Unusual Subtypes of Prostate Tumors

Jonathan I. Epstein
## Financial and Other Disclosures

- Off-label use of drugs, devices, or other agents: None
- Data from IRB-approved human research is not presented

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Prostatic Duct Adenocarcinoma
“Ductal” Terminology Confusing

• “Duct adenocarcinoma” (ductal refers to cytology)
  Ductal morphology (tall pseudostratified columnar cells) typically invasive but also can be growing within ducts and acini

• “Intraductal carcinoma” (ductal refers to location)
  Acinar morphology (cuboidal cells) growing within ducts and acini as either precursor lesion or by extension of invasive high grade carcinoma into ducts
Prostatic Duct Adenocarcinoma

- May arise in large periurethral ducts and project into the urethra around verumontanum clinically mimicking UC.
- Presents with LUTS and hematuria. Rectal often normal.
- Diagnosis made on TURP
• May arise in secondary (peripheral) ducts

• May present as ordinary (acinar) adenocarcinoma with abnormal DRE or elevated serum PSA levels and diagnosed on needle biopsy.
Relation to Acinar Adenocarcinoma

- Separate peripheral acinar and central duct
- Comingling of duct and acinar
- Uncommon for pure duct adenocarcinoma with mixed acinar/duct more common
Grading Duct Adenocarcinoma

- Usual (cribriform; papillary) Ductal: Gleason pattern 4

- With central necrosis: Gleason pattern 5

- PIN-like Ductal: Gleason pattern 3

- Stage for stage similar prognosis compared to usual acinar prostate cancer.
Intraductal Carcinoma of the Prostate (IDC-P)
• IDC-P frequently adjacent to Gleason pattern 4 invasive carcinoma

• Relative rarity of IDC-P to be at a distance from invasive cancer and low frequency within cancers under 2 cc suggest that IDC-P evolves concurrent with the progression of established invasive carcinoma rather than as a precursor to it.
Intraductal Carcinoma of the Prostate Without Invasive Carcinoma on Needle Biopsy: Emphasis on Radical Prostatectomy Findings

Brian D. Robinson and Jonathan I. Epstein*

From the Departments of Pathology (BDR), Urology and Oncology, The Johns Hopkins Hospital (JIE), Baltimore, Maryland
• Of the 21 RPs available for review findings revealed pathological stage pT3a in 8 (38%), pT3b in 3 (13%), pT2 in 8 (38%).

• IDC-P only without identifiable invasive cancer in 2 (10%).

• Median Gleason score 8.
• Definitive therapy is recommended in men with IDC-P on needle biopsy even in the absence of pathologically documented invasive prostate cancer.

• Strict definition of IDC-P on biopsy with relatively high threshold to diagnose IDC-P since recommend definitive therapy

• Consequently, will be cases borderline between HGPIN and IDC-P where repeat biopsy is recommended.
Report if Only Gleason Score 3+3=6

- Gleason score 3+3=6 with intraductal carcinoma. See note:

- Note: Intraductal carcinoma is more frequently seen with Gleason patterns 4-5 carcinoma although these are not present on the current tissue samples.
Biopsy diagnosis of intraductal carcinoma is prognostic in intermediate and high risk prostate cancer patients treated by radiotherapy

T. Van der Kwast a,*, N. Al Daoud a, L. Collette b, J. Sykes c, J. Thoms c, M. Milosevic c, R.G. Bristow c, G. Van Tienhoven d, P. Warde c, R.-O. Mirimanoff e, M. Bolla f

Independent prognosticator of early biochemical relapse and metastatic failure
High Risk Cancer

In multivariate analysis, IDC-P significantly associated with BCR and cancer specific survival.
 Needle biopsy of the prostate in men with metastatic prostate cancer

IDC-P predictive of cancer-free survival even in the subset of men with Gleason score ≥8 cancer
IDC-P on needle biopsy significantly associated with rapid progression of CRPC.

Poor response to initial ADT and sequential docetaxel-based chemotherapy.
The prognostic implication of intraductal carcinoma of the prostate in metastatic castration-resistant prostate cancer and its potential predictive value in those treated with docetaxel or abiraterone as first-line therapy.

IDC-P diagnosed by prostate re-biopsy at the time of mCRPC

IDC-P was an independent prognosticator for clinical outcome.

Abiraterone better therapeutic efficacy than docetaxel as the first-line therapy in IDC-P(+) mCRPC patients.
Grading Intraductal Cancer

• Uncommonly, only IDC-P may be present in the RP so grading biopsy as high grade cancer gives wrong prognostic information.

• Current recommendation is not to grade IDC-P but report its presence.
Intraductal Carcinoma

• Distinctive morphology vs. HGPIN

• Associated with high grade cancer and adverse pathology at RP & relatively poor prognosis with other therapies

• In most cases it is an advanced stage of tumor progression with intraductal spread of tumor; rarely an in-situ high grade cancer

• Justified to treat patients with intraductal carcinoma on biopsy even in the absence of documented infiltrating cancer
Prostate Carcinomas with Neuroendocrine Differentiation
Small Cell Carcinoma

Advanced stage at diagnosis of small cell cancer >90%
stage T3 & T4

• Prior diagnosis of adenocarcinoma – 14% to 35% - median 18-50 months

• At the time of diagnosis of small cell cancer
  – Pure small cell cancer in 70%
  – Mixed small and adenocarcinoma in 30%
Overlap Cases

Transdifferentiation of Usual Prostate Adenocarcinoma to Small Cell Carcinoma
Prognosis of Small Cell Carcinoma

• No difference:
  – Pure vs. mixed
  – Proportion of small cell cancer
  – Prior history of adenocarcinoma

• Following onset of small cell cancer
  – Median survival - 5 months; 17.5 months
  – Range – no 2 yr. survivors; 2 to 90 months

• Widespread metastases mostly small cell
Misdiagnosis of Small Cell Carcinoma

• Usual prostate adenocarcinoma has numerous neuroendocrine (NE) cells if stained with NE markers (synaptophysin, chromogranin) which has no prognostic or treatment ramifications.

• Not uncommon for Gleason score 5+5=10 to be misdiagnosed as small cell carcinoma if stains for NE markers are done.
Small Cell Carcinoma Defined Clinically

Platinum-Based Chemotherapy for Variant Castrate-Resistant Prostate Cancer

Ana M. Aparicio1, Andrea L. Harzstark4, Paul G. Corn1, Sijin Wen2, John C. Araujo1, Shi-Ming Tu1, Lance C. Pagliaro1, Jeri Kim1, Randall E. Millikan1, Charles Ryan4, Nizar M. Tannir1, Amado J. Zurita1, Paul Mathew1, Wadih Arap1, Patricia Troncoso3, Peter F. Thall2, and Christopher J. Logothetis1

19: 3621-30, 2013
Anaplastic Prostate Carcinoma
(1 of the Following Criteria)

- C1. Histologic evidence of small-cell prostate carcinoma. (25.4%)
- C2. Exclusively visceral metastases. (16.7%)
- C3. Radiographically predominant lytic bone metastases. (14.0%)
- C4. Bulky (5 cm) lymphadenopathy or Gleason 8 tumor mass in prostate/pelvis. (43.0%)
- C5. Low PSA ($\leq 10$ ng/mL) at initial presentation (before ADT or at symptomatic progression in the castrate setting) plus high volume ($\geq 20$) bone metastases. (22.8%)
Anaplastic Prostate Carcinoma

• C6. Presence of NE markers on histology (positive staining chromogranin A or synaptophysin) or in serum (abnormal high serum levels for chromogranin A or GRP) at initial diagnosis or at progression. **Plus** any of the following in the absence of other causes: A. elevated serum LDH (>2 IULN); B. malignant hypercalcemia; C. elevated serum CEA (>2 IULN). (18.4%)

• C7. Short interval (<6 months) to androgen-independent progression following the initiation of hormonal therapy

• Recommends treat like small cell carcinoma
Sarcomatoid Carcinoma (Carcinosarcoma)

- 66%–78% prior h/o of prostate cancer
- Interval 6 months – 16 yrs (median 7 yrs)
- Adenocarcinoma can be variable
  - Ductal; Small cell; squamous
- Spindle cell also variable
  - Bizarre giant cells, osteosarcoma, chondrosarcoma, rhabdomyosarcoma
Sarcomatoid Carcinoma of the Prostate: Retrospective Review of a Case Series From the Johns Hopkins Hospital

Mark C. Markowski, Mario A. Eisenberger, Marianna Zahurak, Jonathan I. Epstein, and Channing J. Paller

Urology 86: 539-43, 2015

• Local disease (1/3 of cases) was defined as prostate-confined cancer with or without EPE, in the absence of radiographic evidence of metastatic disease and bladder invasion.

• Poor outcomes for non-local disease. Median OS 9 mo. Bladder invasion and 7.1 mos. distant disease.

• 5/9 local disease survive > 5 years with surgery and/or XRT.
Summary

- Rich and diverse range of histological variants of prostate adenocarcinoma with not only unique histological features, but also having in some cases unique clinical and treatment implications.