COMMENTS TO AMR SEMINAR #51

CASE NO. 1 – CONTRIBUTED BY PHILIP ALLEN:

Carlos Bacchi: Could this be just a cutaneous histiocytoma, hemosiderotic subtype, associated with an approcrine gland cyst due to obstruction of the glandular duct?

David Ben-Dor: The epithelium of the large cyst in my slide looks more flattened and squamoid, while the smaller inclusions to the side are lined by columnar epithelium with apocrine features. The coexistence of epithelium with a particular type of stroma reminds me of the mucinous cysts in the pancreas (with ovarian stroma) or the MESK lesions well known to some members of the group (who popularized the entity). If people still believe that fibrous histiocytomas can be reactive to some sort of insult, then maybe this proliferation is secondary to leaked cyst fluid? We have seen previous contributions by members of hemosiderotic lesions in the ankle, which were thought to be secondary to stasis (I apologize for not remembering the name of this entity which is rather long- I'm getting old) This lesion is on the calf, so maybe there is an element of vascular insufficiency here? The spindle cell proliferation is cellular and mildly atypical, and there is some fat involvement on the side (shades of DFSP), so the possibility of this recurring should be taken into account.

Gerald Berry: I agree with the diagnosis.

Michele Bisceglia: Apocrine gland cyst with hemosiderotic dermatofibroma-like stroma of the skin and subcutis of the calf. I was not aware of this new variant of cutaneous benign fibrous histiocytoma of the skin. Do not understand the relationship between the cyst and the FH, maybe the cyst is the induction effect by FH.

Ira Bleiweiss: New one. Never seen anything like this before.

Tom Colby: I think one can pick any name that they like for this. To me the lesion is benign and apocrine cyst with dermatofibroma-like stroma is entirely reasonable. I wondered if maybe the cystic change were secondary; i.e. which came first: the cyst or the stroma?

Kum Cooper: Thanks Phil for my first encounter with this interesting case. I thought that hemosiderotic FH arising in the wall of an apocrine cyst was more appropriate. Thanks for the great review of the variants of FH. I can never keep up with them all!

Göran Elmberger: New to me. Seems to be a good fit with Gonzales' original description, including apocrine-like epithelium with focal squamous metaplasia and prominent muscularized venules. In my sections, I did not see associated sebaceous structures. AR? GCDFP-15? I personally like the author's discussion on the nature of the lesion when he discussed the possibility of this actually being a neoplastic "proliferative" lesion – dermatofibroma variant - rather than reactive – "dermatofibroma like stroma". To me the spindle cell component seems just a bit too much not to represent a tumorous proliferation in itself. If the cystic component should be viewed as a secondary "induction" phenomenon or part of a collission/hybrid lesion, I have no clue. Misnomer? Hemosiderotic dermatofibroma with stromal induction of apocrine cyst (or steatocystoma simplex) as an alternative.

Giovanni Falconieri: Quite difficult, Phil. We do not have access to the referenced journal; hence I could not see Dr. Gonzalez's paper. Nevertheless, I must confess that I would favor a neoplastic (a "true" hemosiderotic DF) rather than a reactive, DF-like change; in fact, the growth pattern and cellularity look almost identical to those seen in cutaneous dermatofibroma including the indistinct, margins at the periphery. Microscopic changes seen in the adnexal skin units are to me secondary to distortion/compression effect exerted by the fibrohistiocytic lesion growing at a snail rate. Thank you for this submission and the quick overview of DF. I look forward to reading the experts' opinion as to fill another gap of ignorance!

Cyril Fisher: Dermal adnexal cyst with hemosiderotic BFH-like stroma as described, but not yet clear whether this is a defined entity. Nice summary of BFH, thanks, Phil.

Christopher Fletcher: I have seen four or five similar cases in the past and, to be honest, have interpreted them somewhat differently. To me, the appearances are those of a haemosiderotic fibrous histiocytoma (dermatofibroma) within the center of which there is some type of inclusion cyst lined mainly by squamous epithelium but focally showing apocrine metaplasia. I have always assumed that this represents an unusual cystic alteration in an entrapped skin adnexal structure, and I have never thought of the cystic component as the primary 'event'. In cases such as this, one can always see fibrous histiocytoma-type tissue all the way around the cyst, as is pretty much evident in this particular case as well. Perhaps the dermatopathologic experts in our group can provide greater insight.

Jerónimo Forteza Vila: We had never seen this entity previously.

Masaharu Fukunaga: Thank you very much for the very rare case and comments. Cysts and glands are unusual. I did not see before. Hemosiderotic dermatofibroma-like change looked neoplastic rather than reactive. How about a collision lesion?

Thomas Krausz: I feel that the main pathology is a fibrous histiocytoma with entrapment of eccrine appendages leading to cystic change as a result of obstruction. I do not favor a fibrous histiocytoma-like stroma concept. The apocrine features are not entirely convincing.

Janez Lamovec: Of the three cysts present in my slide, there is only a small one that shows some apocrine type epithelium; most of the epithelial lining is represented by flat to cuboidal and squamous cells. The hemosiderotic histiocytoma-like stroma appears to be reactive.

Thomas Mentzel: The lesion represents a relatively deep-seated dermatofibroma with areas of hemorrhage and small pseudovascular spaces in association with an epithelial cyst. The cystic space is lined partly by squamous epithelium partly by one or more layers of epithelial cells. Did epithelial cells stain positively for cytokeratin 7 (to confirm a glandular cyst)?

Liz Montgomery: Seems like much ado about nothing. Looks like a fibrous histiocytoma that is next to a benign skin adnexal cyst to me.

Giuseppe Pelosi: This is a very nice histologic case showing an apocrine cyst (apocrine hidrocystoma) associated with dermatofibroma with angiomatoid features. This association was unexpected for me, and I agree with Dr Allen that this case is absolutely rare.

Juan Rosai: Nice combination of benign cutaneous fibrous histiocytoma and apocrine hidradenoma. The FH component has focal angiomatoid features. It is difficult to figure out which came first, but I have the impression that the basic disease is the fibrous histiocytoma, which perhaps has induced a cystic dilatation of the apocrine ducts due to obstruction.

Josh Sickel: Interesting case. I would have initially guessed these lesions were completely unrelated. The number of reported cutaneous histiocytoma variants is astounding.

Dominic Spagnolo: Looks exactly like the cases described by Dr. Gonzales - what a great case! Was not aware of this lesion. Thanks Phil.

James Strauchen: Cystic DF or cyst with DF-like stroma. I have never seen one before!

Lawrence Weiss: I think that it is a bonafide dermatofibroma, and it is associated with an apocrine cyst. Typical dermatofibromas show a relationship with the overlying epidermis, causing hyperplasia, etc., so it is not surprising to be associated with an epithelial cyst. Twenty-nine references on variants of dermatofibroma just show how variable these lesions can be.

CASE NO. 2 – CONTRIBUTED BY CARLOS BACCHI:

Phil Allen: Possible glomangioma, posterior mediastinum. I always like to see more obvious glomus cells before I feel confident with this diagnosis. Some of this looks a bit like a spindle cell hemangioendothelioma. I have to admit that I betray my conservatism with the term spindle cell “hemangioendothelioma.” Similarly, I have grown rather Reaganesque when interpreting positive smooth-muscle actin and type IV collagen stains, or indeed, all immunohistochemistry from that matter, and like many pathologists, have to beat about the bush.

David Ben-Dor: At first glance, this is a cavernous vascular tumor; the typical glomus cell proliferation is inapparent and found only focally- you have to think of the possibility and look for it. To think of this in the context of a mediastinal mass, well you deserve a lot of credit, Carlos. I hope that in the event that this type of lesion turns up, I will think of this possibility.

Gerald Berry: I have not seen this tumor in this site. Nice example.

Michele Bisceglia: Glomangioma of the posterior mediastinum. Agree with diagnosis. Had the opportunity to see 2-3 cases like this, one in the subcutis of the chest in a young male; this lesion was of very large size (glomangiomatosis). Indeed, this a deceptive variant, which can be misinterpreted as cavernous hemangioma.

Ira Bleiweiss: Very difficult case. Is this another "theme" seminar?-see case 3 (mine). Without the immuno, I would have thought cavernous hemangioma.

Tom Colby: Agree with diagnosis; I initially missed the interstitial cells but assuming they fit immunohistochemically, I would go along with glomangioma.

Kum Cooper: Carlos, I must confess that I was working my way down the hemangioendothelioma route (? Composite ? Kaposiform). I am still not struck with the cytomorphology of glomus tumor. I look forward to the STT guru opinions. Other markers that may be attempted include D2-40 and Fli-1 for the stromal cells.

Göran Elmberger: Challenging case. Dominating "angioma" component and not quite characteristic glomus cell morphology but I guess with the right supportive IHC as you indicated, I would agree with dx. Thanks.

Giovanni Falconieri: Challenging lesion. I wonder how many people would jump straight to cavernous hemangioma given the overall vascular architecture that obscures the diagnostic glomoid features. Excellent case and discussion, Carlos. Thank you for this contribution.

Cyril Fisher: Glomus tumor – very good case.

Christopher Fletcher: The appearances in this case seem to me a little unusual for a glomangioma. The perivascular cells present in this lesion are mainly ovoid or spindled, and lack the sharply defined cell membranes of a usual glomus-type lesion. Also, the vessels are more uniformly dilated than typically seen in that context. There are, however, small foci with very glomoid cytomorphology. Conceptually, I agree that this tumour likely belongs somewhere in the spectrum of myopericytic lesions, but I am not sure that I would have used the 'glomus' word in this particular case.

Jerónimo Forteza Vila: The morphological features raise the differential diagnosis with cavernous hemangioma, hemangioendothelioma and vascular variant of Ewing's tumor.

Masaharu Fukunaga: I agree with the diagnosis of glomangioma. It is very educational. It focally looks like myopericytoma. Thank you for the beautiful case and the description, Carlos.

Thomas Krausz: Cavernous hemangioma with "cellular" septae (mostly pericytes and histiocytes). Histologically strictly defined glomus cells are not so obvious to me on H&E.

Janez Lamovec: Nice case. Vascular spaces very much dominate the histologic appearance and pericytic lining is difficult to appreciate in many fields.

Thomas Mentzel: Histologically, dilated vascular spaces lined by uniform endothelial cells and surrounded by plump spindled and round myoid cells are seen. Vascular structures are set in fibrosed stroma. For me, the perivascular cells do not show convincing features of glomus cells (as in Case 3), and I would label this as a cavernous hemangioma with perivascular proliferation.

Michal Michal: I would diagnose whatever hemangioma but not a glomangioma. The cells of the tumor do not seem to me to be "glomus-like" quality.

Liz Montgomery: This is interesting. The slide I got has mostly a component that looks like cavernous hemangioma with a backdrop of bland spindle cells, and there is a small area with slightly rounded cells. These slightly rounded cells seemed more spindly than those in the usual glomus cell tumor, and the whole picture reminded me more of spindle cell hemangioma/hemangioendothelioma despite the odd size and odd location. Curious what others think.

Giuseppe Pelosi: I agree with the diagnosis of glomus tumor of the mediastinum, even though I recognize that the histologic features of this tumor are quite unusual for such entity also in this anatomical location.

Juan Rosai: This is not exactly my idea of a glomus tumor, although I recognize the fact that we are dealing with a vascular neoplasm having a component of pericytes and perhaps glomus cells. I am more impressed by the complexity of the vascular proliferation and the not insignificant component of endothelial cells. I am also bothered by the fact that the tumor is said to invade the adjacent lung. I'm afraid this tumor may be some sort of hemangioendothelioma, i.e., borderline vascular tumor with the capacity for local aggressive behavior.

Josh Sickel: At first glance, I assumed this was a cavernous hemangioma arising in an unusual location. Carlos, thanks for the histologic tutorial in pointing out the salient features of this peculiar lesion.

Dominic Spagnolo: This is a first for me - have not encountered pulmonary or mediastinal glomus tumors before. I was thinking cavernous hemangioma initially. Wonderful case thanks.

James Strauchen: Glomangioma. I missed the glomus cells altogether!

Saul Suster: Very unusual vascular neoplasm – my initial impression was that we were dealing with a spindle cell hemangioma on account of the cavernous vascular spaces and spindle stromal cells. In some areas there seem to be

clusters of ovoid cells that are reminiscent of glomus cells, but are not quite convincing. The characteristic perivascular hyalinization of glomangioma is not present. I suppose this could represent an unusual glomus tumor of the posterior mediastinum (I have never actually seen one before) provided that the smooth muscle actin stain shows convincing staining in the appropriate cells and there is negative staining for CD31/CD34. But the immunohistochemical results would have to be spectacularly convincing for me to make this diagnosis.

Lawrence Weiss: The glomus component is subtle. It is good to see that others are using collagen IV, which I think can be a very helpful stain at times.

CASE NO. 3 – CONTRIBUTED BY IRA BLEIWEISS:

Phil Allen: Glomus tumour of the stomach. This is more like my idea of glomus tumor. There are a few glomangiomatous areas in this predominantly solid tumor.

Carlos Baachi: This is really a nice classic example of glomus tumor in the stomach.

David Ben-Dor: The fact that we have two glomus tumors in a row- is this the product of intelligent design? In any case, a gastric glomus tumor was presented by Saul at the meeting organized by Michele in Italy in 2002, and I presented another one at Michal's meeting in the Czech Republic two years ago. When I prepared my presentation, I wrote Henry Appelman (who wrote the original article in Cancer in 1969 while he was at the AFIP) to inquire how often he sees these things, and he answered in his colorful fashion that they are "as rare as hen's teeth" (to use a rather quaint expression). So while rare, they do crop up here and there.

Gerald Berry: A second nice example of glomus tumor. I remember your previous submission!!

Michele Bisceglia: Glomus tumor of the stomach. Agree. We have seen 2 cases here as well.

Tom Colby: Agree with diagnosis.

Kum Cooper: Thanks Ira. This certainly looks like a glomus tumor to me. I also saw a case in the stomach here in Vermont in the last year or two!

Göran Elmberger: After seeing the previous case from Carlos, this was simple. Always on top of my differential in future. Ha-Ha. Enough vascularity to indicate glomangioma variant?

Giovanni Falconieri: Another collectible item, thanks Ira. Obviously, I have no objection to your interpretation, nor have I any valid diagnostic alternative.

Cyril Fisher: Nice contrast with previous case- I assume IHC is appropriate.

Christopher Fletcher: A beautiful and convincing case, Ira! Given the prominence of the dilated vascular spaces in this particular example, one could have used the term glomangioma!

Jerónimo Forteza Vila: We agree with you.

Masaharu Fukunaga: Beautiful case of glomus tumor of the stomach.

Thomas Krausz: Great example. I would do a congo red to see whether the focal homogenous/hyalin matrix is just basement membrane/collagen or amyloid (unlikely)?

Janez Lamovec: A good case to complement Case 2.

Thomas Mentzel: Thanks for this nice case of gastric glomus tumour.

Liz Montgomery: This is a beautiful typical glomus tumor. Did not realize these showed calcifications so it was nice to see this beautiful example. Too bad there is no mucosa on the slide.

Giuseppe Pelosi: This is a spectacular case of glomus tumor of the stomach, with classical and diagnostic features for this entity.

Juan Rosai: This is a glomus tumor all right! It is absolutely classic of the entity. Parenthetically, I have now seen three cases of glomus tumor of the stomach that have behaved in an aggressive way, one of them presenting with multiple satellite nodules around the main tumor mass and vascular invasion. The morphological differences with case 2 are obvious to remark on them, CD117 and CD34 ought to be negative, but I would do them just for fun.

Josh Sickel: Ira, thanks to your memorable Seminar 9 case, I was able to diagnose a gastric glomus tumor several years back. Another nice example for the teaching collection!

Dominic Spagnolo: You're kidding, following on from case 2! Nice case of gastric glomus tumor, thank you.

James Strauchen: Neat!

Lawrence Weiss: Classic case. Gorgeous histology.

CASE NO. 4 – CONTRIBUTED BY KUM COOPER:

Phil Allen: Uterine malignant ectomesenchymoma with neuroblastomatous and rhabdomyosarcomatous differentiation associated with adenocarcinomatous components, presumably an unusual variant of malignant mixed mesodermal tumour, with extensive vascular invasion. I did a quick 10-year search of the pathology literature and could not find an exactly similar case. The closest was the article by Cokelaere K, Michielsen P, De Vos R, and Sciot R, entitled "Primary mesenteric malignant mixed mesodermal (Mullerian) tumor with neuroendocrine differentiation," in Mod Pathol, May 2001, 14(5) p515-20, but it is a poor match. Thanks for the contribution of this possibly unique case, Kum.

Carlos Baachi: Thanks Kum for sharing this rare tumor with us. It is interesting that on morphologic grounds only one is able to make the diagnosis of malignant mesenchymoma as the neuroblastic and gangliocytic elements with rhabdomyoblasts and neuropil structures are all very evident on the HE section.

David Ben-Dor: This is quite a primitive tumor and I gave up trying to make sense of it, but with Kum's expert guidance, I could locate the various elements he pointed out (the neuropil and the rhabdomyoblasts). The neuropil looks so much like brain that I was surprised to learn that it is S100 positive, meaning that it is derived from schwannian elements and not the neuronal cells themselves. As for the glomangioma, this case requires thinking "out of the box", given the clinical setting. In contrast to its pastoral nature, you can see some wild pathology in Vermont!

Gerald Berry: I didn't appreciate the ganglionic component on my slide. I was stuck at undifferentiated malignant neoplasm!

Michele Bisceglia: Malignant ectomesenchymoma arising in a uterine MMMT. Given the definition of ectomesenchymoma as a neural crest tumor with rhabdo differentiation, I wonder whether even medulloblastoma with rhabdo differentiation (medullomyoblastoma) and Merkel cell tumor with rhabdo differentiation (Eusebi et al, AJSP 24: 223-230; 2000) can be included in this spectrum. Sometimes rhabdo differentiation is only discovered at the immunohistochemical (and I suppose also only ultrastructural) level without any histologic hints of rhabdomyoblastic morphology, as it happens in 2 cases in our files here (one case of medullomyoblastoma in a child so designated based only on immunohistochemistry and in one case of Merkel cell tumor of the gluteus in a lady).

Ira Bleiweiss: Never knew of this.

Thomas Colby: Agree with diagnosis. I had difficulty finding rhabdomyoblast-like cells but putting the entire scenario together, MMMT seems most reasonable.

Kum Cooper: My case. I hope that all your slides have the rhabdomyoblastic component!

Göran Elmberger: Very interesting and difficult case. Wonder if case should still be classified as carcinosarcoma (MMMT) with sarcomatous overgrowth. The present case illustrates the recommendation to extensively sample any uterine high-grade sarcoma with heterologous differentiation to confirm or rule out a carcinosarcoma.

Giovanni Falconieri: Excellent case, Kum. I do not know the entity. Instructive and challenging contribution.

Cyril Fisher: Terrific case, Kum.

Christopher Fletcher: What a remarkable case! Based on your description of areas of adenocarcinoma elsewhere, then personally I think I might have regarded this as MMMT with heterologous neuroblastomatous and rhabdomyosarcomatous differentiation, rather than using the term 'ectomesenchymoma', since the latter is quite poorly defined in the literature and has been used for quite a variety of different-looking tumors. As you know, rhabdomyoblastic differentiation in MMMT seems to be really quite common, but any type of neural crest differentiation in this context, as far as I know, is vanishingly rare – certainly I have never seen anything like this case!

Jerónimo Forteza Vila: H&E features are not enough to diagnosis this entity. Immunohistochemistry is required. Very interesting case.

Masaharu Fukunaga: Carcinosarcoma with prominent (primitive) neuroectodermal differentiation. There are scattered small glands. I missed rhabdomyoblasts and ganglion cells. I agree with the diagnosis of malignant ectomesenchymal Tumor arising in a uterine MMMT. Thank you very much for the beautiful and rare case, Kum.

Thomas Krausz: Amazing what MMMT can do.

Thomas Mentzel: Thanks a lot for sharing this extraordinary case.

Liz Montgomery: Thanks for sharing this rare and horrible looking neoplasm. Did not think of MMMTs as neoplasms with round cell tumor components so this was very instructive for me.

Giuseppe Pelosi: This is a very difficult case of malignant ectomesenchymoma arising in the setting of uterine MMMT. I congratulate Dr Cooper for this extraordinary tumor, very unusual for me.

Juan Rosai: The sections show a highly undifferentiated malignant neoplasm with features suggestive of a primitive neural nature. In view of the presence (according to the enclosed report) of a glandular component and rhabdomyoblastic differentiation, I would agree with the contributor that this represents a mixed müllerian malignant tumor in which most of the epithelial component is represented by neural/neuroendocrine tissues, an occurrence well documented in the literature (Am J Clin Pathol 86: 438, 1986). Incidentally, the coexistence of small cell neuroendocrine carcinoma and rhabdomyoblastic differentiation in the same tumor is something that we have seen in many situations, and that we commented upon in a paper we wrote some years ago (Am J Surg pathol 24: 223, 2000).

Josh Sickel: Reminds me of a primary endometrial PNET-like tumor we observed in an elderly woman. Despite multiple sections, an epithelial component could not be demonstrated. Thanks for this collectors item!

Dominic Spagnolo: A rare and spectacular case indeed. I agree it is essentially a MMMT with extensive neuroectodermal differentiation, similar to a case reported by Masa in 1996 (Histopathology 1996; 29:565-70). Thanks for the case Kum.

James Strauchen: Ectomesenchymoma in MMMT. I was unaware of this entity. I thought of high-grade endometrial stromal sarcoma.

Saul Suster: Agree with diagnosis. Very exotic case!

Lawrence Weiss: Do you think this may be related to the pure rhabdos that one rarely sees in the uterus? Great case, very convincing workup.

CASE NO. 5 – CONTRIBUTED BY IVAN DAMJANOV:

Phil Allen: Multiple bladder recurrences invading bone of a low grade spindle cell sarcoma with myxoid areas, not further classified, appearing 20 years after excision of urinary bladder "leiomyoma." I can do no better than Drs. Guillou and Jean-Michelle Coindre. I wondered about a clear cell sarcoma but the nucleoli are too small. I can't account for the amianthoid areas either.

Carlos Baachi: Low-grade sarcoma NOS.

David Ben-Dor: The histology looks rather bland in contrast to the aggressive behavior. It's interesting that the luminal cystic component was preferentially necrotic- was this portion different in nature or was this due to a mechanical problem (such as twisting of a pedicle)?

Gerald Berry: Agree. Nice case.

Michele Bisceglia: Low-grade sarcoma of the bladder, multinodular. Agree.

Ira Bleiweiss: Sarcoma, NOS. Not so low grade from the behavior. Nothing fibromyxoid in my slide.

Tom Colby: Agree with diagnosis of low-grade sarcoma, not otherwise specified; major lesions in the differential appeared to have been excluded with the immunohistochemistry and genetic studies.

Kum Cooper: Ivan, I do not have any other suggestions. You seem to have covered all "bases". I enjoyed meeting your colleague, Sam, recently!

Göran Elmberger: Interesting case. No suggestions for subclassification.

Giovanni Falconieri: Clinical history is in keeping with a low grade sarcoma, perhaps a (myo) fibroblastic sarcoma. I do not a have better differential. Stretching a little bit my imagination, the short storiform arrangement of tumor cells along to some "ropy" collagen could raise the possibility of some sort of CD34 negative solitary fibrous tumor.

Cyril Fisher: This does not quite resemble low grade fibromyxoid sarcoma and the term fibrosarcoma NOS might be used here.

Christopher Fletcher: This seems to be a morphologically very unusual tumour, the like of which I cannot recollect seeing in the bladder before. Certainly, I cannot improve on the suggestions which you and the French Sarcoma Group have made in labeling this as an 'unclassified low grade sarcoma'.

Jerónimo Forteza Vila: We had thought about the possibility of "low grade fibrosarcoma with pseudorosettes".

Masaharu Fukunaga: I have only seen a few cases of bladder sarcoma in my hospital. I agree with low grade spindle cell tumor. I considered GIST or SFT, but immunohistochemically it is not compatible.

Thomas Krausz: I have no new suggestion. I assume the biopsy 20 years ago showed a similar tumor. Was that also CD34 negative? Malignant SFT can be focally CD34 negative.

Janez Lamovec: Although there are no giant collagen rosettes present, there is some suggestive arrangement of fibroplastic cells around quite prominent collagen deposits. Perhaps this tumor belongs to the rest of 10% cases of LGFMS without a "specific" genetic alteration.

Thomas Mentzel: Given the histopathological features, I do believe as well that the neoplasm is best regarded as a low-grade fibroblastic sarcoma.

Liz Montgomery: This bladder neoplasm does not look like a low-grade fibromyxoid sarcoma, and I would not have bothered with the search for the fusion products but do not have a name for it either. It seems like it was given the correct descriptive name. It would have been interesting to see the old "leiomyoma".

Giuseppe Pelosi: Morphologically, this tumor looks like a leiomyosarcoma, even though it is a bit strange that the tumor was eroding and infiltrating the bone.

Juan Rosai: I agree that we are dealing with a sarcoma involving the bladder. From a morphologic standpoint, I would favor the diagnosis of leiomyosarcoma (perhaps representing a recurrence from the smooth muscle tumor removed from the bladder many years ago), but the immunohistochemistry does not seem to fit. In any event, it is not an example of Evans' low grade fibromyxoid sarcoma.

Josh Sickel: I can't improve upon your diagnosis. Amazing that such a histologically bland lesion can behave so aggressively. Were you able to retrieve the original "leiomyoma"?

Dominic Spagnolo: A very unusual bladder tumor. I can't do better than recurrent low grade sarcoma unspecified of the bladder. A CD117-negative extraintestinal GIST is a possibility.

James Strauchen: Low-grade sarcoma, considered SFT.

Saul Suster: How about calling it just plain old fibrosarcoma?

Lawrence Weiss: I don't know what to call it, but you just found another CD10+ tumor.

CASE NO. 6A – CONTRIBUTED BY OTTO DIETZE:

Phil Allen: Chronic histiocytic intervillositis at 20-24 weeks gestation. I had never heard of it before and did not even appreciate the intervillous infiltration. Thanks for the contribution.

Carlos Baachi: Thanks for teaching me about chronic histiocytic intervillositis. I was not aware of this entity.

David Ben-Dor: I will admit something that I hope won't be cause for my being drummed out of the group - I usually don't look at slides from placentas that carefully; after reading the comments, I did find rounded cells in the intervillous space but they looked deciduoid to me. I promise that from now on I will examine carefully placenta slides to verify whether decidual cells can ever leak into the intervillous space.

Michele Bisceglia: Chronic histiocytic intervillositis. Nice case. Thank you. I was not aware of the entity and would not have diagnosed it correctly.

Kum Cooper: I recognized the intervillous fibrin deposition due to a paper that was published by a colleague of mine in Vermont: Am J Surg Path 2006; 30(6): 760-765; but am not sure how to distinguish the two entities?

Thomas Colby: Agree with diagnosis. A new entity for me.

Göran Elmberger: Interesting case.

Giovanni Falconieri: This is a didactically valid and beautiful example of chronic intervillositis in a third trimester placenta. In addition to inflammatory cells capping around villi, there is evidence of villous dysmaturity (uneven branching, fibrosis and early ischemic changes of several units, - admitted, however, that the section was taken from the central plate). The syncytiotrophoblastic knots seem to be beyond normal limits and indicate a prolonged hypoxic condition. Nucleated red blood cells are also present within some villous capillaries: this is abnormal after the 12th gestational week and denotes further fetal suffering. If the decidual aspect is enclosed in the section, I may also suppose that there are changes consistent with chronic deciduitis whereas the fetal plate is unremarkable. These features altogether are pretty well consistent with history of fetal IUGR. Nice case of uncommon placental pathology. Thanks for this contribution.

Jerónimo Forteza-Vila: Thank you for sharing this unusual case.

Masaharu Fukunaga: Very nice and rare lesion, thanks a lot. Are there any pathologic features in the cord?

Thomas Krausz: Very nice example. We also have a few cases on our file.

Liz Montgomery: Thank goodness someone knows something about the placenta. Of course, I had never heard of chronic histiocytic intervillositis. This looks very interesting and suspect knowledge of this entity is very helpful in defending our obstetrical colleagues when (not if) they get sued.

Giuseppe Pelosi: I'm sorry, but I pass because I do not have much experience with placental pathology.

Josh Sickel: Fascinating case. I've never encountered this lesion before.

Dominic Spagnolo: A great case of chronic intervillositis. I have only seen this as a seminar case before - thank you.

James Strauchen: Histiocytic intervillitis. I was unfamiliar with this entity but the same certainly describes the pathology!

CASE NO. 6B – CONTRIBUTED BY OTTO DIETZE:

Phil Allen: Haemosiderotic splenomegaly (1100g) of unknown cause with Gamna-Gandy bodies. I wonder if there is any malaria in Albania.

Carlos Baachi: Yes, these are Gamma-Gandy bodies (siderotic nodules). As we all know, they are seen in cases of congestive splenomegaly, sickle cell anemia, and hemochromatosis. In Brazil, they are characteristically seen in hepato-splenic form of schistosomiasis.

David Ben-Dor: Isn't congestive splenomegaly a good enough explanation, secondary to possible liver disease?

Michele Bisceglia: Gandy-Gamna bodies in a megalic spleen likely secondary to an underlying chronic liver disease. Agree.

Tom Colby: I think the Gamna Gandy bodies are a nonspecific finding, particularly in this very enlarged spleen, the cause of which is not clear. Some of the changes would be consistent with congestive splenomegaly, but I gave up on splenic pathology long ago.

Kum Cooper: I agree with the Gamna-Gandy bodies which are nicely demonstrated; but there seems to be micro-collections of neutrophils in the red pulp. Did you rule out infections with special stains (Z-N, GMS, Steiner or WS); the latter to rule out bacillary angiomatosis (even though I do not see any vascular/endothelial proliferation).

Göran Elmberger: Interesting case.

Giovanni Falconieri: Agree with the proffered microscopic interpretation of Gandy-Gamna bodies. I have recently seen a case like this where, alike yours, we were not able to detect any ongoing clinical condition.

Christopher Fletcher: I agree that these are Gamna-Gandy bodies.

Jerónimo Forteza Vila: We think that there is a sinusal capillary transformation.

Masaharu Fukunaga: Difficult case, I did not see similar lesion before. I thought some type of hematopoietic tumor at first. What does Gandy-Gamna body represent? I cannot imagine underlying disease.

Thomas Krausz: Agree with your interpretation.

Janez Lamovec: No explanation for this fibrocongestive splenomegaly and Gamna- Gandy bodies.

Thomas Mentzel: Interesting case indeed, however, honestly I have to admit that I had to luck up for the mentioned Gandy-Gamna bodies that seem to be rather unspecific changes in the spleen.

Liz Montgomery: The lesions indeed look like Gamna-Gandy bodies. It seems as though they can be found associated with a number of conditions other than sickle cell disease. Hope liver biopsy will give a better idea about the etiology.

Giuseppe Pelosi: This spleen shows well-formed Gamna-Gandy bodies, very typical in their histopathologic features.

Juan Rosai: Beautiful demonstration of Gamna – Gandy bodies in the spleen. It has been a long time since I last saw one.

Josh Sickel: Agree with diagnosis of Gandy-Gamna bodies.

Dominic Spagnolo: Have no idea why there is such splenomegaly. I agree with the Gamna-Gandy bodies, the white pulp looks atrophic and the red pulp expanded and "busy" looking. But I can't discern a neoplastic infiltrate. I suspect it could be an infective process and spent time looking for parasitized histiocytes and the like, but have drawn a blank. It does not seem to me to be simply chronic passive congestive splenomegaly.

James Strauchen: Gamna-Gandy bodies ? Portal hypertension due to liver disease and/or portal vein thrombosis (Banti's disease).

Lawrence Weiss: No lymphoma here. Just looks like a very congested spleen, with Gandy-Gamna bodies.

CASE NO. 7 – CONTRIBUTED BY VINCENZO EUSEBI:

Phil Allen: Retroareolar, palpable (20mm), In situ (intraduct), squamous cell carcinoma of the breast with myoepithelial differentiation. I agree with the diagnosis. An astounding case.

Carlos Bacchi: Interesting case of in situ squamous cell carcinoma involving the breast. How are myoepithelial cells related with this carcinoma? Looking forward to seeing the AJSP publication!

David Ben-Dor: Brilliant observation. Histologically, I agree with the squamous differentiation. The question is why squamous and myoepithelial differentiation should go together, since otherwise they are unique phenotypes (though they both share in common p63 reactivity)? Can this be rated using the Van Nuys system? What do you tell the oncologists? They continually browbeat me even when there is no possible answer to their questions. Architecturally, this lesion looks very lobulocentric- maybe other portions looked more “ductal” architecturally speaking. Another possibility albeit crazy: this also reminds me of necrotizing sialometaplasia in the palate, which can demonstrate necrosis and reactive atypia of the metaplastic cells.

Gerald Berry: I thought this looked like adenosquamous carcinoma. I did not see invasion in my slide.

Michele Bisceglia: Never seen such combined/hybrid immunophenotype in DCIS of the breast. Ira Bleiweiss presented a case (seminar #46) of invasive adenosquamous carcinoma (low grade metaplastic carcinoma) with myoepithelial differentiation in the same squamous cells (I also subsequently observed an identical example). Further, a week ago or so another case occurred here of invasive metaplastic spindle cell sarcomatoid carcinoma of the breast (with focal areas of squamous cell differentiation and a small focus of osteosarcoma), in which most of the neoplastic (spindle) cells definitely showed myoepithelial differentiation (several +ve markers). In this latter case, we were not able to differentiate between malignant myoepithelioma and metaplastic sarcomatoid carcinoma, which I considered (at least in this latter case) as equivalent.

Ira Bleiweiss: Agree. I have never seen pure squamous cell carcinoma "DCIS" in breast without "regular" DCIS.

Thomas Colby: Essentially agree with diagnosis. I had also wondered about some sebaceous features in some of the cells. I did not pick up any myoepithelial features on the H & E.

Kum Cooper: It looks very metaplastic to me. However, I concede my ignorance to the breast experts! I showed it to Don Weaver, who called it a metaplastic DCIS. I thought that the latter term sounded really great!

Göran Elmberger: Very interesting. I did appreciate the squamoid differentiation myself before reading your diagnosis. When looking after in high power being fostered in lung pathology, I note that neither prominent intracellular bridges or frank keratinization is present. Some cells show a tendency for glandular – ductular differentiation. CEA? Mucin stains? Adenosquamous differentiation (glassy-cell like)?

Giovanni Falconieri: Excellent case, Vincenzo! This is unheard of to me, and I could not add anything to your assessment. Thanks for this contribution.

Christopher Fletcher: This remarkable lesion certainly looks like DCIS showing squamous differentiation. In this context, such differentiation may well originate from myoepithelial cells, but I do not see convincing morphologic evidence of myoepithelial differentiation in the slide which I received. Another truly remarkable case.

Cyril Fisher: Squamous DCIS with myoepithelial proliferation, nice to have a slide of this rare case.

Jerónimo Forteza Vila: We agree with your diagnosis.

Masaharu Fukunaga: Thank you for a very nice and rare tumor. I considered DCIS with squamous differentiation. Myoepithelial differentiation did not come to my mind light microscopically.

Thomas Krausz: Vincenzo, why not the other way around: in situ myoepithelial carcinoma with squamous differentiation?

Janez Lamovec: In spite of a large number of cases of DCIS seen here, we have never encountered a case of squamous cell type of it. The closest we could get was a case of a DCIS with a small squamous morule in one of the DCIS duct in a core needle biopsy specimen; that was after Vincenzo inquired whether we had seen such cases. Anyway, this must really be a rare event.

Thomas Mentzel: It is wonderful to see this interesting case as it has been published in the last issue of the AJSP, many thanks.

Liz Montgomery: This is really something. Metaplastic carcinoma in situ?

Giuseppe Pelosi: I agree with Dr. Eusebi that this tumor may represent a DCIS with prominent squamous differentiation. The differential diagnosis, in H&E stained sections, may include adenosquamous carcinoma of the breast.

Juan Rosai: Spectacular example of ductal carcinoma in situ involving mammary lobules (so called lobular cancerization) associated with marked squamous metaplasia. I don't think I have seen this phenomenon before, at least not to this degree.

Josh Sickel: Very interesting observation. A few months ago, I diagnosed metaplastic carcinoma of breast, with striking squamous differentiation.

Dominic Spagnolo: Unfortunately, a large central chunk of the lesion was missing from my slide. The carcinoma certainly has a squamoid appearance though I could not see good intercellular bridges, nor was there keratinization in my section. It is exhibiting a mixed basal and myoepithelial phenotype. The proposal to call it squamous carcinoma seems fine to me, but there are also intracytoplasmic lumens in a fair proportion of the cells ?? mixed adenosquamous and myoepithelial. Fascinating case - thanks Vincenzo.

James Strauchen: Unusual (metaplastic?) DCIS!

Lawrence Weiss: Could this be "basal cell phenotype" carcinoma in situ, similar to the ER-, PR-, HER2-, p63+ infiltrating carcinomas?

CASE NO. 8 – CONTRIBUTED BY CYRIL FISHER:

Phil Allen: Large (15 cm), probable inflammatory leiomyosarcoma in HIV positive male, pelvis. I agree that this is different from the virus associated smooth-muscle tumors in immune suppressed patients and that the evidence for smooth-muscle differentiation is not particularly impressive.

Carlos Baachi: Interesting that this case of inflammatory leiomyosarcoma was negative for EBV. I wonder how often EBV is present in this type of sarcoma (in HIV+ patients).

David Ben-Dor: I pulled the AJSP with the cited article off the shelf, and the pictures show more classical smooth muscle differentiation than is seen here. Further, the article also depicts "primitive round cell areas" which I think is prominent in this case. The lymphoid infiltrate seems to be more extensive here than what seems to me to be the situation in the cases in the article, at least according to the illustration and description (the infiltrates are described as "variable, and to the degree seen in IMT" (which was a thought that came to mind).

Gerald Berry: I agree.

Michele Bisceglia: Inflammatory leiomyosarcoma in HIV positive male. Around 1 year ago, I saw a case of what I considered an inflammatory leiomyosarcoma of the bone with multiple location (3 locations in long bones of the limbs) in a lady who a few years previously underwent liver transplantation, which had a similar immunophenotype you describe here, and in addition also expressed CK. I sent this case to 2 consultants (members of this club) one of which agreed on the diagnosis, while the latter also based on the EBV negativity (EBER negative), considered the case in point as metastatic leiomyosarcoma (possibly from uterus). The lady underwent a complete clinico-radiological investigation but no primary was found in other sites. I still continue to think that my case could be immunosuppression driven leiomyosarcoma.

Ira Bleiweiss: I agree.

Thomas Colby: Agree with diagnosis. I was struggling to try to make it into some peculiar proliferative reaction to an infection but finally concluded that the process appeared neoplastic (DRC sarcoma, etc.), and the IPOX would certainly favor leiomyosarcoma and the "inflammatory" descriptor is appropriate.

Kum Cooper: Thanks, Cyril, for reminding us of this entity. My response was one that I always shared with residents in Africa...always rule out mycobacterial spindle cell pseudotumor with a simple Z-N stain!

Giovanni Falconieri: Very tough and challenging. My experience with inflammatory LMS is limited to a few slide seminar cases and I have no insight to offer. Thanks for this valuable contribution.

Cyril Fisher: My case. After I submitted it, I remembered that there have been two previous cases of inflammatory leiomyosarcoma from AMR members Drs. Dei Tos (#23, case 6) and Damjanov (#39, case 6), the latter published in Pathol Res Pract. 2003;199:41.

Christopher Fletcher: The morphology of this man's tumour certainly fits very well with the tumors which we originally described as 'inflammatory leiomyosarcoma'. As Cyril indicates, it is sometimes difficult to know for sure whether one is dealing with a true smooth muscle neoplasm or a myofibroblastic lesion. Either way, the majority of cases in this type which we've seen have indeed proved to be low grade in terms of clinical behavior.

Jerónimo Forteza Vila: We thought that a good alternative are ALK positive myofibroblastic tumor and the inflammatory pseudotumor-like dendritic cells sarcoma.

Masaharu Fukunaga: Nice case, I agree. I considered inflammatory myofibroblastic tumor or FDCT. How do you differentiate inflammatory leiomyosarcoma from inflammatory myofibroblastic tumor, microscopically? I might have missed this type of tumor before. Many thanks, Cyril.

Thomas Krausz: Agree with diagnosis. I have seen only a few cases before. Before reading the clinical history, follicular dendritic cell sarcoma and angiomatoid fibrous histiocytoma without angiomatoid areas were also in my differential diagnosis.

Janez Lamovec: On H&E, I would have problems to recognize a smooth muscle nature of neoplastic cells although spindle cell / epithelioid morphology would fit (with a bunch of other tumors as well); a myofibroblastic origin of the present tumor cannot be entirely dismissed.

Thomas Mentzel: An interesting case. Given the reported features and the cytomorphology, I was thinking on inflammatory myofibroblastic tumour.

Michal Michal: Typical inflammatory leiomyosarcoma. I often wonder, whether at least some of these inflammatory leiomyosarcomas do not represent a variant of follicular dendritic cell-like tumors.

Liz Montgomery: This is fascinating. Thought of inflammatory myofibroblastic tumor before reading Cyril's comments, but certainly the HIV history, strong desmin, and presence of the epithelioid lesional cells with prominent eosinophilic cytoplasm are good for an inflammatory leiomyosarcoma (although the myofibroblastic ultrastructural features and the lack of EBV are less good). It might be fun to try an ALK.

Giuseppe Pelosi: This is a very difficult case showing a spindle cell tumor with inflammatory infiltrate. According to morphology and immunohistochemistry this tumor seems to have myofibroblastic lineage, and a diagnosis of inflammatory myofibroblastic tumor could be also rendered.

Juan Rosai: I am not sure I would buy this tumor as an inflammatory leiomyosarcoma. Neither the ultrastructure nor the immunohistochemistry seem to fit. There is a heavy lymphocytic infiltrate collection of histiocytes and numerous psammoma bodies, none of these being common features in leiomyosarcoma. I would be more inclined to think of something along myofibroblasting lines, perhaps a so-called inflammatory myofibroblastic tumor

Josh Sickel: I have difficulty distinguishing these from inflammatory myofibroblastic tumor. Great case and interesting discussion!

Dominic Spagnolo: Very nice case of inflammatory "leiomyosarcoma" in a HIV+ male. Agree with the incomplete phenotype, which seems closer to the subset of desmin positive myofibroblasts rather than differentiated smooth muscle. Thanks for the case, Cyril.

James Strauchen: Inflammatory leiomyosarcoma. I considered FDCT but ruled out by the immuno.

Saul Suster: Very difficult case! Hard to conceptualize this as a leiomyosarcoma without some of the good morphologic features of smooth muscle differentiation and with the weird staining pattern (strong desmin/weak and focal SMA). The tumor shows a prominent storiform pattern raising the possibility of FDCT. Was CD21/CD35 tried on this tumor?

Lawrence Weiss: Interesting case. Not the best developed smooth muscle features histologically.

CASE NO. 9 – CONTRIBUTED BY CHRISTOPHER FLETCHER:

Phil Allen: Undiagnosed, hemorrhagic, hemosiderin rich, vascular proliferation with extramedullary hematopoiesis, probably benign, parotid of female aged 80. This looks as though it ought to be a distinct entity but I do not recognize it.

Carlos Baachi: I initially thought this was a low-grade sarcoma richly vascularized but considering the clinical history, the presence of somewhat malformed vessels in the periphery of the lesion, the degenerative changes like areas of hyalinization of the stroma and presence of rare mitotic figures, I favored reactive benign process.

David Ben-Dor: I think the fibrohemosiderotic changes raise issues similar to those engendered by the apocrine cyst seen earlier in this seminar which has a similar type of stroma. I did find some foci with thin spindle cells separated by erythrocytes reminiscent of Kaposi's, but this finding was not generalized. I think your approach is reasonable.

Michele Bisceglia: Reactive fibrovascular proliferation, possibly engrafted on a vascular malformation. I agree on the interpretation of the case, and found interesting the subtle finding of extramedullary hemopoiesis you indicated, and which occasionally one can see in vascular lesions (have seen this hemopoiesis in 3-4 vascular lesions, 2-3 of which were cerebellar hemangioblastomas).

Ira Bleiweiss: Granulation tissue gone wild.

Thomas Colby: Difficult case. Assuming that some peculiar pseodoangiosarcomatoid carcinoma is excluded, I was certainly worried about a vascular malignancy. Nevertheless, the overall organization of the process and the chronic scarring would be distinctly unusual for an angiosarcoma, and I would favor some descriptive diagnosis but I probably could not avoid sticking "atypical" in there somewhere.

Kum Cooper: My sentiments mirrored exactly those of yours, Chris: reactive myofibroblastic proliferative lesion probably representing an organizing hematoma.

Göran Elmberger: Difficult case. I have not seen anything quite like it. I agree with your suggestions. I only would like to reinforce the value of complete sampling in cases of presumed salivary gland tumors. Recently, I saw a case of sclerosing mucoepidermoid carcinoma with sparsely occuring epithelial tumor tissue and a mesenchymal dominating component not very unlike the present reaction. That case did not show extramedullary erytropoesis or atypical stromal cells.

Giovanni Falconieri: I don't know how to call this, Chris, but I can honestly say that I do not feel at ease with such a morphology (too cellular, scattered atypical cells, several mitoses though none atypical and no necrosis). Although I agree with the "ancientoid changes" present in this lesion, the overall features make me reluctant to sign this as benign. I would defensively consider this tumor of uncertain malignant potential, at best. Thanks for contributing this nice example of a still problematic area of diagnostic surgical pathology.

Jerónimo Forteza Vila: Thank you for the interesting case.

Masaharu Fukunaga: Difficult case. I agree, a reactive process. I considered a possibility of Kaposiform hemangioendothelioma. In vascular lesions, it is often very difficult to decide a neoplasm or a reactive process.

Thomas Krausz: I also favor the diagnosis of vascular malformation with secondary, FNA-induced reactive changes.

Janez Lamovec: The hemorrhages appear to be of different date and so is the stromal tissue having a sort of organizational aspect. I believe that this is a reactive lesion but I am not sure of the original background lesion. Most difficult lesion to interpret.

Thomas Mentzel: Did endothelial cells show loss of WT1 expression, as it has been reported in vascular malformations (Arch Dermatol 2005; 141: 1297-1300) ? Given the lobular architecture (and if WT1 is expressed), I would think of an example of long-standing inflammatory thick-walled hemangioma.

Liz Montgomery: At scanning power thought of epithelioid hemangioma/angiolymphoid hyperplasia with eosinophilia since there is possibly a "feeder" vessel and a (pathetic) lymphoid cuff with a lobulated appearance, but at 10X this idea vanishes (although one wonders how an EH/ALHE would look if it sat for years and got traumatized and sclerosed and the epithelioid endothelial cells grew bored with being epithelioid). The point, however, is that the architecture does go along with a benign process, but what? The eosinophilic flocculent material is reminiscent of that in bacillary angiomatosis, but that does not compute with the history. The FNA/needle biopsy would have been treacherous with all the crazy secondary changes and extramedullary hematopoiesis – glad it was someone else's problem. Do not have a name for the lesion but believe it is benign, and it looks like it is out and the patient is old enough to reduce the probability of it returning in her remaining years.

Giuseppe Pelosi: In my opinion, this lesion could also be malignant, of vascular derivation, possibly originated from vascular malformation. It is a very difficult case!!

Juan Rosai: Difficult case, but it looks neoplastic to me. I would favor a malignant mesenchymal neoplasm probably of a vascular nature and possibly arisen on a vascular malformation.

Josh Sickel: Whenever I see erythroid islands in weird sites, I wonder if the patient has renal dysfunction. I can't add to your diagnosis and agree that it looks benign.

Dominic Spagnolo: I haven't a clue what this is. I'm not sure it is just a reactive process supervening on a vascular malformation. My hunch is that it is a multinodular low grade vascular tumor, unclassified, with secondary changes of thrombosis affecting larger vessels.

James Strauchen: Organizing hematoma with ? vascular lesion. I don't think this is hematopoietic.

Saul Suster: I feel very certain I have seen similar cases before. To me this looks reactive and benign - along the lines of an exaggerated reaction to an organizing thrombus.

Lawrence Weiss: Looks reactive to me, perhaps related to previous trauma. I do not see definite evidence of a vascular malformation. The EMH indicates that it has been there a long time.

CASE NO. 10 – CONTRIBUTED BY JERONIMO FORTEZA VILA:

Phil Allen: Gliomatosis cerebri, frontal biopsy. We don't have a neuropathologist in this department, and I know absolutely nothing about brain biopsies that are not obvious simple tumors, so I cannot contribute anything on this case.

Carlos Baachi: This is a very difficult case for me. I would have to rely in the imaging findings in order to think about low-grade glioma.

David Ben-Dor: There are fragments of seemingly normal brain and others showing hypercellularity, and populated by gemistocytes and oligodendroglial type cells with mild atypia, without neurons. So this is a diffuse tumor which doesn't form a discrete mass. Sadly despite its slow growing nature, I would think the case is hopeless.

Michele Bisceglia: Gliomatosis cerebri. Difficult case. The few cases I have previously seen here were all grade III astrocytomas.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Low grade glioma. Thank you for sharing this unusual case with us from your precious limited tissue.

Göran Elmberger: Interesting even for a non-neuropathologist.

Giovanni Falconieri: Beautiful case, thanks for contributing this unusual example of astrocytic proliferation. These cases are almost impossible to manage, especially when frozen sections are submitted for intra-operatory consultation.

Cyril Fisher: Gliomatosis cerebri, nice example of a rare entity.

Masaharu Fukunaga: I did not see this type of tumor before. As far as this slide is concerned, it looked like reactive gliosis or low grade astrocytoma, but I agree. Thank you very much for the educational case.

Thomas Krausz: The few cases I've seen before, similarly to this one, were all diagnostically challenging.

Thomas Mentzel: Thanks for sharing this interesting case of gliomatosis cerebri, which represents a challenge if no clinical and radiological information are given.

Giuseppe Pelosi: Unfortunately, I do not have enough experience in gliomatosis cerebri to express personal observations.

Juan Rosai: I pass.

Josh Sickel: It's always nice when the clinicians give us a choice of diagnosis A, B or C! This is a very challenging case and deceptively innocuous at first glance. We recently encountered a similar case in a patient with multifocal white matter abnormalities on MRI scan. The biopsy showed a subtle increase in bland glial-type cells. Ki-67 revealed 20% staining, supporting the diagnosis of gliomatosis cerebri.

Dominic Spagnolo: I will defer to the neuropathologists on this one - the distinction between a reactive gliosis and a low grade diffuse glioma can be impossible for me.

James Strauchen: Gliomatosis cerebri! I have never seen one before. Surprisingly low-grade!

Saul Suster: This is why God created neuropathologists!

CASE NO. 11 – CONTRIBUTED BY JANEZ LAMOVEC:

Phil Allen: Metastatic melan-A and HMB-45 positive tumour associated with recurrent uterine leiomyosarcoma and multiple tumors in lungs, liver and axial skeleton. I think the circulated bone tumor is a metastasis. I don't have a lot of faith in the diagnostic specificity of melan-A and HMB45. The bone tumour looks like a carcinoma to me.

Carlos Baachi: I also think that it is a PEComa.

David Ben-Dor: Based on principles such as Occam's razor, one is tempted to think that this tumor is related to the previous ones, possibly on the basis of a subsequent mutation. I recall seeing papers on PEComas of the uterus (though I'm not implying that the previous uterine tumor was misdiagnosed).

Gerald Berry: This is perhaps the most pleomorphic appearing malignant PEComa that I have seen.

Michele Bisceglia: Perivascular epithelioid cell tumor (PEComa), malignant, probably metastatic (to bone) of unknown primary site. Nice and difficult case. Thank you, Janez.

Thomas Colby: Epithelioid malignant tumor, positive for muscle and melanoma markers. I would favor being somewhat descriptive in this case. I think it is difficult to exclude the possibility that this is not some peculiar epithelioid transformation in a metastasis from the leiomyosarcoma and acquired HMB-45 positivity in leiomyosarcomas has been described. Similarly, I have somewhat of a philosophic problem in the ever broadening spectrum of PEComa. If we accept this as PECOMA, why not primary at this site? They seem to be turning up everywhere else.

Kum Cooper: Janez, thank you for sharing this case. I think it is a metastatic xanthomatous leiomyosarcoma that has been described in the GYN tract. I saw a case about 10 years ago in Africa. My colleagues subsequently published the case: Grayson W, Fourie J, Tiltman AJ. Xanthomatous leiomyosarcoma of the uterine cervix. Int J Gynecol Pathol. 1998;17:89-90.

Göran Elmberger: Poorly differentiated sarcomatous tumor with bizarre nuclear atypia and clear cytoplasm. Given your history and the result of the IHC, I guess your interpretation is plausible. Anyhow, I would personally be somewhat skeptical. The risk of this being a metastatic manifestation of previous high grade uterine leiomyosarcoma from a probabilistic point of view is high.

Giovanni Falconieri: Malignant pleomorphic tumor with predominant epithelioid features; combined with immunostains. I do not see valid alternatives to malignant PEComa though "dismantlers" of the PEComa theory advocate that this is a broad group of clinically different lesions sharing morphologic and immunohistochemical phenotypes. In regard to question 2, you may be interested in the paper by Dr. Silva group, published in Ann Diagn Pathol (2005; 9: 43-45) addressing a case of uterine leiomyosarcoma that became positive for HMB45 in the metastases. The authors also claimed that PEC is a smooth muscle cell capable of becoming positive for HMB45. "God knows" answers to questions 3 and 4. Thank you, Janez, for submitting this difficult and challenging case.

Cyril Fisher: Malignant PEComa – looks good to me!

Christopher Fletcher: The appearances and immunophenotype indeed fit well for metastatic malignant PEComa. We have now seen a number of these cases both primary and metastatic in bone, including at least two cases which presented as bone metastases from a previously unrecognized or clinically undisclosed uterine primary. However, in this case, it does seem that the uterine leiomyosarcoma was quite different and hence the questions raised by Janez may go unanswered. Dedifferentiated clones might have escaped sampling previously. Dedifferentiated tumors can express strange epitopes. EM? I suppose ER/PR was negative.

Jerónimo Forteza Vila: Clinically, it seems a metastatic process.

Masaharu Fukunaga: Very educational and rare case, thank you, Janez. The tumor seemed to be metastatic carcinoma of the kidney or adrenal gland. It is very interesting that PEComa arises in bone tissue. This case lacks the characteristic feature of perivascular proliferation.

Thomas Krausz: Despite the immunoprofile supporting a PEComa diagnosis, I feel your number 2 option is more likely. I assume the patient received chemotherapy following the recurrence of the leiomyosarcoma. If that is the case, then a phenotypic change in the leiomyosarcoma is possible. The histologic features are consistent with a high grade, epithelioid/clear cell leiomyosarcoma. Regarding the positive melanoma immunomarkers ……, that is where my story is limping.

Janez Lamovec: My case. The patient is still alive, with multiple metastases, 8 months following bone surgery.

Thomas Mentzel: Thank you very much indeed for this fascinating case of pleomorphic clear cell PEComa of bone (either primary or metastatic)!

Liz Montgomery: Cannot think of a better diagnosis than malignant PEComa with the appearance of the lesion and the described staining profile.

Giuseppe Pelosi: This case illustrates a spectacular PEComa of epithelioid type. Morphologically, a differential diagnosis with metastatic renal cell carcinoma or clear cell chondrosarcoma should be also done. I never saw PEComas primary to bone, but I trust the extraordinarily vast experience of Dr. Fletcher who had seen occasional cases of primary bone PEComas.

Juan Rosai: I guess we will have to call this tumor a pleomorphic PEComa in view of the immunohistochemical profile, but I'm beginning to have bad feelings about this "entity." At the H&E level, my other considerations were clear cell chondrosarcoma and metastatic renal cell carcinoma.

Josh Sickel: A major diagnostic clue was that it was highly unlikely that Janez would submit a metastatic renal cell carcinoma to the AMR club! Primary PEComa of bone? Thank you for sharing this unique case (is this an upcoming case report in AJSP?)

Dominic Spagnolo: I agree with the diagnosis of malignant PEComa - it is a great example. I have no experience with this as a primary bone lesion though they have been reported rarely. Presumably, scans at the time of diagnosis did not show lesions elsewhere. I would think there is no relation to the uterine leiomyosarcoma.

James Strauchen: Malignant PEComa by immuno. I also considered RCC.

Saul Suster: I agree with your interpretation Janez that this most likely corresponds to a pleomorphic variant of myomelanocytic tumor (PEComa). However, I cannot escape considering the possibility that it represents a metastasis from the uterine leiomyosarcoma, which has now switched on new molecular targets and is expressing smooth muscle and melanocytic markers. Maybe this case is trying to tell us something about the whole concept of these tumors!

Lawrence Weiss: I think that the likelihood is that this tumor is metastatic from the neoplasm in the uterus, despite the fact that you were unable to find a component of PEComa in the primary tumor. If there are primary PEComas of bone, these cases should be published.

CASE NO. 12 – CONTRIBUTED BY MICHAL MICHAL:

Phil Allen: Cribriform adenocarcinoma (CAT), base of the tongue with left lateral neck nodal metastases and two year survival after surgery and radiotherapy. I was not aware of the entity. I found the discussion most convincing, and I think I could recognize the tumour if I see it again. Many thanks to the contribution, Michal.

Carlos Bacchi: Polymorphous low-grade adenocarcinoma of salivary gland.

David Ben-Dor: The question of what makes one lesion seem distinctive from another is perceptual and has a definite subjective component (re: the perpetual debate between "lumpers" and "splitters"). The root of the tongue would seem to be an odd place for salivary gland tumors to arise, PLGA included, and it's reasonable to think that a group of tumors which elects to appear in this location and which shows particular clinical behavior (in this case the early lymph node metastases, though not being a specialist in head and neck pathology I couldn't say how unusual this is for PLGA as a group) might be different than other tumors belonging to the same family which resemble it. In my own mind, I associate PLGA with a greater variety of architectural forms than is displayed here in my slide. I am impressed with a mostly solid appearance more than with glandular lumina or cribriform areas which appear here to be in the minority- with at least some degree of infiltration as single glands or "indian files" which I don't find here. As far as the nuclear features in the AFIP fascicle on salivary gland tumors from the third series (1996), there is in the section on PLGA a high power image (p. 223-fig.5-97) captioned "Bland nuclear morphology" showing overlapping pale enlarged nuclei. Admittedly, these aren't necessarily the light bulb like "orphan Annie" nuclei of thyroid tumors but they do resemble to some extent the nuclei in the slide I have in front of me. This calls to mind another festering issue, that of the "pseudo-clear nuclei" which can be seen in non-neoplastic thyroid conditions such as Hashimoto disease and can lead to over-diagnosis of malignancy vs. true optically clear nuclei (this issue addressed by Saul in an article he wrote in the last century (!- doesn't this really make us feel old?). Whether the nuclei of this condition (as seen in the slide distributed) resemble more the latter than the former, can be debated to the same degree that thyroid pathologists might disagree whether a given case whether is a follicular adenoma or "encapsulated follicular variant of papillary carcinoma".

Gerald Berry: I must admit that I would have placed this low grade carcinoma in the PLGA camp but I agree with your arguments for separating into the CAT lesion.

Michele Bisceglia: Cribriform adenocarcinoma of the tongue (M. Michal). Nice case. Striking similarity to papillary carcinoma of the thyroid. Michal, you say it is difficult to explain why CAT appears to be restricted to the tongue. Elsewhere I heard (probably from M. Luna at a histopathology course in Udine run by Drs. Pizzolitto and Falconieri) that its histogenesis might be related to thyroglossal duct anlage.

Ira Bleiweiss: Areas remind me of solid variant of adenoid cystic carcinoma.

Thomas Colby: I probably would have called this a polymorphous low-grade adenocarcinoma, not being clued in to CAT. Michal's discussion is compelling for a CAT.

Kum Cooper: Cribriform carcinoma of the tongue that you so eloquently described a few years back. I too was reading an excellent review of salivary gland tumors by John Chan in Histopathology (July 2007) that indicated that the WHO views CAT as a variant of PLGA. The cytomorphology of CAT certainly appears to be distinctive (to me at least!).

Göran Elmberger: Agree completely. Michal, I saw one case previously here in Stockholm. Reading your beautiful original paper, I was able to diagnose case preliminary before you confirmed diagnosis. That case had no metastases and extensive blocking of neck resection including levels and IHC was done. I reviewed the present case blindly and came to the same diagnosis, so to me this is a morphologically distinct entity.

Giovanni Falconieri: Beautiful case, Michal. I did not know the entity you have published. I agree, however, that a number of differences exist between this and other conditions such as PLGA. Thanks for this instructive contribution.

Cyril Fisher: Cribriform adenocarcinoma of tongue, thanks for nice slide Michal. Looks myoepithelial in places.

Christopher Fletcher: I have no experience with lesions of this type and look forward to the comments of the head and neck experts.

Jerónimo Forteza Vila: Thank you for this interesting case.

Masaharu Fukunaga: I had not known about CAT at all. I considered that the tumor was papillary carcinoma arising from ectopic thyroid. The immunostaining of thyroglobulin is required for CAT. Thank you for the novel tumor, Michal.

Thomas Krausz: Before reading your excellent discussion, I thought this was PLGA. I am going to look out for the distinguishing features in the future.

Janez Lamovec: Strange tumor. It is not polymorphic enough to be PLGA but at least in my slide, it is not terribly cribriform either.

Thomas Mentzel: Thanks Michal for sharing this example of a seemingly distinct variant.

Liz Montgomery: Thank you for the education on cribriform adenocarcinoma of the tongue. CAT got your tongue?

Giuseppe Pelosi: This case should represent a cribriform adenocarcinoma of the tongue, but segregation from PLGA of the tongue is hard to be done and maybe subjective.

Juan Rosai: I confess I would have called this tumor a polymorphous low grade carcinoma, but then I had never heard of the CAT concept. Now that the cat is out of the bag I will have to reevaluate the case, but it still looks to me pretty good for a PLGC. How far are we going to proceed with this splitting game?

Josh Sickel: Never encountered this lesion before. Thanks for the beautiful review of the literature on this rare entity.

Dominic Spagnolo: Wonderful case, Michal, of cribriform adenocarcinoma of the tongue, which of course I have not seen before. I agree with your reasoning to keep it separate from PLGA.

James Strauchen: Cribriform adenocarcinoma of the tongue. I was unaware of this as a specific entity and considered PLGA.

Saul Suster: It seems that there can be some degree of morphologic overlap between this tumor and polymorphous low-grade adenocarcinoma (PLGA) of minor salivary glands. However, as you point out, the clinical features of this lesion (origin in base of tongue, early spread to lymph nodes and good prognosis) point to a distinct clinicopathologic entity. The similarity with metastatic papillary thyroid carcinoma can also be rather striking. I agree with you that this lesion is sufficiently distinctive that it deserves to be considered as a separate entity from PLGA. Thank you for sharing this great case with us!

Lawrence Weiss: I was unaware of the previous paper. Nice discussion. I am convinced that this is a distinctive entity worthy of recognition.

CASE NO. 13 – CONTRIBUTED BY MARKKU MIETTINEN:

Phil Allen: Amyloid tumor with metaplastic bone, subcutis, left leg. I have not previously seen bone in these lesions. Thanks for the contribution, Markku.

Carlos Baachi: Nice case of amyloid tumor.

David Ben-Dor: Nice slide. Diagnosis of amyloid obvious even without looking at the special stains. Years ago I had a case of a mass in the buttock of an elderly woman with abundant giant cells. It took me a while to realize that there was amyloid and even more time to detect the neoplastic mononuclear cells hidden in the background.

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Amyloid tumor of soft tissue with metaplastic bone. Nice case. I have since recently edited with other colleagues for the Italian journal Pathologica (June 2006) an article on such topic ("amyloid tumors of soft tissue and breast") and made a review on this. Hopefully the literature review might be useful for anyone, and here is the list of references *"Around 30 genuine cases of amyloid tumors of soft tissue have been described so far in either the somatic parts or large cavities (13-33).* **References**: 13. Lipper S, Kahn LB. *Amyloid tumor. A clinicopathologic study of four cases*. Am J Surg Pathol 1978;2:141-5.14. Osnoss KL, Harrell DD. *Isolated mediastinal mass in primary amyloidosis*. Chest 1980;78:786-8. 15. Shaw P, Grossman R, Fernandes BJ. *Nodular mediastinal amyloidosis*. Hum Pathol 1984;15:1183-5. 16. Levitan N, Rubinow A, Bromer RH, Conlon CL, Doos WG, Hong WK. *Transformation of lymphoma to amyloidoma following radiation therapy.* Hum Pathol 1985;16:1072-4. 17. Oyaizu N, Shikata N, Tsubura A, Morii S, Taniguchi N, Miura K. *Systemic amyloidosis with a mesenteric mass which had the appearance of proteinaceous lymphadenopathy*. Acta Pathol Jpn 1987;37:133-9. 18. Sethi D, Hutchison AJ, Cary NR, Brown EA, Curtis JR, Woodrow DF, Gower PE. *Macroglossia and amyloidoma of the buttock: evidence of systemic involvement in dialysis amyloid*. Nephron. 1990;55:312-5. 19. Papla B, Harazda M, Lukasiewicz M, Mlodkowski J. *Amyloid tumour (amyloidoma) of the mediastinum*. Patol Pol 1993;44:227-31. 20. Krishnan J, Chu WS, Elrod JP, Frizzera G. *Tumoral presentation of amyloidosis (amyloidomas) in soft tissues. A report of 14 cases.* Am J Clin Pathol 1993;100:135-44. 21. Vadmal MS, Labate AM, Hajdu SI, Ricci JL. *Primary amyloidoma (amyloid tumor) of soft tissue*. Acta Cytol 1998;42:837-9. 22. Sidoni A, Alberti PF, Bravi S, Bucciarelli E. *Amyloid tumours in the soft tissues of the legs. Case report and review of the literature*. Virchows Arch 1998;432:563-6. 23. Flores M, Nadarajan P, Mangham DC. *Soft-tissue amyloidoma. A case report*. J Bone Joint Surg Br 1998;80:654-6. 24. Romagnoli S, Braidotti P, Di Nuovo F, Coggi G. *Amyloid tumour (amyloidoma) of the leg: histology, immunohistochemistry and electron microscopy*. Histopathology 1999;35:188-9. 25. Murata H, Kusuzaki K, Hashiguchi S,

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Ira Bleiweiss: I agree.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Thanks, Markku, lovely example of amyloid tumor of soft tissue.

Göran Elmberger: Very unusual. How often ossification? Bone predilection area?

Giovanni Falconieri: Nice example of amyloid tumor of soft part. Multinucleated giant cells are often present in these lesions.

Cyril Fisher: Amyloid tumor in soft tissue, great case, Markku,

Christopher Fletcher: Great case of amyloidoma. I agree with Markku that these lesions seem to be really quite uncommon. Most of those which I've seen have been associated with a B-cell/plasma cell disorder, although the most recent example that we saw was associated with chronic renal failure.

Jerónimo Forteza Vila: I am agreement with the diagnosis.

Masaharu Fukunaga: I have not personally experienced amyloid tumor of soft tissue. The lymphoplasmacytoid infiltration seemed to be reactive.

Thomas Krausz: Beautiful example.

Thomas Mentzel: A nice case of tumorous amyloidosis.

Liz Montgomery: Thank you for this beautiful case.

Giuseppe Pelosi: This lesion shows accumulation of amyloid blocks with metaplastic bone and giant cell granulomatous reaction to form a well-developed case of amyloid tumor of soft tissues.

Juan Rosai: Beautiful demonstration of amyloid tumor associated with metaplastic bone formation and foreign-body multinucleated giant cell reaction.

Josh Sickel: Another great case for the teaching files.

Dominic Spagnolo: Agree tumoral amyloid of soft tissue - great example. We recently encountered a massive amyloidoma in a 34 year old male sent from New Guinea for surgery here. He had a 170mmx140mm, 4 Kg "football" overlying his sternum, destroying sternum and massively involving soft tissue on either side of the sternum. The histology was much the same as this AMR case but there appeared to be kappa-restricted plasma cells in the amyloidoma, but not in a separate marrow trephine. It made the TV news over here; such was the interest in the case.

James Strauchen: Soft tissue amyloid tumor. Did it stain for light chains?

Lawrence Weiss: Nice case.

CASE NO. 14 – CONTRIBUTED BY GIUSEPPE PELOSI:

Phil Allen: Poorly differentiated (monophasic), recurrent synovial sarcoma, vagina, with pulmonary metastases locally excised, patient now apparently disease free. Although the tumour is poorly differentiated, it looks like a synovial sarcoma to me, even in the H&E. It seems that synovial sarcoma can occur almost anywhere. Many thanks for the extensive workup and discussion.

Carlos Baachi: Very difficult case! Thanks for sharing this case with excellent discussion.

David Ben-Dor: I suppose the clinical presentation (a lobular mass protruding into the vagina) could be typical for alveolar rhabdomyosarcoma as seen in young girls; can this also be the case for mature women? The depth, thoroughness, and erudition displayed by this presentation put it in the same league as Michele's. Is this a result of a classical Italian education going back to Da Vinci?

Gerald Berry: Beautiful example of synovial sarcoma. Thank you for the comprehensive discussion.

Michele Bisceglia: Poorly differentiated synovial sarcoma of the vagina. Impressive case under several points of view: rarity of occurrence, completeness of (elegant) investigations, and expertise. What can one say, except to thank you very much for such a highly educational case.

Ira Bleiweiss: I agree.

Tom Colby: Agree with diagnosis; in addition to synovial sarcoma, I had also wondered about a malignant SFT with lots of small stubby cells. Excellent discussion in this case!

Kum Cooper: You have comprehensively covered the diagnosis with all the available armamentaria. Great case. Thank you and welcome to the AMR club!

Göran Elmberger: Thanks for presenting this tumor in a new location. Illustrates value of open mind and broad panels.

Giovanni Falconieri: Impossible case, thanks for this submission and welcome to the club!

Cyril Fisher: Nice case of PD synovial sarcoma in exceptional location. SS can occur just about anywhere, but is very rare in vagina where I have seen perhaps two examples.

Christopher Fletcher: The morphologic appearances in this case would indeed fit well with poorly differentiated synovial sarcoma, and the molecular results which you have obtained seem to confirm this beyond doubt. This is certainly a very uncommon location.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Welcome Dr. Pelosi. Thank you very much for the rarest and convincing case and detailed description. I agree with the diagnosis.

Thomas Krausz: Highly educational case. Thank you for the comprehensive discussion.

Thomas Mentzel: Thanks for this difficult case and the detailed description and discussion.

Liz Montgomery: It is nice to have an example of a poorly differentiated synovial sarcoma that has been evaluated in such detail.

Juan Rosai: Good example of monophasic synovial sarcoma, confirmed at the molecular level. It would have been hard to substantiate the diagnosis without it.

Josh Sickel: Spectacular case. Thanks for your excellent review of the literature.

Dominic Spagnolo: Unique case of vaginal synovial sarcoma - thanks for the informative discussion as per your publication of which I was unaware.

James Strauchen: Vaginal synovial sarcoma. Elegant work up. I didn't know they occurred there!

Saul Suster: Thank you for this great example of synovial sarcoma in an unusual location, and...welcome to the Club!

CASE NO. 15 – CONTRIBUTED BY ELVIO SILVA:

Phil Allen: Well-differentiated pseudoendometrioid Sertoli-Leydig cell tumour, left ovary. I have used McCluggage's terminology which I find it easier to remember than his name is to pronounce. My colleague, Professor John Skinner, knows him and says he is a very nice fellow with a Northern Irish accent. His name is apparently pronounced Mac-Clue-Gage. His article is certainly of the highest quality, exceeded perhaps only by Dr. Silva's scholarly dissertation.

Carlos Baachi: Thanks Elvio for the practical information about how to reach the diagnosis of well-differentiated Sertoli-Leydig cell tumor.

David Ben-Dor: Eye opening case, and thanks for sharing your practical and easy-to-apply approach to resolving the differential diagnosis. It's amazing how endometrioid this looks. If I got this (especially on a frozen!), I doubt that I would have thought much beyond the diagnosis of endometrioid carcinoma. But on close examination, the nuclei don't have the atypia of carcinoma; rather they show more of the grooves seen in GCT. The stroma is not the desmoplastic type usually associated with carcinoma. There is some cytoplasmic clearing and also many cells with seemingly signet ring appearance- this wasn't brought out in the discussion and I wonder if it has any significance? Signet ring like cells can also be seen in the sclerosing stromal tumor so they don't always signify malignancy. While in my own mind, I tend to associate stromal/germ cell tumors of the ovary with younger patients in who surface epithelial tumors are relatively rare. This case shows that they can also occur in older women in whom the latter can also be found, so age isn't a wholly satisfactory discriminant in the differential diagnosis. Can the existence of a simultaneous endometrioid carcinoma in the uterus of a patient with an ovarian endometrioid tumor be considered as adequate proof of the latter being carcinoma without doing immunohistochemistry even if it doesn't fill the criteria enumerated by Dr Silva?

Michele Bisceglia: Well-differentiated Sertoli-Leydig cell tumor. It is identical to the cases reported in the series you quoted, Elvio. Thank you for this timely update.

Ira Bleiweiss: I agree.

Thomas Colby: Agree with diagnosis. There are subtleties on the H & E against endometrioid adenocarcinoma but the results of the IPOX were comforting.

Kum Cooper: Elvio, I love your approach! Beautiful example.

Göran Elmberger: Great case with great algorithm. Practical value. Thanks. Just before signed out case with endometrioid adenocrcinoma of ovary without IHC. Case showed squamous subtle differentiation, endometriosis and adenofibroma component.

Giovanni Falconieri: Nice case Elvio. I have no experience with this. Thanks for the valuable comment

Cyril Fisher: Sertoli Leydig tumor. It seems this can have almost any pattern.

Jerónimo Forteza Vila: I agree with your diagnosis.

Masaharu Fukunaga: Pure Sertoli cell tumor. There is a cluster of luteinized interstitial cells, however, I would not call Sertoli-Leydig cell tumor on this slide. Thank you very much for the educational case and description.

Thomas Krausz: Agree with diagnosis. Excellent differential diagnostic discussion, thank you. I assume the clear cytoplasmic vacuoles represent lipid?

Thomas Mentzel: Thanks for the case and for the pragmatic approach to the diagnosis of these kinds of tumors. I found the diagnosis quite difficult, because I had problems to find the eosinophilic Leydig cells in the fibrosed stroma.

Liz Montgomery: Thanks so much for your helpful discussion of your practical approach to such neoplasms in the ovary. You have narrowed the clues down so this novice at ovarian pathology can understand them.

Giuseppe Pelosi: This tumor is consistent with well-differentiated Sertoli-Leydig cell tumor. I do not have specific comments for the case.

Juan Rosai: Whatever you say, Elvio.

Josh Sickel: I fell into the trap of endometrioid adenocarcinoma. Thanks for your very instructive (and humbling) lesson.

Dominic Spagnolo: Very nice example of a well-differentiated Sertoli-Leydig cell tumor, with focal lipidisation. Thanks.

James Strauchen: Sertoli cell tumor predominately!

Saul Suster: Great case for the club, Elvio! Reading your elegant discussion was like watching a Tango show in Buenos Aires with a cup of Argentinian Malbec wine in your hand....Salud, Che!

Lawrence Weiss: Nice practical discussion.

CASE NO. 16 – CONTRIBUTED BY JAMES STRAUCHEN:

Phil Allen: Subcutaneous panniculitis-like T-cell lymphoma involving the breast. Yet another wonderful case with a very helpful discussion.

Carlos Baachi: Beautiful example of subcutaneous panniculitis-like T-cell lymphoma involving the breast. This is a rare location for this type of lymphoma indeed.

David Ben-Dor: On low power, this looks hematopoietic though, of course, on high power the cells are neoplastic. Can the possibility of a granulocytic sarcoma be ruled out completely without immunohistochemistry? The rimming of the fat cells by tumor is typical for this condition. There is also easily visible nuclear debris which can be interpreted as the "bean bag histiocytes" seen in this condition (though it's hard to be certain whether the particles are lying loosely or associated with the histiocytes).

Michele Bisceglia: Subcutaneous panniculitis-like T-cell lymphoma involving the breast. We had one such case here in a child. Parenthetically (but different case) in Seminar #38, Carlos Bacchi contributed a case of granulomatous slack skin which also involved the skin and subcutis of breasts and axillae.

Thomas Colby: Agree with diagnosis; lovely case!

Kum Cooper: Beautiful example (never seen it involve breast tissue before!) and there is even evidence of hemophagocytosis. Thank you.

Giovanni Falconieri: Spectacular case! Thanks for this excellent contribution.

Göran Elmberger: Nice case. Never saw this before. Respecting dermis. Rather lobulated appearance not engaging septae as opposed to description in WHO text.

Cyril Fisher: Subacute panniculitis-like T-cell lymphoma, beautiful example for the teaching set.

Christopher Fletcher: What a wonderful and convincing example of this very rare disease, which so many people like to talk about in lectures, even though many seem never to have seen a case of their own!

Jerónimo Forteza Vila: I agree with your diagnosis. There are multiple images of T cell around the adipocytes typical feature of this entity.

Masaharu Fukunaga: Panniculitis-like T cell lymphoma, very unusual site, agree. Nice case.

Thomas Krausz: Dramatic pathology. Not seen in the breast before. The rare cases of panniculitis-like T cell lymphoma I came across before had a less dense T cell and a more striking histiocytic component which made diagnosis difficult.

Janez Lamovec: We just recently saw a case of this lymphoma, not in the breast, though. Very interesting case.

Thomas Mentzel: A nice case, many thanks.

Liz Montgomery: Thank you for a wonderful T cell lymphoma case.

Giuseppe Pelosi: Extraordinary case of T-cell lymphoma involving the breast. Additional DD include extramedullary hematopoiesis or simple panniculitis. Among unusual lymphoproliferative disorders I saw in breast, I'd like to add (taking from my personal experience at the European Institute of Oncology of Milan) some cases of dendritic cell sarcomas and CD30 +ve anaplastic lymphomas arising around breast prosthesis after surgery for cancer.

Juan Rosai: Subcutaneous panniculitis-like T-cell lymphoma involving the breast. The tumor sure simulates panniculitis or even extramedullary hematopoiesis.

Josh Sickel: I've seen a few of these distinctive tumors, but never in this location.

Dominic Spagnolo: A very typical example of subcutaneous panniculitis-like T-cell lymphoma - thank you. Have not encountered this in the breast.

Saul Suster: Great example of panniculitic T-cell lymphoma! Many thanks.

Lawrence Weiss: Spectacular histology—I shall be using these slides to illustrate the entity. There are even some breast ducts on my slides to convince one that we are actually in the breast.

CASE NO. 17 – CONTRIBUTED BY PAUL WAKELY, JR.:

Phil Allen: Large pedunculated, submucosal atypical fatty tumour with rhabdomyomatous component, distal third of the oesophagus. This looks to me like an atypical fatty tumour with very convincing lipoblasts and an inflammatory component. I think the rhabdomyomatous component is neoplastic rather than included voluntary muscle from the upper oesophagus. Moreover, this tumor arose in the lower third of the oesophagus where voluntary muscle should not be present. I can find no accounts of rhabdomyomatous differentiation in fatty tumors. I suspect the fatty component is analogous to the submucosal atypical fatty tumors (liposarcomas) of the pharynx, but the voluntary muscle component seems to be unique.

Carlos Baachi: Great case. I was leaning towards the diagnosis of liposarcoma. Thanks for teaching me about this entity.

David Ben-Dor: You and your surgical colleagues have my deepest admiration for figuring this case out and doing the right thing for this patient. The stromal cells and the rhabdomyoblasts look very strange. I didn't see any lipoblasts, and I think that your analysis is correct. Fortunately, this was submitted in toto and presumably relatively intact and not as a small biopsy or in a piecemeal fashion with numerous cautery artifacts. In the latter situation, this could be an impossible case to figure out!!

Michele Bisceglia: Rhabdomyomatous giant fibrovascular polyp of the esophagus. Agree. Bizarre stromal cells. I do not see any malignant histology in this tumor.

Ira Bleiweiss: Very neat case, never seen such a thing.

Thomas Colby: Agree with diagnosis; would be somewhat descriptive. This appears to be a classic example as well as the first example. I would favor somewhat of a descriptive diagnosis because I was not 100% sure this was not some peculiar low-grade sarcoma.

Kum Cooper: Paul, great case. Are you certain this is not a liposarcoma with rhabdomyoblastic differentiation? The atypical cells look like true lipoblasts to me and not ancient change. (J Clin Pathol. 1996 September; 49(9): 770-772; Archives of Pathology & Laboratory Medicine </p/articles/mi_qa3725> , Aug 1998 </p/articles/mi_qa3725/is_199808>).

Göran Elmberger: Great case. Interesting hypothesis about connection with skeletal muscle from upper esophagus. Some of atypical stromal cells do, in my opinion, show hyperchromatic dense "dead" nuclei of degenerative ancient character like in SN polyps. MIB-1? Some stromal cells look awfully like lipoblasts, but I do not think their appearance would make me go malignant.

Giovanni Falconieri: Never seen before, Paul. Many thanks for this exotic case.

Cyril Fisher: Rhabdomyomatous giant stromal polyp, great case Paul.

Christopher Fletcher: In my personal experience, the majority of giant polyps in the esophagus have proved to be liposarcomas, most often well-differentiated or dedifferentiated. In this regard, I note the presence of quite numerous bizarre stromal cells in this lesion, and I would strongly suspect that this is in fact a well-differentiated liposarcoma with heterologous rhabdomyoblastic differentiation. Was it possible to stain the lesion for CDK4 or MDM2?

Jerónimo Forteza Vila: I had never seen a similar case before.

Masaharu Fukunaga: Great case! Thank you very much for the beautiful case and comprehensive description, Paul. I did not have any idea of giant fibrovascular polyp of the esophagus, so I considered well-differentiated liposarcoma with rhabdomyoblastic differentiation. The adipose element seems to be liposarcoma or spindle cell lipoma.

Thomas Krausz: Unique case. I favor well differentiated liposarcoma. I feel the cellular composition (adipocytes, lipoblasts, spindle cells and atypical/bizarre stromal cells) of the tumor favors liposarcoma. It would be interesting to do FISH studies/immunohistochemistry to see whether the appropriate chromosomal aberration and amplification for cdk4 and mdm2 of WD liposarcoma are present or not. As far as I know rhabdomyoblastic differentiation (in contrast to smooth muscle) has not been seen in conventional well differentiated liposarcoma but only in dedifferentiated liposarcoma. I see no evidence of dedifferentiation.

Janez Lamovec: I have never seen a case of giant fibrovascular polyp of the esophagus let alone the one with rhabdomyoblasts. Thank you for educating me.

Thomas Mentzel: For me the lipogenic cells show at least focally variations in size and shape, contain enlarged and hyperchromatic nuclei, and few multivacuolated cells as well as atypical stromal cells are seen as well. Have you performed MDM2 and CDK4 stainings?

Michal Michal: The lipomatous component contains lipoblasts. Therefore, I would rather diagnose the case as a well differentiated liposarcoma with rhabdomyoblastic differentiation.

Liz Montgomery: This is a real treat. In our "in-house" files here at JHU, we have only one giant fibrovascular polyp of the esophagus, testimony to how rare they are, but your case is so much better! The skeletal muscle differentiation indeed seems unique. I would agree with you that the large hyperchromatic cells akin to those in well-differentiated liposarcomas can be dismissed in this setting. Years ago, I was told by both Les Sobin and Franz Enzinger that in their [anecdotal] experience, there were no recurrences in giant fibrovascular polyps of the esophagus when such cells were seen. I was told this because as an eager young thing working at AFIP, I had such a case and wanted to call it well differentiated liposarcoma and had the good sense to show it to both of them (who both reined me in)!

Giuseppe Pelosi: In this case, I have seen atypical cells consistent with well-differentiated liposarcoma or atypical lipomatous tumor. I'm wondering if skeletal fibers seen in the lesions are neoplastic in nature or simply entrapped fibers considering the position of the lesion in the proximal part of the esophagus. I'm not sure of the diagnosis of rhabdomyomatous giant fibrovascular polyp of esophagus, and I'd like to know what is the feeling of other AMR members about this interesting case.

Juan Rosai: This looks to be like a pretty good case of atypical lipomatous tumor (well differentiated liposarcoma) to me. I wonder whether the scattered skeletal muscle fibers are simply entrapped normal structures from the region rather than a component of the lesion.

Josh Sickel: Paul, thanks for submitting this unique case to the seminar. I focused on the atypical cells and wondered about liposarcoma. The rhabdomyomatous cells are quite impressive. I've never encountered this entity in my practice. Thanks for the great discussion.

Dominic Spagnolo: The uniform spread of the rhabdoid cells through the lesion suggests this is an integral part of the lesion rather than entrapped, anatomical muscle. I agree the atypia in the stromal cells is probably degenerative, which is the stated dogma in several texts. What of the univacuolar and multivacuolar lipoblast-like cells??

James Strauchen: RGFPE! A new one to me! I considered a pleomorphic lipoma.

Lawrence Weiss: I'd never personally seen this entity before. I would agree that the stromal cells are just stromal cells.

CASE NO. 18 – CONTRIBUTED BY LARRY WEISS:

Phil Allen: Histiocytic sarcoma, stomach, 27 years after adjuvant chemotherapy for lower extremity osteosarcoma. I don't suppose you would countenance a malignant fibrous histiocytoma with vascular invasion, Larry!!!!!

Carlos Baachi: Very difficult case Larry. I spent a lot of time looking for osteoid and missed the diagnosis of histiocytic sarcoma or even to think about it!!

David Ben-Dor: This looks more sarcoma and less histiocytic (though maybe this tumor is called histiocytic sarcoma for that reason!).

Gerald Berry: Nice case Larry!

Michele Bisceglia: Histiocytic sarcoma. Thank you. For sure, it is pure ignorance on my side, but I confess I did not know about CD163 as a histiocytic marker.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Thanks Larry for a genuine case of histiocytic sarcoma.

Göran Elmberger: Just very beautiful case.

Giovanni Falconieri: Eextraordinary case. Thanks for submitting another collectible item!

Cyril Fisher: Histiocytic sarcoma – it's good to have a true example of this now rare entity.

Jerónimo Forteza Vila: Thank you for this interesting case.

Christopher Fletcher: For sure this is a beautiful example of histiocytic sarcoma with a convincing immunophenotype – many thanks, Larry.

Masaharu Fukunaga: Wonderful case. I considered anaplastic large cell lymphoma or metastatic high grade tumor or anaplastic carcinoma. It showed focally an epithelioid arrangement.

Thomas Krausz: Great case.

Janez Lamovec: This is a spectacular case of histiocytic sarcoma that I wouldn't recognize as such without immuno. The site of its growth would even confuse me further. Thank you for submitting it.

Thomas Mentzel: Thanks for this interesting case that looks like pleomorphic, "MFH"-like sarcoma.

Giuseppe Pelosi: This is a high-grade neoplasm that is reported to be a histiocytic sarcoma. I do not have any specific comments to this interesting case.

Juan Rosai: I think it is a good example of true histiocytic sarcoma, the diagnosis being backed by the immunohistochemistry. I have seen several examples of this tumor lately, most of them in the GI tract.

Josh Sickel: This is an amazing case. I did a quick Google search under histiocytic sarcoma and found a web site devoted to *canine* histiocytosis disorders. Did you know that histiocytic sarcoma is found most commonly in Bernese Mountain Dogs? Not sure if they mentioned CD163!

Dominic Spagnolo: I agree this is a beautiful example of a histiocytic sarcoma. I have also found CD163 to be a great histiocytic marker.

James Strauchen: Histiocytic sarcoma! Very nice case! We just got CD163.

Saul Suster: Morphologically this doesn't look "histiocytic" at all! There is definite nesting of tumor cells and alternating epithelioid/spindle cells reminiscent of melanoma. I get very nervous whenever I have to make a diagnosis that is exclusively based on results of immunostains or other ancillary studies. Also, I don't know that I can trust any of the current "histiocytic" markers to be that reliable or specific.

FOLLOW-UP COMMENTS TO AMR SEMINAR #50

CASE NO. 10 – CONTRIBUTED BY GIOVANNI FALCONIERI:

Michele Bisceglia: Focal nodular hyperplasia of the liver with sarcoid-like granulomas. Falco asked if anyone of us had previously seen granulomata in FNH of the liver. Most of us (obviously including myself) answered and stated not having seen such findings in the lesion in point, while others (few) did not state whether they had or had not ever seen such finding. However, while preparing the description of the case I contributed for Seminar # 52, on a debated telangiectatic variant of FNH of the liver, I found in the literature that "nine lesions had epithelioid granulomas" out of 305 FNH - classical and non-classical variant (Nguyen BN, et al. Am J Surg Pathol 23:1441-1454; 1999 [page. 1444, left column, last but one line].

CASE NO. 18 – CONTRIBUTED BY DOMINIC SPAGNOLO:

Dominic Spagnolo: Apologies for inadvertently omitting in the case presentation that the melanocytic markers HMB-45 and Melan-A were both negative. The ultrastructure was not that of a melanocytic neoplasm.