

IRAP

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EVANSTON HOSPITAL
NORTHSHORE UNIVERSITY
HEALTHSYSTEM

Case #1 (Esther Bit-Ivan, D.O.)

CASE HISTORY: 79-year-old female presents to the emergency department after experiencing dizziness and a subsequent fall at home. Work up reveals a heterogeneous 1.9 x 1.4 x 1.3 cm intracranial/intranasal mass.

DIAGNOSIS: **Grade III Olfactory Neuroblastoma with ganglion cell differentiation**

DIFFERENTIAL DIAGNOSES: Sinonasal undifferentiated carcinoma, Small cell undifferentiated neuroendocrine carcinoma, Ewing's sarcoma/PNET, Mucosal malignant melanoma

KEY DIAGNOSTIC FEATURES:

- The tumor is composed of circumscribed nests of uniform round cells sometimes surrounded by sustentacular cells.
- Pleomorphism is absent to mild in low grade tumors but marked in high grade tumors.
- Cells have a high N/C ratio.
- Nuclei have dispersed coarse to fine nuclear chromatin.
- The stroma is hyalinized or fibrillary and vascular.
- Homer Wright and/or Flexner-Wintersteiner rosettes may be present.
- Necrosis is present in high grade tumors.

UNCOMMON FEATURES:

- Ganglion cells
- Stromal calcifications
- Clear cell change
- Divergent differentiation
 - Melanocytic, neural, myogenic or epithelial

SPECIAL STUDIES:

- Neuron specific enolase positive
- Variable staining with chromogranin, synaptophysin, neurofilament protein
- CD 56 and CD 57 are often positive.
- If sustentacular cells are present, they are S100+.
- 1/3 of cases have stain for cytokeratin either within the tumor nests or in areas of divergent differentiation.
- Negative stains include EMA, CD99, desmin, melanoma markers, hematoxyphoid marker.

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Case #2 (Rick Bains, D.O.)

CASE HISTORY: A 55-year-old Caucasian female with a history of breast cancer status post bilateral mastectomy with complaints of indigestion and weight loss is found to have a 1.9 cm submucosal mass in the antrum of the stomach. The mass is removed by laparoscopic partial gastrectomy and submitted to pathology for examination.

DIAGNOSIS: **Plexiform Fibromyxoma/Plexiform Angiomyxoid Myofibroblastic Tumor**

DIFFERENTIAL DIAGNOSES: Other soft tissue tumors which can occur in the stomach including myxoid GIST, Leiomyomas, Schwannomas and Neurofibromas and Desmoid Fibromatosis. Some of these lesions can have a myxoid appearance or a plexiform pattern of growth.

KEY DIAGNOSTIC FEATURES:

- Plexiform fibromyxoma is a rare and recently described soft tissue tumor.
- To this point it has only been identified in the antrum region of the stomach.
- It has a wide age range, and patients can be asymptomatic to having GI bleeding and perforation.
- The plexiform nature of the lesion may be appreciated grossly with the tumor infiltrating the muscularis propria in what has been described as a “bag of worms”.
- Microscopically the tumor will be composed of large and small plexiform nodules with bland ovoid cells with scant cytoplasm in a myoid, fibromyxoid to fibrous stroma with and prominent vascular network.
- Mitotic rates are very low, from 0-4/50 hpf.
- Although only recently classified as a distinct entity, data suggest that these are a benign lesion that requires complete excision, even in cases with extragastric extension or lymphovascular invasion.
- Initially described by Takahashi *et al* in 2007 who suggested the name Plexiform Angiomyxoid Myofibroblastic Tumor based on the vascular myxoid stroma and myofibroblastic characteristics of the lesional cells.
- A case series by Miettinen in 2009 describes more heterogeneity of the stroma and posit the term Plexiform Fibromyxoma.

SPECIAL STUDIES:

- Plexiform Fibromyxoma will stain positive for vimentin, smooth muscle actin and focal positivity for CD10, caldesmon, calponin and desmin.
- Plexiform Fibromyxoma will be negative for CD34, CD177 and DOG1, which will help to distinguish it from GIST.
- It is also negative for S100 unlike Peripheral Nerve Sheath Tumors and negative for beta-catenin as opposed to Desmoid Fibromatosis.
- Mutational analysis for CKIT and PDGFRA are negative in Plexiform Fibromyxoma.

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Case #3 (Beenu Thakral, M.D.)

CASE HISTORY: A 45-year-old woman presented in April 2009 with a two month history of painful mass in the right anterior thigh. MRI of the thigh demonstrated a 17.3 x 4.0 x 2.5 cm mass between rectus femoris and vastus lateralis muscle with no evidence of muscle or bone invasion. The patient underwent right thigh mass resection.

DIAGNOSIS: **Soft tissue myoepithelioma**

DIFFERENTIAL DIAGNOSES: Mixed tumors, myoepithelial carcinoma, extraskeletal myxoid chondrosarcoma (EMC), ossifying fibromyxoid tumor (OFMT), and parachordoma.

KEY DIAGNOSTIC FEATURES:

- Most tumors arise in limbs and limb girdles, peak in 3rd-5th decade.
- Heterogeneous tumors containing mixture of epitheloid, spindle cells, clear cells or plasmacytoid in the background of myxoid to hyalinized stroma.
- Cytological atypia (nuclear pleomorphism, coarse or vesicular nuclear chromatin, prominent nucleoli), and not tumor infiltrative growth pattern, differentiate myoepithelial carcinoma from myoepithelioma of the soft tissue.
- 18% of myoepithelioma recurs locally but none metastasize. No association is found between rate of recurrence and margin status, nature of border of tumor (circumscribed vs. infiltrative) or tumor size.

SPECIAL STUDIES:

- Immunoreactivity for at least one epithelial marker (keratin or EMA) with S-100 positivity or myogenic marker positivity (calponin or SMA).

IHC	Myoepithelioma	EMC	Parachordoma	OFMT
S-100	+ (90%)	± (20%)	+	+ (70%)
CK/EMA	+ (75%)	Neg	+	Neg
GFAP	+ (50%)	Neg	Neg	±
SMA	+ (40%)	Neg	Neg	+
Desmin	± (14%)	Neg	Neg	+ (50%)

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Case #4 (Melanie Fox, D.O.)

CASE HISTORY: The patient is a 70-year-old female who was found to have an abdominal/pelvic mass upon physical examination. She had an elevated CA-125 of 59.8 and a CT scan that revealed a 15.7 x 14.5 x 10.3 cm septated, complex, predominantly cystic pelvic mass containing both fat and calcifications. She underwent an exploratory laparotomy with a total abdominal hysterectomy, bilateral salpingo-oophorectomy, infracolic omentectomy, and peritoneal biopsies.

DIAGNOSIS: **Poorly differentiated adenocarcinoma, mucinous and signet ring type, arising in association with a mature teratoma**

KEY DIAGNOSTIC FEATURES:

- Grossly, the tumor was a multi-nodular cystic mass with solid components. The gross measurements were 21.0 x 18.0 x 1.5 cm. The cut surfaces were variegated, demonstrating a viscous mucoid material and cystic degeneration. Both fat necrosis and calcifications were identified.
- Microscopically, the majority of the mass was composed of copious amounts of extracellular mucin with associated malignant glands and signet ring cells. Additionally, a very small portion of the tumor contained foci of fat, cartilage, keratinizing squamous epithelium, and ciliated respiratory epithelium.
- Immunohistochemical profile of the malignant cells was CK7+, CK20+, CDX2+, Chromogranin patchy/focal +, TTF-, and Synaptophysin-.

DISCUSSION:

- Following the criteria as set forth by Lee and Young (5), one can generally distinguish between a primary and a metastatic mucinous ovarian carcinoma based solely on gross and histopathologic findings.
- Investigation for an occult lower GI primary tumor should be undertaken.
- Immunohistochemistry is typically of little value in these cases due to shared expression profiles.
- When a mucinous ovarian carcinoma arises in association with a teratoma, the possibility of a germ cell origin must be given consideration.
- Signet ring cells are reported to rarely occur in primary ovarian mucinous tumors and when they do they must be distinguished from a Krukenberg tumor. The neoplasm should be classified based on the histologic features of the associated primary ovarian tumor (non-signet ring areas). A comment addressing the signet ring cell component should be included in the diagnostic report.

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Case #5 (Nirali M Patel M.D.)

CASE HISTORY: An 82-year-old male was found to have an incidental 1.7 cm lung nodule. A wedge resection was performed, and the diagnosis of poorly differentiated non-small cell carcinoma was made on frozen section of the nodule.

DIAGNOSIS: Metastatic melanoma, primary unknown, with areas of lepidic growth

DISCUSSION: The presence of a lepidic pattern of growth in association with a poorly differentiated tumor is usually suggestive of adenocarcinoma, most often of pulmonary origin. In this patient with no history of melanoma or adenocarcinoma, the lepidic component revealed on permanent sections led to staining for AE1/AE3 and TTF-1. When these stains were negative, the presence of pigment in the main tumor nodule led to staining with melanoma markers, which demonstrated positive staining in both the main nodule and the adjacent areas of lepidic growth.

DIFFERENTIAL DIAGNOSES: Primary pulmonary adenocarcinoma, Metastatic adenocarcinoma

SUGGESTIVE DIAGNOSTIC FEATURES:

Primary

- Solitary nodule
 - Spiculated edges
- Fibroinflammatory cuff
- Entrapment of normal pulmonary structures
- Mixed patterns
 - Solid
 - Acinar
 - Bronchioloalveolar
- Adjacent atypical adenomatous hyperplasia

Metastatic

- Multiple peripheral nodules
 - Rounded “cannonballs”
- Well demarcated margin
- Complex or cribriform architecture
- Cytologically bland or uniform cells (breast)
- Dirty necrosis (colon)

Adenocarcinoma Staining Patterns

	CK7	CK20	Specific Markers
Lung	+	-	TTF-1
Endometrial	+	-	ER, PR
Pancreatic	+	+	CA19-9
Cholangiocarcinoma	+	+	Monoclonal CEA
Colon	-	+	CDX-2
Renal	-	-	RCC-Ma, CD 10
Prostate	-	-	PSA
Mesothelioma	+	-	WT-1, calretinin

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Case #6 (Tiffany Thurow, D.O.)

CASE HISTORY: 82-year-old female presented to her primary care physician with post-menopausal vaginal bleeding. Endometrial curettings showed well differentiated adenocarcinoma of the uterus, grade 1, with villoglandular features. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed. Upon examination of the uterus, an incidental 0.8 cm nodule in the myometrium was identified.

DIAGNOSIS: **Perivascular epithelioid cell tumor (PEComa)**

DIFFERENTIAL DIAGNOSES: Leiomyoma, leiomyosarcoma, endometrial stromal nodule, endometrial stromal sarcoma

KEY DIAGNOSTIC FEATURES:

- Clear to eosinophilic cytoplasm
- Perivascular arrangement
- Immunopositivity with melanocytic markers, particularly HMB-45, and with CD1a

SPECIAL STAINS:

- HMB-45
- CD1a
- Desmin
- Smooth Muscle Actin
- CD10

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