Case # 4

Peiguo Chu, M.D., Ph.D.

Clinical history: A 63 year-old man presented with elevated serum PSA of 6.0 ng/ml in August 2005. His PSAs ranged from 4.0 ng/ml to 5.0 ng/ml over prior two years. Fourteen needle core biopsies were performed in an outside hospital in June 2005 with a diagnosis of “prostate carcinoma, Gleason score 7”. Prostate triple immunostains were performed on needle core slides and showed that atypical glands were positive for AMACR and negative for CK 34βE12 and p63. The patient was referred to City of Hope in August 2005 for surgery. Laparoscopic radical prostatectomy was performed at City of Hope.

Pathologic findings: Prostate weighted 99.5 grams. The entire prostate was submitted for histologic examination. Thirteen of sixty-five H&E sections (20%) had atypical glands (volume of involvement 5-10%) that were identical to those seen in prostate core biopsy. Atypical glands:
- Small acini or nests
- Present at the peripheral zone of prostate and at multiple peripheral margins
- Single layer of luminal cells
- Pink luminal secretion and gland dilatation
- Focally infiltrating pattern
Atypical cells:
- Minimal nuclear atypia
- Occasional centrally placed small nucleoli
- No mitotic figures
Immunohistochemistry:
- Positive: AMACR, CK 34βE12 (focal), keratin 7 and CD10 (focal)
- Negative: p63, PAS, PAcP, calretinin, and RCC

Differential diagnoses:

Prostate adenocarcinoma, Gleason score 3+4=7: The Differential diagnosis of small atypical glands in prostate stroma with single cell lining and presence of nucleoli should always include prostate adenocarcinoma.
- Findings favor adenocarcinoma: Small atypical glands, single layer of luminal cells, presence of nucleoli, focal infiltrating pattern, AMACR+, P63-
- Findings against adenocarcinoma: Peripheral location, no stromal reaction, PSA-/PAcP-, CK 34βE12+

Atrophic glands/postatrophic hyperplasia:
- Findings favor atrophy: Small atypical glands, presence of nucleoli, infiltrating pattern, CK 34βE12+
Findings against atrophy: Peripheral location, PSA-/PAcP-, AMACR+

**Atypical adenomatous hyperplasia/atypical small acinar proliferation (ADH/ASAP):**
- Findings favor ADH/ASAP: Small atypical glands, AMACR+, CK 34βE12+
- Findings against ADH/ASAP: Infiltrating pattern, single layer of luminal cells, PSA-/PAcP-, P63-

**Sclerosing adenosis (SA):**
- Findings favor SA: Small atypical glands, infiltrating pattern, CK 34βE12+
- Findings against SA: Single layer of luminal cells, AMACR+, PSA-/PAcP- P63-

**Nephrogenic adenoma (NA):**
- Benign, tumor like lesions within the urothelial mucosa of the urinary tract
- Most are found in bladder
- Other locations: pelvic urothelium, ureter, and urethra
- Tissue origins: metaplasia, hamartoma, and renal tubule implantation
- Immunohistochemistry:
  - Positive: AMACR, CD10, RCC, calretinin
  - Negative: CK 34βE12, P63^-, PSA

- Findings favor NA: Small atypical glands, single layer of luminal cells, AMACR+, CD10+, PSA-/PAcP-
- Findings against NA: Peripheral location, RCC^-, CK 34βE12^+

**Mesonephric remnant (hyperplasia):**
- Rarely identified (0.6%), about 0.1-0.7 cm. in diameter
- Closely spaced acini arranged in lobules or infiltrating between muscle bundles (periphery) or prostate acini
- Single layer of cuboidal cells with scant amount of eosinophilic cytoplasm, finely dispersed chromatin, and small round punctuate nucleoli
- Sometimes with tubular dilation, epithelial tufting and micropapillary formation
- Occasionally undergo hyperplasia
- May demonstrate perineural spread and extraprostatic extension
- No stromal desmoplastic or inflammatory response
- Dense eosinophilic luminal secretion
- No mitotic figures
- Immunohistochemistry:
  - Positive: AMACR; keratin 34βE12, keratin 7,
  - Negative: PAS, PacP, P63, CD10, RCC
Findings favor mesonephric remnant hyperplasia: Diffuse peripheral location (size >1.0 cm.), single layer of luminal cells, AMACR+, CK34βE12+, PAS-/PAcP-

Summary of immunohistochemical features of benign mimickers of prostate adenocarcinoma

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<th>Lesions</th>
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<th>PSA</th>
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<th>CK 903</th>
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