

Diagnosis of PIN and prostate cancer

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The histological diagnosis of prostate cancer relies on the *synthesis of a constellation of cytoarchitectural, nuclear, cytoplasmic and intraluminal features rather than on one finding in isolation.*

Cytoarchitectural features:

- Infiltrative pattern (around and between benign glands)
- Often small glands (not always!)
- Absence of basal cells
- Crowded glands
- Straight luminal border
- May have periglandular clefts
- Fused glands/ciriform glands/individual cells in high grade tumours

Nuclear features:

- Prominent enlarged nucleoli
- Multiple nucleoli
- Parachromatin clearing
- Nuclear enlargement
- Hyperchromasia
- Mitotic figures (relatively uncommon; highly suggestive of malignancy if present)

Cytoplasmic features:

- Amorphophilic, clear or pale granular cytoplasm

Intraluminal features

- Blue wispy mucin
- Crystalloids (also seen in AAH and some benign glands)
- Eosinophilic amorphous secretions
- Intraluminal necrosis in high grade tumours
[Corpora amylacea are extremely rare and should suggest benign glands]



Features unique to cancer (though recommend the diagnosis be based on a constellation of findings)

- Mucinous fibroplasia (collagenous micronodules)
- Perineural invasion
- Glomerulations



High grade prostatic intraepithelial neoplasia (HGPIN or PIN)

- Amorphophilic cytoplasm (usually readily detectable at low magnification)
- Enlarged monomorphic nuclei
- Enlarged nucleoli (easily observed with x20 objective)
- Nuclear hyperchromasia
- Preserved or discontinuous basal cell layer
- Four major architectural patterns:
 - tufted, micropapillary, cribriform, flat
- May show 'maturation' towards luminal aspect
- Comedonecrosis is extremely rare



High grade PIN: differential diagnosis

- Basal cell hyperplasia
- Ejaculatory duct/seminal vesicle type epithelium
- Reactive atypia e.g. with inflammation
- Intraductal adenocarcinoma
- PIN-like invasive adenocarcinoma



Intraductal adenocarcinoma of prostate Guo

and Epstein Mod Pathol 2006;19:1528-1535

Defined as:

Malignant epithelial cells forming large acini and ducts [at least 2x normal size] with preservation of basal cells forming either -

- Solid or dense cribriform patterns

or

- Loose cribriform or micropapillary patterns with either marked nuclear atypia (nuclear size 6 x normal or larger) or comedonecrosis

[the presence of intraductal adenocarcinoma found to have a strong association with high grade invasive adenocarcinoma and the limited number of cases of isolated intraductal carcinoma with follow up have almost all had invasive carcinoma on rebiopsy that is often high volume with Gleason patterns 4 or 5]



Intraductal adenocarcinoma of prostate

May represent intraductal or intra-acinar spread of prostatic adenocarcinoma or intraluminal progression of HGPIN



Intraductal adenocarcinoma of prostate: differential diagnosis

- High grade PIN
- Invasive adenocarcinoma (Gleason pattern 4 or 5)
- Urothelial carcinoma in situ in prostatic ducts



Urothelial carcinoma in situ in prostatic ducts

- A basal cell layer is often retained (stains more intensely for basal cell markers than the lesional cells)
- Racemase is often positive (not helpful marker to distinguish from prostate cancer)



Variants of prostate cancer

- Acinar variants
 - atrophic
 - pseudohyperplastic
 - PIN-like (stratified double cell layer)
 - foamy gland (xanthomatous)
 - with Paneth cell-like differentiation
 - oncocytic
- Ductal adenocarcinoma
- Mucinous adenocarcinoma
- Signet ring adenocarcinoma
- Carcinoma with squamous differentiation
 - adenosquamous carcinoma
 - squamous cell carcinoma
- Basal cell carcinoma/adenoid cystic carcinoma
- Neuroendocrine carcinoma (small cell, carcinoid, large cell neuroendocrine)
- Lymphoepithelioma-like carcinoma
- Sarcomatoid carcinoma
- Undifferentiated carcinoma



Ductal adenocarcinoma of prostate

- Papillae and large glands/cribriform and/or solid areas
- Lined by pseudostratified tall columnar epithelium
- Typically a greater degree of cytological atypia/chromatin irregularity than in acinar subtypes of prostatic adenocarcinoma
- Commonly occurs admixed with acinar adenocarcinoma and rare in pure form (<1% cases)
- Gleason pattern 4 by ISUP; pattern 5 if necrosis



Radiotherapy effects on prostate cancer

- Foamy vacuolated cytoplasm
- Atrophic changes
- Pleomorphic nuclei (including in benign glands)
- 'Grade inflation'
- Immunohistochemistry for basal cell makers remains useful



Hormonal therapy effects on prostate cancer

- Shrunken glands or single malignant cells
- Xanthomatous cytoplasm
- Pyknotic fragmented nuclei
- Mucin extravasation
- [Benign glands show marked atrophy, basal cell hyperplasia +/- squamous metaplasia]

