Demystifying Endometrial Hyperplasia

A review from Diagnostic Histopathology 19:7

Dr R Hadden ST5 Histopathology
Derriford Hospital
Plymouth
Endometrium

• Target for sex-steroid hormones

• Glands
• Stroma

• Proliferate under influence of oestrogen
• Mature/differentiate with progesterone
Hyperplasia

Unopposed oestrogenic stimulation

- Anovulatory sequence
- Granulosa cell tumours
Simple hyperplasia

• Gland and stromal proliferation

• Exaggeration of normal

Normal

Simple hyperplasia
Complex hyperplasia

- Only glandular proliferation (without cytological atypia)
- Crowding and branching
Atypical hyperplasia

- Simple or complex (more often)
- With cytological atypia
- Strong association with endometrioid adenocarcinoma
Independent assessment

• Architecture
  – Simple
    • Wide spaced, smooth outlines
  – Complex
    • Crowded, branching

• Cytology
  – Hyperplastic
    • Like normal, slight enlargment
  – Atypical
    • Cytological atypia
<table>
<thead>
<tr>
<th>Cytology</th>
<th>Simple</th>
<th>Complex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperplastic</td>
<td>Simple hyperplasia</td>
<td>Complex hyperplasia</td>
</tr>
<tr>
<td>Atypical</td>
<td>Atypical hyperplasia (Rare)</td>
<td>Atypical hyperplasia</td>
</tr>
</tbody>
</table>
Simple hyperplasia - glands

• Perimenopausal - anovulatory cycles
• Often maintenance of gland/stroma ratio
• No crowding
• Diffuse/entire thickness
• Variability in size/shape of glands
  – Cystic/budding + small/smooth
• Columnar but can have patches of vesicular/clear cells or ciliated cells
Simple hyperplasia - stroma

- Stroma abundant
- “Naked nuclei”
- Spiral arteries poorly developed
- Superficial thin-walled vessels
  - Congestion, dilation, thrombosis
    - Stromal haemorrhage/necrosis
    - Polymorphs/oedema
Overall

- Resembles late proliferative phase
- Exuberant growth
- Association with carcinoma <1% (same as random occurrence).
Complex hyperplasia - glands

- May occur in young women with normal cycles
- More focal
- >gland:stroma
- Crowded/branching glands
- Blunt, columnar epithelium
- Pseudostratification, mitoses
Complex hyperplasia - stroma

- Compressed
- Maintained between glands
Overall

• Focal glandular proliferation mimics late proliferative phase

• Elsewhere normal endometrium exists
  – Appropriate to age/hormone status

• <3% associated with carcinoma
Atypical hyperplasia - glands

- Focal or multifocal
- Exclusively affects glands
- Cytoplasmic and nuclear atypia
- Crowding/back-to-back glands
  - Although a thin rim of stroma remains
- Multiple branching, infoldings and tufts (lacking FV cores).
Stroma

- Thin rim maintained between glands
  – Subjective, no?
Overall

• Diagnosis relies on nuclear/cytoplasmic features of atypia.

• Architecture is of secondary importance.
Cytological atypia

- Large nuclei (twice normal)
- Round instead of elongated
- Vesicular, not hyperchromatic
- One or more prominent nucleoli
- Loss of polarity
- Loss of cell/cell or cell/basement cohesion
  - Irregular masses, tufts
- Abundant cytoplasm, eosinophilia, indistinct cell borders.
Well-diff EACa

- Myometrial invasion most reliable criteria

- Invasion into “new stroma” (hyalinised/oedematous)
I can has Poland?
• Cytologically atypical proliferation plus:
  – Small clusters/glands invading “new stroma” (hyalinised/oedematous fibrosis)
  – Solid growth of atypical cells (NOT squamous)
• Formation of tumour giant glands/cribiforming/loss of stroma
• Dominance of large, elongated, papillary fronds.
• Newly formed stroma (even without obvious invasion)
• Gland debris/neuts
Stromal proliferations

Summary

• Simple/complex hyperplasia is OK

• Atypia is subjective

• Determining atypical hyperplasia from EACa can be almost impossible
Schrödinger's Cat is alive...

and very pissed off

LOLCATS.COM
How do you solve a problem like classification?

An amendment to my initial presentation
WHO94

- Most widely used system
- Basis of this paper
- Some say overly complex
  - Not the opinion of the authors in this paper
Other systems proposed

• Amalgamate simple/complex hyperplasia

• Amalgamate AEH with EACa
  – Endometrial neoplasia (EN)

• OR redefine AEH
Endometrial Intraepithelial Neoplasia (EIN)

- Molecular, morphometric, and morphological criteria
- Includes exclusion of benign conditions and EACa
- Increased reproducibility (only supported by affiliated groups)
• Independent validation showed each system to be equally satisfactory.

• WHO more so for progression to EACa.