**The University of Illinois Hospital & Health Sciences System Combined Residency Program**

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Illinois Registry of Anatomic Pathology (IRAP)

Case Summaries

10/29/2018

**Case #1: Florid cystitis glandularis cystica of intestinal type with mucin extravasation**

*Presenter:* Charisse Baste, MD; *Attending:* David Allison, DO

**Clinical History:** The patient is a 49-year-old male with past medical history of benign prostatic hyperplasia, resolved sexually transmitted infection and well-controlled hypertension presented for resection of residual bladder mass. One year ago, the patient presented initially with a complaint of hematuria for 1 year. Computed tomography scan showed nodular asymmetric thickening of the bladder base. A cystoscopy showed a bladder mass that was subsequently biopsied. Diagnosis on biopsy at that time was cystitis glandularis. Recently, the patient then underwent transurethral resection of bladder tumor (TURBT). The operative report described a 6.0 x 1.0 cm mass immediately proximal to the bladder neck.

**Diagnosis: Florid cystitis glandularis cystica of intestinal type with mucin extravasation**

**Differential Diagnosis:**

* Florid cystitis glandularis cystica of intestinal type with mucin extravasation
* Adenocarcinoma of bladder, primary
* Metastatic adenocarcinoma

**Key microscopic features:**

* Cytologically bland epithelial cells with small, basal nuclei without atypia
* Acellular pools of mucin without floating epithelial cells
* Lack of destructive stromal invasion in the myxoid stroma

**Immunohistochemical stains:**

* Positive: CK7, CK20, CDX2, Beta-catenin (cytoplasmic)
* Negative: PSA

**Take Home Points:**

* Florid cystitis glandularis of intestinal type may mimic a neoplasm on gross evaluation and the propensity of the mucin extravasation to cause diagnostic difficulty

**References:**

1. Dadhania V, Czerniak B, Guo CC. Adenocarcinoma of the urinary bladder. *American journal of clinical and experimental urology* 2015;3(2):51.
2. Ito A, Sakura Y, Sugimoto M, Kakehi Y, Kuroda N. Villous Tumor of the Urinary Bladder Resembling Low-grade Mucinous Neoplasm of the Appendix. *Urology case reports* 2016 May 1;6:4-6.
3. Song YS, Jang KS, Jang SH, Min KW, Na W, Song SY, Moon HS, Lee TY, Paik SS. The Intestinal Type of Florid Cystitis Glandularis Mimics Bladder Tumor. *Korean Journal of Pathology* 2007;41(116):8.
4. Sung MT, Lopez-Beltran A, Eble JN, MacLennan GT, Tan PH, Montironi R, Jones TD, Ulbright TM, Blair JE, Cheng L. Divergent pathway of intestinal metaplasia and cystitis glandularis of the urinary bladder. *Modern pathology* 2006;19(11):1395.
5. Xin Z, Zhao C, Huang T, Zhang Z, Chu C, Lu C, Wu M, Zhou W. Intestinal metaplasia of the bladder in 89 patients: a study with emphasis on long-term outcome. *BMC urology* 2016;16(1):24.
6. Young RH, Bostwick DG. Florid cystitis glandularis of intestinal type with mucin extravasation: a mimic of adenocarcinoma. *Am J Surg Pathol* 1996;20(12):1462-8.

**Case 2: Dysplastic lipoma**

*Presenter*: Hui Zhang, MD; *Attending*: Michael R. Pins, MD

**Clinical History:** A 34-year-old male with no significant past medical history presented with a left scrotal mass. The surgical resection showed a 6.4 cm subcutaneous mass on left scrotum. The operative impression was that the mass was adherent to the scrotal skin.

**Diagnosis:** **Dysplastic lipoma**

**Differential diagnosis:**

* Dysplastic lipoma
* Conventional lipoma
* Spindle cell / Pleomorphic lipoma
* Atypical lipomatous tumor/well-differentiated liposarcoma

**Key Microscopic Features:**

* Well-demarcated subcutaneous masses
* Striking adipocytic size variation
* Patchy single-cell fat necrosis
* Scant or absent spindled stromal cells and collagenous matrix
* Sparse adipocytes with one or more atypical nuclei are always present
* Mild adipocytic atypia
* Atypical adipocytes have enlarged variably sized nuclei with coarsened chromatin, small nucleoli and often times, focal Lochkern change.
* Rare lipoblast-like cells and infrequent multivacuolated atypical fat cells

**Immunohistochemical stains:**

* Positive: p53, p16

**Molecular cytogenetic studies**:

* FISH analysis for MDM2 gene amplification: Negative

**Take Home Points:**

* Dysplastic lipoma is a recently described, distinct, clinicopathologic entity that may morphologically mimic atypical lipomatous tumor/well-differentiated liposarcoma but has an indolent clinical course with occasional instances of local recurrence

**References:**

1. Agaimy A. Anisometric cell lipoma: Insight from a case series and review of the literature on adipocytic neoplasms in survivors of retinoblastoma suggest a role for RB1 loss and possible relationship to fat-predominant (“fat-only”) spindle cell lipoma. *Ann Diagn Pathol* 2017;29:52–6.
2. Allen PW, Strungs I, MacCormac LB. Atypical subcutaneous fatty tumors: a review of 37 referred cases. *Pathology* 1998;30:123–35.
3. Dei Tos AP, Doglioni C, Laurino L, et al. p53 protein expression in non-neoplastic lesions and benign and malignant neoplasms of soft tissue. *Histopathology* 1993;22:45–50.
4. Enzinger FM, Harvey DA. Spindle cell lipoma. *Cancer* 1975;36:1852–9.
5. Evans HL. Subcutaneous minimally atypical lipomatous tumors with variable fat cell size-a study of 13 cases. *Mod Pathol* 2015;28(suppl 2):17A.
6. Evans HL. Anisometric cell lipoma: a predominantly subcutaneous fatty tumor with notable variation in fat cell size but not more than slight nuclear enlargement and atypia. *AJSP Rev Rep* 2016;21:195–9.
7. Michal M, Agaimy A, Contreras AL, et al. Dysplastic lipoma a distinctive atypical lipomatous neoplasm with anisocytosis, focal nuclear atypia, p53 overexpression, and a lack of MDM2 gene amplification by FISH: a report of 66 cases demonstrating occasional multifocality and a rare association with retinoblastoma. *Am J Surg Pathol* 2018;42(11):1530-1540.
8. Shmookler BM, Enzinger FM. Pleomorphic lipoma: a benign tumor simulating liposarcoma. A clinicopathologic analysis of 48 cases. *Cancer* 1981;47:126–33.
9. Thway K, Wang J, Swansbury J, et al. Fluorescence in situ hybridization for MDM2 amplification as a routine ancillary diagnostic tool for suspected well-differentiated and dedifferentiated liposarcomas: experience at a tertiary center. *Sarcoma* 2015;2015:812089.

**Case 3: Liposarcoma Presenting as Giant Fibrovascular Polyp**
Presenter: Aleksandar Krbanjevic, MD, PhD; Attending: Michael R. Pins, MD

**Clinical History:** An 87-year-old male with history of hypertension, diabetes mellitus and chronic musculoskeletal debilitating condition presented to an outside hospital emergency department with the complaint of an oropharyngeal mass. The patient stated that he began coughing while eating and “coughed out the mass.” The patient denied fever, vomiting, and recent illness.

**Diagnosis: Liposarcoma**

**Differential Diagnosis:**

* Lipoma
* Liposarcoma
* Giant fibrovascular polyp

**Key Macroscopic Features:**

* A large esophageal pedunculated fibro-fatty mass
	+ Smooth shiny tan-yellow lobulated surface
	+ Grows frequently from upper esophagus and partially obstructs its lumen

**Key Microscopic Features:**

* Heterogeneous lesion with:
	+ Tumor centered in subepithelial stroma and lined by intact squamous nonkeratinized epithelium
	+ Morphological features of esophageal polyp are commonly not diagnostic for malignant lesion (mature adipose tissue with benign looking stroma)
	+ Rarely focal areas of lipoblasts can be found

**Immunohistochemical and special stains:**

* None

**Molecular cytogenetic studies**: FISH positive for MDM2 amplification

**Take Home Points:**

* Liposarcoma can sometimes present clinically as giant fibrovascular polyp
	+ Giant fibrovascular polyp = liposarcoma until proven otherwise
* It is comprised of benign looking spindle cells surrounded by subepithelial stroma and covered by squamous nonkeratinized epithelium
* It is critical to test this lesion for MDM2 amplification as a positive result suggests malignancy

**References:**

1. Boni A, Lisovsky M, Dal Cin P, Rosenberg AE, Srivastava A. Atypical lipomatous tumor mimicking giant fibrovascular polyp of the esophagus: report of a case and a critical review of literature. *Hum Pathol* 2013; 44(6):1165-70.
2. Graham RP, Yasir S, Fritchie KJ, Reid MD, Greipp PT, Folpe AL. Polypoid fibroadipose tumors of the esophagus: 'giant fibrovascular polyp' or liposarcoma? A clinicopathological and molecular cytogenetic study of 13 cases. *Mod Pathol.* 2018;31(2):337-342.
3. Momand J, Jung D, Wilczynski S, Niland J. The MDM2 gene amplification database. *Nucleic Acids Res* 1998;26:3453-3459.
4. Nag S, Qin J, Srivenugopal KS, Wang M, Zhang R. The MDM2-p53 pathway revisited. *J Biomed Res* 2013;27:254-271.
5. Vassilev LT. MDM2 inhibitors for cancer therapy. *Trends Mol Med* 2007;13: 23-31.

**Case #4: Glandular odontogenic cyst***Presenter*: Ismail Younes, MBChB*; Attending:* John Groth, MD

**Clinical History:** A 70-year-old male with no significant past medical history presented for repeat enucleation and curettage for an anterior mandibular lesion that was found radiologically. The patient previously underwent enucleation and curettage without complications. The lesion had regressed significantly and was followed over the course of multiple years, but now has recurred. The lesion was grossly multicystic associated with teeth #20, 21, 22, 27. The patient then underwent a repeat enucleation and curettage with extraction of teeth without complications.

**Diagnosis: Glandular odontogenic cyst**

**Differential Diagnosis:**

* Dentigerous cyst
* Radicular cyst
* Central mucoepidermoid carcinoma
* Glandular odontogenic cyst

**Key microscopic features:**

* Cystic lesion
* Variable thickness of the epithelium associated with goblet cells and microcysts
* Lined by squamous epithelium with ciliated cells with occasional cuboidal eosinophilic cells and papillary proliferation

**Special stain:**

* Mucin stain highlighted occasional goblet cells

**Molecular Studies**:

* *CRTC1-MAML2* fusion gene for FISH was negative

**Take Home Points:**

* Glandular odontogenic cyst is a locally aggressive cyst within the jaw
	+ - Most commonly in the mandible
* Morphologic overlap with other odontogenic cysts
	+ - Most importantly exclude mucoepidermoid carcinoma
* Has high rate of recurrence between 20-50%

**References:**

1. Fowler CB, Brannon RB, Kessler HP, Castle JT, Kahn MA. Glandular Odontogenic Cyst: Analysis of 46 Cases with Special Emphasis on Microscopic Criteria for Diagnosis. *Head and Neck Pathol* 2011;5:364-375.
2. Kaplan I, Anavi Y, Manor R, Sulkes J, Calderon S. The use of molecular markers as an aid in the diagnosis of glandular odontogenic cyst. *Oral Oncol*2005;41:895.
3. Lo Muzio L, Santarelli A, Caltabiano R, et al. p63 expression in odontogenic cysts. *Int J Oral Maxillofac* Surg 2005;34(6):668.
4. Tosios KI, Kakarantza‐Angelopoulou E, Kapranos N. Immunohistochemical study of bcl‐2 protein, Ki‐67 antigen and p53 protein in epithelium of glandular odontogenic cysts and dentigerous cysts. *Journal of oral pathology & medicine* 2000;29(3):139-44.

**Case 5: Eosinophilic Solid and Cystic Renal Cell Carcinoma**

Presenter: Luis Manon, MD; Attending: Karen Ferrer, MD

**Clinical History:** A 64-year-old female with a past medical history of hypertension, osteoarthritis, and complicated diverticulitis was referred to clinic for an incidental right renal mass discovered on computed tomography scan. The patient denied any symptoms related to the mass and her physical exam was unremarkable. An ultrasound was consistent with a 6.6 cm heterogeneous, vascular mass at the right upper pole. A right total nephrectomy was performed and the specimen obtained consisted of a 440 g kidney with a 6.3 x 5.9 x 5.6 cm well-circumscribed, markedly hemorrhagic, cystic mass in the upper pole.

**Diagnosis: Eosinophilic solid and cystic renal cell carcinoma**

**Differential Diagnosis:**

* Oncocytoma
* Chromophobe Renal Cell Carcinoma
* Clear Cell Renal Cell Carcinoma (with predominant eosinophilic morphology)
* Epithelioid Angiomyolipoma

**Key Microscopic Features:**

* Solid and cystic architecture
* Neoplastic cells with voluminous eosinophilic cytoplasm
* Granular cytoplasmic stippling

**Immunohistochemical stains:**

* Immunoreactive: CK20 (strong, diffuse), CD20, CD15, and p504S
* Nonreactive: CAIX, EMA, CD117, and e-cadherin
* Scattered cells show focal & patchy immunoreactivity with CK7, and vimentin

**Ancillary Testing:**

* Copy number analysis showed DNA copy number increase along the SMO gene on chromosome 7q32 and the entire chromosome 16 where TSC2 is located

**Summary/Discussion:**

* Renal neoplasms characterized by eosinophilic cytoplasm and solid and cystic growth should consider the differential diagnosis of Eosinophilic Solid and Cysitc Renal Cell Carcinoma (ESC RCC). It has been described as a new subtype of renal cell carcinoma based on the solid and cystic architecture, in addition to the neoplastic cells containing voluminous eosinophilic cytoplasm with granular cytoplasmic stippling. Also, there is consistent immunoreactivity for cytokeratin 20 which is unique to this entity. ESC RCC has been postulated to be analogous to a subtype of RCC consistently identified in tuberous sclerosis complex patients. TSC1 and TSC2 mutations are consistently seen in these tumors and infrequently seen in established subtypes of renal cell carcinoma. This further supports ESC RCC as a unique renal neoplasm based on molecular analysis in addition to morphologic and immunohistochemical features. Further characterization of this neoplasm can lead to targeted treatment and also give a category to a group of neoplasms that may represent the same entity (as ESC RCC) but otherwise categorized as “unclassified RCC” or “unclassified renal neoplasm (or carcinoma) with oncocytic or eosinophilic morphology.”

**References:**

1. Kryvenko ON, Jorda M, Argani P, Epstein JI. Diagnostic Approach to Eosinophilic Renal Neoplasms. Arch Pathol Lab Med 2014;138(11):1531-1541.
2. Palsgrove DN, Li Y, Pratilas CA, Lin MT, Pallavajjalla A, Gocke C, De Marzo AM, Matoso A, Netto GJ, Epstein JI, Argani P. Eosinophilic Solid and Cystic (ESC) Renal Cell Carcinomas Harbor TSC Mutations. *Am J Surg Pathol* 2018 Sep 1;42(9):1166-81.
3. Trpkov K, Abou-Ouf H, Hes O, Lopez JI, Nesi G, Comperat E, Sibony M, Osunkoya AO, Zhou M, Gokden N, Leroy X. Eosinophilic Solid and Cystic Renal Cell Carcinoma (ESC RCC). *Am J Surg Pathol* 2017;41(10):1299-308.
4. Trpkov K, Hes O, Bonert M, Lopez JI, Bonsib SM, Nesi G, Comperat E, Sibony M, Berney DM, Martinek P, Bulimbasic S. Eosinophilic, Solid, and Cystic Renal Cell Carcinoma. *Am J Surg Pathol* 2016;40(1):60-71.