
  - quality (criteria)
Atypical EC NOS

- Examples:
  - XRT situation: too much atypia
  - Atypical repair
  - IUCD changes, but no IUCD

Management

- Benign mimics ➔ Routine screening
- HSIL ➔ Colposcopy
- Glandular atypia ➔ Colposcopy, EC/EM sample
  NOS, neoplastic, AIS

Summary

- Glandular atypia mimics
  - LUS sampling, tubal metaplasia
  - HSIL in glands
- Spectrum of glandular atypia
  - use criteria to classify (NOS, Neopl)
  - colposcopic/gyn referral in all
Take Home Pearls

When considering glandular atypia:

- Rule in benign mimics
- Think squamous!
- Respect (don’t ignore) atypia

QUESTIONS?