Pseudomalignant Lesions of the Prostate

Thomas M. Ulbright, M.D,
Indiana University School of Medicine
Prostatic Atrophy

• Most common benign lesion of prostate misinterpreted as carcinoma
• Affects both old and young men, increasing with age
• Associated with chronic prostatitis, hormonal deprivation Rx and radiation
• PZ> TZ and CZ

Prostatic Atrophy

• Classification:
  – **Simple atrophy**: Normal-sized to large glands with shrunken cytoplasm [basophilia]; not usually lobular
  – **Simple atrophy with cyst formation**: Large, round glands with shrunken cytoplasm
  – **Post-atrophic hyperplasia**: Lobular groupings of small glands with shrunken cytoplasm [basophilia] (formerly lobular and sclerotic atrophy)
  – **Partial atrophy**: Lobular to non-lobular arrangement of small glands with shrunken apical cytoplasm but abundant lateral cytoplasm; not basophilic

Post-atrophic Hyperplasia - Pathologic Features

- Low power – lobular arrangement of small, darkly staining glands, often with a central, larger duct
- Stroma may be sclerotic and chronically inflamed, with gland distortion (angulated)
- High power – atrophic secretory cells causes nuclear crowding and therefore “pseudohyperchromasia” but bland cytologic features; basal cells intact but often compressed

Post-atrophic Hyperplasia (PAH)
PAH
- Lobular
- Prominent basophilia at low power
- Cuboidal to flattened secretory cells with scant apical cytoplasm
- Bland nuclei
- Basal cells present

Adenocarcinoma
- Invasive growth
- Less basophilia
- Columnar secretory cells with more abundant clear to eosinophilic cytoplasm
- Atypical nuclei
- No basal cells

Differential: Atrophic Prostatic Adenocarcinoma
- Low power mimics atrophy, but there are occasional admixed non-atrophic glands with nuclear enlargement, nucleolomegaly and other features of prostate carcinoma (increased cytoplasmic density, crystalloids, absence of basal cells, etc.)
- The diagnostic features may only become apparent at intermediate or high magnification, making close inspection of atrophic-appearing foci important
Differential: Atrophic Prostatic Adenocarcinoma

- Immunostains should be performed in questionable cases:
  - Basal cells are absent
  - Racemase present in two-thirds

**PIN 4 stain**
Partial Atrophy (PA)

- Lobular to partially disorganized arrangement of glands having cells with scant apical cytoplasm and abundant lateral, pale cytoplasm
- Thin needle cores may not permit appreciation of the lobular organization
- The ample, pale cytoplasm causes concern for low grade adenocarcinoma, but the **glands have undulating contours, “ruffled” luminal borders and relatively bland nuclei**
- In needle Biopsies, basal cells may be focal or absent, even with HMW keratin stains; racemase may be positive
Partial Atrophy in Needle Bxs

- 4% of consultation cases
- ↑ nuclei: 15%
- ↑ nucleoli: 20%
- + basal cells, + AMACR: ~45%
- + basal cells, - AMACR: ~24%
- - basal cells, + AMACR: ~24%
- - basal cells, - AMACR: ~ 7%


Differential Diagnosis

<table>
<thead>
<tr>
<th></th>
<th>PA</th>
<th>Carcinoma</th>
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<tbody>
<tr>
<td>Infiltrative</td>
<td>Uncommon</td>
<td>Common</td>
</tr>
<tr>
<td>Cytoplasm</td>
<td>Pale</td>
<td>Often basophilic</td>
</tr>
<tr>
<td>Luminal border</td>
<td>Ruffled/undulating</td>
<td>Often straight</td>
</tr>
<tr>
<td>Blue mucin</td>
<td>No</td>
<td>Frequent</td>
</tr>
<tr>
<td>Pink secretions</td>
<td>Rare</td>
<td>Frequent</td>
</tr>
<tr>
<td>↑ Nuclei</td>
<td>Mild</td>
<td>Mild to marked</td>
</tr>
<tr>
<td>↑ Nucleoli</td>
<td>Mild</td>
<td>Mild to marked</td>
</tr>
<tr>
<td>Basal cells</td>
<td>Patchy to absent</td>
<td>Absent</td>
</tr>
<tr>
<td>AMACR</td>
<td>Negative to positive</td>
<td>Positive to negative</td>
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Sclerosing Adenosis (SA)

- Rare lesion of older men
- TZ lesion and mostly seen in TUR material rather the needle cores
  - Circumscribed proliferation of small glands, nests and individual epithelial cells in a spindle cell stroma
- Basal cells may be prominent and undergo myoepithelial metaplasia, possibly contributing to the stroma
Sclerosing Adenosis (cont’d)

- Basal cells (and some stromal cells) therefore are + for myoepithelial markers – HMWCK, S-100, MSA, p63, etc.
- Hyalinized periglandular/pericellular basement membrane in some cases
- Occasional cases show glandular crystalloids and rarely acid mucin
Sclerosing adenosis

SA – S100

Atypical SA
SA vs. High Grade Adenoca

- **SA**
  - Circumscribed margin
  - Glands usually have bland secretory cells
  - Prominent spindle cell stromal component
  - Single cells with thick pericellular basement membrane
  - TZ predominant

- **Gleason 4-5 Adenoca**
  - Infiltrative margins
  - Glands with atypical secretory cells & no basal cells
  - Absent to minimal stromal component
  - “Naked” single cells
  - PZ predominant
Atypical Adenomatous Hyperplasia/Adenosis

- Incidental finding in TUR specimens (up to 20%) more commonly than needle cores (~1%)
- Usually located in TZ, periurethral area or apex
- Mean age 65-70 years
- Controversy regarding biological significance

Atypical Adenomatous Hyperplasia/Adenosis

- Circumscribed nodule of **variably sized glands** with abundant, pale cytoplasm
- Larger glands have papillary infoldings; smaller have straight luminal borders
- Secretory cells have abundant, pale cytoplasm and cytologically bland nuclei
- Basal cells are present but may be inconspicuous
- HMWK stains are spotty and discontinuous; occasional cases + for racemase
AAH-Adenosis vs. Low Grade Adenoca

- **AAH-Adenosis**
  - Larger glands with intraluminal infoldings & branching
  - Pale or clear glands
  - Inconspicuous to medium-sized nucleoli
  - Rarely intraluminal blue mucin
  - Basal cells present

- **LG Adenoca**
  - Uniformly small glands with straight luminal edges
  - Some glands with amphophilic cytoplasm
  - Sometimes large nucleoli
  - Intraluminal blue mucin common
  - Basal cells absent

(Clear Cell) Cribriform Hyperplasia (CH)

- Mean patient age ~ 70 years
- Patients present with prostatism
- Incidental TZ lesion seen mostly in TUR specimens
- Complex, intraglandular cribriform hyperplasia of often pale cells in a nodular configuration
- Basal cells are very conspicuous in foci
- Clear cells are cytologically bland
Basal Cell Hyperplasia (BCH)

- TZ > PZ
- Mostly seen in TUR specimens (~10%)
- May result from anti-androgen Rx
- Nodular pattern at low power
- Peripheral cuffs of proliferated basal cells around glands with ("incomplete BCH") or without ("complete BCH") residual lumens
- Psammoma body-like Ca++ in 50%
- ± nucleolar prominence in basal cells ("atypical BCH")
Adenoid cystic-like BCH

Atypical BCH

Courtesy of Dr. J. Epstein
Atypical BCH

- Small acinar process
- Often solid nests
- Flat to round lesional cells
- Residual secretory cells are bland
- Atypical cells + for p63, HMWCK

Atypical BCH

BCH vs. HGPIN

- BCH
  - Normal-sized glands
  - Distinct lumens
  - Columnar, often stratified lesional cells
  - Secretory cells are atypical
  - Atypical cells + for p63, HMWCK

- HGPIN
  - Small acinar process
  - Often solid nests
  - Flat to round lesional cells
  - Residual secretory cells are bland
  - Atypical cells + for p63, HMWCK
BCH vs. Basal Cell Ca (BCC)

- **BCH**
  - Confined to prostate
  - Relatively uniform nests & glands
  - Non-necrotic
  - No perineural invasion
  - Minimal stromal reaction

- **BCC**
  - May infiltrate outside prostate (bladder neck)
  - Irregularly sized & shaped nests
  - Central necrosis
  - May show perineural invasion
  - Desmoplastic stroma
Nephrogenic Adenoma (NA)
- Usually in patients with prior procedures, catheterization, stones, etc.
- Bladder more common than prostatic urethra
- Prostatic urethra cases may extend into prostatic stroma, mimicking carcinoma
- Various patterns: tubular, papillary, cystic, diffuse (solid), fibromyxoid
- Characteristic small tubules, with cuboidal, hobnail cells or rare signet ring cells

Nephrogenic Adenoma
- Peritubular, thickened, hyalinized basement membrane
- Absent to very rare mitotic figures
- Inflamed, vascular stroma
- Multifocality in ~20%
- Racemase + in ~60%
- Secretions in tubular lumens may be + for PSA and PAP
NA vs. Adenoca

- **NA**
  - Multiple patterns (tubular, cystic papillary, diffuse)
  - Occasional hobnail cells & flattened cells
  - Thickened peritubular basement membrane
  - Inflamed stroma
  - “Hard” colloid-like secretion

- **Adenoca**
  - Mostly spectrum of glandular patterns
  - Cuboidal or columnar cells, not hobnail
  - Lacks periglandular basement membrane prominence
  - Normal stroma
  - Amorphous, “loose” eosinophilic secretion

NA vs. Adenoca - Immuno

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<tr>
<th></th>
<th>NA</th>
<th>PCa</th>
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<tbody>
<tr>
<td>PSA</td>
<td>-</td>
<td>+ (90%)</td>
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<tr>
<td>PAX8</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>CK7</td>
<td>+</td>
<td>-(84%)</td>
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<tr>
<td>PAX2</td>
<td>+</td>
<td>-(75%)</td>
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N.B. – AMACR is positive in 55% of NA
Seminal Vesicle (SV)/Ejaculatory Duct

- Usually sampled in biopsies directed at the base
- Small glands around a dilated duct
- Pleomorphic lining cells with hyperchromatic nuclei, nuclear pseudoinclusions, lipofuscin pigment
- No mitotic figures
- - for PSA, PAP; basal cells + for p63, HMWCK
SV/ED vs Adenoca

- **SV/ED**
  - Lobular with central dilated duct
  - Pleomorphism
  - Nuclear pseudoinclusions
  - Often prominent cytoplasmic pigment
  - PSA & PAP -; basal cells present

- **Adenoca**
  - Infiltrative, no central dilated duct
  - Minimal pleomorphism
  - No nuclear pseudoinclusions
  - Cytoplasmic pigment rarely prominent
  - PSA & PAP +; no basal cells
Mesonephric Remnant Hyperplasia (MRH)

• Usually incidental finding in TURP or prostatectomy specimens
• Misinterpretation as adenocarcinoma has resulted in unnecessary prostatectomy
• Usually near base or anterior fibromuscular stroma
• Typically lobular clusters of small to dilated glands with colloid-like secretions
• PAX8 +; PSA & p63 – ; variable HMCK, AMACR
