Evaluation of Prostate Cancer and “Atypical” on Needle Biopsy
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Difficulty in Underdiagnosing Prostate Cancer

- Limited tissue on needle biopsy (1 cm. x <1mm.)
- Limited cancer on needle biopsy
- Histologic findings often subtle

Diagnosis of Prostate Cancer

- Use a systematic approach to the diagnosis of prostate cancer based on specific architectural, cytological, and ancillary features.

*Diagnostic criteria of limited adenocarcinoma of the prostate on needle biopsy (Epstein: Hum Pathol 1995)*

- With the exception of three findings that by themselves are specific for cancer, the diagnosis of prostate cancer is based on a constellation of features.
Features Favoring The Diagnosis of Adenocarcinoma

- Abnormal architectural pattern
- Nuclear enlargement
- Nuclear hyperchromasia
- Prominent nucleoli
- Mitotic/apoptotic figures
- Amphophilic cytoplasm
- Blue mucinous secretions
- Pink amorphous secretions
- Crystalloids
Apoptosis & Nucleoli

- Mitotic figures (13%) and apoptotic bodies (34%) more common in cancer and HGPIN.

- Number and position of nucleoli do not distinguish between cancer and benign mimickers.

*Number & location of nucleoli and presence of apoptotic bodies in diagnostically challenging cases of prostate adenocarcinoma on prostate needle biopsy. Aydin, Zhou, Herawi, & Epstein (Hum Path 2005)*
Features Diagnostic of Adenocarcinoma

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

Perineural invasion, mucinous fibroplasia, and glomerulations: diagnostic features of limited cancer on prostate needle biopsy. Baisden, Kahane, & Epstein (AJSP 1999)
Perineural and Intraneural Involvement by Benign Glands

**Cancers Mimicking Benign Glandular Proliferations**

- Pseudohyperplastic prostate cancer
- Foamy gland prostate cancer
- Atrophic prostate cancer

**Pseudohyperplastic Adenocarcinoma**

Architecturally resembles benign glands

Patterns include:
- Glands with papillary infolding
- Branching glands
- Large dilated glands
Foamy Gland Carcinoma

Architecturally cancer but very bland cytology

Adenocarcinoma with Atrophic Features

- Can be seen de novo or in prostates treated with hormonal therapy
- In biopsy or TURP material, most have no history of anti-androgen therapy

*Adenocarcinoma of the prostate with atrophic features. Cina & Epstein (AJSP 1997)*

### Diagnostic Criteria

1. Infiltrative growth pattern
2. Macronucleoli
3. Presence of adjacent non-atrophic cancer
Features Against The Diagnosis of Adenocarcinoma

- Atrophic cytoplasm
- Merging in with benign glands (r/o adenosis)
- Corpora amylacea
- Inflammation
- Adjacent PIN (r/o PINATYP)

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.
Use of Basal Cell Markers

- Atypical favor cancer - negative staining, confirm diagnosis of cancer
- Atypical favor benign - negative staining, call atypical
- Benign - negative staining, call benign

Pitfalls with Basal Cell Markers

- Entirely benign glands may not stain for basal cell markers.

- More commonly negative staining non-cancerous glands include: adenosis, partial atrophy, and high grade PIN.

- Cancer cells may occasionally stain nonspecifically (not in a basal cell distribution).

- Very rarely, cancers can demonstrate basal cells.
Use of AMACR (P504S)

Marker that selectively stains adenocarcinoma of the prostate and is negative in benign prostate glands
Pitfalls with AMACR

FALSE POSITIVES:
• Labels high grade PIN
• Occasionally stains entirely benign glands
• Occasionally partial atrophy and adenosis

FALSE NEGATIVES:
• Up to 20% of small foci of adenocarcinoma may be negative

Pitfalls with AMACR

- FALSE NEGATIVES:
  - Difficult to diagnose variants of prostate cancer less frequently positive.
    - Foamy - ~65% (+)
    - Atrophic - ~ 65% (+)
    - Pseudohyperplastic - ~75% (+)

Farinola MA, Epstein JI. Utility of immunohistochemistry for alpha-methylacyl-coa racemase (AMACK) in distinguishing atrophic prostate cancer from benign atrophy. (Hum Pathol 2004).


Atypical Needle Biopsies

- Not use term “atypical hyperplasia"
- Problem with the term “atypical small acinar proliferation” (ASAP)
- Sign out descriptively

Atypical Signout

Prostate with small focus of atypical glands. See note:

Note: Although the findings are atypical and suspicious for adenocarcinoma, there is insufficient cytologic and/or architectural atypia to establish a definitive diagnosis. Follow up is warranted with serum or urine tests, imaging and in some cases repeat biopsy with relative increased sampling of the atypical site may be recommended.
Incidence of Atypical on Biopsy
Mean 5%

Atypical on Biopsy: Subsequent Risk of Cancer
Mean 40%

Post Benign Needle Biopsy: Risk of Cancer
Mean 19%

Atypical Follow-up Biopsy Strategy

• Cancer on repeat biopsy often at or adjacent to initial atypical site.

• Initial biopsies should be submitted to preserve location of each biopsy.

Atypical Signout

Prostate with small focus of atypical glands. See note:

Note: Although the findings are atypical and suspicious for adenocarcinoma, there is insufficient cytologic and/or architectural atypia to establish a definitive diagnosis. Follow up is warranted with serum or urine tests, imaging and in some cases repeat biopsy with relative increased sampling of the atypical site may be recommended.
Summary

• With the exception of a few findings, the diagnosis of adenocarcinoma of the prostate is based not on any single feature, but on a constellation of features.

• One should weigh features for and against the diagnosis of cancer.

• Even in the setting of a few atypical glands, if there are several features in favor of cancer and nothing against cancer, a definitive diagnosis of cancer can be made.
• Partial Atrophy: The most common mimicker of prostate cancer on needle biopsy

Partial Atrophy in Prostate Needle Cores: Another diagnostic pitfall for the surgical pathologist. Oppenheimer & Epstein (AJSP 1998)
Adenosis – Needle Biopsy

- 16% with more than 1 focus
- One of the more difficult diagnoses on biopsy
- Difficult to appreciate lobular architecture
Nonspecific Granulomatous Prostatitis

Pitfalls

- Mimics cancer clinically
- Most histological patterns do not resemble cancer
- Rare epithelioid variant easily confused with high grade cancer
