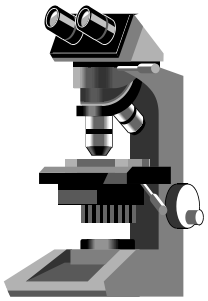
CALIFORNIA
TUMOR TISSUE REGISTRY

HEAD AND NECK PATHOLOGY

Minutes – Subscription A

March 2016



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FILE DIAGNOSES

CTTR Subscription A March 2016

Case 1: **CYSTIC SQUAMOUS CARCINOMA,** Neck

Case 2: **PLEOMORPHIC ADENOMA,** Benign Submandibular Gland

Case 3: **WARTHIN TUMOR,** Parotid Gland

Case 4: **ACINIC CELL CARCINOMA,** Parotid Gland

Case 5: **PIGMENTED NEUROFIBROMA,** Scalp

Case 6: **HIGH GRADE NEUROENDOCRINE CARCINOMA,** Maxillary Sinus

Case 7: **HEMANGIOPERICYTOMA,** Neck

Case 8: **EMBRYONAL RHABDOMYOSARCOMA**, Face and Right Parotid Region

Case 9: **PARAGANGLIOMA,** Thyroid Gland

Case 10: **HODGKIN LYMPHOMA,** Left Neck and Supraclavicular Area

CASE #1: **Accession No. 15359**

DIAGNOSIS: CYSTIC SQUAMOUS CARCINOMA, Neck

Diagnoses submitted in decreasing order of frequency:

Squamous cell carcinoma arising in branchial cleft cyst
Branchial cleft cyst, branchial cleft cyst with dysplasia
Cystic squamous cell carcinoma (metastatic)
Squamous cell carcinoma
Lymphoepithelioma
Lymphoepithelial cyst

Discussion

This archival case of a multilocular cystic squamous cell carcinoma case was donated to the CTTR as a possible primary squamous cell carcinoma arising in a branchial cleft cyst.

The differential diagnosis of a cystic squamous cell mass in the upper neck of an adult over the age of 40 years is a branchial cleft cyst, cystic metastatic squamous cell carcinoma or a branchial cleft cyst carcinoma (BCCC). Investigation must include diagnostic imaging, biopsy or excision biopsy of likely primary sites, such as oropharyngeal sub-sites including bilateral tonsillectomies, and testing for HPV, Epstein-Barr virus immunological status.

Primary carcinoma arising in a pre-existing branchial cleft cyst-is an extremely controversial clinicopathologic entity, with less than 40 cases considered proven. Consensus agreement has been proposed on making such a diagnosis. The diagnosis of a BCCC should be one of exclusion after all other possible diagnoses have been considered and excluded.

Branchial cleft cysts arise from the incomplete obliteration of any branchial tract, which results in a sinus or cyst. As the cyst is usually lined with stratified squamous epithelium, there is a possibility for the development of carcinomatous transformation in the cyst lining. However, there has never been unanimity about the existence of true branchiogenic carcinoma. Many authors argue that this malignancy is more conceptual than a true clinicopathologic entity. This argument is based on the recognition that a variety of head and neck sites - including in particular the tonsil - have a propensity to give rise to cervical metastases while the primary tumors themselves remain undetected. The majority of branchiogenic carcinomas are in fact cystic metastases from oropharyngeal carcinoma, most commonly originating in the tonsils, and not true carcinomas arising in a branchial cleft cyst.

However, Martin and Khafif have proposed a set of conditions which need to be satisfied for a diagnosis of branchiogenic carcinoma. The most important criteria emphasized are demonstration of a normal lining epithelium, zone of transition, and frank malignancy in the cystic squamous lining. Exhaustive search for a local primary and five years or greater follow-up with no other squamous head and neck tumor that may have been the primary site of origin are required, however as most patients are treated with radiation therapy the likelihood of finding the possible primary are extremely low.

Current consensus is that almost all presumed BCCC are actually a metastatic primary from Waldeyer’s ring.

CASE #2: **Accession No. 15384**

DIAGNOSIS: PLEOMORPHIC ADENOMA, Benign Submandibular Gland

Diagnoses submitted in decreasing order of frequency:

Pleomorphic adenoma / benign mixed tumor

Discussion

Pleomorphic adenoma (PA) is a benign salivary gland tumor that exhibits wide morphologic and architectural diversity with an admixture of epithelial, myoepithelial and chondromyxoid stromal/mesenchymal components. The solid areas appear to "melt" into the adjacent chondroid areas of the tumor. The epithelial components show trabecular, tubular, solid, cystic, and papillary patterns. The stromal component may appear mucoid, myxoid, hyaline, chondroid, or myxochondroid.

PA is the most common salivary gland tumor in both children and adults and is twice as common in females. It is most common in the third to sixth decades; the average age at presentation is between 43 and 46 years. Etiology is unknown; however there is an increased incidence 15-20 years after exposure to radiation, the simian virus (SV40) may also play a causative role.

PA presents as a slow-growing, painless mass, which may be present for many years. Rapid enlargement of a tumor nodule should raise concern of malignant change. Malignant change occurs in 2-7% of cases and shows some association with multiple recurrences, deep lobe tumors, male gender, and older age. Microscopic satellite tumor nodules and capsular penetration may be seen beyond the capsule. This may be the cause of recurrence of PA after surgery with inadequate margins.

Epithelial and myoepithelial markers are positive (CK, CAM 5.2, EMA, P63, Calponin, maspin, S-100, MSA, HHF-35, GFAP). *PLAG1*and *HMGA2* gene translocations have been identified as tumor-specific in PA. *MUC1* has been found to be related to the recurrence of PA and to be associated with malignant transformation.

CASE #3: **Accession No. 14936**

DIAGNOSIS: WARTHIN TUMOR, Parotid Gland

Diagnoses submitted in decreasing order of frequency:

Warthin Tumor

Discussion

Warthin tumor (WT) is the second most common benign salivary gland tumor, and occurs most commonly in the parotid gland. WT may be multifocal and bilateral, and consists of a double layer of epithelial cells with subjacent dense lymphoid stroma. Primary tumors may also arise in the oral cavity and larynx. There is a strong association with smoking; hence the male predominance. There is cystic and oncocytic change caused by the inflammatory infiltrate. Tumors are not clonal. Rare cases may give rise to lymphoma.

CASE #4: **Accession No. 14902**

DIAGNOSIS: ACINIC CELL CARCINOMA, Parotid Gland

Diagnoses submitted in decreasing order of frequency:

Acinic cell carcinoma (microcystic variant)
Mammary analogue secretory carcinoma
Adenoid cystic carcinoma
Mucoepidermoid carcinoma, low grade
Sebaceous adenoma
Low grade cribriform cystadenocarcinoma
Polymorphous low grade adenocarcinoma

Discussion

Acinic cell carcinoma (ACC) is a low-grade malignant salivary neoplasm that constitutes ~ 17% of primary salivary gland malignancies. In the head and neck region, the parotid gland is the predominant site of origin and women are usually more frequently diagnosed than men. Previous radiation exposure and familial predisposition are risk factors for ACC. The most frequent presentation is of a slowly enlarging mass in the tail of the parotid gland.

ACC cells are round or polygonal with lightly basophilic fine to coarsely granular cytoplasm, eccentrically placed nuclei and inconspicuous nucleoli. Some tumors may show numerous intercellular microcysts and cysts as in this case. There is a prominent lymphoid infiltrate. Aggressive tumors are often associated with frequent mitoses, focal necrosis, neural invasion, pleomorphism, infiltration, and stromal hyalinization.

Tumor cells are positive for CK, A1 antitrypsin, amylase, and PAS-D.

Differential diagnosis:
MASC (mammary analogue secretory carcinoma, S100+, GCDFP +, ETV6-X fusion)
Adenocarcinoma NOS
Low grade cystadenocarcinoma

CASE NO #5: **Accession No. 14891**

DIAGNOSIS: PIGMENTED NEUROFIBROMA, Scalp

Diagnoses submitted in decreasing order of frequency:

Pigmented neurofibroma, diffuse
Neurofibroma, diffuse cutaneous

Discussion

Neurofibromas with melanin-laden pigmented cells are rare, accounting for 1-5 % of all neurofibromas. Head and neck and lower extremities are the most common sites. There may be an association with

neurofibromatosis. Recurrences may occur, as in our case. There are no documented cases of malignant transformation.
There is a loose spindle cell proliferation of tumor cells with scant cytoplasm and scattered melanin pigment. MelanA, S100 and MITF, Masson Fontana stain +. CD 117-. A pigmented neurofibroma can be confused with a pigmented dermatofibrosarcoma protuberans (Bednár tumor); however the latter exhibits a classic extensive storiform growth pattern, greater immunoreactivity for CD34, and lacks a diffuse proliferation of S-100+ Schwann cells. Other differentials include: cellular blue nevus, melanotic schwannoma, congenital neuronevus.

CASE #6: **Accession No. 32043**

DIAGNOSIS: HIGH GRADE UNDIFFERENTIATED NEUROENDOCRINE CARCINOMA, Maxillary Sinus

Diagnoses submitted in decreasing order of frequency:

Olfactory neuroblastoma
Olfactory neuroblastoma, high grade
Basal cell adenoma
Small round blue cell malignancy
Sinonasal undifferentiated carcinoma
Esthesioneuroblastoma
PNET vs embryonal rhabdomyosarcoma
Merkel cell carcinoma
Alveolar rhabdomyosarcoma
High grade neuroendocrine carcinoma
High grade basaloid tumour (differentials:olfactory neuroblastoma, neuroendocrine carcinoma, high grade adenoid cystis carcinoma
Low-grade polymorphous adenocarcinoma
Diffuse large B cell lymphoma
Small cell undifferentiated neuroendocrine carcinoma vs SNVC

Discussion

This is a poorly differentiated tumor with round cell infiltrates forming nests and lobules. Nuclei are vesicular to hyperchromatic, with focal molding, numerous mitoses, and indistinct nuceoli.

There was dot-like (perinuclear) synaptophysin reactivity, CD 99+ and very high Ki-67 indices, with apoptotic bodies, and rare CK cocktail +. Mesodermal and lymphoid markers were negative. These findings, given the location and involvement of sino-nasal area are consistent with a small cell undifferentiated neuro-endocrine carcinoma (SCUNC).

EWSR1 rearrangement was negative for Ewing sarcoma/PNET. No abrupt squamous differentiation was present making a NUT midline carcinoma (NMC) unlikely. Immunostains for TTF-1, CDX2, and Merkel Cell CA polyoma virus were negative, ruling out a metastasis from a distant primary.

Primary sinonasal neuroendocrine carcinomas are rare and represent a histological spectrum. Poorly differentiated sinonasal neuroendocrine carcinoma is an extremely rare and aggressive neoplasm with a high

recurrence rate and a tendency to metastasize to other sites. No specific etiologic factor has been identified. They are thought to arise from a multi-potential stem cell. However, there is recent molecular evidence that small cell elements may arise as a late-stage phenomenon in the genetic progression of more organ-typical carcinomas.

Sinonasal neuroendocrine carcinoma has to be differentiated from other neoplasms involving nasal cavity and paranasal sinuses such as squamous cell carcinoma, lymphoma, melanoma, olfactory neuroblastoma (Keratin-, EMA-, sustentacular cell S100+, calretinin+), and sinonasal undifferentiated carcinoma (NE markers-).

CASE #7: **Accession No. 14887**

DIAGNOSIS: HEMANGIOPERICYTOMA, Neck

Diagnoses submitted in decreasing order of frequency:

Solitary fibrous tumor, Hemangiopericytoma
Monophasic synovial sarcoma
Malignant schwannoma
Fibrosarcoma
Extra-abdominal desmoid tumor
Spindle cell sarcoma, NOS

Discussion

The tumor shows diffuse growth pattern of solid or focally whorled spindle or round/oval tumor cells with admixed prominent, small, thin-walled gaping blood vessels with a staghorn appearance. No necrosis, marked atypia or no/rare mitotic activity is identified.

Hemangiopericytoma of soft tissue is a rare controversial entity; most cases are solitary fibrous tumor, monophasic synovial sarcoma or myofibromatosis. In the head and neck region WHO designates this tumor as a glomangiopericytoma (myopericytoma). Tumors are positive for vimentin, smooth muscle actin, muscle specific actin, factor XIIIa, laminin, D2-40; and stain negative for CD31, CD34 (usually), factor VIII, and keratin. Differential diagnosis includes: solitary fibrous tumor (more prominent collagen D2-20-, CD 34+), synovial sarcoma: t(X;18)(p11.2; q11)

CASE #8: **Accession No. 14882**

DIAGNOSIS: EMBRYONAL RHABDOMYOSARCOMA, Face and Right Parotid Region

Diagnoses submitted in decreasing order of frequency:

Rhabdomyosarcoma (embryonal, pleomorphic)
Post treatment round cell sarcoma
Rhabdoid tumor
PNET / Ewing's sarcoma
Malignant neoplasm, sebaceous carcinoma

Discussion

Tumor is composed of primitive cells with variably prominent nucleoli, minimal cytoplasm as well as cells with rims of eosinophilic cytoplasm. Tumor necrosis is present.

Embryonal rhabdomyosarcoma (RMS) is a rare malignant tumor arising from cells of skeletal muscle lineage. Subtypes of RMS: alveolar, anaplastic, embryonal, botryoid, pleomorphic, and sclerosing. Embryonal RMS is the most common sarcoma of the head and neck region in pediatric patients 2 -6 years, with a slight male predominance. This subtype has an intermediate prognosis (botryoid and spindle cell types have the best prognosis). There is poor survival if anaplasia is present, as in this case. Tumors are usually large at time of diagnosis. Strap or tadpole cells and more eosinophic plump tumor cells may be present.

Tumor cells are positive for myogenin, desmin, myoD1, negative for FLI-1.

Differential diagnosis: PNET/EWS , rhabdoid tumor (keratin+, EMA+, INI1 -) S

CASE #9: Accession No. 14469

DIAGNOSIS: **PARAGANGLIOMA,** Thyroid Gland

Diagnoses submitted in decreasing order of frequency:

Paraganglioma, Glomus tumor
Medullary carcinoma, Paraganglioma-like medullary thyroid carcinoma
Hemangiopericytoma
Adenoid cystic carcinoma- solid pattern
Papillary Thyroid Carcinoma, Solid Variant

Discussion

Round and oval tumor cells are present in nesting (zellballen) and trabecular patterns, with a prominent vascular network.

Paragangliomas may occur in various body sites, those arising in the adrenal medulla are designated as pheochromocytomas. They may be multiple and associated with Carney and MEN 2a and 2b syndromes, neurofibromatosis type 1, and von Hippel-Lindau disease or single sporadic tumors. Tumor cells are positive for neuroendocrine markers, also S100+ in surrounding sustentacular cells. Malignant paragangliomas are uncommon, and present at sites where no normal paraganglionic tissue exists, and also show high mitotic activity, necrosis.

Differential diagnosis: alveolar RMS, low grade neuroendocrine tumor, medullary thyroid carcinoma, hyalinizing trabecular tumor.

CASE #10: **Accession No. 15280**

DIAGNOSIS: HODGKIN LYMPHOMA, Left Neck and Supraclavicular Area

Diagnoses submitted in decreasing order of frequency:

Hodgkin lymphoma, mixed cellularity type, nodular sclerosing variant
Thymoma
Malignant lymphoma, atypical lymphoid process
Toxoplasmosis
Infectious mononucleosis
Rosai-Dorfman disease
Langerhans cell histiocytosis

Discussion

The lymph node sections show partial involvement by Hodgkin lymphoma, with Hodgkin cells, classic Reed-Sternberg cells and a background of scattered eosinophils, lymphocytes and a few plasma cells. No special stains are available.

Classic Hodgkin lymphoma (HL) is a monoclonal lymphoid neoplasm (usually of B cell origin) composed of mononuclear Hodgkin and multinucleated Hodgkin Reed-Sternberg cells in an infiltrate containing a mixture of non-neoplastic small lymphocytes, eosinophils, neutrophils, histiocytes, plasma cells, fibroblasts and collagen fibers. There are four histological subtypes: lymphocyte-rich, nodular sclerosis, mixed cellularity and lymphocyte-depleted (latter two are more commonly associated with EBV).

In developed countries HL shows a bimodal age distribution with peaks in adolescents and young individuals, and a second peak in late life. Developing countries show early childhood tumors that are EBV related. There is a higher incidence in patients with HIV and with history of infectious mononucleosis. Familial and geographical clustering has been reported.

Cervical lymph nodes are the commonest sites for HL. Abdominal involvement is most common in mixed cellularity type. CD 30+, CD 15+.

Differential diagnosis: infectious mononucleosis (children, young adults), anaplastic large cell lymphoma.

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