A good H & E helps!

ADENOCARCINOMA DIAGNOSTIC CRITERIA

Relatively uniform proliferation
Small round glands
Single cell layer
Some prominent nucleoli

Relatively Uniform Proliferation of Small Round Glands
**Infiltrative growth**

**Relatively Uniform Proliferation of Small Round Glands**
Relatively Uniform Proliferation of Small Round Glands

Atrophic pattern

Relatively Uniform Proliferation – Atrophic pattern
Relatively Uniform Proliferation of Small Round Glands

Pseudohyperplastic pattern

Relatively Uniform Proliferation of Small Round Glands

Pseudohyperplastic pattern
Single cell layer and at least some prominent nucleoli

Single cell layer (loss of basal cells)
Single cell layer (loss of basal cells)

Single cell layer (pseudostratification) “PIN-like”
Small acinar HGPIN

PCa DIAGNOSTIC CRITERIA
THE NUCLEOLUS
THE NUCLEOLUS

THE NUCLEOLUS
MITOTIC FIGURES

ADENOCARCINOMA

MITOTIC FIGURES

ATROPHY
ADENOCARCINOMA
ANCILLARY DIAGNOSTIC CLUES

Crystalloids
Basophilic (acid) mucin
Eosinophilic secretions
Collagenous micronodules
Cytoplasmic amphophilia
Glomerulations
Perineural invasion
IHC markers

PROSTATIC CRYSTALLOIDS
BASOPHILIC MUCIN/CRYSTALLOIDS

BASOPHILIC MUCIN
COLLAGENOUS MICRONODULES

COLLAGENOUS MICRONODULES
COLLAGENOUS MICRONODULES

CYTOPLASMIC FEATURES
CYTOPLASMIC FEATURES

GLOMERULATIONS
PERINEURAL INVASION
PERINEURAL INVASION - BENIGN

PCa DIAGNOSTIC CRITERIA IMMUNOHISTOCHEMISTRY

- Basal cell markers: HMW cytokeratins + p63
- Cancer markers: AMACR (racemase, p504s) + ERG

Cytokeratin 34βE12
HIGH MOLECULAR WEIGHT CK

HIGH MOLECULAR WEIGHT CK
Alpha-methylacyl-CoA racemase (AMACR, p504s)

- Enzyme involved in β-oxidation of branched chain fatty acids
- Identified as upregulated in prostate cancer through DNA microarray studies of prostate cancer
- Over-expression of protein in ~80% of cancers
- Not specific for cancer: overexpression also seen in:
  - Normal, hyperplasia, AAH (adenosis) and atrophy
  - Usually patchy and weaker but can be strong
Alpha-methylacyl-CoA racemase

ADENOCARCINOMA - AMACR
Alpha-methylacyl-CoA racemase

IHC – p504s + p63 + hmwck

ATROPHY

HYPERPLASIA

Adenocarcinoma

High Grade PIN
Alpha-methylacyl-CoA racemase

Positive adenocarcinoma

Negative adenocarcinoma

Alpha-methylacyl-CoA racemase

Prostate – Nephrogenic adenoma
**PROSTATE CANCER**

**TMPRSS2:ERG FUSION**

- 15% - 78% of prostate cancer may have a chromosomal rearrangement at 21q22.3
- Are multiple different breakpoints
- This involves several genes
  - **TMPRSS-2** (transmembrane protease serine 2)
  - ETS family transcription factors
    - **ERG** (21q22.2) or **ETV1** (7p21.2) or **ETV4** (17q21)
- **TMPRSS-2** is highly expressed in normal and neoplastic prostate under androgen regulation
- Appears to be an early event (present in HGPIN)

**ERG - IMMUNOHISTOCHEMISTRY**
PROSTATIC ADENOCARCINOMA
MOST USEFUL DIAGNOSTIC CRITERIA

- Prominent nucleoli
  - largest nucleolar diameter
  - mean nucleolar diameter
  - nucleolar diameter > 1μm
- Infiltrative borders
- Crystalloids
- Basophilic mucin

Bostwick et al Hum Pathol 24:19 1993
**SMALL ACINAR PROLIFERATIONS DIFFERENTIAL DIAGNOSIS**

<table>
<thead>
<tr>
<th>Normal tissues</th>
<th>Proliferative lesions</th>
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</thead>
<tbody>
<tr>
<td>Cowper’s glands</td>
<td>Basal cell hyperplasia</td>
</tr>
<tr>
<td>Seminal vesicle</td>
<td>Clear cell cribriform hyperplasia</td>
</tr>
<tr>
<td>Paraganglionic tissue</td>
<td>Sclerosing adenosis</td>
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<tr>
<td>Inflammatory</td>
<td>VMGH</td>
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<td>Granulomatous prostatitis</td>
<td>Mesonephric hyperplasia</td>
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<tr>
<td>Xanthoma</td>
<td>AAH (adenosis)</td>
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<tr>
<td>Atrophy</td>
<td>Other</td>
</tr>
<tr>
<td>PIN (outpouching)</td>
<td>Nephrogenic adenoma</td>
</tr>
</tbody>
</table>

**PROLIFERATIVE LESIONS**
BASAL CELL HYPERPLASIA

- TZ lesion – variation on usual hyperplasia
- Round or slightly irregular glands completely or partially filled with basal cells
BASAL CELL HYPERPLASIA

BASAL CELL HYPERPLASIA
BCH vs CARCINOMA

CLEAR CELL CRIBRIFORM HYPERPLASIA

- TZ lesion – variant of usual hyperplasia
- Cribriform glands with cells having pale cytoplasm and no nuclear atypia
CLEAR CELL CRIBRIFORM HYPERPLASIA

- Rare TZ lesion – incidental finding in TURP or RP
- Busy lesion with small to irregular glands
- Basal cells undergo myoepithelial metaplasia

SCLEROSING ADENOSIS

- Rare TZ lesion – incidental finding in TURP or RP
- Busy lesion with small to irregular glands
- Basal cells undergo myoepithelial metaplasia
SCLEROSING ADENOSIS

ATYPICAL ADENOMATOUS HYPERPLASIA (ADENOSIS)

- Predominantly TZ lesion – part of usual hyperplasia
- Transition of obvious benign to worrisome small glands
- Patchy loss of basal cells and overexpression of racemase
ATYPICAL ADENOMATOUS HYPERPLASIA (ADENOSIS)
**Atypical Adenomatous Hyperplasia**

- Infrequently involves the prostatic urethra
- Tubules (with thick BM) and papillary structures
- Positive for AMACR and PAX8

**NEPHROGENIC ADENOMA**

- Infrequently involves the prostatic urethra
- Tubules (with thick BM) and papillary structures
- Positive for AMACR and PAX8
NEPHROGENIC ADENOMA

AMACR
PROSTATIC ATROPHY

- Foci appear as early as 3rd decade
- Associated with prior inflammation
- May be side by side with BPH
- Clinical significance:
  - Can mimic CA on US (hypoechoic)
  - Can mimic CA on histology
  - Can cause elevated PSA (?)

LOBULAR ATROPHY
SIMPLE LOBULAR ATROPHY

SCLEROTIC ATROPHY
POSTATROPHIC HYPERPLASIA

PARTIAL ATROPHY
PARTIAL ATROPHY

High molecular weight cytokeratin 34βE12
ATROPHY – “Infiltrative growth”

ATROPHY vs CARCINOMA
ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)

- Term used for cases where a definitive benign or malignant diagnosis cannot be rendered
- Is not a specific pathologic entity
- In many cases represents small foci of carcinoma that do not fulfill diagnostic criteria
- Others represent benign processes such as atrophy where cancer cannot be excluded
- Re-biopsy yields cancer in about 50% of cases
ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)

ATYPICAL SMALL ACINAR PROLIFERATION (ASAP)

HMWCK
DIAGNOSIS:
1. Right prostate: SMALL ACINAR PROLIFERATION HIGHLY SUSPICIOUS FOR ADENOCARCINOMA INVOLVING <5% OF THE SPECIMEN.
2. Left prostate: benign prostatic hyperplasia

SMALL ACINAR PROLIFERATION HIGHLY SUSPICIOUS FOR ADENOCARCINOMA INVOLVING RIGHT LOBE

Gleason Score: 3 + 3 = 6 out of 10.
Percent of area of needle biopsies involved by tumor: <5%.
Tumor involves 1 of a total of 11 needle biopsy specimens.
Maximal longitudinal tumor dimension = 0.4 mm.
Perineural invasion: Absent
Angiolympathic invasion: none identified.
Local extraprostatic invasion: none identified