Mimickers of Prostate Cancer From Adenosis to Xanthoma

Benign Mimickers of Well-Moderately Differentiated Carcinoma

- Adenosis
- Atrophy
- Basal cell hyperplasia
- Nephrogenic adenoma
- HGPIN
- Radiation atypia
Adenosis
(Atypical Adenomatous Hyperplasia)

Incidence

- TURP - 1.6%
- Needle - 0.8%
- Multifocal
Diagnostic Criteria of Adenosis

<table>
<thead>
<tr>
<th>Adenosis</th>
<th>Cancer</th>
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<tbody>
<tr>
<td>Lobular</td>
<td>Haphazard growth pattern</td>
</tr>
<tr>
<td>Small glands share cytoplasmic and nuclear features with admixed larger benign glands</td>
<td>Small glands differ in either nuclear or cytoplasmic features from adjacent benign glands</td>
</tr>
<tr>
<td>Pale-clear cytoplasm</td>
<td>Occasionally amphophilic cytoplasm</td>
</tr>
<tr>
<td>Medium sized nucleoli</td>
<td>Occasionally large nucleoli</td>
</tr>
<tr>
<td>Blue mucinous secretions rare</td>
<td>Blue mucinous secretions common</td>
</tr>
<tr>
<td>Corpora amylacea common</td>
<td>Corpora amylacea rare</td>
</tr>
<tr>
<td>Basal cells present</td>
<td>Basal cells absent</td>
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Features Shared in Adenosis and Cancer

- Crowded glands
- Crystalloids
- Medium sized nucleoli
- Scattered poorly formed glands and single cells
- Minimal infiltration at periphery
Relation of Adenosis to Cancer

- No difference in risk of subsequent diagnosis of cancer following TURP diagnosis as compared to BPH

- “Adenosis is a mimicker of prostate cancer which is not associated with an increased risk of cancer”

Atrophy

- Post-atrophic hyperplasia
- Partial atrophy
- Simple atrophy
• Proliferative atrophy linked to prostate carcinogenesis

• Atrophy & inflammation associated with increased proliferation.

• Gives rise to reactive oxygen and nitrogen species which in the setting of increased turnover results in mutations.

• If atrophy is associated with cancer, it is not a proximate cause.

• Proliferative atrophy seen in 47% of sextant biopsies

• Not associated with cancer on repeat biopsy

• Not typically even mentioned in pathology report unless florid as a mimicker of cancer.
Partial Atrophy
Basal Cell Hyperplasia

Basal Cell Hyperplasia in the Peripheral Zone of the Prostate

- BCH in peripheral zone – 23% of whole prostates
- BCH on needle biopsy – 10.2%
Nephrogenic Adenoma of the Prostatic Urethra: A Mimicker of Prostate Adenocarcinoma

- Features mimicking prostate cancer:
  - Presence of tubules, cords, and signet ring-like tubules
  - Prominent nucleoli
  - Muscle involvement
  - Blue-tinged mucinous secretions (32%)
  - Focal PSA (36%) and PSAP (50%)
  - Negative staining for HMWCK in some cases
Nephrogenic Adenoma vs. Prostate Ca.

- Focal PSA and PSAP positivity in 1/3 of cases
  - Tends to not be diffusely strong
- Negative staining for HMWCK in 62%-75% of cases
- Cases with positive HMWCK rules out prostate cancer
- Positive AMACR (racemase) in 35%-58% of cases
- Positive PAX2 in NA and not in prostate cancer
PINATYP

High grade PIN with small focus of atypical glands. See note:

Note: Adjacent to glands of high grade PIN are a few small atypical glands. While these small glands may represent a small focus of infiltrating cancer, we can not exclude that they represent outpouching or tangential sections off of the adjacent high grade PIN.
Radiation Change in the Prostate

- RT affect in Benign Prostate - Differential Diagnosis from Prostate Cancer

- RT results – Affect on Prognosis
  - Positive for cancer (w/o treatment affect)
  - Negative for cancer
  - Positive for cancer (with treatment affect)

- More atypia in cases treated with IRT (seeds) than XRT

- No change in epithelial atypia over time in men treated with IRT. With XRT, less epithelial atypia in cases biopsies >48 months after treatment

- RT atypia may persist for a long time: Prominent RT atypia detected 72 months after IRT

- Some cases clinicians not aware of remote h/o of RT or do not relay this on to pathologists. Pathologists must be able to recognize RT atypia w/o relying on the clinician to provide this history
Radiation Biopsy Results: Cancer with Treatment Affect

Histologically cancer is seen, yet shows treatment effect with degenerative features. Cancer is present, yet is it viable?

Prognosis: Similar to cases with no cancer.

Do not grade radiated cancer with treatment effect.

Radiation Biopsy Results: Positive

Histologically, ordinary prostate cancer is seen, which resembles non-radiated cancer.

If biopsy performed too soon (<12 months), can not tell if the cancer is resistant or has not had enough time to be destroyed by the treatment.

If biopsy is done >12 months following radiation, indicates progression of cancer. Can assign a Gleason grade.

Benign Mimickers of Moderately-Poorly Differentiated Adenocarcinoma

- Nonspecific granulomatous prostatitis
- Paraganglia
- Urothelial carcinoma
- Xanthoma
Nonspecific Granulomatous Prostatitis
Paraganglia of Prostate
High Grade Prostatic Adenocarcinoma
vs.
Poorly Differentiated Urothelial Carcinoma
Direct Invasion of UC Into the Prostate (pT4): Invasive UC versus High Grade Prostatic Adenocarcinoma

PROSTATE ADENOCARCINOMA

- Large solid sheets or cords of cells
- Uniform nuclear size & shape with prominent nucleoli, yet advanced prostate cancer may be as pleomorphic as UC
- Microacinar formation
- Lacks stromal inflammation
Immunohistochemistry UC vs. Prostate Adenocarcinoma

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<thead>
<tr>
<th></th>
<th>UC</th>
<th>Pr. Ca.</th>
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<tbody>
<tr>
<td>PSA, PSAP</td>
<td>0%</td>
<td>&gt;95%</td>
</tr>
<tr>
<td>HMWCK/p63</td>
<td>60%-70%</td>
<td>0%</td>
</tr>
<tr>
<td>Thrombomodulin</td>
<td>60%</td>
<td>0%</td>
</tr>
<tr>
<td>CK7</td>
<td>70%-100%</td>
<td>19%-35%</td>
</tr>
<tr>
<td>CK20</td>
<td>15%-71%</td>
<td>2%-72%</td>
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PSA-Poor Prostate Cancers

- Make sure that positive control is not just positive in benign prostate glands, but labels it intensely, as poorly differentiated cancers have lower expression than benign prostate glands.
- P501S (prostein)
- PSMA (prostate specific membrane antigen)
Recommended Panel

- PSA
- P501S
- PSMA
- NKX3.1
- Thrombomodulin
- p63
- HMWCK
- GATA3
Prostatic Xanthoma
Summary

Prostate biopsies and TURs are some of the most difficult specimens to evaluate, in part due to the wide range of mimickers of both moderately and poorly differentiated adenocarcinoma of the prostate.

Recognition of these mimickers’ unique histologic features can prevent an overdiagnosis of prostate cancer.