

# AMR Seminar #63

## Case – 1

**Contributed by:** Abbas Agaimy, M.D.

**Clinical history:** A 51-year-old woman presented with constitutional symptoms (unexplained fever, general illness and arthritis) thought to be of infectious etiology but no focus of infection could be found on thorough clinical workup. Abnormal laboratory findings upon admission included elevated erythrocyte sedimentation rate (56 mm), CRP (11.32 mg/dl), Hemoglobin of 10.8 g/dl, ANA of 1:800, ASMA of 1:40 and pANCA titer of 1:16. All other findings including relevant liver function tests, rheumatoid factor, AMA and ferritin level were within normal ranges. Abdominal ultrasound and MRI showed a 4.3 cm circumscribed round mass within the left liver lobe (segment 2/4) in addition to a 1.2 cm lesion typical of hemangioma in segment VIII of the right lobe. The mass was removed via segmental resection of the left lobe. The patient recovered well and her initial symptoms resolved completely and the serological inflammation parameters returned to normal after surgery. Currently she is alive and well 7 years after surgery.

**Macroscopic features:** The resection specimen contained a well demarcated but not encapsulated 4.3 cm tumor with brown soft cut-surface.

**Histological and immunohistochemical findings:** Histological examination showed a predominance of mixed inflammatory infiltrates composed of prominent plasma cells admixed with small mature lymphocytes, scattered neutrophils, histiocytes, fibroblasts and a few eosinophils associated with diffuse fine reticular sclerosis/hyalinosis. Several small to medium-sized thick-walled veins within the lesion and the adjacent liver showed complete lumen obliteration by inflammatory cells and fibrosis. The tumor contained scattered large mono-, bi- or multinucleated cells with pale to eosinophilic granular cytoplasm and overall histiocytoid appearance, occasionally superficially mimicking Reed-Sternberg cells. Isolated scattered fat vacuoles were seen but there were no areas of classical angiomyolipoma. The interphase to the surrounding liver was partially sharp, but in other areas irregular where focal obliterative angiitis involving thick-walled vessels and isolated portal tracts surrounded by prominent concentric periductal mononuclear inflammation associated with sclerosis were seen. Otherwise, the liver parenchyma away from the mass showed no significant pathological changes. Immunohistochemical staining with HMB45 and Melan-A highlighted numerous immunoreactive cells with predominantly spindled morphology and multiple slender dendritic-like cytoplasmic processes that were barely discernible on H&E stain (Fig. 1). Scattered medium to large sized polygonal histiocytoid cells stained also for melanocytic markers. ASMA stained many of these slender myoid cells in addition to stromal myofibroblasts in areas of sclerosis. IgG4 antibody revealed numerous staining plasma cells that were either scattered within the tumor or forming occasional clusters (Fig. 2) with an average of 37 IgG4 positive cells/HPF (range, 28-54). Although focal areas rich in IgG4 positive plasma cells were seen at the interphase with the surrounding liver parenchyma, the pericholangitis lesions away from the main mass did not contain increased numbers of IgG4 plasma cells. Kappa and lambda light chains showed polytypic plasma cells. All other relevant markers (CD30, CD15, CD21, CD23, CD163, ALK, EBER ISH and others) were negative in the lesional cells.

**Diagnosis:** Inflammatory angiomyolipoma of the liver with features overlapping with IgG4-related pseudotumor.

**Comment:** The inflammatory variant of hepatic angiomyolipoma is exceedingly rare (7 cases reported to date) [1-3], mainly affects women (mean age: 41 yrs) and originates in the left lobe (5/8). None was associated with chronic liver diseases, or the tuberous sclerosis complex. Two cases (including this case) presented with constitutional symptoms. The tumor mean size was 6.5 cm. None recurred or metastasized at a mean follow-up of 5.3 yrs. All tumors showed predominantly inflammatory pattern (>90%). Reviewing illustrations of reported cases, I found that the case reported by Kojima et al was strikingly similar to the current case and both closely mimicked inflammatory pseudotumor including the presence of obliterative phlebitis and the current case showed in addition inflammatory lesions involving adjacent portal tracts.

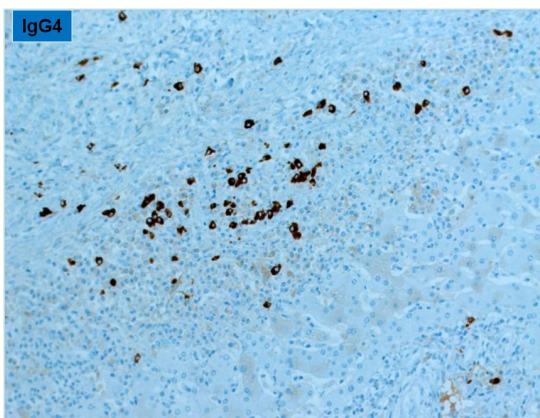
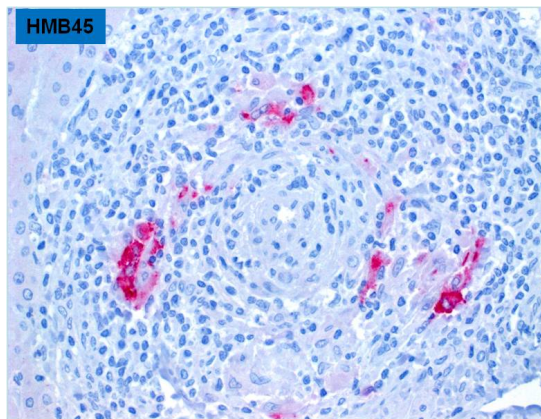
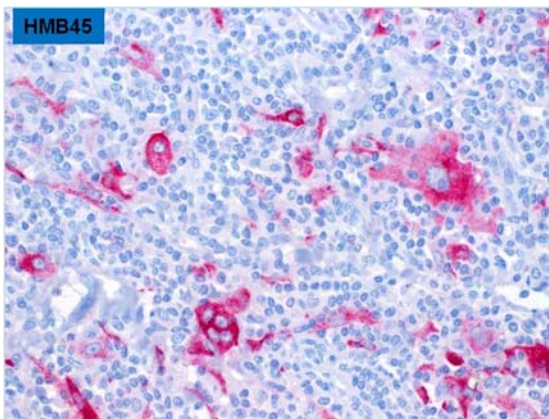
The current case features unusual findings that merit special discussion. Admittedly, without the scattered fatty vacuoles and IHC for HMB45, the lesion would have been classified as inflammatory pseudotumor. Notably, the lesion showed clear-cut features of IgG4-related inflammatory pseudotumor (prominent storiform reticular sclerosis, prominent plasma cells, obliterative phlebitis and increased IgG4-positive plasma cells).

Thus, the classification of this lesion raises several questions. Is this really a hepatic inflammatory AML or an IPT with secondary "non-specific or metaplastic" myomelanocytic immunophenotype? Is the adjacent inflammatory liver change a secondary associated phenomenon or a precursor lesion that ultimately would be incorporated into the growing tumor? What is the role and clinical significance of IgG4 in this lesion?

Regarding the first question, a diagnosis of angiomyolipoma seems justified on the basis of histological features (scattered fatty cells), immunoprofile (HMB45+) and similarity to previously reported cases that showed in addition a classical angiomyolipoma component.

The role of IgG4 in this peculiar lesion remains obscure. Recent studies showed significant numbers of IgG4 positive plasma cells as a constituent of intra- and peritumoral inflammatory response in different carcinomas of different subtypes from various organs, but none was associated with features of hyper-IgG4 disease [4]. However, the overall histological similarity of the tumor in the current case to the IgG4-related lesions strongly suggests a role for IgG4 in the pathogenesis of the inflammatory infiltrate and the associated vascular and stromal changes. Furthermore excessive IgG4 production by the tumor-associated inflammatory response might be responsible for the constitutional clinical symptoms of this patient. This is strengthened by complete resolution of her clinical symptoms after tumor resection. Unfortunately, preoperative or perioperative serum IgG4 level was not available due to the retrospective nature of this case. However, absence of extra-hepatic manifestations and the uneventful follow-up for the next 7 years indicates a localized disease with paraneoplastic (probably IgG4-mediated) symptoms and strongly argues against a systemic disorder. A recent report described a case of cholangiocarcinoma associated with IgG4-related pseudotumor in the same liver specimen where both lesions formed a single bilobated gross mass [5]. The presence of IgG4 plasma cells has been implicated in the prominent stromal sclerosis commonly seen in a subset of mucoepidermoid carcinomas [6].

Given that HMB45 staining might represent the only clue to diagnosis and that most hepatic inflammatory pseudotumors reported earlier have not been stained with HMB45, this variant of hepatic angiomyolipoma might be under-recognized. Thus, HMB45 and Melan-A need be included in the marker panel used for classifying lesions in the spectrum of "hepatic inflammatory pseudotumor". It would be of interest to test hepatic inflammatory pseudotumor in other settings (particularly those lesions with features of IgG4-related disease) for HMB45 expression as some of them might display overlapping features with inflammatory angiomyolipoma. The differential diagnosis of this unusual case should include inflammatory pseudotumor-like FDC tumor [7], inflammatory myofibroblastic tumor [8], IgG4-pseudotumor in patients with systemic disease [9], non-specific tumefactive inflammatory lesions in the liver, lymphomas as well as primary and secondary liver neoplasms with prominent inflammatory component.



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# AMR Seminar #63

## Case – 2

**Contributor:** Phil Allen, M.D.

**Case Identification:** FMC 12/S09662, St Vincent's 12B015084

**Contributor:** Dr. John Slavin, St Vincent's Pathology, PO Box 2900, Victoria, Australia 3065.

**History:** Male aged 37 with a firm, solid nodule in the vastus medialis muscle. On the basis of a small biopsy it was initially thought to be proliferative myositis. The entire lesion was excised (this specimen). The AE1/AE3 is positive in many of the lesional cells.

**Diagnosis:** Possible ectopic myxoinflammatory hyaline tumour with minimal myxoid areas, vastus medialis muscle.

**Comments:** I have had great difficulties with this case. Many of the lesional cells resemble the ganglion-like cells of proliferative myositis but there is no chequerboard pattern nor are there any areas that resemble nodular fasciitis.

Does anyone recognise this as a specific entity or is it really an ectopic myxoinflammatory hyaline tumour with minimal myxoid areas?

# AMR Seminar #63

## Case – 3

**Contributor:** Michele Bisceglia, M.D.

**Clinical history:** (case seen in consultation): A 23-year old woman underwent surgical excision of a 10 cm subcutaneous mass of the anterior chest wall. Actually this tumor mass was the local recurrence of a congenital lesion which had already been removed at the age of 2 months at another institution, where the diagnosis of congenital lymphangioma was established. Glass slides relating to the primary tumor were reviewed at the consulting institution and the diagnosis was confirmed.

**Histology:** As one can easily notice the eye-catching finding of this tumor is represented by many irregularly distributed vascular lobules with a “cannon-ball” pattern, in the context of a classical lymphangioma. Each lobule is composed of aggregates of endothelial cells and undifferentiated mesenchymal cells, part of which can be supposed to be pericytes. Some lobules are uncanalized cellular aggregates but others form slit-like spaces or truly newly well formed vessels, containing erythrocytes. Immunohistochemically the lobules showed fair immunoreactivity for CD34 and CD31, while stained weakly with F-VIII Rag. Many cells were also immunopositive with actins.

**Diagnosis:** Tufted angioma arising in/on a recurrent congenital lymphangioma.

**Follow-up:** Subsequently, for completeness sake and research purposes, small pieces of tumor tissue were recovered from paraffin blocks, dewaxed and processed for ultrastructural analysis. Foci of tissue containing those vascular lobules were selected on semithin sections and fine sections were obtained from these areas. In agreement with previous reports, describing cases which were examined with electron microscopy, two types of differentiated cells we could demonstrate ultrastructurally, endothelial cells and pericytes. Also cells showing no sign of differentiation of neither lineage were seen. These fine features were consistent with and even supportive for the above histological diagnosis.

**Discussion:** The discussion of this case will entirely revolve around its vascular component showing the “cannon-ball” pattern. Because of the histologic finding mainly characterized by small circumscribed angiomatous lobules scattered apart, in 1989 Edward Wilson Jones and Milton Orkin in a clinicopathologic report of 20 cases suggested for this lesion the name of “tufted angioma”, a designation which had already been used earlier in 1976 by one (EWJ) of the authors for the former cases of their series. At the time of the publication of that seminal paper the two patronymic authors were well aware that tufted angioma corresponded to the same entity, which had already been termed “angioblastoma of the skin” [in 1949 by Nakagawa] as well as “progressive capillary haemangioma” (in 1971 by McMillan & Champion). In 1987 Rosai and coworkers considered this unusual angiomatous proliferation as yet a distinct entity, but closely related to lobular capillary hemangioma (i.e. pyogenic granuloma). Tufted angioma commonly arises on the neck, back and upper trunk, although extremities are also on record. Rarely tufted angioma has also been reported as arising in the oral mucosa. Most of the cases are observed under 10 years of age, without sex predilection, with one fourth seen at birth and over half within the first 5 years of life. However tufted angioma has also been observed (around 10% of cases) in the young and even in adults. The lesion is usually single, but may be multiple. The size commonly ranges from 2 to 5 cm, but may be larger and even giant forms have been recorded. Tufted angioma behaves always in a benign manner, with no differences in the clinical behaviour between childhood-onset and adult-onset conditions. Systemic manifestations have occasionally been recorded, such as isolated thrombocytopenia and Kassabach-Merritt syndrome. Tufted angioma is an acquired lesion (“acquired tufted angioma”) for which a reactive pathogenesis has been hypothesized. Associations with sites of previous trauma is notable. Rosai and coll. had originally pointed to this possibility, based on the observation that “the lesion in one of [their] patients developed following a possible injury to the region, and was accompanied by the presence of peripheral ‘satellite’ nodules”. Another example of isotopic response is that of a tufted angioma which arose in the site a healed herpes zoster. Associations with pregnancy, acquired immunodeficiency, post-solid organ transplant and Crohn’s disease have also been noticed: usually as eruptive forms, then followed by complete regression. Familial predisposition has also been reported. All these events are clearly indicating that modification of angiogenesis due to several causes, including immunosuppression or drugs, may well play a role in the development and regression of this lesion. On occasions tufted angioma has also been observed as coexisting with other types of vascular lesions (port wine stain, conventional hemangioma, angioma serpiginosum), either as a separate new growth or as located on it. Tufted angioma is usually located in the dermis, but occasionally it has been seen as extending into the subcutaneous tissue. Analogously to pyogenic granuloma deep-seated form may turn up.

**Conclusion:** We believe that this case of tufted angioma arising in a recurrent congenital lymphangioma is a form of deep-seated lesion which was triggered by trauma, represented by the surgical intervention of two decades earlier.

# AMR Seminar #63

## Case – 4

**Contributor:** Ira Bleiweiss, M.D.

**Short Summary:** F. 39 presented with a palpable right breast mass.

**Case History:** A 39 year old woman presented with a large palpable mass in her right breast. On imaging the lesion was well-circumscribed and superficial. The lesion was biopsied at a different institution and was thought to be an adenomyoepithelioma. A lumpectomy with attached overlying skin was performed at our affiliate hospital in Queens.

Grossly the lesion was partially cystic(probably due to the biopsy), measured 2.7x2.5x1.5 cm, and was 0.7cm below the skin surface.

Microscopically the tumor is gland forming with two cell types – basaloid (also known as lymphocytoid) with hyperchromatic nuclei and ductal-type cells with clear cell change and occasional cytologic atypia. There is also a hyalinizing stroma.

**Diagnosis:** Eccrine spiradenoma.

**Comment:** You all know I always like to submit breast tumors, so here's a breast tumor that's not really a breast tumor. Not particularly challenging except because of its location. When a supposed breast lesion doesn't quite fit the right patterns, I start to think of sweat gland tumors (probably the only time I think of them). The dermatopathologists tell me this one is totally benign, should not recur, and the cytologic atypia is of unclear (sorry) significance.

# **AMR Seminar #63**

## **Case – 5**

**Contributor:** Kum Cooper, M.D.

**Clinical History:** An endocervical polyp (uterine) removed in a 23-year-old.

**Diagnosis:** Benign endocervical polyp with exuberant gestational-associated changes.

**Discussion:** This endocervical polyp was removed at the time of Caesarian section, which I deliberately omitted from the history. Both the exaggerated gestational architectural and cytological changes raise the possibility of clear cell carcinoma. However, careful examination reveals the “decidualized”/metaplastic changes superimposed on microglandular (cribriform) hyperplasia and papillary metaplasia. This was a consult I received from India and at that time I shared the case with Dr. Elvio Silva, who agreed with the benign interpretation. I had not seen this degree of gestation-associated changes in an endocervical polyp and wanted to share with the group.

# AMR Seminar #63

## Case – 6

**Contributor:** Ivan Damjanov, M.D.

**Clinical History:** A 21 year-old man with a testicular nonseminomatous germ cell tumor (NSGCT), for which he was treated by chemotherapy, presented for retroperitoneal lymph node dissection. AFP and hCG were not detectable in patient's serum. Two lymph nodes, one of which is included here, contained the same viable tumor tissue.

**Diagnosis:** Yolk sac carcinoma, parietal yolk sac type, in a lymph node metastasis of a testicular NSGCT.

**Comment:** This tumor is composed of neoplastic cells with vesicular nuclei, prominent nucleoli and well developed cytoplasm. These cells are arranged in sheets and nests. The extracellular spaces are filled with eosinophilic matrix resembling basement membranes. In parts of the tumor the hyaline matrix is quite prominent. This material is PAS positive and reacted strongly with antibodies to collagen type IV. No embryonal carcinoma cells were detected, and the multinucleated giant cells seen in one corner were hCG negative.

This tumor is reminiscent of the murine parietal yolk sac (PYS) carcinoma, first described by G.B.Pierce in mice germ cell tumors (1). During the retransplantation of these tumors from one mouse to another the PYS cells cloned themselves and started forming tumors that had a characteristic basement membrane-rich extracellular matrix. By the way, the PYS tumor of Pierce was the source of many basement matrix components, such as laminin, entactin etc, which were first isolated from this tumor.

I first time saw a pure human PYS type of yolk sac carcinoma at an autopsy of a woman treated for classical AFP + yolk sac carcinoma of the ovary (2). The tumor cells that survived the chemotherapy and filled the entire abdominal cavity at the autopsy were all of the PYS type and were typically encased in the basement membrane material alike to the mouse tumors described by Pierce. Neither human nor the mouse PYS cells secrete AFP. A good review of the entire topic was published recently by Nogales et al (3).

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# AMR Seminar #63

## Case – 7

**Contributor:** Otto Dietz, M.D.

**Clinical History:** A 76 year old lady with invasive lobular carcinoma of the right breast (2008; pt2 N 0 (sn) R 0) died from recurrent episodes of pulmonary thromboembolism. Postmortem revealed disseminated metastasis of the spine without local tumor recurrence and without other organ involvement (macroscopic and microscopic). Additionally, a 7 cm large tumor with a lipoma – like appearance was found in the vicinity of the left adrenal gland.

Microscopically the lipomatous tumor displayed the typical morphology of a myelolipoma with small infiltrates of the metastatic lobular breast carcinoma.

**Comment:** In the absence of any other organ involvement by metastatic disease this “tumor in tumor” emphasizes/supports an affinity of metastatic breast cancer to hematopoietic tissue. Has anyone seen this before, hitherto I did not find something similar in the literature.

# AMR Seminar #63

## Case – 8

**Contributor:** Vincenzo Eusebi, M.D.

**Case History:** In December 2010 a 59 year-old female not showing von Recklinghausen syndrome, was admitted to our Hospital, having a palpable nodule located in the soft tissue of the right forearm. Magnetic resonance imaging (MRI) showed that the lesion was located between the flexor muscles and the radial diaphysis and was adherent to the median nerve and ulnar artery. In January 2011 the nodule was excised . No recurrent tumour was evident at a second MRI obtained in August 2011. No other lesions in other organs were evidenced after a total body computerised tomography scan. Patient was in good health when last seen in June 2012.

**Pathologic Findings:** The following prediluted Ventana antibodies were employed: TTF-1, ER, EMA, S100, CK 7, and MNF 116. A tissue block was selected for RNA extraction where SS18-SSX synovial sarcoma fusion transcripts analysis was performed.

*Macroscopically* the nodule had smooth circumscribed borders, was grey-yellowish in colour and measured 3,7x3x2,5 cm.

*Histologically* the tumour was well circumscribed and surrounded by a dense sclero-hyaline capsule. The lesion was constituted of numerous glands. These were lined by one layer of cuboidal to columnar cells showing eosinophilic cytoplasm and round to ovoid nuclei with a single small nucleolus. Lumina were round to irregular and their calibre varied from small to medium large. Their content was composed of dense eosinophilic strongly PAS positive material . Glands were immersed within tightly packed spindle cells with nuclei similar to those of the glandular structures. Mitoses were scanty and averaged 1 to 2 per 10 HPF (400X). Necrosis was absent. EMA strongly stained most of the glandular elements. Spindle cells were occasionally EMA positive. The dense luminal content was also strongly positive. MNF 116 decorated most of the glands (Fig. 5 A) while keratin 7 stained occasional glands and rare spindle stromal cells. ER, TTF1 , and S-100 protein were consistently negative. Occasional elongated spindle cells with bland, small, central nuclei were entrapped within the sclerotic capsule. These same cells consistently stained for EMA and were negative for keratins (Fig. 5 B).

In this neoplasm molecular analysis gave a positive signal for SS18-SSX1 transcript, while no positivity was observed for SS18-SSX2 and SS18-SSX4 rearrangements.

**Diagnosis:** Synovial sarcoma arising within the median nerve of the right forearm.

**Discussion:** In favour of the origin from the nerve is the evidence of a thick fibrous capsule that surrounded the neoplastic proliferation indicative of a pre-existing structure. This was also suggested by the presence within the capsule of numerous elongated EMA positive and Keratin negative cells with bland nuclei that were very reminiscent of perineural cells. Synovial sarcomas classically are seen in limbs, but other locations are occasionally seen such as heart, lung, small intestine, soft palate, and retroperitoneum[1]. Peripheral nerves have been shown to be site of origin of this neoplasm, as reported in 22 instances[2]

This case has been recently published in the Turk Patoloji Dergisi (Turkish Journal of Pathology) 28, 266-269, 2012. You will find there most of the immunos of the present case. This Journal is very nice, the only problem is they want an abstract in Turkish.

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# AMR Seminar #63

## Case – 9

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

**Clinical History:** A 59-year-old man had a mass in deep soft tissue of the thigh. It had remained unchanged for 30 years, but had doubled in size in the preceding 8 months. A mass 10 cm diameter was excised from right sartorius. There has been no local recurrence or metastasis after one year.

**Pathology:** A peripheral rim of pale spongy tissue surrounded a hemorrhagic focally necrotic tumor (image 1). Microscopically the peripheral zone (slide 1) had randomly oriented bland spindle cells with focally dense fibrosis and calcification and a marked hemangiopericytic pattern. The central area (slide 2) showed pleomorphic sarcoma with osteosarcomatous areas with associated osteoclast-like giant cells. Immunohistochemistry (image 2) showed CD34 positivity that was lost in the malignant component, which also had foci of malignant cells that expressed desmin and myogenin (nuclear). Ki67 showed higher proliferation in the malignant area. FISH showed no *MDM2* amplification.

**Diagnosis:** Dedifferentiated solitary fibrous tumor with divergent osteosarcomatous and rhabdomyosarcomatous differentiation.

**Comment:** Dedifferentiation in solitary fibrous tumor is a recent concept developed by Chris Fletcher<sup>1,2</sup> with a nice pleural example submitted by Hugo Dominguez- Malagon in AMR 61 (case 10). It can be regarded as differing from malignant solitary fibrous tumor by the usually abrupt transition between benign and dedifferentiated components as well as the undifferentiated pleomorphism of the latter.

Recently, two of 7 dedifferentiated SFT were identified with divergent osteosarcomatous differentiation, and one with rhabdomyosarcoma.<sup>3</sup> Our case,<sup>4</sup> arising in soft tissue, is exceptional in having both osteosarcomatous and rhabdomyosarcomatous components. This can be distinguished from dedifferentiated liposarcoma by the absence of a well-differentiated component and of *MDM2* gene amplification.<sup>5</sup> Recently *NAB2-STAT6* gene fusions have been described in many SFT<sup>6,7</sup> and conceivably this might become of use in identifying purely dedifferentiated SFT.

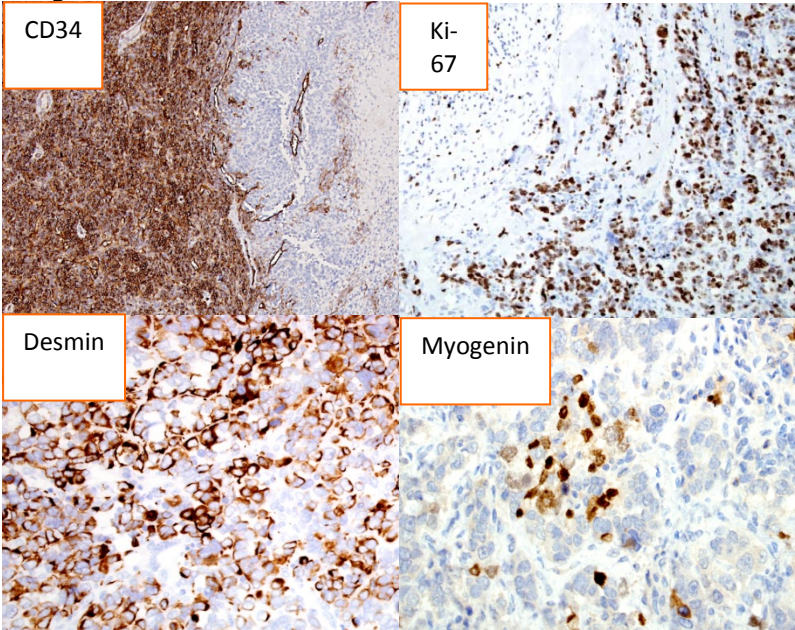
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Image 1



Image 2



# AMR Seminar #63

## Case – 10

**Contributor:** Christopher Fletcher, M.D.

**Clinical History:** A 60-year-old man who was being worked up for kidney stones was found, by chance on radiology, to have a 3 cm mass on the lesser curve of the stomach. The mass was excised with clear margins. Eighteen months postoperatively, the patient is free of disease.

**Diagnosis:** Malignant glomus tumor of stomach.

**Comments:** As Markku Miettinen noted in his 2002 study (*Am J Surg Pathol* 2002; 26:301-311), it is very difficult to reliably predict behavior of glomus tumors arising in the GI tract but frankly malignant behavior seems to be very uncommon. In this lesion, some areas of the tumour have more spindled atypical cytomorphology and we counted up to 5 mitoses per 50 HPF. In addition, there was multifocally prominent lymphovascular invasion (as seems quite often to be found in gastric glomus tumors) – although, regrettably, this feature is not evident in all of the sections submitted. Immunostains showed positivity for SMA and caldesmon, supporting the diagnosis of glomus tumor. At least in my experience, truly clinically malignant examples of glomus tumor arising at almost any anatomic location seem to be extremely rare.

# AMR Seminar #63

## Case – 11

**Contributor:** Andrew Folpe, M.D.

**Clinical History:** A 43-year old female nursing home resident with a 3-4 year psychiatric history presented with a fracture of the left proximal tibia. A curettage was performed.

**Pathological Findings:** Sections from the curettage specimen showed spicules of medullary bone and associated adipose tissue. The adipose tissue contained a highly distinctive accumulation of membranous material arranged in a complex folded to papillary pattern. The membranous material was positive with luxol fast blue and PAS special stains. In areas, this membranous material elicited a foreign body giant cell reaction. Radiographical studies showed multiple bilateral lytic and sclerotic lesions as well as extensive demineralization.

**Diagnosis:** Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy (PLOSL).

**Comment:** I confess that I had never heard of this syndrome until I got this case. My initial reaction on viewing the biopsy was something along the lines of “this fat looks funny”, and it took me a little while to realize it was some type of membranous foreign material. Then I just hit PubMed until the right thing came up.

The following paragraph is directly copied from an excellent online review article on this subject, available at <http://www.ncbi.nlm.nih.gov/books/NBK1197/>

**Disease Characteristics.** Polycystic lipomembranous osteodysplasia with sclerosing leukoencephalopathy (PLOSL) is characterized by fractures (resulting from radiologically demonstrable polycystic osseous lesions), frontal lobe syndrome, and progressive presenile dementia beginning in the fourth decade. The clinical course of PLOSL can be divided into four stages: (1) The latent stage is characterized by normal early development. (2) The osseous stage (3rd decade of life) is characterized by pain and tenderness, mostly in ankles and feet, usually following strain or injury. Fractures are typically diagnosed several years later, most commonly in the bones of the extremities. (3) In the early neurologic stage (4th decade of life), a change of personality begins to develop insidiously. Affected individuals show a frontal lobe syndrome (loss of judgment, euphoria, loss of social inhibitions, disturbance of concentration, and lack of insight, libido, and motor persistence) leading to serious social problems. (4) The late neurologic stage is characterized by progressive dementia and loss of mobility. Death usually occurs before age 50 years.

**Diagnosis/testing.** The combination of radiologically demonstrable polycystic osseous lesions, frontal lobe syndrome, and progressive presenile dementia beginning in the fourth decade is diagnostic. Fractures of the wrists or ankles after minor trauma with typical polycystic osseous lesions identified on x-ray examination suggest the possibility of PLOSL. In uncertain cases, molecular genetic testing helps to establish the diagnosis. Molecular genetic testing of *TYROBP (DAP12)* and *TREM2*, the only two genes known to be associated with PLOSL, is available in clinical laboratories.

# AMR Seminar #63

## Case – 12

**Contributor:** Janez Lamovec, M.D., Institute of Oncology, Ljubljana, Slovenia

**Clinical history:** The patient is an 83-year-old woman who had a vulvectomy and bilateral inguinal lymph node dissection because of infiltrating squamous cell carcinoma of vulva 10 years previously performed in another hospital. In two lymph nodes metastases were found. The depth of invasion was 5 mm. A few months after surgery, she had a local recurrence treated with wide excision. She had been referred to our institution where she received postoperative irradiation in total dose of 6600 cGy. In November 2012, she was admitted with a polypoid lesion in the left inguino-femoral fold of 2 months duration.

**Pathologic findings:** The specimen was a skin ellipse with subcutaneous adipose tissue with a nodular polypous tumor measuring 2.5 x 2 cm. The surface of the polyp was ulcerated, the cut surface of variegated appearance.

Microscopically, the surface of the polyp is hemorrhagic and necrotic while the rest of the lesion features a great number of dilated blood filled or empty vascular structures with intervening stroma composed of spindle cells many of them with hyperchromatic or bizarre nuclei. Many atypical mitoses are seen. Some cells have myoid appearance. Stroma is focally edematous, moderately collagenized, with extravasated blood and fibrin and scattered inflammatory cells. The rest of the skin and subcutaneous tissue shows thickened blood vessels, fibrosis and hyalinosis, focal lymphoid infiltrates and underneath the lesion rare scattered multinucleated fibroblastic cells. Immunohistochemically, the stromal cells exhibited strong smooth muscle actin positivity; they were negative for desmin and steroid receptors.

**Diagnosis:** Pseudosarcomatous fibroepithelial stromal polyp of perivulvar skin.

**Comment:** I believe that this lesion represents an extravulvar example of the lesion called pseudosarcomatous fibroepithelial stromal polyp. Most commonly such polyps arise in lower female genital tract but it appears that they may develop in a wider perigenital region too; some other locations (gastrointestinal, respiratory tract, urotract ) are also on record . . More cellular and even more sarcoma-looking examples were also described. I don't think that in this case, the polyp is the complication of irradiation, at least I am not aware that the reaction to irradiation may have a similar morphologic manifestation. Although I know that such polyps have been known for a long time, I still think they are not that common and that due to their peculiar pseudosarcomatous appearance an example of such lesion deserves to be submitted to AMR seminar.

### References:

1. Burt RL et al. Fibroepithelial polyp of the vagina. A report of five cases. *Obst Gynecol* 1976; 47: 52S-4S.
2. Miettinen M et al. Vaginal polyps with pseudosarcomatous features. A clinicopathologic study of seven cases. *Cancer* 1983; 51:1148-51.
3. Nucci MR et al. Cellular pseudosarcomatous fibroepithelial stromal polyps of the lower female genital tract: an underrecognized lesion often misdiagnosed as sarcoma. *Am J Surg Pathol* 2000; 24: 231-40.

# AMR Seminar #63

## Case – 13

**Contributor:** Michal Michal, M.D. Plzen, Czech Republic

**Patient:** Woman, 71 years old had a tumor of the uterus 15,3x15,5x7,4 cm.

The tumor was sampled in 40 blocks and looked the same everywhere. It contained well differentiated endometrioid adenocarcinoma and widespread hyalinization.

**Diagnosis:** Hyalinized endometrioid adenocarcinoma.

**Comment:** In my opinion this can be a great pitfall. All cases, without exception, I ever saw in consultation, were diagnosed by referring pathologists as Mullerian carcinosarcomas (Mullerian malignant mixed tumors) and the hyalinized parts were considered as hyalinized cartilage so that the hyalinized parts was considered as sarcomatoid differentiation! In contrast to Mullerian carcinosarcomas this hyalinized endometrioid adenocarcinoma is an indolent lesion. There is, up to my knowledge only one paper describing series of this lesion **(1)**. It is an excellent paper I recommend all to read it.

**Reference:**

1. S.K.Murray, P.B.Clement, R.H.Young . Endometrioid carcinomas of the uterine corpus with sex cord-like formations, hyalinization, and other unusual morphologic features. A report of 31 cases of a neoplasm that may be confused with carcinosarcoma and other uterine neoplasms. Am J Surg Pathol 2005;29:157-166



# AMR Seminar #63

## Case – 14

**Contributor:** Markku Miettinen, M.D.

**Clinical History:** 56-year-old man with a 1 cm subcutaneous nodule in the thigh.

**Diagnosis:** Adult myofibroma.

**Comments:** This is a benign entity related to childhood myofibroma. These adult myofibroblastomas are related to and overlap with myopericytomas. The most common sites of involvement are head and neck and lower extremity. Histologically there is a well-defined nodule containing partly hyalinized, differentiated myofibroblastic component and a less-differentiated vascular/primitive pericytic component. The differentiated myofibroblastic elements are seen as spherical to ovoid nodules that are actually myofibroblastic/vascular myointimal proliferations originating from vessel walls, and in some case the entire lesion may intravascular. Immunohistochemically the myofibroblastic nodules are positive for smooth muscle actin and negative for desmin.

**References:**

1. Daimaru Y, Hashimoto H, Enjoji M. Myofibromatosis in adults (adult counterpart of infantile myofibromatosis). *Am J Surg Pathol* 1989;13:859-865.
2. Smith KJ, Skelton HG, Barrett TL, Lupton GP, Graham JH. Cutaneous myofibroma. *Mod Pathol* 1989;2:603-609.
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4. Mentzel T, Dei Tos AP, Sapi Z, Kutzner H. Myopericytoma of skin and soft tissues: clinicopathologic and immunohistochemical study of 54 cases. *Am J Surg Pathol* 2006;30:104-113.

# AMR Seminar #63

## Case – 15

**Contributor:** Manuel Sobrinho-Simoes, M.D.

**Clinical History:** A twenty year-old female (DOB 08-08-1992) was seen in September 2011 for two episodes of pneumonia in the left lung. Her clinical situation deteriorated and in March 2012 a bronchoalveolar lavage was performed at another Institution. The diagnosis of neuroendocrine carcinoma was made.

In April 2012 she was admitted to our Hospital. A PET – TC scan displayed a mass (36 x 28 x30 mm) located in the left pulmonary hilum. In the left lower lobe, multiple nodular opacities with sizes ranging from 6 mm to 12 mm were also seen. Surgical bronchial biopsy showed a poorly differentiated small round cell tumour. The neoplastic cells contained glycogen in the cytoplasm and immunoexpressed CD99, synaptophysin, Cam 5.2 and p63, in the absence of immunoexpression for CD56 (N-CAM), Bcl2 and desmin. A tentative diagnosis of PNET was advanced. The patient started chemotherapy with VIDE protocol for PNET.

In January 2013 a left partial pneumectomy (lower lobe) was performed. At section, and in the lower lobe bronchus, there was a solid and whitish neoplasia measuring 3.5 x 2.9 x 1.8 cm.

**Diagnosis:** ??????

# AMR Seminar #63

## Case – 16

**Contributor:** Elvio Silva, M.D.

**Case History:** A 32-year old woman, gravida 3, para 2, gave birth to a female infant at term. The delivery was normal. The placenta weighted 480 grams and had a 2 cm necrotic nodule. The section included is from this nodule.

**Diagnosis:** Intraplacentral gestational choriocarcinoma.

It is not unusual to see trophoblastic proliferations with cellular atypia in areas of placental villi; however, most of these are proliferations of intermediate trophoblasts in placental cell islands. These are proliferations of only one cell type and the HCG titers are low. It is highly unusual to see proliferations of cyto and syncytiotrophoblast in a term placenta. The differential diagnosis in this case would be a complete mole but the presence of an infant would rule out the possibilities of a hydatidiform mole in over 99% of the cases. The diagnosis of this case is not difficult, but the case is extremely unusual.

### References:

1. Henningsen AK, Maroun LL, Havsteen H, Svare J. Massive fetomaternal hemorrhage caused by an intraplacentral choriocarcinoma: a case report. *Case Rep Med.* 2010;2010:767218.
2. Aso K, Tsukimori K, Yumoto Y, Hojo S, Fukushima K, Koga T, Sueishi K, Takahata Y, Hara T, Wake N. Prenatal findings in a case of massive fetomaternal hemorrhage associated with intraplacentral choriocarcinoma. *Fetal Diagn Ther.* 2009;25(1):158-62.
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5. *International Journal of Gynecological Pathology.* Official journal of the International Society of Gynecological Pathologists. 2013 Jan; 32(1):1-147.

# AMR Seminar #63

## Case – 17

**Contributor:** James A. Strauchen, M.D.

**Clinical History:** 26 year old Asian female presented with a liver mass. Clinical impression was hepatic adenoma versus hepatocellular carcinoma. Hepatitis B surface antigen positive with history of oral contraceptive pill usage.

**Pathology:** The specimen designated "left lateral lobe liver" consisted of a 22 x 8 x 4.5 cm partial hepatectomy specimen weighing 285.9 grams. This contained a 4.2 x 3.5 x 3.3 cm tan white mass. Sections showed a circumscribed nodule composed of small and large lymphocytes, plasma cells, histiocytes, and scattered spindle cells. Immunohistochemical stains demonstrate the lymphocytes consist predominantly of CD8-positive cytotoxic-suppressor T-cells (CD3 positive, CD5 positive, CD7 positive, CD8 positive, Granzyme B positive). The spindle cells are positive for vimentin, variably positive for smooth muscle actin, and negative for CD21, CD23, and CD35. In-situ hybridization for Epstein-Barr virus (EBER) is positive in the spindle cells. T-cell receptor gene rearrangement studies are positive for both clonal TCR gamma and TCR beta gene rearrangements.

**Diagnosis:** ? EBV-positive inflammatory pseudotumor of liver with oligoclonal T-cell expansion secondary to EBV infection versus peripheral T-cell lymphoma.

**Comment:** This was a challenging case eventually seen at NYU, Memorial Sloan Kettering, National Cancer Institute, and Massachusetts General Hospital. Both Elaine Jaffe and Nancy Harris favored an EBV-positive inflammatory pseudotumor with oligoclonal T-cell expansion secondary to EBV infection rather than peripheral T-cell lymphoma, based on the circumscription, EBV-positive spindle cells, and cytologically bland population of lymphocytes, histiocytes, and plasma cells. The absence of FDC markers (CD21, CD23, CD35) excluded an EBV-positive follicular dendritic cell tumor. The marked predominance of CD8-positive, Granzyme B-positive cytotoxic suppressor T-cells was a feature concerning for peripheral T-cell lymphoma, however, there is surprisingly little in the literature on the phenotype of the lymphocytes in inflammatory pseudotumor. EBV infection is a well recognized cause of "false" positive T-cell receptor gene rearrangement studies and there is at least one case report of oligoclonal T-cell populations in an inflammatory pseudotumor of the pancreas unrelated to EBV.

**Reference:** Esposito I, et al. Oligoclonal T-cell populations in an inflammatory pseudotumor of the pancreas possibly related to autoimmune pancreatitis: an immunohistochemical and molecular analysis. *Virchows Arch* 2004; 444:119-126.

# AMR Seminar #63

## Case – 18

**Contributor:** Saul Suster, M.D.

(Case submitted by Dr. Felipe Rosales, National Cancer Institute, Quito, Ecuador).

**Clinical History:** A 32 year old woman was seen for constipation, proctorrhagia, abdominal pain and distention of one year's evolution. En endoscopy, a submucosal lesion was noted in the gastric antrum. At laparotomy, a well-circumscribed 3.5 cm. mass was resected from the gastric wall. Clinical and radiographic examination did not disclose evidence of any tumor elsewhere.

**Diagnosis:** Low-grade stromal tumor of the gastric wall – type undetermined ???

**Discussion:** I received this case in consultation and I'm afraid I don't know what this is. The morphology looks quite distinctive. My obvious first choice was a peculiar GIST, but the GIST workup was completely negative. We did a panel of IHC stains that showed convincing positivity for bcl-2 and SMA, but stains for CD117, DOG-1, CD34, S-100, desmin, calponin, and H-caldesmon were all negative. I suppose the SMA positivity could be interpreted as favoring smooth muscle differentiation, but I've never seen a leiomyoma/leiomyosarcoma with these morphologic features in this (or any other) location. I've seen very few cases of gastroblastoma that can look similar but have very limited experience with such tumors. I'm circulating this in the hope that someone can take me out of my misery and tell me that they've seen this before and what it is. In fact, any suggestions for additional work-up would be appreciated!

# AMR Seminar #63

## Case – 19

**Contributor:** Saul Suster, M.D.

(Case submitted by Dr. Hector Cohen, Western Galilee Hospital, Nahariya, Israel).

**Clinical History:** A 56 year old man was seen for a pericardial effusion that did not resolve over a period of 3 weeks, prompting a biopsy of the pericardium. At the time of the procedure, the pericardium contained a thick, fibrinous material adhering to the wall of the heart. The biopsy samples consisted in irregular rubbery tan-gray tissue fragments of up to 1 cm. in thickness. The patient apparently has no underlying condition that would explain this process.

**Pathologic Findings:** The biopsy shows thickening of the pericardium with extensive fibrosis and a proliferation of small vacuolated and empty spaces evenly scattered throughout. On superficial examination these empty vacuoles resemble mature adipose tissue, but closer examination shows a large number of flattened nuclei applied against the periphery of the vacuoles resembling signet-ring cells.

**Diagnosis:** Don't know.

**Discussion:** This was another consultation case in which I was unable to help the consulting pathologist. The case was extensively worked up at the original institution; stains for calretinin, CK5/6, HMB45, S100 and caldesmon were negative. The referring pathologist considered the diagnostic possibility of an adenomatoid tumor but the vacuoles are negative for cytokeratins, calretinin and HBME-1. We repeated some of the stains here, and found a few spindle cells at the edges of the tissue that were positive for cytokeratin and SMA that may correspond to entrapped keratin-positive submesothelial fibroblasts. Stains for HMB45, S-100 and CD31 were also negative. The process appears infiltrative but I'm having a hard time conceiving of this as malignant. I even considered the possibility of some foreign material like silicone (no birefringence is observed on polarized microscopy). So, I don't know what this is – any suggestions? Has anyone ever seen this or something like this before?

# **AMR Seminar #63**

## **Case – 20**

**Contributor:** Lawrence M. Weiss, M.D.

**History:** 76 yo man with 7.0 cm. renal mass.

**Gross:** Well-circumscribed lesion.

**Immunos:** The neoplasm was strongly positive for cytokeratin Oscar and PAX-8, and was weakly positive for CD56 and CD99. Cytokeratin 7, CD117, RCC, chromogranin, CD10, CDX-2, TTF-1, cytokeratin 20, synaptophysin, S-100 and SF-1 stains were negative. The Ki-67 index was about 1%. (The case was received with immunostains already performed).

**Diagnosis:** Renal metanephric adenoma.

**Comment:** This is a pretty case that I have not often seen outside of teaching sets. Interestingly, I received two of these within one week, from the same hospital (the other was a needle biopsy). As far as I am aware this is a completely benign lesion. I include it in the seminar because it is a photogenic example of a rare benign tumor.

# AMR Seminar #63

## Case – 21

**Contributor: Bruce M. Wenig, M.D.**

**Clinical History:** 82 year old man presented with a slowly enlarging right thyroid lesion over several months. There is no known past history of thyroid gland lesions/neoplasms. A PET CT scan showed a hypermetabolic mass (Standard Uptake Value 27) inseparable from the right thyroid lobe. The patient has a remote history of a cutaneous malignant melanoma of the left ear. A fine needle aspiration biopsy was performed and reported as “positive for malignant cells; high-grade malignant neoplasm” Immunostains performed on a cell block from the aspiration showed the lesional cells to be positive for TTF-1, thyroglobulin (rare) and cytokeratins (AE1/AE3, CK7) but negative for CK20, p63, p40, Melan A, HMB45, tyrosinase and RCC. Based on the above findings a diagnosis of an undifferentiated (anaplastic) thyroid carcinoma was favored.

**Gross:** The patient subsequently underwent a total thyroidectomy. In the right thyroid lobe there was a well circumscribed mass measuring 3.1 x 2.8 x 2.4 cm that on sectioning with appeared yellow to tan with areas of necrosis and a small rim of uninvolved appearing parenchyma. Grossly, there was no evidence of invasion into adjacent thyroid parenchyma and/or outside the thyroid gland proper. Within the undifferentiated carcinoma there are foci of a differentiated follicular epithelial cell proliferation characterized by colloid-filled follicles and uniform appearing nuclei lacking the high-grade histologic features of the undifferentiated carcinoma.

**Microscopic:** The neoplasm identified in sections of the right thyroid lobe is circumscribed to encapsulated comprised of cells with features of lymphoepithelial-like carcinoma characterized by diffuse growth, pleomorphic vesicular nuclei with prominent nucleoli, increased mitoses including atypical forms and necrosis. In addition, there are areas of the neoplasm showing angiomatoid features (the latter may not be present in all distributed slides) characterized by irregular and anastomosing vascular channels lined by neoplastic cells. Foci of a differentiated follicular epithelial cell proliferation characterized by colloid-filled follicles and uniform appearing nuclei lacking the high-grade histologic features are present. Once the initial sections of the neoplasm were reviewed and the lesion was found to be completely encapsulated without evidence of invasion, we sectioned the entire tumor and found it to be completely encapsulated without evidence of invasive growth. For completion, sections of the left thyroid lobe showed the presence of adenomatoid nodules and multiple resected lymph nodes were negative for carcinoma.

### **Immunohistochemical staining:**

Undifferentiated components:

- Lymphoepithelial-like carcinoma component: Reactive for cytokeratins (AE1/AE3, CAM5.2), PAX8 and vimentin but negative for thyroglobulin, TTF1, CD5, CD31, Factor 8-related antigen, S100 protein and HBME1.
- Angiomatoid variant component immunoreactive for CD31, Factor 8-related antigen and vimentin but negative for cytokeratins, thyroglobulin, TTF1, PAX8, HBME1 and CD34.

The malignant components showed an increase proliferation rate of > 50% as seen by Ki67 (MIB1) staining.

Differentiated component:

- Reactive for thyroglobulin, TTF1, cytokeratins (AE1/AE3, CAM5.2), PAX8 and HBME1. Numerous foamy (benign) histiocytes are present in association with the neoplastic proliferation; the histiocytes were reactive for CD68.

**Diagnosis:** Thyroid gland with encapsulated (noninvasive) undifferentiated (anaplastic) thyroid carcinoma arising in association with a differentiated follicular epithelial cell lesion measuring 3.1 cm in greatest dimension without evidence of extrathyroidal extension. (pTNM: pT4aN0MX - pT4a = Intrathyroidal anaplastic carcinoma.)

**Discussion:** The typical clinical scenario for thyroid undifferentiated (anaplastic) carcinoma is that of a rapidly enlarging neck mass that is extensively invasive at the time of presentation directly contributing to its aggressive biology and dire outcome. Thyroid undifferentiated (anaplastic) carcinomas typically occur in association with a pre- or coexisting differentiated thyroid lesion/neoplasm to include adenomatoid nodules, follicular adenomas/carcinomas and papillary carcinoma. The majority of thyroid undifferentiated (anaplastic) carcinomas show sarcomatoid histologic features but there may be a wide histologic spectrum to include several morphologic variants. This patient's neoplasm lacked sarcomatoid features but included an admixture of features that included lymphoepithelial-like carcinoma and angiomatoid variants. Some authorities feel that angiosarcomas of the thyroid represent undifferentiated carcinomas. However, angiosarcoma as an independent primary malignancy of the thyroid gland occurs although it may share overlapping clinical and pathologic features with undifferentiated



carcinoma. In any event, from a practical standpoint it may be more of an academic matter in trying to differentiate undifferentiated carcinoma from angiosarcoma as the typical biologic behavior for both tumor types is extremely poor with patient deaths occurring over short time periods irrespective of treatment.

In this patient's case there is high-grade undifferentiated malignancy arising in association with a differentiated follicular epithelial cell lesion that we felt represented adenomatoid nodules. While the overall pathologic features are those of a thyroid undifferentiated (anaplastic) carcinoma, including lymphoepithelial-like carcinoma and angiomatoid variants, the relatively innocuous clinical presentation and corresponding complete encapsulation without invasion are quite unusual for this tumor type. However, there is a recognized subset, albeit rare, of thyroid undifferentiated (anaplastic) carcinomas that include encapsulated (noninvasive) ones (see references below). This patient's clinical presentation was decidedly unusual (in retrospect) for an undifferentiated (anaplastic) thyroid carcinoma. In spite of the morphology being that of a thyroid undifferentiated (anaplastic) carcinoma, in the absence of invasion the prognosis may be favorable and not follow the dire prognosis usually associated with (invasive) undifferentiated (anaplastic) thyroid carcinomas.

#### **References:**

Guimarães L, Meneses A, Carrara W, Kefalás A. Encapsulated anaplastic thyroid carcinoma with three-year disease-free survival. *Pathol Res Pract* 2000;196(12):867-70; discussion 871.

Ito Y, Matsuzuka F, Yoshida H, Morita S, et al. A. Encapsulated anaplastic thyroid carcinoma without invasive phenotype with favorable prognosis: report of a case. *Surg Today* 2003;33(4):277-81.

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Voutilainen PE, Multanen M, Haapiainen RK, Leppäniemi AK, Sivula AH. Anaplastic thyroid carcinoma survival. *World J Surg.* 1999 Sep;23(9):975-8; discussion 978-9.

# AMR Seminar #63

## Case – 22

**Contributor:** – Ady Yosepovich. M.D.

**Clinical History:** This is a consultation case sent to me by one of our breast oncologists.

A 58 yo lady had routine screening mammography that revealed a 2CM mass in her left breast, subsequent breast ultrasound showed a 2.7 cm. irregular mass that was biopsied. The CNB and the subsequent excision biopsy was reported as invasive papillary carcinoma, the immunoprofile was triple negative and the KI 67 was low. The SLN was free of tumor.

The patient came for adjuvant treatment ( large triple negative tumor) but the oncologist asked me to revise the receptor status ( papillary carcinoma is usually ER positive).

**Pathologic Findings:** The tumor is well circumscribed, composed of cells arranged in solid, microcystic and tubular patterns, at areas the tumor simulates thyroid follicles. The neoplastic cells are uniform round to polygonal and display a finely granular or vacuolated cytoplasm showing a dense eosinophilic secretion. They show mild atypia and low mitotic activity. The nuclei are round to oval, occasionally with vesicular chromatin and discrete nucleoli.

On immunostains the cells are positive for AE1/3, CAM5.2, S-100, E-Cadherin and CK5/6. The cells are negative for calponin, p63, CEA, ER, PR, HER-2, Ki-67 was positive in 2% of the cells.

We performed FISH study that showed break apart rearrangement involving chromosome 12 at the ETV6 region (12q13) – please see the picture below.

**Diagnosis :** Secretory carcinoma of the breast.

**Discussion:** This is a rare subtype of infiltrating breast carcinoma accounting for less than 0.1 of all breast cancers. Initially it was described in children but subsequently over 100 cases have been reported leading to the observation that 2/3 of the cases are in adults ranging all ages.

In the majority of patients it has a low grade clinical course resulting in an exceptionally favorable prognosis albeit it's triple negative phenotype. There is no clinical evidence that radiation or systemic treatment is beneficial in this special tumor subtype.

The most striking molecular feature of secretory carcinoma is the presence of the recurrent chromosomal translocation t(12;15)(p13;q25), which results in the ETV6-NTRK3 fusion gene that is specific and diagnostic for this histological subtype.

REF:

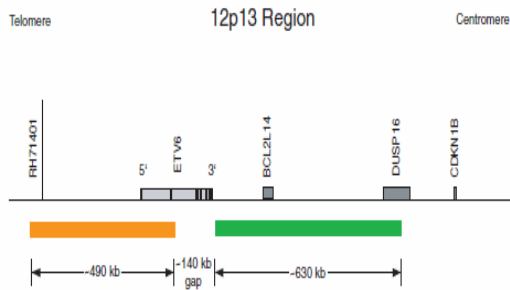
Rosen's breast pathology, 3<sup>rd</sup> Ed.

Dabbs Breast pathology (2012).



Hybridization with the Vysis LSI ETV6 Dual Color, Break Apart Rearrangement Probe:

Hybridization of this probe to interphase nuclei of normal cells is expected to produce two pair of overlapping, or nearly overlapping, orange and green (yellow fusion) signals. The anticipated signal pattern in abnormal cells having a chromosomal breakpoint within the gap between the two probe targets on one chromosome 12 is one orange, one green, and one fusion signal (encircled nucleus).



LSI ETV6 (TEL) Dual Color, Break Apart

# **AMR Seminar #63**

## **Quiz Case – #1**

**Contributor:** Saul Suster, M.D.

(Consult case submitted by Dr. Pablo Ortega from Ecuador, South America).

**Clinical History:** A 43 year old man in previous good health is seen for localized inguinal lymphadenopathy. Thorough clinical examination does not disclose evidence of tumor or other evidence of disease elsewhere. An inguinal lymph node is removed.

# **AMR Seminar #63**

## **Quiz Case – #2**

**Contributor:** Saul Suster, M.D.

(Consult case submitted by Dr. Pablo Ortega from Ecuador, South America).

**Clinical History:** A 68 year old man was seen for a large (8cm.) soft tissue mass in the lumbar region. No other significant history available. No other tumor on extensive clinical workup.

# **AMR Seminar #63**

## **Quiz Case – #3**

**Contributor:** Saul Suster, M.D.

**Clinical History:** A 19 year old man was seen for shortness of breath. CT scan of the chest revealed a left lung mass involving the pleura and irregularly infiltrating the left lower lobe. A left lower lobectomy was performed. The resected specimen showed an ill-defined 6.5 x 4.5 x 4.0 area within the lung parenchyma composed of tan-yellow soft tissue extending to the pleural surface.