AMR Seminar #51 – Short Summary of Cases

Case 1: F.42 with cystic skin lesion in medial calf.

Case 2: F.65 with 9 cm. posterior mediastinal mass.

Case 3: M.79 with gastric mass.

Case 4: F.59 with large pelvic mass.

Case 5: M.62 with large bladder mass eroding into the pubic ramus.

Case 6: F.22 with C-section at 28 weeks gestation for placental insufficiency.

Case 7: F.35 with a 2cm. retroareolar nodule in the nipple.

Case 8: M.27, HIV+, with 15 cm. pelvic soft tissue mass.

Case 9: F.80 with slow-growing tumor in the parotid.

Case 10: F.63 with seizures and diffuse lesions in white matter.

Case 11: F.74 with pathologic fracture of the left femora neck.

Case 12: F.66 with 3.5 cm. tumor in the root of the tongue.

Case 13: F.66 with 4 cm subcutaneous mass in her left leg.

Case 14: F.40 with polypoid mass in the vaginal wall.

Case 15: F.43 with 10cm. tumor in the ovary.

Case 16: F.73 with a right breast mass.

Case 17: M.68 with a large polypoid esophageal mass.

Case 18: M.48 with history of amputation of lower extremity for osteosarcoma now presents with a large mass in the mid-body of the stomach.

AMR SEMINAR #51
CASE 1

Contributed by: P W Allen. Case referred by Dr Lesley Joblin, Southern Communities Hospital, Hawkes Bay, Hastings, New Zealand.

History: Female aged 42 in 2006. Cystic mass in the skin and subcutis of the right medial calf. It was an incidental finding at the time of varicose vein surgery.

Diagnosis: Apocrine gland cyst with haemosiderotic dermatofibroma-like stroma, skin and subcutis, right medial calf.

Comment: I had never previously seen one of these and was not even aware of the existence of the apparent entity until I saw this case. To the best of my knowledge, there are only two previously reported cases, both in Am J Dermatopathol 2005; 27: 36-38.   The author, Dr Gonzales, who works in the Department of Pathology, Catholic University of Chile School of Medicine, Santiago, Chile, called the condition "apocrine gland cyst with hemosiderotic dermatofibroma-like stroma."   I originally thought that the cysts resembled steatocystoma simplex but they could well be apocrine, as Dr Gonzales suggests.

What do club members think of this as an entity?

My current list of the variants of cutaneous histiocytoma is: cellular with or without necrosis;[5] aneurysmal (angiomatoid);[4,18] hemangiopericytoma-like;[29] hemosiderotic (elusive);[27] lipidised (xanthomatous or cholesterol rich);[10] epithelioid;[7,8,20,24] myofibroblastic;[3,28] monstrocellular (atypical);[11,15,22] keloidal (sclerotic or hyalinised);[13] palisaded;[19] clear cell;[16,23] granular cell;[21,26] myxoid;[25] histiocytoma with diffuse eosinophilic infiltrate;[1] lichinoid, erosive and ulcerated;[17] ossified;[12] apocrine gland cyst with hemosiderotic dermatofibroma-like stroma;[9] multinodular of Franquemont and Cooper;[6] proliferative;[14] and metastasizing.[2]

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AMR SEMINAR #51
CASE 2

Contributed by: Carlos E. Bacchi, MD (CB 3278/06)

History: The patient was a 65-year-old woman without any significant past medical history who presented with a posterior mediastinal tumor detected by image studies. I am sorry but I don't have details about the gross findings of this tumor but it measured 9 x 5 cm.

Histopathologic findings: Histological examination showed a neoplasm composed of a striking trabecular network of cavernous-type of vessels some of which are surrounded by collection of bland, epithelioid small to medium-size tumor cells with sharply outlined round-to-oval nuclei with vesicular chromatin and eosinophilic or clear cytoplasm. The vessels have lumens of different diameter caliber filled with red cells. There are also foci of hemossiderin deposition.

Immunohistochemical findings: Immunohistochemical studies showed focal positivity staining for smooth muscle actin and for type IV collagen, this one showing a strong intercellular staining pattern. Chromogranin A, CD34, S-100 protein, CD31 and desmin were all negative in those cells.

Diagnosis: Glomangioma (glomus tumor) of posterior mediastinum.

Discussion: Glomus tumors are relatively uncommon lesions of presumed glomus cell origin with ultrastructural and immunohistochemical features of smooth muscle. They occur as solitary or multicentric lesions, predominantly in the dermis or subcutis, with characteristic subungual location. Infrequently they involve unusual sites, including the mediastinum and respiratory tract. Mediastinal tumors are even more unusual, with only few cases reported. Gaertner et al (including Tom Colby) reported the clinical pathological features of four cases of pulmonary glomus tumors and one mediastinal glomus tumor. In their case, the tumor was located in the left aortic arch and it surrounded and partially invaded the aortic wall. Histologically, glomus tumors are subdivided into three general categories based on the prominence of glomocytes, vessels, and smooth muscle: the common glomus tumor type ("glomus tumor proper"), a glomangioma type, and a glomangiomyoma type. The distribution of these subtypes varies somewhat anatomically, but this histologic distinction is not thought to correlate with clinical differences. I believe that this cases fits well for the glomangioma "variant". I shared this case with Saul who agreed with this diagnosis. In fact, the histology of this tumor is quite characteristic. It is the anatomic location and the clinical presentation that are unusual. In four cases reported in the literature of mediastinal glomus tumor, 2 occurred in the posterior and two in the superior mediastinum. Three of the four cases were reported as infiltrative, atypical and malignant. Our case showed no atypia but the surgeon informed that the tumor infiltrated the pulmonary parenchyma and this was the reason the inferior lobe of the right lung was also surgically removed. Spindle cell morphology, which is described in glomangiosarcoma, was not identified in the current case. Differential diagnoses in this particular case include cavernous hemangioma and paraganglioma. The presence, in this case, of monomorphic epithelioid cells with central, round nuclei and clear cytoplasmic change, along the wall of some vessels, and the immunophenotype (expression of muscle actin and type IV) are findings that ruled out the aforementioned neoplasms. It is important to mention that glomus tumor, including those with clinical or histological features of malignancy, are generally indolent tumors.

References: Gaertner, E. M., D. M. Steinberg, et al. (2000). "Pulmonary and mediastinal glomus tumors: report of five cases including a pulmonary glomangiosarcoma: a clinicopathologic study with literature review." Am J Surg Pathol **24**(8): 1105-14.

AMR SEMINAR #51
CASE 3

Contributed by: Ira Bleiweiss

History: A 79 year old man presented with a gastric mass. A partial gastrectomy was performed.

Diagnosis: Glomus tumor of stomach.

Comment: The older members of the AMR (by membership period, not chronologic age) may remember an identical case which I submitted in Seminar 9- a LONG time ago. When I saw this case, I immediately recognized it for what it was because of that other case, which, in fact, was also originally misdiagnosed as carcinoid (both on frozen and permanent sections at an outside institution). There are fewer than 100 cases of gastric glomus tumor in the literature, and, as I wrote back then, both glomus and carcinoid of the stomach are benign, but given a choice, I'd rather have the glomus. Lightning DOES strike twice, despite what they say.

AMR SEMINAR #51
CASE 4

Contributed by: Kum Cooper

History: This is a 59-year old woman who presented with a pelvic mass.

Macroscopic Findings: The hysterectomy specimen demonstrated a massive uterine tumor (15 x 10 x 1.5cm) in the posterior wall of the uterus that filled the endometrial cavity. The cut surface appeared tan with focal areas of hemorrhage and necrosis. The ovaries, fallopian tubes and cervix were unremarkable.

Microscopic Examination: The tumor section is from the posterior wall of the uterus and is dominated by a malignant small round blue cell differentiating neuroblastomatous component (Synaptophysin/chromogranin positive) with distinct foci of neuropil (S-100 positive) and ganglionic differentiation. Other focal areas of Schwannian stroma were also evident (not present in submitted sections). The small blue cells merge with larger cells (vesicular chromatin with nucleoli and more amphophilic cytoplasm) amongst which are discernible distinct rounded rhabdomyoblasts (desmin, MSA, and myogenin positive). Both these components dominate the microscopy to support a diagnosis of malignant ectomesenchymoma (ME). However, after examination of several blocks, isolated foci of adenocarcinoma were evident, suggesting that the ME arose in a background of MMMT.

Diagnosis: Malignant ectomesenchymoma arising in a uterine MMMT.

Comment: Ectomesenchyme refers to neural crest tissue that shows mesenchymal differentiation during embryogenesis. Hence the neural crest tumor (neuroblastoma or ganglioneuroblastoma) with rhabdomyoblastic differentiation is referred to as ectomesenchymoma. These are exceptionally rare tumors (under 25 reported in the literature) occurring predominantly in infants (retroperitoneum, pelvis, paratesticular are rarely soft tissue) and only rarely in adults. This case is therefore, highly unusual in that this ME is located in the uterus of an adult and probably arose from an MMMT which has largely been obliterated or overridden. I share this case with members to enjoy this rare tumor with highly unusual features.

AMR SEMINAR #51
CASE 5

Contributed by: Ivan Damjanov, MD

History: A 62 year-old man had a radical cystectomy for urinary bladder sarcoma that was diagnosed 3 months before final surgery. During surgery the ramus of the pubic bone was also removed because the tumor infiltrated and eroded the bone. Some 20 years ago he had urinary bladder surgery, during which a "leiomyoma" was removed.

Pathologic findings: The urinary bladder was distorted with several discrete or confluent nodules measuring from 0.5 to 8 cm in diameter . These nodules were either fibrotic and firm or soft and gelatinous. Three large nodules protruded into the lumen of the urinary bladder severely reducing the lumen to a volume of less than 100 ml.
Microscopically, all tumors were composed of spindle shaped fibroblastic cells arranged into bundles and sheets. Parts of the tumor were myxoid and the cells in these areas were separated one from another by mucoid extracellular matrix that stained with Alcian blue, pH 2.5. The mitotic count was low in the range of 1-2 mitoses per 50 HPF.MIB-1 staining was in the range of 4%.

The tumor invaded and partially destroyed the pubic bone and was obviously malignant. The intraluminal parts of the tumor were necrotic, but in other parts there was very little necrosis.

Immunohistochemistry gave the following results: Positive for vimentin and CD 10.Negative for cytokeratins, smooth muscle cell actin, desmin. CD34, CD117, EMA, S100.

Diagnosis: Low grade sarcoma of the bladder, multinodular.

Comment: We felt comfortable with our diagnosis of low grade sarcoma, but also wanted to use the qualifier "fibromyxoid" , to account for the changes that we saw histologically. We sent the blocks to Dr L.Guillou of Lausanne, Switzerland who performed genetic studies for FUS-CREB3L2 and FUS-CREB3L1 genes. These genes are found, namely, in 90% of fibromyxoid sarcomas. The genetic studies gave negative results. Dr. J-M Coindre, Bordeaux saw the tumor as well and agreed with Dr Guillou's diagnosis of "low grade sarcoma, that cannot be further classified".

Sarcomas of the urinary bladder account for less than 2% of all malignant tumors of the urinary bladder. Most sarcomas are histologically high grade and the low grade tumors are obviously quite rare. We were thus quite eager to classify this tumor as precisely as possible, but unfortunately we ran out of ideas on how to do it. Any suggestions on how to classify this tumor would be welcome.

AMR SEMINAR #51
CASE 6

Contributed by: Otto Dietze

Case A

History: Caesarian section was performed at the 28th week of gestation due to fetal growth restriction and placental insufficieny. The mother, a 22-year-old primipara, had no previous diseases or infectious episodes. Shortly after delivery the child died of respiratory insufficiency.

Pathological findings:
The body weight was 381g and the external measurements corresponded to the 20th – 24th week of gestation. The weight of the heart (7g) was consistent with the 28th week, the weight of the lungs (8g) distinctly below the mean age-matched normal organ weight (normal 12,6g).
The placenta (170g) had an increased consistency, but no focal changes.

Histological investigation of the placenta showed massive fibrin deposition and a dense histiocytic infiltrate in the intervillous space, intermixed some T-lymphocytes.

Diagnosis: Chronic histiocytic intervillositis.

Comment: Chronic (massive) intervillositis was first described in 1987 by Labarrere and Mullen. To date there are several reports with spontaneous abortion, poor pregnancy outcome, intrauterine fetal growth restriction and intrauterine fetal death in the 2nd and 3rd trimester. The disease was observed to recur in consecutive pregnancies and lead to the hypothesis of an immunological background. The differential diagnosis includes placental malaria, unusual infections, intervillositis of unknown cause but with a polymorphic inflammatory infiltrate and maternal floor infarction. If the diagnosis of histiocytic intervillositis is established, immunomodulatory therapy (steroids) might be of interest in recurrent cases.

References / Literature:
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Chronic histiocytic Intervillositis: A placental lesion associated with recurrent reproductive loss. Boyd TK and Redline RW Hum Pathol 2000: 31, 1389-1396

Case B

History: A 26-year-old male patient from Albania was investigated for suspected lymphoma. He presented with B-symptoms and splenomegaly but without lymphadenopathy. Bone marrow biopsy was negative. To rule out splenic lymphoma, splenectomy was performed. Postoperatively the patient had a infectious complication at the site of surgery but recovered well within the short time of follow up (8 weeks).

Pathological findings : enlarged spleen, 20 x 14 x 8 cm, 1100g, homogenous red-brown cut surface. Histology reveals an enlarged red pulp with fibrotic changes along the arteries with deposition of hemosiderin pigment and partially calcified material.

Comment: We think the lesions are most consistent with Gandy-Gamna bodies. We were unable to detect any causative underlying disease (e.g. sickle cell anaemia).
We could not reach a definitive diagnosis. The consistently elevated LFT and LDH levels in absence of haematological abnormalities are in our opinion suggestive of an underlying liver disease.

AMR SEMINAR #51
CASE 7

Contributed by: Vincenzo Eusebi

History: A 35 yr-old woman (lady) from Istanbul presented with a retroareolar lump, of 20 mm in greatest axis, which had been present for some time. It was diagnosed as in situ duct carcinoma and simple mastectomy was performed together with axillary sentinel node excision, which proved negative. Patient is alive and well 15 months later.

Histology: Numerous lobes were filled by a solid proliferation of atypical cells with large and irregular nuclei. Their cytoplasm was eosinophilic to clear and no luminal differentiation was evident. Necrosis was present and also occasional squamous pearls.

The neoplastic cells were positive for P63, Keratin 14 and EGFR .
The case was interpreted as DCIS (positive staining for basal lamina, collagen IV) showing squamous cell differentiation.

To the best of our knowledge no similar case has been reported, previously, especially in view of the fact that usually only "ordinary" DCIS accompany the rare invasive pure squamous cell carcinomas.
This case also showed several neoplastic cells positive for smooth muscle actin and calponin, indicating myoepithelial cell differentiation. This phenomenon did not surprise us very much since myoepithelial and squamous cell differentiation, together, is also observed in metaplastic spindle cell carcinoma or in invasive myopithelioma(2; 3). In addition, carcinomas showing both squamous and myoepithelial cell differentiation have already been reported in other tissues, (a part from breast), such as oesophagus(3), lung(4), cervix(1), larynx and in some skin basal cell carcinomas(5).

Diagnosis: I would like to propose the diagnosis of In situ Squamous cell carcinoma of the breast with myoepithelial cell differentiation.

We have collected two additional similar cases and the small series has been recently accepted for publication (Am J Surg Pathol 2007).

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AMR SEMINAR #51
CASE 8

Contributed by: Cyril Fisher, Royal Marsden Hospital, London, UK.

History: An HIV-positive male aged 27 presented with a large pelvic tumor. After needle core biopsy diagnosis, this was excised as a 15 cm diameter firm mass with solid cut surface.

Pathology: The tumor is composed of fascicles of spindle cells with mild pleomorphism, low mitotic index and an inflammatory infiltrate. There is focal necrosis and scattered calcifications are seen.   Immunohistochemistry shows diffuse positivity for desmin (illustration provided, Fig 1), very focal staining for SMA, and none for h-caldesmon, myogenin, MyoD1, S100pr, CK, EMA, CD34, EBVLMP or EBER.   Electron microscopy (illustration provided, Fig 2) shows peripheral myofilaments adjacent to plentiful rough endoplasmic reticulum.

Diagnosis: Inflammatory leiomyosarcoma in HIV-positive male.

Comment: Inflammatory leiomyosarcoma is an incompletely defined entity that is not conclusively of smooth muscle lineage. Chris's original report[1] described the morphologic resemblances to regular leiomyosarcoma, and emphasized a xanthomatous component. The immunophenotype, notwithstanding the diffuse desmin positivity, is inconclusive for this (absence of h-caldesmon, relative paucity of SMA) and ultrastructural features of smooth or skeletal muscle differentiation are not usually seen.[2]   A near-haploid karyotype has been demonstrated.[2]   In this case, the EM suggests myofibroblastic differentiation. The calcifications seen here are unusual although psammoma bodies were seen in 25% of cases in the original series.

Concerning the clinical setting, smooth muscle tumors in patients who are immunocompromised have been described for some years, and are usually EBV-associated. Dr Sharon Weiss and colleagues recently published a large series of cases following renal transplantation, AIDS, or steroid therapy.[3]   I showed Sharon this case and she agreed the diagnosis of inflammatory leiomyosarcoma but also found EBV to be negative and thought it differed from her published cases.

It is difficult to predict behavior. Inflammatory leiomyosarcoma has been considered to be a low-grade sarcoma but one of the original series and two of three recent cases metastasized to lung.[2]   The case submitted here is very recent, but the unusual features and presence of necrosis warrant caution about the outcome.

References:

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3.   Deyrup AT, Lee VK, Hill CE et al. Epstein-Barr virus-associated smooth muscle tumors are distinctive mesenchymal tumors reflecting multiple infection events: a clinicopathologic and molecular analysis of 29 tumors from 19 patients. Am J Surg Pathol 2006;30:75-82.

AMR SEMINAR #51
CASE 9

Contributed by: Christopher D. M. Fletcher MD FRCPath

History: An 80 year old female had a slowly growing tumour in the parotid gland for some years, measuring approximately 4 cm. Following an FNA diagnosis of "possible fibrohistiocytic lesion" (at an outside institution), the lesion was excised.

Diagnosis: Reactive fibrovascular proliferation, possibly engrafted on a vascular malformation.

Comment: This case, which came to me in consultation, caused me considerable difficulties and I would much appreciate the thoughts of those with more experience in dealing with unusual salivary gland or head and neck lesions. Initially, given the presence of some erythroid extramedullary haematopoesis, and the presence of atypical stromal cells (possibly representing dysplastic megakaryocytes), I had wondered about an extramedullary haematopoetic pseudotumour – however, the somewhat atypical stromal cells are negative for CD61 and VWF. In the end, after considerable angst, I decided that this lesion was most likely reactive in nature, rather than a true neoplasm and, given the very prominent thick-walled blood vessels (with degenerative changes), I wondered if there had been a
long-standing vascular malformation at this site. I note, however, that these vessels are variably prominent in the multiple sections now prepared. In truth, I remain quite uncertain as to the best diagnosis for this lesion and I will welcome the thoughts of this august group recognising, nevertheless, that there may result in a variety of rendered diagnoses!

AMR SEMINAR #51
CASE 10

Contributed by: Jeronimo Forteza Vila

History: The patient is a 63-year-old woman with previous diagnosis of uveitis and thyroid hyperplasia. Now, the patient courses with seizure.
Image studies show diffuse lesions at the white matter, with focal infiltration of the cortex with features of demyelinization. Clinical diagnosis are Vasculitis, Lymphoma or Gliomatosis Cerebri. A frontal biopsy was performed.

Microscopic findings: Histologically cellular proliferation was identified with two different cells populations, one showing features of astrocytes and the other one, with oligondendrocytes aspect. Nuclei shows different shape and size, and few binucleational forms are identified, there is no vascular proliferation nor mitotic figures. Inmunohystochemistry showed PGFA positivity in astrocytes-like cells and not in oligodendroglial cells. Proliferation index was low (5-7%) (MIB-1/k 67). Histopathological findings are consistent with a Low Grade Glyoma with high infiltrative capacity.

Diagnosis: Gliomatosis Cerebri

Comment: Gliomatosis cerebri was originally coined by Nevin in 1938 to describe diffuse infiltration by glial cells of extreme areas of the brain without formation of an obvious tumours mass.
WHO defines this entity as diffuse glial tumour infiltrating the brain extensively, involving more than two lobes, frequently bilaterally and often extending to infratentorial structures and not to the spinal cord.
It used to cause corticospinal tract deficits (58%), but it will also present dementia (44%), headache (39%), seizures (38%), cranial nerve signs (37%), etc.
Molecular studies have showed p53 and PTEN mutations and a EGFR amplification. Similar findings are described in diffuse Astrocytoma.

References:
Chamberlain, MC. Glomatosis cerebri: Better definition, better treatment. Neurology 2004; 63:204-205.

Herrlinger U, Felsberg J, Küker W, et al. Gliomatosis cerebri: molecular pathology and clinical course. Ann Neurol 2002;52: 390-399.

AMR SEMINAR #51
CASE 11

Contributed by: Janez Lamovec, M.D. (kindly contributed by Dr. Janez Jančar, Institute of Oncology)

History: A 74- year-old female patient was admitted to the hospital because of spontaneous fracture of the left femoral neck. A resection of epiphysis and of the femoral neck was performed.
Five years previously, she had had a hysterectomy with adnexectomy performed in another institution because of leiomyosarcoma of uterine body. A year later, she presented with a recurrent tumor in the pelvic cavity that was operated upon and a wide resection of the tumor with partial resection of vagina, urinary bladder and rectosygmoid colon was carried out. Histologically, both uterine and pelvic tumor were identical; they were high grade leiomyosarcomas.

Pathological findings: Grossly, bone lesion appeared yellow-pinkish and soft .
Histologically, this malignant tumor is composed of nests of predominantly clear cells with marked nuclear pleomorphism and not so numerous mitoses. Nests of tumor cells are surrounded by thin-walled capillaries. Focally, there were necrotic areas found. Immunohistochemically, the tumor cells were positive for MSA, SMA, desmin and also for Melan –A and HMB-45. S-100 protein in cytokeratins were negative.
Tumor was morphologically and immunohistochemically different from uterine leiomyosarcoma and its recurrence in the pelvic cavity. The latter two tumors were positive for SMA. desmin and calponin and totally negative for Melan-A and HMB-45.

Follow up: At the last follow up, 3 months following bone surgery, CT showed multiple metastases to lungs, liver and axial skeleton. Kidneys appeared normal The patient is receiving symptomatic treatment and is alive with disease.

Diagnosis: PEComa, malignant, probably metastatic (of unknown primary site)

Comment: There are several unknowns in this case : 1. Could this tumor be something else and not what we think it is? 2. Is there any relation between uterine leiomyosarcoma (different morphologically or on immuno) and the bone tumor? Uterine tumor and its recurrence were extensively sampled and no foci alike to PEComa were found. 3. Is it possible that the bone tumor would be a primary (bone PEComa)? 4. The nature of present metastases to skeleton liver and lungs are not known since they were not biopsied (?metastases of leiomyosarcoma or PEComa)
I am looking forward to your opinions and comments.
The case was seen by Chris who concurred with our diagnoses and commented that he had seen occasional cases of primary bone PEComa.

AMR SEMINAR #51
CASE 12

Contributed by: Michal Michal, Czech Republic

History: A 66-year old woman presented with a tumor of the root of the tongue 3,5 cm in greatest diameter. At the time the patient had a left lateral neck lymphadenopathy. The tumor and enlarged lateral neck lymph node was surgically excised and the patient was irradiated. Two years after the surgical excision the patient is well, free of recurrences and metastases. Grossly the tumor of the tongue was unencapsulated, white in color, hard in consistency and devoid of hemorrhage or necrosis.

Pathological findings: The tumor grew under the uninvolved superficial epithelium and infiltrated the surrounding skeletal muscle of the tongue. The tumor was divided by fibrous septa into lobules, and major parts were composed of areas with solid and microcystic growth patterns. Morphologically the tubules of the tumor were composed of one cell type. The lumina of the tubules were focally filled with mucin, which stained strongly with Alcian Blue at pH 2.5, but poorly with HE, PAS and mucicarmine. Cytologically, the tumor was composed of one cell type; characteristically, the nuclei, which often overlapped one another, were single, pale and vesicular with a "ground glass" quality. There were one to three nucleoli of varying conspicuousness in the nuclei of the cells. The overall morphology of the neoplasm, particularly with its pale, overlapping nuclei was remarkably similar to solid and follicular variants of the papillary carcinoma of the thyroid. The metastasis in the neck lymph nodes had identical appearance to the primary tumor.
Immunohistochemically, the tumor reacted strongly with antibodies to cytokeratins AE1-AE3 and CAM 5.2 and S-100 protein. The tumor was negative with both monoclonal DAK-Tg6 and polyclonal antibodies to thyroglobulin. Actin antibodies reacted with only minor areas. Ultrastructurally, each cell had an irregularly clefted nucleus with a nucleolus. The cytoplasm was poor in organelles, which included a few mitochondria, lysosomes and Golgi apparatus. The cells were attached to each other by well formed desmosomes. The secretory spaces were composed of well formed microvilli on the apical borders of the cells. An unusual feature was that many of the secretory cells displaying the apical microvilli also contained groups of microfilaments in the cytoplasm. These cells thus had features of hybrid myoepithelial-secretory cells. Many cells were found to contain numerous bundles of cytoplasmic tonofilaments.

Diagnosis: Cribriform adenocarcinoma of the tongue (CAT).

Comment: I believe that CAT represents a distinct entity, different from PLGA and other tumors of the minor salivary glands due to its characteristic histopathological appearance, specific location in the tongue and biological behavior. We have recently published a series of these tumors and we chose the name of CAT, because greatest parts of the tumors had solid or cribriform appearance at light microscopical level (1). In the last WHO classification (page 224) (2) CAT is included as a possible variety of PLGA, with which I do not agree. CAT appears to be morphologically so distinctive from adenocarcinomas previously diagnosed as PLGA that the microscopic appearance alone enables the right diagnosis to be made even without knowledge of its location. CAT is an infiltrative tumor largely consisting of areas with solid and microcystic growth patterns, composed of cells with pale, vesicular "ground glass" nuclei, which often overlap one another. These nuclear morphological characteristics thus closely resemble solid and follicular variants of papillary carcinoma of the thyroid. We were unable to find any other example of CAT at any site other site than the tongue among the 5000 cases of salivary gland tumors in our registry. We therefore concluded that CAT occurs mostly in the tongue, and perhaps exclusively so (1).

The most distinguishing clinical feature of CAT is its behavior; all eight tumors in our series and all potential candidates in the literature had unilateral or bilateral neck lymph node metastases, but none of these patients died of disease (1). This suggests that CAT is a tumor with early lymphotropic metastases into the regional lymph nodes, but in spite of this it has an excellent prognosis, either due to inherent slow biological growth or the result of sensitivity to radiotherapy. Since of our original publication (1), we found a couple of cases of CAT, which at the time of the diagnosis, were avoided of the lymph node metastasis. In spite of theta most of the CAT are at the time of the diagnosis already metastatic to LNs. The clinical behavior and many morphological features of CAT are strikingly similar to the usual type of papillary carcinoma of the thyroid, which also often displays early metastatic spread to the cervical lymph nodes, but yet has an excellent prognosis.

The literature records several possible examples of CAT published as PLGA or under other names. Perez-Ordonez et al (3) described 17 PLGAs among which were two examples of "PLGA" of the tongue. In this series there was a much higher metastatic rate than is usual for PLGA, as 5 of the 17 cases had secondaries in the neck lymph nodes. Two of these five had a papillary appearance, and figures 4a and 4b of this paper show a tumor with an appearance very similar to that of our cases of CAT (3). It is reasonable to speculate that the tumor pictured in these two figures is likely to be a CAT. Another possible candidate was reported by Colmenero et al (4). In a series of 14 PLGAs, one tumor arose at the base of the tongue and metastasized to the neck lymph nodes. Their figure 2 (and possibly also figure 3) shows a tumor very similar to CAT. Interestingly, Figure 55 of the previous edition of the World Health Organization (WHO) classification of salivary gland neoplasms (5) illustrates under the heading of PLGA, a tumor quite similar to ours, and perhaps another example of CAT. Two other possible candidates for CAT were published under different names, and both carcinomas metastasized to the cervical lymph nodes. Yajima et al reported a tumor of the tongue in a 59-year old man which was called "tubular adenocarcinoma" (6), and Crocker et al described a 5 year old boy with an adenocarcinoma, which they called "papillary adenocarcinoma of minor salivary gland" (7). Even allowing for the difficulties of proper assessment of figures in reprints, there are many similarities to the microscopic appearance of CAT. In the differential diagnosis of CAT, it is most difficult to distinguish it from solid and follicular variants of the papillary carcinoma of the thyroid, either metastatic or as a primary from the lingual thyroid. Most importantly, CAT is always thyroglobulin negative, but there are a few morphological clues visible on HE; the deeply eosinophilic colloid seen in most cases of the follicular variant of papillary thyroid carcinoma is lacking in CAT. Furthermore, unlike in the thyroid neoplasm, there is immunohistochemical and ultrastructural evidence of myoepithelial differentiation in CAT. Many of the features of CAT are also seen in PLGA, for example solid and cribriform tumor islands, papillary structures and even vacuolated nuclei. What distinguishes them is the much wider range of architectural patterns seen in PLGA, as well as the characteristic extensive nuclear ground glass change of CAT. CAT can be easily differentiated from adenoid cystic carcinoma of the tongue by the nuclear morphology of dark hyperchromatic angulated nuclei which are often closely packed. CAT also lacks the characteristic collagen depositions of adenoid cystic carcinoma. Mitotic figures are more frequent in the latter. It is difficult to explain why CAT appears to be restricted to the tongue. I am aware of only one other tumor entity, ectomesenchymal chondromyxoid tumor of the anterior tongue, which is similarly limited to this site (8), but it seems totally unrelated to CAT, both in appearance and location. Ectomesenchymal chondromyxoid tumor arose exclusively on the anterior parts of the tongue, while most cases of CAT were described as involving the root of the tongue.

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AMR SEMINAR #51
CASE 13

Contributed by: Markku Miettinen

History: A 66 y old woman had a hard subcutaneous mass of 4 x 2 x 2 cm in the left leg.She had been healthy otherwise.

Diagnosis: Amyloid tumor of soft tissue with metaplastic bone. Amyloid tumors of soft tissue are quite rare. We have approximately 30 cases in the Soft Tissue files of AFIP. These lesions often contain a clonal plasma cell component, and therefore represents forms of plasmacytomas or lymphoplasmacytoid lymphomas, often with quite indolent behavior. Also characteristic is a histiocytic giant cell component surrounding some of the amyloid deposits.

This tumor showed abundant kongo-positivity with green birefringence in the acellular material but it was negative for amyloid precursor (BAPP). There was only scant lymphoplasmacytic component. Small clusters of CD20-positive B-cells were present, and the scant plasmacytoid component showed roughly equal numbers of kappa and lambda-positive plasma cells. Therefore, we could not establish the diagnosis of lymphoma in this case. Nevertheless, clinical follow-up (and possible work-up) is warranted in terms of lymphoma. Also, evaluation of amyloid A might be useful; of some reason, it was not done in this case. However, there was no evidence for systemic amyloidosis in this case.

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AMR SEMINAR #51
CASE 14

Contributed by: Giuseppe Pelosi, MD, Division of Pathology and Laboratory Medicine, European Institute of Oncology and University of Milan School of Medicine, Milan, Italy

Abstract: Reported is a hitherto unrecognized occurrence of synovial sarcoma developing as a polypid lesion of the vaginal wall in a middle-aged patient. The tumor presented with morphological features of poorly differentiated synovial sarcoma with necrosis and high mitotic count. The finding of FISH-detected 18q11.2 translocation, the ultrastructural study revealing focal epithelial differentiation of tumor cells, and RT-PCR assay documenting a SYT-SSX1 fusion gene product allowed the diagnosis of synovial sarcoma to be confirmed. The pathologist should be aware of poorly differentiated synovial sarcoma arising in the vagina, distinguishing this tumor from other more common lesions developing at this anatomical site.

Patient's history (1st part): A 40-year-old Caucasian albino woman (gravida 0, para 0), previously in good health, began to suffer on July 2004 from abnormal bleeding during the period associated with important anemia. A gynecological visit revealed a necrotic, friable and blueish polypoid lesion grossly measuring about 40-50 mm of cranio-caudal axis spanning from the external urethral meatus to the middle part of the anterior wall of the vagina whose lumen was almost totally obliterated. Transvaginal ultrasonographic examination with color-doppler modality showed a 32x22 mm-large dishomogeneous tumor of the vaginal wall with several randomly dispersed and irregular blood vessels in the central part of tumor that presented with poorly defined but not infiltrating margins towards perineum or thight root soft tissues. A large tissue biopsy, performed elsewhere at the end of July 2004, was reported as a high-grade leiomyosarcoma with necrosis, hemorrhage and high mitotic count. Pretreatment work-up including computed tomography (CT) scan and chest-X ray examination was unremarkable for distant metastases. The patient was then admitted to our Institution at the end of the same month when the tumor had grown up to a 6-cm-large mass, and a formal histologic revison was immediately required.

Microscopic description (1st part): Histopathologic revision of the original sections performed at the Division of Pathology of the European Institute of Oncology revealed a high-grade sarcoma with abundant necrosis and numerous mitoses (more than 10/10 high power fields), composed of spindle to roundish tumor cells either haphazardly arranged or forming densely cellular short fascicles (Fig 1A).

Immunohistochemical results (1st part): Standard and previously refined immunohistochemical methods on unstained paraffin sections of this tissue biopsy revealed in either spindle or roundish tumor cells variable reactivity for vimentin, epithelial membrane antigen, CD99, low to high molecular weight cytokeratins (clones AE1-AE3 and 34βE12), cytokeratins 7 and 19, bcl-2 protein, and calretinin, but not for smooth or skeletal muscle (smooth muscle actin and myosin, desmin), melanocytic (HMB-45, PNL2), or neural (S-100 protein) markers, as well as for CD10, CD34, CD117, WT1, alpha-inhibin, and estrogen and progesterone receptors.

Fluorescence *in situ* hybridization study results: As there was a strong suspicion of synovial sarcoma according to morphologic and immunohistochemical data, a rearrangement of SYT gene (located in the breakpoint region of the chromosome 18q11.2) was detected by means of two-color fluorescence in situ hybridization (FISH) (LSI® SYT Dual Color, Break Apart Rearrangement Probe, PathVision, Vysis, Downers Grove, IL, USA) on paraffin sections, allowing a final diagnosis of synovial sarcoma. In particular, FISH analysis was carried out with the LSI® SYT Dual Color, Break Apart Rearrangement Probe (Vysis), which

documents t(18q11.2) but not the specific translocation partner. Tumor cells showed one orange (probe of 650kb extending distally from the SYT gene) and one green (probe of 1040 kb liying 3' or proximal to the SYT gene) signal, which were indicative of a rearrangement of one copy of the SYT gene region (Fig 2).

Patient's history (2nd part): Given tumor histology and tumor size spanning from the external urethral meatus to the middle part of the vagina anterior wall, the patient underwent neoadjuvant chemotherapy with three courses of epirubicin and ifosfamide to facilitate surgical removal and to reduce the risk of distant metastases. Total body CT-scan performed after chemotherapy completion did not document recognizable distant metastases, and gynecological examination carried out at the same time revealed a polypoid mass of the vaginal wall that almost completely occluded the vaginal lumen, even partially protruding outside the vaginal introitus and presenting with a large implant basis from the external urethra meatus to the middle part of the vagina anterior wall. As the patient refused an aggressive surgery, she underwent conservative removal consisting in a wide local resection of the anterior vaginal wall with preservation of the external urethral meatus.

Gross pathology: The surgical specimen obtained from re-excision showed a polypoid growth of the tumor with friable tissue, necrosis and hemorrhage that infiltrated the vaginal wall (Fig 3).

Microscopic description and immunohistochemical results (2nd part): Histopathologic examination of this surgical specimen showed a polypoid, high-grade spindle to roundish cell sarcoma that exhibited high mitotic count and the same morphologic and immunophenotypic features as seen in the previous biopsy (Fig 1 B).

Electron microscopy study: In order to have a more complete documentation on the case, an ultrastructural study using fresh tumor fragments from the re-excision of the tumor (fixed in glutaraldehyde/osmium tetroxide, and stained with uranyl acetate and lead citrate) was also performed. This study revealed fibroblast-like spindle cells with irregularly outlined nuclei, small nucleoli, and features of early epithelial differentiation in the form of intercellular cleft-like spaces and poorly developed junctional complexes (Fig 4).

Molecular study results: RT-PCR assay (carried out on snap-frozen tissue taken immediately after surgery) documented a SYT-SSX1 fusion gene product of 158 bp (Fig 5). Briefly, the junctional region of the SYT-SSX1 and SYT-SSX2 fusion gene transcripts was amplified using the SYT 1100 forward primer (5'-AGGATATAGACCAACACAGCC-3') in combination with the SSX1 or SSX2 reverse primer as previously described [1]. PCR assay conditions were 40 cycles at 94ºC for 30 sec, 58ºC for 30 sec and 72ºC for 30 sec. The positive PCR product was then sequenced with an automated sequencing system (3100 Genetic Analyser, Applied Biosystem, Foster City, CA) to confirm the type of fusion gene. As shown in Fig 5, RT-PCR assay documented SYT-SSX1 fusion transcript (B=blank [no template]; N=negative control [Ewing sarcoma]; P=positive control; SS[1] and SS[2]=synovial sarcoma case, 2 different reverse transcriptions; MK=1kb ladder) (A). The partial sequence of the fusion gene product was also obtained to demonstrate the SYT-SSX1 transcript breakpoint, with the fusion point being indicated by the arrow (B).

Patient's history (3rd part): Due to the extension of the tumor close (< 1 mm) to the surgical margins, the patient received adjuvant brachytherapy. Eleven months after completing chemotherapy and surgery, however, she experienced distant metastases in the peripheral parenchyma of the right lung with no signs of local recurrences. Therefore, the patient successfully underwent wedge resections of three pulmonary metastases at the beginning of January 2006, ranging from 0,6 to 0,9 cm in their greatest diameter. Currently, the patient is alive with no signs of further residual disease confirmed by positron emission tomography-scan analysis.

Final diagnosis: Poorly differentiated synovial sarcoma of the vagina

Discussion: In general, synovial sarcoma accounts for approximately 10% of all soft tissue sarcomas, and for the large majority they arise near the large joints of the extremities in adolescents and young adults [2,3]. These tumors usually appear as either biphasic tumors (with glandular or solid epithelial structures intermingled with a spindle cell component) or fibrous monophasic tumors composed exclusively by spindle cells. An uncommon poorly differentiated variant has also been described that may be histologically indistinguishable from other small, blue, round cell soft tissue tumors [4]. Although synovial sarcoma may arise at unexpected sites, including head and neck region, skin, heart, pleura, retroperitoneum, mesentery, lung and mediastinum, kidney, prostate, bone, central nervous system, esophagus, penis, and vulva [2,3,5,6,7], its occurrence in the vagina has not been previously recorded. Therefore, I hope the AMR members will

enjoy having an apparently unique example of synovial sarcoma developing as a polypid, poorly differentiated tumor of the vaginal wall. The differential diagnosis of synovial sarcoma in the vagina includes potentially several malignancies given its capability of presenting with different histologic features of either biphasic or monophasic tumor. In the event of vaginal tumor, the differential diagnosis includes spindle cell carcinoma and poorly differentiated adenocarcinoma, carcinosarcoma, malignant hemangiopericytoma, fibrosarcoma, myoepithelioma, malignant peripheral nerve sheath tumor, malignant mixed tumor, leiomyosarcoma, rhabdomyosarcoma, alveolar soft tissue sarcoma, angiosarcoma, malignant mixed mesonephric tumors, mullerian stromal sarcoma, Ewing's sarcoma-primitive neuroectodermal tumor, mullerian adenosarcoma, and even malignant lymphoma, granulocytic sarcoma, reticulum cell sarcoma, malignan melanoma, and aggressive angiomyxoma. In single tumor series, however, leiomyosarcoma accounts for the most common histology occurring in this anatomical location [8-10]. While all these entities can be reliably distinguished by means of an integrated use of morphology, immunohistochemistry and clinical evaluation, I cannot completely exclude that a few of the previously reported spindle cell sarcomas of the vagina (especially leiomyosarcomas) could actually correspond to synovial sarcoma, just as initially misdiagnosed in our case at another institution. Leiomyosarcoma, however, is said to be composed by tumor cells that are arranged in better-defined fasicles intersected at right angles to each other and supplied with sigar-shaped nuclei, more densely eosinophilic cytoplasm and paranuclear vacuoles [3]. Moreover, most leiomyosarcomas stain diffusely for smooth muscle actin, myosin and desmin and to some extent for cytokeratins and epithelial membrane antigen [11], but usually not for bcl-2 [12]. Many synovial sarcomas express cytokeratins 7 and/or 19, which is diagnostically helpful because either the malignant peripheral nerve sheath tumor [13] or the Ewing's sarcoma/pPNET family of tumors [14] are typically unreactive for them. The most important and difficult differential diagnosis, however, is with the spindle cell variant of squamous cell carcinoma and with the extremely rare mixed tumor of the vagina, either benign or malignant [15-19]. Although these entities may share some morphologic, immunohistochemical and ultrastructural traits with synovial sarcoma, our case lacks either the biphasic growth pattern with both epithelial and spindle tumor cells that is usually seen in mixed tumors of the vagina, or the continuity with the squamous epithelial coating of the vagina that is common in the spindle cell variant of squamous cell carcinoma. Moreover, the covering vaginal squamous epithelium did not show any dysplastic changes or *in situ* neoplasia, arguing against the hypothesis of squamous cell carcinoma.

It has been stated that molecular assays (FISH or to some extent RT-PCR) are particularly useful tools to establish the correct final diagnosis [20-22], especially in the event of poorly differentiated monophasic fibrous synovial sarcoma which may be particularly hard to distinguish from other spindle cell and round cell sarcomas [2,3]. Although a strong association of SYT-SSX1 fusion transcript has been reported in biphasic synovial sarcomas and of the SYT-SSX2 fusion transcript in monophasic tumors [23], a half of the latter variant may also involve the SYT-SSX1 [24] translocation as documented in our case.

The prognosis of synovial sarcoma is generally related to tumor size, margin status [25,26], extent of necrosis, vascular invasion and occurrence of poorly differentiated areas [27], whereas the clinical relevance of fusion gene typing in synovial sarcoma remains uncertain at the present time [20,28,29], even though SYT/SSX1 fusion transcript has been associated in some studies with a shorter disease-free survival [24], and SYT-SSX fusion type has even been indicated as the single most significant prognostic factor by multivariate analysis in patients with localized disease at diagnosis [30]. The occurrence of pulmonary metastases after eleven monthy from radical surgery indicates the inherent biological aggressiveness of this tumor arising in the vagina characterized by SYT/SSX1 fusion transcript, even though the power of correlation of a single case is always disputable.

A careful evaluation of hematoxylin&eosin-stained sections with special emphasis to lower grade areas more typical of monophasic synovial sarcoma, as well as the judicious use of an adequate immunohistochemical panel, however, remain important tools in the identification of this tumor (at least at the level of consistency) and in its differential diagnosis, remitting the final diagnosis of problematic cases to more expensive and cumbersome investigations such as electron microscopy, RT-PCR and especially FISH analysis. In particular, CD99, bcl-2 protein, cytokeratins and epithelial membrane antigen (all typically positive) on one hand, and CD34, desmin and smooth muscle actin (all typically negative) on the other hand, emerge as the most suitable immunohistochemical markers for the vaginal synovial sarcoma, in keeping with the classical immunophenotypic profile of this tumor [2,3].

Although such an occurrence could simply be considered a variation of anatomical type on the general theme of the ubiquity of synovial sarcoma, I feel it is worth remembering the possibility of poorly

differentiated synovial sarcoma arising in the vagina to avoid misinterpreting it as being related to other more common lesions developing at this anatomical site. To this respect, H&E-stained sections, immunohistochemistry and possibly additional studies (especially FISH analysis) should resolve most diagnostic dilemmas.

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AMR SEMINAR #51
CASE 15

Contributed by: Elvio G. Silva, M.D.

History: This is a 43-year-old female patient who was found to have a pelvic mass. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy. Multiple Biopsies were also obtained from the peritoneum. A 10x8x7cm tumor was found in the left ovary.

Pathology: During the operative procedure a frozen section was obtained and the diagnosis was: Adenocarcinoma, primary vs. metastatic. A careful search of the gastrointestinal tract, including the pancreas, failed to demonstrate another neoplasm, therefore multiple biopsies from the peritoneum were obtained. The right ovary was unremarkable. Our differential diagnosis was: endometrioid adenocarcinoma, metastatic adenocarcinoma and Sertoli-Leydig cell tumor. By immunohistochemistry the tumor cells were positive for inhibin and calretinin and negative for keratin 7 and EMA.

Diagnosis: Well differentiated Sertoli-Leydig cell tumor.

Comment: My approach to this type of tumor is the following: first I look for features typical of endometrioid carcinoma because this is the only one of the three possible diagnoses that can be made with certainty on H&E. I would make a diagnosis of endometrioid carcinoma when I see: squamous metaplasia, clear cells (subnuclear vacuols, foamy cytoplasm like in a previous AMR case, or focal clear cell Ca), adenofibroma, or associated endometriosis. If I do not see these features I look for two other histologic features diagnostic of Sertoli-Leydig: the presence of the frequently associated foci of granulosa cell tumor and the rare retiform pattern. If I were unable to find these diagnostic features on H&E I would request immuno: Keratin 7 and EMA for adenocarcinoma, Inhibin and calretinin for Sertoli-Leydig. If the Keratin 7 and EMA are positive the tumor is an adenocarcinoma and since the typical features for endometrioid carcinoma are not present I would say that I cannot distinguish endometrioid from metastatic adenocarcinoma. I would sign out the case as Sertoli-Leydig cell tumor if the Keratin 7 and EMA are negative and Inhibin and calretinin positive. If the tubules are well differentiated and there is no spindle cell component it would be a well differentiated Sertoli-Leydig, always benign. If the tubules are not well differentiated or there is a spindle cell component it would be a moderately differentiated Sertoli-Leydig cell tumor with a 10% possibility for recurrence. Other feature that would favor the diagnosis of Sertoli-Leydig is the almost absence of mitotic figures in the epithelial cells. Unfortunately I believe that neither Leydig cells nor a spindle cell component would be diagnostic of Sertoli-Leydig because it is impossible to differentiate Leydig cells from luteinized cells (except in the rare situation when crystals are seen), and a spindle cell component can be present in endometrioid tumors, as well as sex-cords. EM could separate these tumors because crystals can be found (Reinke in Leydig cells and Charcot-Bottcher in Sertoli cells).

Terminology can be questioned on a case like this one because depending on the presence or the number of Leydig cells the tumor could be designated as Sertoli-Leydig or pure Sertoli. I believe there are no specific guidelines to make this distinction.

After I finished the preparation of this case I found an article on this subject in the last issue of AJSP 31:592-7,2007.

AMR SEMINAR #51
CASE 16

Contributed by: James A. Strauchen, M.D.

History: A 73 year old woman presented with a right breast mass. Incisional biopsy was performed.

Diagnosis: Subcutaneous panniculitis-like T-cell lymphoma involving the breast.

Pathology: The specimen was received fixed. Sections show an atypical lymphoid infiltrate involving the subcutaneous tissue with sparing of the dermis. The infiltrate is composed of medium-sized atypical lymphocytes with infiltration between individual fat cells with "rimming" of the fat cells and characteristic "lace-like" pattern of infiltration. Focally, nuclear karyorrhexis and necrosis is present and admixed reactive histiocytes.

Immunohistochemistry: Immunohistochemical stains were positive for CD3, CD43, CD45; negative for CD20, CD79a, CD30, ALK-1. CD68 stained reactive histiocytes.

Comment: Subcutaneous panniculitis-like T-cell lymphoma is a characteristic form of peripheral T-cell lymphoma. Patients typically present with multiple subcutaneous nodules on the legs or trunk, mimicking a panniculitis. Patients are usually adults, but cases in childhood have been reported. A hemophagocytic syndrome may be present at presentation or develop in the course of the disease. The lymphoma cells are cytotoxic-suppressor T-cells, positive for CD3 and usually CD8, and express various cytotoxic molecules, including granzyme B, perforin, and TIA-1. Most cases are alpha-beta T-cell, however, cases of gamma-delta T-cell are reported, particularly in immunosuppressed patients. T-cell antigen receptor rearrangements are demonstrable in most cases. "Histiocytic cytophagic panniculitis" is likely a related entity. Cases of subcutaneous panniculitis-like T-cell lymphoma involving the breast are rare, but have been reported.

References: Sy ANL, Lam TPW, Khoo US. Subcutaneous panniculitis-like T-cell lymphoma appearing as a breast mass. A difficult and challenging case appearing at an unusual site. J Ultrasound Med 2005; 24:1453-1460.

AMR SEMINAR #51
CASE 17

Contributed by: Paul E. Wakely, Jr.

History: A 68-year old man presented with a 3-month history of progressive dysphagia. Barium swallow showed a massively dilated proximal esophagus and a possible cervical esophageal stricture. CT scan was interpreted as retained food particles versus a soft tissue mass. Repeat chest CT with contrast was interpreted as consistent with known achalasia. Esophagoscopy 3 weeks later showed a large area of extrinsic compression of the lumen of the distal third of the esophagus. A 3rd chest CT scan with contrast was interpreted as showing a large pedunculated heterogenous esophageal mass. Right thoracotomy and esophagotomy produced a smooth intraluminal pedunculated mass that was amputated flush with the esophageal wall.

Pathology: A firm, elongated club-shaped 15.0 x 7.5 x 4.5 cm mass with a 2.3 cm stalk was resected. The outer surface was smooth, finely granular and the distal end had a 2.6 cm ulcer. Cut sections showed a central core consisting of various-sized lobules of adipose tissue and fibrous tissue with focal areas of hemorrhage. The polyp is composed of lobules of mature adipose tissue separated by dense and loose connective tissue consisting of bland spindle cells. Within this fibrovascular tissue are areas of chronic inflammation with lymphoid follicle formation. Also scattered throughout the polyp are aggregates of large round and elongated cells with abundant eosinophilic cytoplasm typical of rhabdomyomatous differentiation. Many of these displayed long strap-like shapes with multiple nuclei arranged in tandem analogous to primitive myofibers. Immunohistology showed these cells to stain intensely with myoglobin, myogenin, HHF-35, and vimentin.

Diagnosis: Rhabdomyomatous Giant Fibrovascular Polyp of Esophagus.

Comment: Large pedunculated polyps (> 5 cm) of the upper esophagus are rare intraluminal tumors with at least 111 cases reported in the world's literature as of 2006. Over 90% are best classified as giant fibrovascular polyp (GFVP) as described by Stout et al. GFVP is typically seen in middle aged men, however, there is a broad age range (18 months to 88 years). Approximately 2/3rd of patients present with progressive dysphagia and weight loss. In about 25% a dramatic presentation involving regurgitation of the polyp into the oral cavity with respiratory compromise occurs. The most feared immediate complication is asphyxiation due to glottic obstruction. There seems to be agreement that these are likely derived from an outpouching of loose submucosal tissue into the lumen of the cervical esophagus in an area known as Laimer-Haeckmann or Laimer's triangle, where more than 80% of GFVP originate. Through normal peristaltic action of the esophagus, and eventual tractional forces produced by the polyp's own weight, the submucosal outpouching slowly grows to "giant" proportions (mean length, 13.3 cm; mean width, 3.8 cm) and assumes a club or sausage shape.
　　　　Since any one of these components may predominate a varied nomenclature has been applied to GFVP including lipoma, fibromyxoma, fibroma, hamartoma, fibrolipoma, and fibroepithelial polyp. The World Health Organization recommends the term *fibrovascular polyp* for any lesion with these previously described characteristics. To our knowledge, our case is unique in that rhabdomyomatous differentiation has not been described previously. We believe this rhabdomyomatous component arose from the muscularis propria of the upper esophagus which is normally and predominately skeletal, rather than smooth muscle.

Despite the reported benign nature of GFVP, several cases of malignant transformation were found by Caceres et al. These have been of two types, either squamous cell carcinoma or liposarcoma.

Despite its large size, initial imaging studies fail to demonstrate the presence of GFVP as an intraluminal mass 20-30% of the time. A number of reasons account for this difficulty. These include the fact that these polyps are covered by the same mucosa as the normal esophagus, and they can span almost the entire length of the esophagus. In addition, GFVP can position itself against the esophageal wall and the small stalk may be overlooked. Barium swallow may be interpreted as normal because the contrast is allowed to pass smoothly down the esophagus without getting around the polyp to demonstrate its intraluminal location. It may also show a pseudoachalasia narrowing of the distal esophagus caused by compression of the distal esophagus from the bulbous end of the polyp as in our case. Misinterpretation of the barium swallow along with other findings such as esophageal manometry showing a hypertensive lower esophageal sphincter can erroneously lead to the patient being misdiagnosed as having achalasia. Esophagoscopy may be misinterpreted as an intramural mass or extrinsic compression by a thoracic mass, or may even be reported as normal. Reports from 2 different patients showed a GFVP being missed repeatedly by numerous radiographic modalities over a period of years such that the patients were referred for psychiatric evaluation due their continued symptomatology.

I would appreciate club members opinion of the large non-rhabdomyomatous cells scattered throughout the tissue. I am unwilling to designate these large hyperchromatic irregularly contoured nuclei as evidence of liposarcoma. Rather, they remind me of the atypical stromal cells that have been described in sinonasal polyps, and in fibroepithelial polyps of the vagina and cervix. From their photographs, my suspicion is that the papers that have described "liposarcoma" arising in GFVPs are really describing these atypical stromal cells.

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AMR SEMINAR #51
CASE 18

Contributed by: Larry Weiss, M.D.

History: This is a 48 yo man with a previous history of a lower extremity osteosarcoma at age 21, treated with amputation and adjuvant chemotherapy. He presented with fatigue, and was found to have profound anemia. Endoscopy revealed a large mass in the mid-body of the stomach with central cavitation occupying half of the greater curvature. PET scan confirmed the mass and showed involved retroperitoneal lymph nodes.

Diagnosis: Histiocytic sarcoma

Comment: I think this is a beautiful example for the members of the club. CD163 is a wonderful marker for these neoplasms. The case is somewhat atypical in that CD4 and CD43 were negative.

Gross: We received a total gastrectomy, pancreatectomy, and splenectomy. There was a 13 cm. fungat\ing tumor mass, which extended to the serosa. Tumor also involved perigastric lymph nodes, omentum, peripancreatic lymph nodes, and peripancreatic soft tissue. The spleen and pancreas were free of tumor.

Stains:		
	Keratin, EMA, desmin, actin	NEGATIVE
	CD2, CD3, CD5, CD7	NEGATIVE
	CD4, CD8	NEGATIVE
	CD20, PAX5, CD79A	NEGATIVE
	CD10, CD43, CD56, BCL-2	NEGATIVE
	CD34, CD117A, CD138	NEGATIVE
	CD163	STRONG POSITIVE
	CD68	POSITIVE
	CD45	POSITIVE
	CD1A	NEGATIVE
	S-100 PROTEIN	FOCAL POSITIVE
	LYSOZYME	NEGATIVE
	EBV-LMP	NEGATIVE
	KI-67	NEGATIVE

Genes:		
	IgH, IgK, Gamma-TCR	GERMLINE