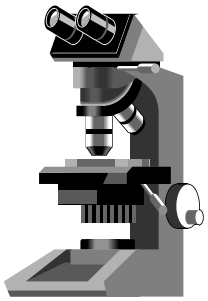
CALIFORNIA
TUMOR TISSUE REGISTRY

GENITOURINARY PATHOLOGY

Minutes – Subscription A

April 2016



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FILE DIAGNOSES

CTTR Subscription A April 2016

Case 1: **VERRUCOUS CARCINOMA,** Penis

Case 2: **VILLOUS ADENOCARCINOMA,** Urethra

Case 3: **SEMINOMA,** Testis

Case 4: **URACHAL ADENOCARCINOMA,** Bladder

Case 5: **RHABDOMYOSARCOMA,** Prostate

Case 6: **GRANULOMATOUS PROSTATITIS,** Prostate

Case 7: **MALAKAOPLAKIA,** Kidney

Case 8: **LOW GRADE ONCOCYTIC RENAL EPITHELIAL NEOPLASM**, Left Renal

Case 9: **TUMEFACTIVE PRIMARY AMYLOIDOSIS,** Bladder

Case 10: **CARCINOSARCOMA,** Bladder

CASE #1: **Accession No. 23481**

DIAGNOSIS: VERRUCOUS CARCINOMA, Penis

Diagnoses submitted in decreasing order of frequency:
Condyloma accuminatum
Verrucous Carcinoma
Giant Condyloma

Discussion

This patient has a verrucifom, slow growing, recurring, and locally destructive squamous proliferation. This tumor shows hyperkeratotic and acanthotic papillae with keratin cysts. A basal dense lymphohistiocytic infiltrate is present.

First described by Buschke and Löwenstein in 1925, the giant condyloma of Buschke and Löwenstein is a slow-growing, locally destructive verrucous plaque that typically appears on the penis but may occur elsewhere in the anogenital region. It most commonly is considered to be a regional variant of a well differentiated squamous verrucous carcinoma, with limited metastatic potential. It is a rare sexually transmitted HPV-related tumor; the incidence is estimated to be 0.1% in the general population. Low-risk genotypes (HPV-6 and 11) predominate. It usually involves the foreskin and coronal sulcus; also glans and perianal regions. It is associated with chronic irritation and poor hygiene in uncircumcised men. It may also occur in women in the mucosal anogenital regions. Majority of cases occur in patients younger than 50 years. It has a cauliflower-like growth with a broad pushing base and prominent bulbous endophytic expansion into underlying tissue.

Giant condyloma acuminatum is differentiated histologically from ordinary condyloma acuminata by its thicker stratum corneum and the presence of an endophytic downgrowth, along with a tendency to invade deeper.

CASE #2: **Accession No. 23332**

DIAGNOSIS: VILLOUS ADENOCARCINOMA, Urethra

Diagnoses submitted in decreasing order of frequency:
Villous adenocarcinoma
Invasive adenocarcinoma arising in villous adenoma
Adenocarcinoma r/o metastasis from colon, bladder, prostate
Papillary adenoma
Adenocarcinoma of Cowper glands

Discussion

This is a case of a villous carcinoma arising from a villous adenoma of the urethra. The neoplasm bears close similarity to intestinal villous carcinomas. Beneath the villous surface elements there is less differentiated invasive adenocarcinoma.

Primary urethral carcinoma is rare, the most frequent histologic types are urothelial carcinoma, squamous cell carcinoma and adenocarcinoma (not otherwise specified, clear cell). For male primary urethral carcinoma various predisposing factors have been reported, including urethral strictures, chronic irritation after intermittent catheterisation/urethroplasty, external beam irradiation therapy, radioactive seed implantation and chronic urethral inflammation/urethritis following sexually transmitted diseases (condylomata associated with HPV 16). African Americans are more commonly affected. In females urethral carcinomas urethral diverticula, and recurrent urinary tract infections have been associated with primary carcinoma.

Adenocarcinoma may originate anywhere along the urethra. It may arise from urothelial metaplastic mucosa or from periurethral glands. Urethral adenocarcinoma shows positive staining for CK20, CDX2 and beta-catenin (cytoplasmic). Negative staining for PSA, PSMA, AMACAR, PAX2 and PAX8.

Differential Diagnosis: Extension of cancer from adjacent organs (bladder, prostate, colon - more frequent), extension from squamous cell carcinoma of penis, vulva or cervix, nephrogenic metaplasia.

CASE #3: **Accession No. 17715**

DIAGNOSIS: SEMINOMA, Testis

Diagnoses submitted in decreasing order of frequency:

Seminoma
Seminoma versus embryonal carcinoma / hepatoid yolk sac tumor
Embryonal carcinoma

Discussion

Testicular germ cell tumors represent the most frequent solid malignancy in white males between the ages of 20 and 35 but are relatively uncommon among African Americans. Epidemiologically, clinically, and histologically, 3 entities of germ cell tumors can be distinguished in the testis. The first group includes teratomas–yolk sac tumors, which become manifest usually within the first 4 years of life and almost always before puberty. The second group comprises seminomas and non-seminomatous germ cell tumors, which manifest after puberty. The third group includes spermatocytic tumors, which usually affect older men. These groups differ in their presentation, treatment, and prognosis.

Seminoma is the most common testicular tumor; it responds well with radiation treatment. Features of classic seminoma include: fibrous stroma, lymphocytic and/or granulomatous stromal reaction, cells with abundant glycogen, positivity for placental alkaline phosphatase, and germ cell neoplasia in situ component.

The risk of testis cancer is higher in patients with a history of cryptorchidism, intersex disorders, infertility and prior contralateral germ cell tumor. Germ cell carcinoma in situ (CIS) is a premalignant condition with intratubular atypical germ cells within seminiferous tubules and a natural history of progression to seminoma or embryonal cancer. Most patients with seminomas have CIS associated with the primary tumor. 5% of patients may harbor CIC in the contralateral testis. An elevated AFP level rules out pure seminoma, despite possible contrary histopathologic orchiectomy findings. Beta–human chorionic gonadotropin (beta-hCG) levels are elevated in 5-10% of patients with seminomas. Classic seminomas reveal a consistent structural chromosomal abnormality of isochromosome 12p.

CASE #4: **Accession No. 13200**

DIAGNOSIS: URACHAL ADENOCARCINOMA, Bladder

Diagnoses submitted in decreasing order of frequency:
Urachal adenocarcinoma
Mucinous adenocarcinoma
Tubulovillous adenoma
Cystitis glandularis

Discussion

Urachal adenocarcinoma arises from embryologic urachal remants in the anterior wall or dome of the bladder. There is predominant invasion of muscularis and deeper tissues with sharp demarcation between the tumor and surface urothelium, which is free of glandular and polypoid proliferations. No carcinoma in situ or glandular intestinal metaplasia is present. The presence of urachal remnants is helpful but not always identifiable. There should be no primary adenocarcinoma elsewhere.

Urachal adenocarcinoma represents 0.3% of all bladder cancers. It is usually a well-differentiated, mucin-producing adenocarcinoma, often enteric type. Colloid type (tumor cells floating in mucin lakes) and signet-ring cell carcinoma types may also occur. Tumor is CK7+ with variable CK20 and CDX2 staining; also shows diffuse positivity for 34BE12.

Differential diagnosis: Local extension of colonic or other adenocarcinoma - clinical history is important. Non-urachal adenocarcinoma of bladder: presentation with an intraluminal mass, carcinoma in situ or extensive glandular metaplasia of adjacent urothelium. Villous adenoma: noninvasive

CASE NO #5: **Accession No. 7843**

DIAGNOSIS: RHABDOMYOSARCOMA, Prostate

Diagnoses submitted in decreasing order of frequency:
Rhabdomyosarcoma (embryonal, botryoid types)

Discussion

This is the most common malignant tumor in children/infants. There is firm, smooth enlargement of prostate. Morphologic features with striated rhabdomyoblasts and positivity for the muscle markers (desmin, myogenin, MyoD1+) are helpful for diagnosis. Genitourinary rhabdomyosarcoma are usually of the embryonal subtype. Patients usually present with stage 3 disease, sometimes with distant metastases. The long-term disease-specific survival rate is poor.

CASE #6: **Accession No. 18662**

DIAGNOSIS: GRANULOMATOUS PROSTATITIS, Prostate

Diagnoses submitted in decreasing order of frequency:
Granulomatous prostatitis
Severe acute and chronic prostatitis
Benign prostatic hyperplasia with chronic inflammation
Pulse Granuloma

Discussion

Granulomatous prostatitis is an inflammatory condition of the prostate that histologically features the presence of granulomas. It is subclassified as infectious granulomas, nonspecific granulomatous prostatitis, post-biopsy granulomas, and systemic granulomatous prostatitis.

Rarer forms of granulomatous prostatitis include xanthogranulomatous prostatitis and sarcoidosis. Xanthogranulomatous prostatitis is histologically similar to granulomatous prostatitis, the main difference being the prominence of foamy histiocytes, which constitute the xanthomatous component. In mycobacterial prostatitis, granulomas predominate within the peripheral zone of the prostate. Nonspecific granulomatous prostatitis and xanthogranulomatous prostatitis may occur in the transition and peripheral zones, whereas post-biopsy granulomatous prostatitis occurs around the resection site and along the biopsy tract. The granulomas in systemic granulomatous conditions may be centered on blood vessels.

CASE #7: **Accession No. 17873**

DIAGNOSIS: XANTHOGRANULOMATOUS PYELONEPHRITIS, FOCAL MALAKAOPLAKIA, Kidney

Diagnoses submitted in decreasing order of frequency:
Xanthogranulomatous pyelonephritis
Malakaoplakia
Renal abscess suggestive of acute pyelonephritis
Oncocytic renal cell carcinoma
Oncocytic carcinoma versus metastasis

Discussion

This gentleman was also found to be in shock due to Gram negative sepsis, and expired despite treatment. At autopsy the kidneys showed severe acute necrotizing papillitis and xanthogranulomatous pyelonephritis (XGP) with malakoplakia. The pathognomonic microscopic features of XGP are the lipid-laden foamy macrophages with accompanying acute and chronic inflammatory cells and focal abscess formation. The macrophages can be difficult to distinguish from clear cell carcinoma on gross examination (yellow mass with necrosis and hemorrhage, may extend through the capsule to involve adjacent structures and organs), H&E and at the time of frozen sections. There are case reports of XGP and renal cell carcinoma occurring together in the same kidney. Oncocytic neoplasms have plump cells with granular eosinophilic cytoplasm and may show diffuse sheet-like or nested growth patterns. The XGP cells display abundant finely vacuolated cytoplasm, lack prominent cell borders and may contain Michaelis-Gutmann bodies (laminated cytoplasmic concretions, malakoplakia). The histiocytes are CD68 and CD163 positive.

XGP is a rare, serious, chronic inflammatory disorder of the kidney characterized by a diffuse destructive mass that invades the renal parenchyma. It is most commonly associated with *Proteus* and *E. coli* infections. *Pseudomonas* species have also been implicated. XGP is often associated with long term urinary tract obstruction (staghorn calculi), infection, diabetes, and/or immunocompromised status. The kidney is usually nonfunctional.

CASE #8: **Accession No. 31743**

DIAGNOSIS: LOW GRADE ONCOCYTIC RENAL EPITHELIAL NEOPLASM, Left Renal

Diagnoses submitted in decreasing order of frequency:

Papillary renal cell carcinoma (Type 1, oncocytic)
Oncocytoma
Chromophobe RCC
Tubulocystic Carcinoma
Adenocarcinoma
Collecting duct carcinoma

Discussion

This is a challenging case, it was reported as a low grade oncocytic unclassified renal neoplasm consistent with tumor of distal nephron origin. The mostly "tubular" presentation is unusual. CD 117 is diffusely positive in oncocytomas, however this tumor is negative. The immunostain profile and absence of overt papillary, clear cell or chromophobe-like features prevent classification into a classic RCC subtype.

Tumors in the differential diagnosis of oncocytic renal cell neoplasms include: oncocytoma, chromophobe renal cell carcinoma (RCC), hybrid tumor, tubulocystic carcinoma, papillary RCC, clear cell RCC with predominant eosinophilic cell morphology, follicular thyroid-like RCC, hereditary leiomyomatosis-associated RCC, acquired cystic disease-associated RCC, rhabdoid RCC, microphthalmia transcription factor translocation RCC, epithelioid angiomyolipoma, and unclassified RCC.

Eosinophilic epithelial neoplasms with architecture, cytology, and/or immunoprofile not qualifying for either of the established types of RCC should be classified as unclassified eosinophilic RCC and arbitrarily assigned a grade (low or high).

CASE #9: **Accession No. 23340**

DIAGNOSIS: **TUMEFACTIVE AMYLOIDOSIS,** Bladder

Diagnoses submitted in decreasing order of frequency:

Amyloidosis
Necrosis, foreign material and foreign body giant cell reaction

Discussion

This is an example of primary localized or "tumefactive" amyloidosis. A neoplasm was suspected due to the prolonged patient history of dysuria, hematuria and cystoscopic findings of an ulcerated mass. The amyloid deposits are present in the submucosa, muscularis and vessel walls, and stained appropriately with Congo red, methyl violet stains. Further workup showed no evidence of abnormal serum proteins, plasma cell neoplasia or systemic amyloidosis.

Amyloidosis consists of extracellular deposition of amyloid, a protein with a fibrillary structure, in one or more body sites. Amyloidosis may be inherited or acquired. The organs commonly involved are urinary bladder, lung, larynx, skin, tongue and the region around the eye. Primary amyloidosis arises from diseases with disordered immune cell function such as multiple myeloma. Secondary (reactive) amyloidosis occurs as a complication of some chronic inflammatory or tissue destructive diseases. The kidney is nearly always involved in secondary amyloidosis and in approximately 50% of the cases of primary amyloidosis. This is in contrast to the urinary bladder, which is usually affected in primary localized amyloidosis.

CASE #10: **Accession No. 4904**

DIAGNOSIS: CARCINOSARCOMA, Bladder

Diagnoses submitted in decreasing order of frequency:

Carcinosarcoma
Sarcomatoid, poorly differentiated urothelial carcinoma with heterologous differentiation
Malignant teratoma
Urothelial carcinoma with squamous differentiation
High grade urothelial carcinoma

Discussion

This is a high grade urothelial neoplasm varied patterns and morphology including epithelial, spindle cell and cartilaginous components. There is abundant necrosis.

Carcinosarcomas are neoplasms characterized by the presence of both malignant epithelial and mesenchymal components. Carcinosarcomas of the urinary bladder are rare, with fewer than 80 documented cases. There is a male predominance in the urinary bladder cases, with a mean age of 66.4 years, e similar to those of conventional urothelial carcinoma. Smoking has been implicated as a risk factor. There is also an association between previous radiation exposure, BCG and chemotherapies and development of carcinosarcomas in the urinary bladder.

The most common epithelial component in bladder carcinosarcomas is urothelial carcinoma, followed by squamous cell carcinoma. There may be a 2 or more epithelial components in the same tumor. The most common mesenchymal component is osteosarcoma, followed by chondrosarcoma, rhabdomyosarcoma and others. Overall prognosis for these tumors is poor.

The histogenesis of carcinosarcomas remains uncertain, they may develop as a result of the capability of the undifferentiated neoplastic cells undergoing multiple pathways of terminal differentiation into mesenchymal and epithelial elements. This is supported by the presence of immunoreactivity for epithelial markers (cytokeratin or EMA) in mesenchymal areas as well as the presence of ultrastructural features (desmosomes or tonofilaments) of epithelial differentiation in sarcomatoid elements. A few carcinosarcomas may also be the result of collision tumors, where both malignant epithelial and mesenchymal components arise independently from each other.

Differential diagnosis: Carcinomas with pseudosarcomatous stroma, sarcomas with pseudoepitheliomatous hyperplasia, and teratomas. Pseudosarcomatous stroma, and other proliferations such as inflammatory pseudotumors and postoperative spindle cell nodules are usually highly vascularized with numerous small slitlike vessels. The cells show minimal reactive-type atypia; atypical mitotic figures are absent. Teratomas may resemble carcinosarcomas due to the presence of multiple histologic elements. However, by definition, teratomas are tumors derived from all 3 embryologic layers and contain abundant histologically benign epidermoid elements with admixed dermal adnexal structures.

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