DECEPTIVELY BENIGN-APPEARING PROSTATE CANCER

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DISCLOSURE

I have nothing to disclose

FALSE NEGATIVE DIAGNOSES OF MALIGNANCY IN SURGICAL PATHOLOGY: TOP 5 MALPRACTICE CLAIMS

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>% False negatives in claims</th>
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<tbody>
<tr>
<td>Melanoma</td>
<td>95%</td>
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<tr>
<td>Breast biopsy</td>
<td>48%</td>
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<tr>
<td>Gyn path</td>
<td>74%</td>
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<tr>
<td>Sarcomas</td>
<td>80%</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>57%</td>
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<tr>
<td>Prostate (#8)</td>
<td>67%</td>
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Troxel DB. Arch Pathol Lab Med 2006; 130:617-619

FALSE NEGATIVE DIAGNOSIS OF PROSTATIC ADENOCARCINOMA

- Overall false negative rate in needle core biopsy tissue = 1.1% to 1.7%
- Reasons:
  - Low # of glands (<10)
  - Intermingled with benign glands
  - Lack of architectural disorder
  - Foamy gland or pseudohyperplastic variants
FALSE NEGATIVE DIAGNOSIS OF PROSTATIC ADENOCARCINOMA

- 793 needle biopsies diagnosed as benign by H and E stained for AMACR
- 9/793 (1.1%) diagnosed as carcinoma – all less than 1 mm (minimal or limited carcinoma)
- Atrophic, foamy, and pseudohyperplastic pattern adenocarcinomas accounted for most false-negative prostate needle biopsy interpretations

PSEUDOBENIGN PROSTATIC ADENOCARCINOMAS

- Pale Minimal Adenocarcinomas
- Atrophic Pattern Adenocarcinoma
- Foamy Gland Adenocarcinoma
- Pseudohyperplastic adenocarcinoma
- Ductal Adenocarcinoma
- Crushed Small Cell Carcinoma
- Single cell and linear array Gleason grade 5
- Hormonal and radiation treatment effect

MINIMAL SMALL PALE ACINAR ADENOCARCINOMA: CROWDED GROWTH

CROWDED BENIGN GLANDS IN NEEDLE BIOPSY
MINIMAL SMALL PALE ACINAR ADENOCARCINOMA

SMALL PALE ACINAR MINIMAL ADENOCARCINOMA MAY BE MISTAKEN FOR BENIGN GLAND OUTPOUCHINGS AT SCANNING MAGNIFICATION

C,D : p63/AMACR immunostain

ATROPHIC PATTERN ADENOCARCINOMA

- CAN BE SEEN WITH OR WITHOUT PRIOR HORMONAL THERAPY
- ATROPHY IN BENIGN OR MALIGNANT GLANDS = CYTOPLASMIC VOLUME LOSS

PERINEURAL INVASION

HORMONAL THERAPY EFFECT ON PROSTATIC CARCINOMA: ATROPHY
ATROPHIC PATTERN ADENOCARCINOMA

CYSTIC ATROPHIC ADENOCARCINOMA: MICROCYSTIC ADENOCARCINOMA

Cyctic atrophic adenocarcinoma in needle biopsy

Sclerotic atrophy

Atrophy = cytoplasmic volume loss

Misdiagnosed as adenocarcinoma

Nuclear atypia in benign atrophy
PARTIAL ATROPHY

POSTATROPHIC HYPERPLASIA

IN NEEDLE BIOPSY

POSTATROPHIC HYPERPLASIA: CASE MISDIAGNOSED AS ADENOCARCINOMA

DIAGNOSIS: ATROPHIC ADENOCARCINOMA

- Infiltrative process with individual small atrophic glands situated between larger benign glands
- Presence of co-existing non-atrophic adenocarcinoma
- Greater cytological atypia than benign atrophy
ATROPHIC PATTERN ADENOCARCINOMA

- VS. BENIGN ATROPHY: NUCLEAR ATYPIA AND DIFFUSE LOSS OF BASAL CELLS, BEST DEMONSTRATED BY HIGH MOLECULAR WEIGHT CYTOKERATIN AND/OR p63 IMMUNOSTAINS

ALPHA-METHYLACYL-CoA RACEMASE (AMACR; P504S) AS A MARKER FOR ATROPHIC PROSTATIC ADENOCARCINOMA

"TRIPLE STAIN" TRAP: PARTIAL ATROPHY

GENE EXPRESSION PROFILES OF ATROPHY VS. NORMAL VS. PIN VS. CARCINOMA

ATROPHIC PATTERN ADENOCARCINOMA: A PROLIFERATIVE, NON-QUIESCENT GROWTH

- Proliferation index (by KI-67 labeling): 4% for atrophic pattern vs. 5.3% for usual pattern
- Apoptotic index (by TUNEL labeling): 0.4% for atrophic pattern vs. 0.4% for usual pattern

ATROPHIC VS. NONATROPHIC ADENOCARCINOMA

- WITH ATROPHIC CHANGE:
  - MEDIAN GLEASON SCORE = 6
  - MEDIAN TUMOR VOLUME = 1.4 CC
  - pT3: 26%
  - MARGIN+: 26%

- WITHOUT ATROPHIC CHANGE:
  - MEDIAN GLEASON SCORE = 6
  - MEDIAN TUMOR VOLUME = 1.1 CC
  - pT3: 31%
  - MARGIN+: 32%

All non-significant differences

FOAMY GLAND ADENOCARCINOMA

- First formally described in 1996
- Incidence in needle biopsy: 17% (2% pure)
- Incidence in radical prostatectomy: 15% to 23%

INITIAL DEFINITION: FOAMY GLAND ADENOCARCINOMA

- Infiltrative small acini with characteristic xanthomatous cytoplasm without nuclear enlargement or nucleolar prominence in most cases
- Intraluminal pink secretions in about one-half of cases
- AJSP 20:419, 1996
NUCLEAR ATYPIA IN USUAL ACINAR VERSUS FOAMY GLAND ADENOCARCINOMA

VALUE OF p63/AMACR COCKTAIL IN DIAGNOSIS OF MINIMAL FOAMY GLAND CARCINOMA

AMACR positive in 68% of cases (AJSP 27:772, 2003)

FOAMY GLAND ADENOCARCINOMA IN NEEDLE BIOPSY

GLEASON GRADE OF FOAMY GLAND ADENOCARCINOMA

- Needle biopsy: 80% 6s
- Radical prostatectomy: median Gleason score = 7

- Warrick JI and Humphrey PA. AJSP 37:1709, 2013
SPREAD OF FOAMY GLAND ADENOCARCINOMA

Extraprostatic extension  Lymph node metastasis

DIFFERENTIAL DIAGNOSIS: XANTHOMA OF PROSTATE

Xanthoma  Foamy gland carcinoma

FOAMY GLAND CARCINOMA VS. BENIGN ATROPHY WITH FOAMY FEATURES

OUTCOME AFTER RADICAL PROSTATECTOMY: FOAMY VS. NON-FOAMY ADENOCARCINOMA

**PSEUDEHYPERPLASTIC ADENOCARCINOMA**

- A variant included in 2004 WHO Blue Book

**HISTORICAL PERSPECTIVE**

- WILLIS, 1948: “Other tumors show tubular, cystic, or papillary structure…”
- ACKERMAN, 1964: “Epithelium formed in early carcinoma often shows small acini, numerous papillae, increased columnar cells…”
- EPSTEIN, 1992: “Prostate adenocarcinomas resembling benign glands”
- RO et al, 1997: Transition zone carcinomas may closely mimic BPH
PSEUDOHYPERPLASTIC ADENOCARCINOMA: BRANCHING PATTERN

MIXED BRANCHING AND PAPILLARY PATTERNS

PSEUDOHYPERPLASTIC ADENOCARCINOMA: MICROCYSTIC ADENOCARCINOMA

MIXED PATTERN – LARGE AND SMALL GLANDS

MICROCYSTIC ADENOCARCINOMA

MICROCYSTIC ADENOCARCINOMA

p63/AMACR cocktail

34betaE12 immunostain
PSEUDOHYPERPLASTIC ADENOCARCINOMA: NODULOCYSTIC PATTERN

CYSTIC CHANGE IN PROSTATIC GLANDS: USUALLY A BENIGN INDICATOR

NODULOCYSTIC PSEUDOHYPERPLASTIC ADENOCARCINOMA

NODULOCYTIC PATTERN PSEUDOHYPERPLASTIC ADENOCARCINOMA IN METASTATIC DEPOSIT (IN TESTIS)
PSEUDOHYPERPLASTIC ADENOCARCINOMA IN TURP CHIPS

IMMUNOSTAINS FOR BASAL CELLS AND AMACR : PSEUDOHYPERPLASTIC CARCINOMA IN NEEDLE BIOPSY

34βE12 IMMUNOSTAIN
AMACR IMMUNOSTAIN
Note : 77% of cases positive

PSEUDOHYPERPLASTIC ADENOCARCINOMA : APPEARANCE IN NEEDLE BIOPSY TISSUE

PSEUDOHYPERPLASTIC ADENOCARCINOMA VS. BPH NODULE

NEOPLASTIC MIMICS IN GENITOURINARY PATHOLOGY, 2013
PATHOLOGIC ATTRIBUTES OF PSEUDOHYPERPLASTIC CARCINOMA

- **ANATOMIC LOCALIZATION**: Transition or peripheral zone
- **TUMOR SIZE**: 14.2% of whole gland involved vs. 9.9% for usual carcinoma (P=0.038)
- **pT3 STAGE**: 36% vs. 30% for carcinoma without pseudohyperplastic features (P=0.7)
- **GLEASON GRADE = 3**

DECEPTIVELY BENIGN DUCTAL CARCINOMA IN NEEDLE BIOPSY TISSUE

SMALL CELL CARCINOMA VS. CRUSHED LYMPHOCYTES
GLEASON PATTERN 5: SINGLE CELLS


GLEASON GRADE PATTERN 5: LINEAR ARRAY

NEOPLASTIC MIMICS IN GENITOURINARY PATHOLOGY, 2013

HORMONAL TREATMENT EFFECT ON PROSTATIC ADENOCARCINOMA

RADIATION TREATMENT EFFECT ON CARCINOMA

"Triple stain"
DIAGNOSIS OF DECEPTIVELY BENIGN-APPEARING (PSEUDOBENIGN) CARCINOMAS

- Stout criteria hold true for usual and pseudobenign prostatic carcinomas
- **GLANDULAR PATTERN** – disordered infiltrative growth
- **LACK OF BASAL CELLS**
- **CELLULAR DETAILS** – large deeply-staining nucleoli
- Arch Pathol 55:131, 1953

PSEUDOBENIGN CARCINOMAS: ADDENDA TO STOUT CRITERIA

- Diagnose with great caution in needle biopsy tissue
- Search for continuity with usual adenocarcinoma
- Apply markers: basal cell stains (high molecular weight cytokeratin, p63) and AMACR