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Illinois Registry of Anatomic Pathology

Case Histories and Diagnoses
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Case 1: Phosphaturic Mesenchymal Tumor

Presenter: Nathan Aardsma DO; Attending: Andre Balla MD PhD

Clinical History: The patient is a 48-year-old Hispanic female with a previous medical history of a high grade sarcoma of the left thigh who presented with a new mass in the previous tumor bed. She was treated with resection and chemotherapy 2 years ago. She has a complicated medical history with a 10 year history of severe osteomalacia, muscle weakness, and pain in the setting of recent hypophosphatemia, normocalcemia and elevated FGF-23 levels, consistent with oncogenic osteomalacia.

Diagnosis: Malignant Phosphaturic Mesenchymal Tumor

Differential Diagnosis:

- Spindle cell lipoma
- Spindle cell hemangioendothelioma
- Lipomatous hemangiopericytoma

Key Microscopic Features:

- Spindle cells with small normochromic nuclei with indistinct nucleoli. Usually low mitotic activity and low cellularity
- The matrix is described as myxoid or chondromyxoid with "grungy" calcifications and prominent vasculature
- Areas of infiltration into the adjacent soft tissue is common
- The heterogeneity of the tumor often leads to misdiagnosis

Immunohistochemical stains:

- Positive: Vimentin
- Negative: S100, Smooth muscle actin, CD99, and CD34

Ancillary Study:

- Elevated serum FGF-23

Discussion:

- Phosphaturic mesenchymal tumor is a rare entity that requires awareness for diagnosis
- Recognition of the entity in patients with oncogenic osteomalacia and secretion of FGF-23
- The importance of clear surgical margins to avoid recurrence
- Malignant behavior can be seen with minimal atypia

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Case 2: Primitive Neuroectodermal Tumor with EWSR/FLI1 translocation

Presenter: Nemencio R. Ronquillo Jr. MD; Attending: Andre Balla, MD PhD

Clinical History: The patient is a 37-year-old male with history of hypertension who presented to the emergency department complaining of a two-month history of dyschezia and the constant urge to defecate. An initial compute topography (CT) scan showed a heterogeneous pelvic mass measuring 10 cm in greatest dimension that replaced the prostate and displaced the rectum to the left. Additionally there were enlarged pelvic lymph nodes and pulmonary and liver nodules. The patient received chemotherapy and subsequently underwent total pelvic exenteration.

Diagnosis: Primitive Neuroectodermal Tumor of the Prostate with EWSR/FLI1 translocation

Differential Diagnosis:

- High grade prostatic adenocarcinoma
- Neuroblastoma
- Rhabdomyosarcoma
- Small cell carcinoma
- Desmoplastic small round cell tumor
- Monophasic synovial sarcoma
- Lymphoma
- Melanoma
- Primitive neuroectodermal tumor

Key Morphologic Features:

- Microscopic: At low power, typical tumor cells show sheet-like to vaguely lobular growth pattern. At higher power, the cells are uniform, small, round, ovoid, or plump spindle with a small amount of clear and PAS positive cytoplasm. Nuclei are round and regular with finely dispersed chromatin, and small nucleoli.

Immunohistochemistry:

- Positive: CD99 (diffuse and membranous)
- Negative: Desmin, vimentin, high and low-molecular weight cytokeratin, EMA, PIN4 cocktail (AMACR, p63, 34betaE12), PSA, PLAP, CD45, CD30, CD56, Bcl-2, NSE, chromogranin, synaptophysin, GFAP, calcitonin, S-100, HMB45, MelanA

Ancillary Study:

- RT-PCR or FISH: EWSR/FLI1 or t(11;22)(q24;q12)

Discussion:

- Ewing Sarcoma and Primitive Neuroectodermal Tumor comprise the same spectrum of neoplastic diseases now known as Ewing Sarcoma family of tumors (EFTs)
- Nonepithelial neoplasms of the prostate are rare and they only represent <1% of all prostatic tumors
    - 6 cases of primary PNET of the prostate have been reported previously
- CD99 is positive in 90-100% but also stains rhabdomyosarcoma, acute lymphoblastic lymphoma, synovial sarcoma, melanoma and neuroendocrine tumors

- FLI1 immunostain is positive in 71-100% but also stains lymphoblastic lymphoma and benign and malignant vascular tumors are also positive
- EWS and FLI1 fusion happens in 90-95% of cases followed by EWS-ERG in 5-10%, and rarely, EWS fusion with ETV1, E1AF, and FEV
- Neural differentiation and non-type 1 EWSR/FLI1 fusion are some of the poor prognostic factors

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Case 3: Primary Nonurachal Bladder Adenocarcinoma

Presenter: David Stephen DO; Attending: Elizabeth Wiley MD

Clinical History: The patient is a 61-year-old male with a history of hypertension, hyperlipidemia and stroke who presented with a complaint of gross hematuria. He had a smoking history of 1-2 pack/day for 40 years, although he stopped smoking 6 months prior to this visit and denied alcohol and drugs of abuse. He is retired, having worked 25 years as a day laborer.

Diagnosis: Primary nonurachal bladder adenocarcinoma, mixed type with enteric, mucinous and signet ring components in the setting of diffuse cystitis glandularis, intestinal metaplasia and a villous adenoma

Differential Diagnosis:

- Cystitis glandularis
- Local extension of prostatic adenocarcinoma
- Metastatic colon carcinoma/ local extension
- Urachal adenocarcinoma
- Primary adenocarcinoma of the bladder

Key Microscopic Features:

- Glandular component predominates, resembles colonic carcinoma
- Produces mucin, deeply invades muscularis propria
- High grade at diagnosis
- Intestinal metaplasia may be seen
- Bladder adenocarcinomas can show multiple growth patterns including: enteric, NOS, mucinous, signet ring and mixed

Immunohistochemical and special stains:

Positive: CK20, CDX-2, AMACR, Beta-catenin (membranous)
Negative: PSA, HMWK, CK5/6, Beta-catenin (nuclear)

Discussion:

- Primary adenocarcinoma of the bladder constitutes only 0.5-2% of all primary bladder malignancies
- Poor prognosis 5 year survival is 20-40%
- Bladder adenocarcinomas can show multiple growth patterns including: enteric, NOS, mucinous, signet ring and mixed.
- Pathogenesis is thought to occur via two main pathways
    - Develop from embryologic rests
    - In the setting of chronic irritation with subsequent metaplastic changes (cystitis glandularis, intestinal metaplasia and villous adenoma)
- Using the combination of CK7, CK20 and beta-catenin will discriminate between adenocarcinoma of bladder and colorectum
- Ultimate diagnosis rests on systemic exclusion of other adenocarcinomas

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Case 4: Mesonephric Adenocarcinoma of the Cervix

Presenter: Anthony Sisk DO; Attending: Michael Pins MD

Clinical History: The patient is a 46-year-old female (G4P0040) with a history of menorrhagia and uterine leiomyomata presented to her obstetrician-gynecologist complaining of heavy post-coital bleeding. A recent endometrial biopsy at an outside institution showed an atypical spindle cell proliferation suspicious for a low grade endometrial stromal sarcoma and the immunohistochemical profile favored an epithelioid trophoblastic tumor. On physical exam there was red polypoid soft tissue present at the cervical os. A cervical biopsy was diagnostic of endometrioid adenocarcinoma with sex-cord like formation. The patient subsequently underwent a radical total abdominal hysterectomy.

Diagnosis: Mesonephric Adenocarcinoma of the Cervix

Differential Diagnosis:
- Endometrioid Adenocarcinoma
- Clear Cell Carcinoma
- Serous Papillary Carcinoma
- Carcinosarcoma (MMMT)

Key Microscopic Features:
- Irregular tubular gland proliferation
- Inspissated intra-luminal eosinophilic material
- Variable coexisting morphologies including duct, tubule, sex-cord like and solid

Immunohistochemical and special stains:
- Positive: CD10 (apical), Calretinin (patchy)
- Negative: Estrogen Receptor, Progesterone Receptor, Androgen Receptor

Discussion:
- Rare cervical tumor thought to arise from mesonephric remnants
- Usually low grade at diagnosis and may have a better prognosis than other types of cervical adenocarcinomas of similar grade
- Usually associated with mesonephric hyperplasia
- Distinct immunoprofile distinguishes this tumor from other cervical based lesions

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Case 5: Retroperitoneal Bronchogenic Cyst

Presenter: Wei Song, MD PhD; Attending: Grace Guzman, MD

Clinical History: The patient is a 41-year-old Caucasian male with acute right-sided neck pain which radiated to the chest. His past medical history was unremarkable. A computed tomography (CT) scan revealed a 6.4 x 4.8 cm retroperitoneal mass in the right upper quadrant of his abdomen along his diaphragm. The patient subsequently underwent laparoscopic enucleation of the mass.

Diagnosis: Retroperitoneal Bronchogenic Cyst

Differential Diagnosis:

- Cystic teratoma
- Bronchogenic cyst
- Cystic lymphangioma
- Mucinous cystadenoma
- Retroperitoneal enteric duplication cyst
- Pseudomyxoma retroperitonei
- Cystic mesothelioma
- Pseudomyxoma retroperitonei
- Tailgut cyst
- Mullerian cyst

Key Morphologic Features:

- Gross: Cut surface exhibits heterogenous, multi-loculated, cystic soft tissue that is brown and filled with mucinous areas
- Microscopic: Multiple cysts with different diameters; cysts predominantly lined by ciliated pseudostratified columnar cells; submucosal cartilage and seromucous glands present; no other types of epithelial cells identified; no neuronal cells or structures identified

Immunohistochemical stains:

Positive: CK7, TTF-1
Negative: CK20, CDX2

Discussion:

- Retroperitoneal bronchogenic cysts are relatively rare (77 cases reported) foregut-derived developmental anomalies
- They most commonly are encountered in the mediastinum and are rarely present in the cervical, cutaneous, diaphragmatic, gastric, abdominal, and retroperitoneal regions
- They are lined by ciliated columnar epithelium with submucosal cartilage and bronchial glands present
- The most important differential diagnosis is primary or metastatic teratoma; the whole specimen needs through search for other types of tissue than bronco-tracheal origin; CK20 and CDX2 negativity argues against a diagnosis of a teratoma and is supportive of a diagnosis of bronchogenic cyst

References:

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Case 6: Nuclear Protein in Testis (NUT) Midline Carcinoma

Presenter: Rachel A. Mariani MD; Attending: Michael Pins MD

Clinical History: The patient is a 30-year-old male with no significant past medical history, who presented to an outside hospital with left mandibular swelling thought to be a dental abscess. The lesion persisted and a biopsy showed a poorly differentiated malignancy. An extensive immunopanel was negative except for PLAP and a diagnosis of germ cell tumor was rendered. Staging showed evidence of visceral and bone metastases. The oral lesion progressed to a disfiguring, fungating mass in a matter of months despite chemotherapy. The patient presented to our institution where one of the bone lesions was biopsied and additional studies were performed; however, the patient progressed rapidly and died approximately 5 months after his initial presentation. Autopsy revealed multiple additional sites of involvement including posterior mediastinum, liver, and retroperitoneum.

Diagnosis: Nuclear protein in Testis (NUT) Midline Carcinoma

Differential Diagnosis:

- Metastatic Seminoma
- Dedifferentiated Salivary Gland Carcinoma
- Ewing Family Tumors/PNET
- Melanoma
- Follicular Dendritic Sarcoma/Hematologic Malignancy
- Poorly-Differentiated Squamous Cell Carcinoma
- Nuclear protein in testis (NUT) midline carcinoma

Key Microscopic Features:

- Sheets of infiltrative cells without any obvious differentiation or other architectural pattern with extensive necrosis
- Cells appear undifferentiated with scant amphophilic cytoplasm, nuclei with irregular contours, vesicular chromatin and small prominent nucleoli

Immunohistochemical and special stains:

Positive: p63 (strong, diffuse)**,** CK7 (focal)**,** CAM5.2 (focal)
Negative: PLAP, AFP, βhCG, Myogenin, Synaptophysin, Desmin, CD45, MAK-6

Ancillary Study:

Karyotype: 49,XY,add(1)(q42),der(2)t(2;3)(q33;p21),t(3;6)(p21;p23),+6,+8,der(8)t(3;8)(p21;p23),+12, del(12)(p11.2),**t(15;19)(q14;p13.3)[**11]/49, idem,der(7)t(4;7)(q31.1;q32)[2]/46,XY[7]

Discussion:

- NUT midline carcinoma is an underdiagnosed malignancy presenting mostly in the head, neck, and mediastinum with no age or sex predilection
- It is an undifferentiated tumor with no specific IHC profile currently thought to be a distinctive genetic variant of squamous cell carcinoma or an undifferentiated tumor arising from a common squamous precursor
- Defined by rearrangement of *NUT* gene, most commonly t(15;19)

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