COMMENTS TO AMR SEMINAR #45

CASE NO. 1 – CONTRIBUTED BY DR. ALLEN

Phil Allen: Primary borderline mucinous tumor, right infrarenal retroperitoneum. My Case.

Carlos Bacchi: I agree with the diagnosis of borderline mucinous tumor. I believe that Dr. Silva could clarify some of the raised questions in this case.

David Ben-Dor: I have two thoughts, the first being whether a true mucinous peritoneal borderline tumor (similar to serous peritoneal borderline tumor) can arise outside the ovary- then maybe one can speculate whether this tumor originally arose in the peritoneum and somehow pinched off and migrated to the kidney. Second, the spindle stroma looks vaguely ovarian- could this be akin to the mucinous cystadenomas described in the pancreas (albeit with the added atypia)?

Michele Bisceglia: Primary borderline mucinous tumor, right infrarenal retroperitoneum. Great case. I was not aware of this entity. Now that I am aware, I wonder - in case of association with analogous tumors in the ovaries- how we could discriminate association versus metastasis.

Ira Bleiweiss: Agree. This has such a colonic look to it, but the underling stroma looks ovarian. I wonder how it would stain with CK 7/20 and WT-1.

Tom Colby: Agree with diagnosis. Was not really aware of this entity either.

Kum Cooper: Thanks Phil for this lovely example. I saw a case a couple of years ago that had the full spectrum of changes: adenoma/BL/intra-epithelial carcinoma and invasive carcinoma. Clearly primary tumors must be ruled out before this diagnosis is entertained: appendix, pancreas, GIT and ovaries. Behavior is unpredictable and close follow-up is warranted.

Hugo Dominguez: I agree with the diagnosis of mucinous cystic tumor (borderline) primary of retroperitoneum. The ovarian-like stroma is very striking in this case. Retroperitoneal mucinous tumors are similar to those occurring in the pancreas an other organs of the region, we have seen cases in the retroperitoneum and one in the spleen, all tumors are seen in women and have ovarian-type stroma. The behavior is similar to those occurring in the ovary and depends on the histological grade (cystadenoma, borderline and cystadenocarcinoma) and the clinical stage.

Giovanni Falconieri: I agree with the diagnosis straight, yet several features of this case are unusual indeed

Cyril Fisher: This looks very atypical in places and I would be concerned about adenocarcinoma. Thanks for the literature.

Christopher Fletcher: A very convincing and educational case – many thanks. I have no personal experience of such lesions at this site.

Andrew Folpe: Mucinous cystadenocarcinoma. Obviously a subjective area, but I think this tumor shows sufficient architectural and cytologic features to be considered a non-invasive carcinoma (CIS). Have not seen one of these with ovarian-type stroma in this location before- thanks Phil.

Jeronimo Forteza-Vila: I agree with the diagnosis. Origin is relevant. (localization).

Masaharu Fukunaga: Extraovarian mucinous tumor of borderline malignancy. Dr. Allen, thank you very much for the very informative references. I have experienced a mucinous carcinoma of the pelvic cavity, but no follow-up information is available.

Allen Gown: Thank you for this example of a lesion I have not seen before.

Thomas Krausz: I have seen a few examples with either benign or borderline histology. All behaved in an indolent fashion: only incompletely excised ones recurred locally, but none of them metastasized. All of them had an ovarian-type stroma.

Thomas Mentzel: Thanks for sharing this interesting case of primary retroperitoneal mucinous cystadenocarcinoma.

Michal Michal: It is interesting that all these cases of retroperitoneal mucinous tumors are always of intestinal type. We have several cases of this tumor in our files and none of them resemble Mullerian (endocervical type) mucinous cystic tumor as seen in the ovaries.

Elizabeth Montgomery: Mucinous cystic neoplasms seem to retain their ovarian-like stroma no matter where they live! The slide I have has carcinoma in situ so I hope this was well-sampled to exclude invasive carcinoma. It seems likely that there was some invasive carcinoma hiding among the initial specimen, especially since the patient has a massive recurrence (presumably overt malignancy) and the prognosis would not seem too good if the follow-up in extra-pancreatic lesions mirrors that in pancreatic ones with CIS.

Cesar Moran: The more I get to know about this so-called "borderline tumors" the more I dislike them. I think a better designation would be to call them carcinomas of low-grade malignancy. Many years ago someone wanted to do the same thing with similar tumors in the lung.

Joshua Sickel: I've never seen such a case. If I have, I probably mis-classified it as being ovarian in origin. Thanks for the great references!

Dominic Spagnolo: I agree with your diagnosis Phil. I'm pretty sure I've seen a couple of these before, and of both serous and mucinous variety, but it has been a while. Your case seems to have both intestinal and endocervical type mucinous epithelium. Was there any endometriosis?

James Strauchen: Thank you for the references. We recently saw a benign mucinous cyst presenting in the substance of the kidney.

Paul Wakely: I have no experience with this lesion except for its counterpart in the ovary, which this certainly looks similar to.

Bruce Wenig: Wow, what a cool case. I have never seen such a case. Other than the ovary I have seen quite a few similar type lesions in the pancreas. I would be somewhat circumspect in predicting behavior and am not sure whether this tumor type in this specific location will follow the biologic guidelines of similar ovarian type or pancreatic type tumors. The latter even when showing essentially benign histology (i.e., mucinous cystadenoma) or borderline histology may behave in a more malignant fashion (i.e., metastasis). I am not surprised that this woman's lesion has recurred.

Lawrence Weiss: I had never heard of this entity, separate from the pancreas. Given the cytological features, I diagnose intraepithelial carcinoma, and mention that without complete sampling an invasive carcinoma cannot be ruled out. It's hard to predict the behavior of the neoplasm without knowing for sure what it is.

CASE NO. 2 — CONTRIBUTED BY: DR. BACCHI

Phil Allen: I accept this as a metastasizing cutaneous histiocytoma similar to Harry Evans' two published cases. I have one other similar unpublished metastasizing case in my consultation files and a visitor to the AFIP in the late sixties told me he had seen a metastasizing case in Venezuela. It seems that vanishingly rare cases of tumors histologically indistinguishable from benign cutaneous histiocytomas may repeatedly recur and then metastasize. I also have about 15 referred cases of cutaneous histiocytomas that have recurred once, but most incompletely excised cutaneous histiocytomas do not recur. I should add that benign cutaneous histiocytoma is one of the commonest lesions referred to me in consultation. I believe that cutaneous histiocytoma commonly extends into the subcutis and may be predominantly subcutaneous, with minimal dermal attachment. Cutaneous histiocytoma has no adequately substantiated counterpart in the deep soft tissues, nor is it related to either atypical fibrous histiocytoma of the sun damaged skin of elderly individuals, which behaves as a squamous cell carcinoma of the skin, nor to dermatofibrosarcoma protuberans, which has nothing in common with cutaneous histiocytomas except a storiform pattern. I see a lot of cellular benign cutaneous histiocytomas and in my experience, they are no more likely to recur than any of the many other histological variants of this common and *almost* invariably benign tumor.

David Ben-Dor: I would call it dermatofibroma with focal pleomorphism secondary to degeneration (as seen in dermatofibroma with monster cells or ancient schwannoma). To be honest I don't think I would have been too concerned at the time about this coming back later as metastatic disease (all this provided that it was totally excised, as this seems to be). On first glance I wasn't too worried about the cellularity but on careful examination (the slide being of such high quality and this being an AMR case after all) there does seem to be some diffuse atypia. The lymph node metastasis looks more cellular and more atypical than the first occurrence does; in fact based on the histology of the lymph node lesion alone I would think of metastatic DFSP. Of course if the lesion kept on coming back and looking worse on each occasion one would need to take precautions.

Michele Bisceglia: Metastasising cellular dermatofibroma of the skin. I have just contributed an analogous case for this current Seminar n. 46: please refer to it. With my case contribution I not only invite Carlos in putting his case and mine together in order to publish them both, but am also pleased to expand this invitation to anyone else of the members who has other similar cases he wants to publish as a case report. Please contact me.

Ira Bleiweiss: I did and would still call "A" a dermatofibroma. Metastasis from this lesion is certainly a surprise.

Tom Colby: Agree with diagnosis. Admittedly there is some atypia there, particularly in the metastasis, but I am not sure I would have used that solely for a diagnosis of sarcoma. I will be interested to hear what our colleagues say.

Kum Cooper: Yes, I agree with your differential diagnosis. Both DFSP and BFH were in my differential.

Hugo Dominguez: I agree with the diagnosis of metastasizing dermatofibroma, I would feel more comfortable if FXIIIa had been positive.

Giovanni Falconieri: No experience with this. The metastasis looks pretty much cellular dermatofibroma.

Cyril Fisher: I would regard the original lesion as atypical cutaneous fibrous histiocytoma.

Christopher Fletcher: This is a very convincing example of cellular fibrous histiocytoma associated with lymph node metastasis. I have now seen perhaps 10 examples of otherwise ordinary cases of cellular or aneurysmal (as well as atypical) FH associated with metastasis to either lymph node or lung. As far as I can tell, there are no morphologic features, which separate these cases from their far more common non-metastasizing counterparts. As such, this seems to be an entirely unpredictable phenomenon, although, as in Carlos' case, some of these lesions do appear to be associated with repeated local recurrence prior to metastasis. Whenever I encounter cases of cellular FH with repeated recurrence, I always raise the possibility that the lesion might subsequently metastasize. The suggestion, propagated by some dermatopathologists, that all of these lesions should, by definition, be regarded as misdiagnosed sarcomas seems, to my mind, both illogical and delusional.

Andrew Folpe: Very nice case. I would have called the primary a benign fibrous histiocytoma, perhaps a cellular FH. I don't see sufficient cytologic atypia to label it an "atypical fibrous histiocytoma". The lymph node metastasis also appears to be a relatively conventional FH, with aneurysmal changes, except for the fact that it is in the lymph node! There is perhaps a bit more cytologic atypia in the metastasis, but not that much. I've seen several of these cases, and they have all been rather ordinary BFH's in the primary lesion. Certainly these cases put the lie to the notion promulgated by the Zelgers- that these all represent misdiagnosed sarcomas.

Jeronimo Forteza-Vila: The diagnosis of metastasizing dermatofibroma should be accepted.

Masaharu Fukunaga: A great case, Dr. Bacchi, thank you very much. This is the first time I see a cellular fibrous histiocytoma with metastasis. Both A and B seem me to be conventional dermatofibroma (benign fibrous histiocytoma).

Allen Gown: 'Metastasizing dermatofibroma' does sound a bit oxymoronic, and I would prefer a term with 'sarcoma' in the name, given the fact that it has metastasized.

Thomas Krausz: I agree that this is metastasizing fibrous histiocytoma rather than something else. Apart from the literature data of rare event of metastasis I have seen one case personally before.

Thomas Mentzel: Many thanks for this rare example of metastasizing dermatofibroma. Given the lack of cellular fascicles I would classify the lesion as dermatofibroma with scattered enlarged atypical cells (usually cellular dermatofibroma is characterized by the presence of cellular fascicles).

Elizabeth Montgomery: Truly horrifying case since it does not look different from a non-metastasizing fibrous histiocytoma.

Joshua Sickel: Fantastic case, Carlos! I've seen a similar lesion which metastasized to the lungs in a multicentric fashion...patient was asymptomatic (found on routine CXR). Both skin and lung tumors were rich in hemosiderin. The skin lesion was surprisingly bland in appearance. The diagnosis was confirmed by Chris Fletcher, who first introduced me to this weird phenomenon.

Dominic Spagnolo: I see no reason not to call the primary a dermatofibroma/benign cutaneous fibrous histiocytoma. There are no features on my slide that would have allowed me to predict this behavior. I think your interpretation of this as a metastasising dermatofibroma is absolutely correct. Thanks for the case.

James Strauchen: Agree, metastasizing cellular Dermatofibroma.

Saul Suster: "Benign metastasizing dermatofibroma"? I have seen a couple of cases like this that metastasized despite rather banal histology. Pretty scary proposition. Maybe our molecular friends and acolytes can come up with something that will help separate these tumors from otherwise conventional FHs.

Bruce Wenig: My opinion is skewed given the presence of metastatic disease, but in the presence of nuclear pleomorphism and scattered mitotic figures present in slide A I might have suggested a "prospective" diagnosis of atypical fibrous histiocytoma.

Lawrence Weiss: I would have just called the original lesion a dermatofibroma and gone on to the next case. There's nothing too atypical about it in my mind.

CASE NO. 3 — CONTRIBUTED BY: DR. COOPER

Phil Allen: To me, some of the myxoid areas are indistinguishable from a neurothekeoma, but the non-myxoid areas looked like a neurilemoma, which is confirmed by the location and immunohistochemistry. I suspect that neurothekeomas "never" occur outside the skin and subcutis.

Carlos Bacchi: Myxoid schwannoma. Nice example!

David Ben-Dor: Myxoid schwannoma- the transition between the two phases here is more abrupt than that usually seen in conventional schwannomas. As in everything else, clinicopathologic correlation (to rule out neurothekeoma) is essential.

Michele Bisceglia: Myxoid schwannoma. Nice case in a rare location.

Ira Bleiweiss: Agree. Myxoid schwannoma. I can't recall seeing such prominent myxoid elements.

Kum Cooper: My case, no further comment; although the morphology still strikes me!

Hugo Dominguez: Nice case. Thank you.

Giovanni Falconieri: Thanks for contributing this unusual case.

Cyril Fisher: Beautiful Schwannoma with myxoid change (Antoni B-like in places). I have seen a similar case recently and, apart from considerations of location, found the absence of EMA helpful in the diagnosis from nerve sheath myxoma.

Christopher Fletcher: Many thanks – indeed this schwannoma has strikingly myxoid areas, as one occasionally sees. However, the very cellular intervening elements would help distinguish this lesion from a deep-seated nerve sheath myxoma, convincing examples of which seem to be exceedingly rare.

Andrew Folpe: Excellent example of a myxoid schwannoma. The myxoid areas certainly do resemble typical neurothekeoma- you can only teach an old Schwann cell so many tricks, I guess. This would be hard if you didn't get the whole lesion- there is one very nice Verocay body, and an occasional thick walled vessel. Thanks Kum.

Jeronimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: Kum, thank you very much for the great and educational case. There is a limited area of a typical palisading arrangement.

Allen Gown: Nice case, Kum. Thank you.

Thomas Krausz: Excellent case, thanks Kum. I haven't seen a schwannoma exactly like this before. Myxoid change in neurofibroma and MPNST is much more common. I agree with all your comments. The focal similarity to neurothekeoma is close, though perhaps the lesional cells in the latter are a bit more plump.

Thomas Mentzel: An interesting case of schwannoma with prominent myxoid changes. In addition scattered enlarged cells with enlarged nuclei are noted, representing most likely ancient-like, degenerative changes. Histologically, the lesion resembles the recently described hybrid lesions of schwannoma/perineurioma (Virchows Arch 2004; 445: 347-353), however, the spindled cells in the myxoid area were negative for EMA.

Michal Michal: Many of these myxoid schwannomas have areas resembling perineuriomatous differentiation. These areas are, however in our experience, EMA and other perineuriomatous markers (claudin and glut-1) negative.

Elizabeth Montgomery: The diagnosis of myxoid schwannoma makes sense once the ordinary schwannoma backdrop is spotted but this took me for a loop!

Cesar Moran: Nice example of myxoid Schwanoma.

Joshua Sickel: Myxoid schwannoma sounds like a good fit.

Dominic Spagnolo: Thanks Kum for this beautiful example of neurothekeoma-like myxoid Schwannoma.

James Strauchen: Cellular myxoid Schwannoma. Thank you.

Bruce Wenig: My immediate thought was that of a neurothekeoma but given the location I considered alternative diagnoses including myxoid type of Schwannoma. Thanks for providing such a beautiful example of a rare tumor.

Lawrence Weiss: Nice case.

CASE NO. 4 — CONTRIBUTED BY: DR. DAMJANOV

Phil Allen: . Malignant sertoli cell tumor metastatic to abdominal lymph nodes. Thanks for the contribution. I have not seen one of these previously.

Carlos Bacchi: Thanks for the case. This is a rare tumor indeed.

David Ben-Dor: The monomorphous round cells look so much like lymphoma!! I wonder how many members of the group would have figured this out had they received the lymph node either as a frozen section or even as a routine surgical specimen, especially if it came

without the testicle or without knowledge of the existence of a testicular mass? Especially since lymphoma is the most common testicular tumor in elderly men.

Michele Bisceglia: Malignant Sertoli cell tumor metastatic to the abdominal lymph nodes. Beautiful case.

Ira Bleiweiss: Agree, but I would not have been able to figure this one out on its own. The age is very helpful.

Kum Cooper: Thank you Ivan for this case. Given the recent interest in tubular structures in seminomas, I probably would have resorted to a couple of germ cell and sex-cord immuno-markers. Was so good to eventually meet you in San Antonio!

Hugo Dominguez: Nice example of malignant Sertoli cell tumor, thank you.

Cyril Fisher: Most unusual case, which would be difficult to recognize without knowledge of the testicular primary. I guess inhibin is positive?

Christopher Fletcher: Many thanks for sharing this uncommon lesion. We recently saw an example of malignant Sertoli cell tumor which was striking in that it showed abrupt transition to a dedifferentiated pleomorphic/sarcoma-like appearance.

Andrew Folpe: This would be very hard without the history of the testicular tumor. I suspect that many of the cells with more abundant pink cytoplasm are showing Leydig cell differentiation, making this a malignant Sertoli-Leydig cell tumor.

Jeronimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: A beautiful case. Thank you very much for sharing a rare testicular tumor with you.

Allen Gown: Thank you, Ivan, for this tumor. Out of curiosity, I wonder what its immunophenotype was.

Thomas Krausz: Whenever I see a Sertoli cell tumor in the testis it always gives me a problem in determining its biological potential. Seeing the metastasis helps.

Thomas Mentzel: In my opinion a very difficult case, many thanks.

Cesar Moran: Interesting case.

Joshua Sickel: Thanks for the collectors item!

Dominic Spagnolo: Rare tumor indeed!

James Strauchen: I thought these might be malignant Leydig cells.

Saul Suster: Agree with the diagnosis. Thanks for this interesting contribution.

Bruce Wenig: What a case. Thanks!

Lawrence Weiss: Great case. I realize that these tumors are, by convention, called sertoli cell tumors, but it sometimes strikes me, as in this case, that there may be some focal Leydig cell differentiation in it—particularly those solid areas with abundant eosinophilic cytoplasm. Why do the Leydig cells have to be in a spindled area to be recognized as such?

CASE NO. 5— CONTRIBUTED BY: DR. DEI TOS

Phil Allen: Stromal endometriosis with sex cord differentiation, uterus. I still refuse to call these sarcomas, although they metastasize like an aggressive endometriosis.

Carlos Bacchi: I totally agree with the diagnosis. I have seen a case similar to this one where the EST metastasized to the heart. There was also presence of sex cord elements.

David Ben-Dor: Endometrioid stromal sarcoma with sex cord differentiation- I hope I never come across something like this in a curettage specimen!

Michele Bisceglia: Low-grade endometrial stromal sarcoma with sex cord differentiation. Agree.

Ira Bleiweiss: The stromal component may be low grade, but the "sex cord"/epithelial component is extremely mitotic. How does this behave? I wasn't aware of the combination of the two.

Tom Colby: Agree with diagnosis. A particularly dramatic example.

Kum Cooper: Paolo, thank you for this lovely example. There is also focal vascular invasion. Interesting that the sex-cord component is both CD 10 AND inhibin positive indicating that the stromal cells show true differentiation towards sex-cord elements. Rosai first showed this a few years ago.

Hugo Dominguez: Uterine tumor resembling ovarian sex cord tumor Type I (a variant of endometrial stromal sarcoma). Inhibin reactivity has been only described in Type II tumors, however the separation of subtypes could be artificial.

Giovanni Falconieri: Nice case, Paolo. Thanks for this contribution.

Cyril Fisher: Lovely example of ESS with sex cord elements.

Christopher Fletcher: The sex cord-like component in this case is very striking and impressive – more extensive than in previous cases which I can recollect. Many thanks!

Andrew Folpe: Spectacular example of an endometrial stromal sarcoma with sex cord like elements. Definitely one for my resident teaching conference. Thanks, Paolo.

Jeronimo Forteza-Vila: I agree with the diagnosis. We had thought of neuroendocrine differentiation in the cord component.

Masaharu Fukunaga: Thank you for convincing case, Angelo. Although it is positive for inhibin, I always wonder if the element truly shows sex-cord differentiation.

Allen Gown: Lovely example of this tumor; thank you, Paolo.

Thomas Krausz: Superb example, thanks Paolo.

Thomas Mentzel: Many thanks Paolo for this beautiful example.

Elizabeth Montgomery: What a beautiful case.

Joshua Sickel: Beautiful case. We've recently had two examples of low grade stromal sarcoma, one which had sex cord features. Both cases were suggested on endometrial curettage…."stromal neoplasm, cannot exclude a more serious process". I assume this case would resemble a "uterine tumor resembling sex cord stromal tumor", most of which is benign. A minority turn out to be malignant on hysterectomy.

Dominic Spagnolo: This ESS shows a striking degree of sex-cord like differentiation – a very nice case, thanks Angelo. Were it not for the typical ESS areas, a number of other considerations would have arisen.

James Strauchen: Stromal sarcoma with sex cord differentiation. Thank you.

Saul Suster: Never seen this combination before. Thanks for sharing the case.

Bruce Wenig: Agree; yet another great case.

Lawrence Weiss: Great case with classic histology.

CASE NO. 6 — CONTRIBUTED BY: DR. DOMINGUEZ

Phil Allen: I don't know what this is but the basis for chordoid meningioma (Am J Surg Pathol 24: 899-905, 2000) does not seem to me to be particularly strong.

Carlos Bacchi: I would favor meningioma.

David Ben-Dor: This is something for an experienced pediatric neuropathologist! This dilemma could be approached as a question of values or attitude, whether a diagnosis can be made if the histology and clinical context agree with each other, despite discordant immuno and ultrastructural findings.

Michele Bisceglia: Chordoid meningioma. Agree. A similar case was contributed in AMR Seminar n. 19 by Dr. JC Manivel (case 12).

Ira Bleiweiss: My first thought was chordoma, but for the location.

Tom Colby: Not sure I can do much with this other than a descriptive diagnosis.

Kum Cooper: Would have been nice to have EMA positivity.

Giovanni Falconieri: Unfortunately, my slide section has almost all gone off so I cannot say so much. The most important differential is with chordoid glioma, a tumor that is made up of polygonal, loose and bland cells within a myxoid, acidic-rich substance associated with scattered lymphoplasmocytic infiltrate. Immuno are not helpful: although chordoid gliomas are often GFAP+, yet totally erratic and deceitful patterns have been described, including keratin positivity.

Cyril Fisher: I guess chordoid meningioma but not supported by EM/immuno. The other possible diagnoses, eg EMC, seem unlikely.

Christopher Fletcher: Morphologically, this case seems very convincing for chordoid meningioma, so it is disappointing that the immunostains and EM did not support this. It is hard to come up with a sensible differential diagnosis at this anatomic site, although I suppose one might consider an exceedingly rare example of myxoid chondrosarcoma, which likely could only be proved by cytogenetics/molecular genetics.

Andrew Folpe: I'm afraid I can't do any better than "myxoid neoplasm" here. I shared it with Dan Brat, our excellent neuropathologist, who trained with both Sheithauer and Berger, and he also can't make this into anything specific.

Jeronimo Forteza-Vila: The myxoid background supports chordoma diagnosis. In Electron Microscopy wide contact among membranes is compatible with meningioma. In our slide, areas of typical meningioma are not observed.

Masaharu Fukunaga: Chordoid meningioma, thank you, Hugo, I have never seen this type of meningioma. Is there any conventional meningioma element in this particular case?

Allen Gown: The immunos do not specifically support this diagnosis, but they do not rule it out. I'm not sure I could come up with an alternative diagnosis.

Thomas Krausz: No slide received.

Thomas Mentzel: Only few tumor cells were left on the slide, I've received, and I do not have a sensitive idea.

Elizabeth Montgomery: I have no experience with chordoid meningioma, but this looks like what I understand to be one (except no lymphocytes on my slide). If this came to me, suspect a huge IHC panel would have been ordered as I fretted over whether it could be a weird sarcoma.

Cesar Moran: I cannot offer a better alternative.

Joshua Sickel: Strange myxoid tumor….I have no experience with this lesion.

Dominic Spagnolo: I can't do any better. I too considered chordoid meningioma most likely, and also a myxoid chondrosarcoma and chordoid glioma. The EM and the immunos however don't support meningioma or glioma. Chondrosarcoma is not entirely ruled out. What was the size of the lesion? Is the histology the same throughout?

James Strauchen: No idea. Wondered about extraskeletal myxoid chrondrosarcoma.

Saul Suster: Sorry – don't know what this is. Although IHC was not helpful for either one, I would favor myxoid glioma over chordoid meningioma. The cells simply do not look meningothelial at all. The EM (if representative) would also rule out meningioma.

Bruce Wenig: I have a healthy respect and am quite wary of myxoid lesions in general and those of head and neck sites in specific. I am not sure what this tumor is but I am concerned given the overall unpredictable behavior of myxoid lesions in general and the presence of fairly readily identifiable mitoses that this child's lesion represents a malignancy. I would suggest excluding the possibility of a rhabdomyosarcoma (RMS), which from the submitted IHC staining it does not appear that myogenic markers (e.g., desmin, myf-4,myoglobin) were performed. Also, it may be worthwhile to perform cytogenetic evaluation if tumor is still available to be sampled.

Lawrence Weiss: This is the chordoidest meningioma I ever saw. But, I have no better suggestion.

CASE NO. 7 — CONTRIBUTED BY: DR. EUSEBI

Phil Allen: Undiagnosed, histologically bland, locally resected, fibroxanthoma-like lesion, condyle of left humerus with local recurrence and metastases to two axillary lymph nodes eight years after the initial excision. I do not think the malignancy is histologically apparent in the 1996 biopsy. The nodal metastasis appears to me to be histologically identical to the primary lesion and still seems to be histologically benign, despite the fact that it has metastasized. I can see no sign of osteoid or bone production and giant cells are scanty, so I could not support a diagnosis of osteosarcoma or giant cell tumor of bone. I don't know what this is.

Carlos Bacchi: I believe the extensive bone infiltration and the hypercellularity in the first biopsy would raise the possibility of malignant behavior. I would call this lesion MFH and I think the present bone is both metaplastic and reactive.

David Ben-Dor: Concerning the slide from the earlier jaw tumor, there are some giant cells especially in one portion of the slide but I would expect more of them in a jaw related giant cell lesion. The bulk of the lesion is composed of rather large mononuclear cells with mild atypia; I even saw one or two with intranuclear inclusions. I saw no mitoses (normal or atypical) or obvious necrosis and the only osteoid I could see was in the form of broad seams at one end consistent with reactive. The question is whether the radiology of the original tumor was wholly consistent with a giant cell lesion. I can't say how smart I would be if this came to me at first but I don't think it fits for a giant cell lesion. But I'm not sure I would call it outright malignant in the absence of supportive radiological findings.
In slides from the lymph node I saw a few patches cytologically resembling the initial lesion but without giant cells, with foci of eosinophilic deposits which might be osteoid but could also be necrotic or maybe degenerative material. Is it logical for an osteogenic sarcoma of the jaw to metastasize to an axillary lymph node after 8 years? Could a metastatic epithelioid sarcoma (originating in the hand) look like this (we weren't given the patient age)?

Michele Bisceglia: I would call it malignant GCT.

Ira Bleiweiss: Very strange. I've never seen anything like this.

Tom Colby: I don't know what the lesion is so I am not sure what criteria of malignancy to apply. To me obvious features of malignancy are not present in the bone lesion. I am not convinced this is an osteosarcoma but whatever this is it is definitely gotten into the lymph node and I think that finding and the cytologic atypia that is present lead me to conclude it is indeed malignant. Has histiocytic differentiation been excluded?

Kum Cooper: Sorry I only received the A slide. However, I agree that it is very difficult to call this morphology malignant. Was LCH ruled out?

Hugo Dominguez: In both specimens it resembles (to me) villonodular synovitis, (diffuse type? Metastasizing?)

Giovanni Falconieri: Sorry, I do not have good names for these.

Christopher Fletcher: I agree that the bone present in the original condylar lesion appears entirely benign. The tumor in both the primary lesion and metastasis appears to consist of syncytial sheets of plump palely eosinophilic cells with granular cytoplasm, in places admixed with foamy cells (presumably reactive). I do not believe that it is possible to sustain a diagnosis of osteosarcoma in this case. Instead, I would want to exclude the possibilities of some type of true histiocytic neoplasm or perhaps even a PEComa. This is a fascinating and challenging case!

Andrew Folpe: This is an extremely interesting case. The primary lesion, I think, is a diffuse giant cell tumor (possibly PVNS if it was related to the temperomandibular joint). It nicely displays the characteristic admixture of small round cells, larger eosinophilic cells (often desmin-positive), foam cells and osteoclasts seen in tenosynovial GCT's. There are perhaps some atypical cells, but I would not have called it malignant at that time. The metastasis maintains the overall architecture of a tenosynovial GCT, but now clearly has overgrowth of a malignant appearing cell population. So my diagnosis would be "metastatic malignant tenosynovial giant cell tumor". I don't see any evidence of osteoid production. Thanks for sharing this case, Vincenzo.

Jeronimo Forteza-Vila: The tumor osteoid does not bear a relationship with malignant cells. Taking evolution into account, we should consider a well-differentiated metastasizing osteosarcoma.

Masaharu Fukunaga: I appreciate very much for sharing this unusual lesion. My impression was giant cell tumor of tendon sheath. How about immunostaining of desmin? The lesion seems to me recur locally, but no ability of metastasis. I would not call it osteosarcoma.

Thomas Krausz: I am also puzzled. It does not look like any osteosarcoma I have seen before. The bone looks more metaplastic. What is the immuno-profile of the tumor cells? – I would like to know before I can commit. They appear histiocytic or synovial-like. Before reading the history/discussion I was even considering the possibility of giant cell tumor of tendon sheath, diffuse type. Rarely it can invade the bone or even metastasize.

Thomas Mentzel: What about malignant giant cell tumor with focal ossification ?

Michal Michal: It seems to me that there are luminized epithelioid cells. Some of these cells are having red blood cells inside of these lumina. I would diagnose this case as epithelioid hemangioendothelioma.

Elizabeth Montgomery: Don't have a name for this with any certainty. The cytologic features remind me of angiomatoid [malignant] fibrous histiocytoma [except that it was in bone] or a peculiar PEComa but of course I have no name. When I am clueless, I like to regard things as "low grade" to prompt excision. The lesion does not strike me as osteosarcoma but the 2004 material is clearly a metatastasis from the original lesion.

Cesar Moran: I think the initial tumor I would have interpreted as giant cell tumor.

Joshua Sickel: Doesn't look like osteosarcoma to me. How about a malignant giant cell tumor of tendon sheath--PVNS (still looking for a real case…could this be it??). The admixture of plump stromal cells (some containing hemosiderin), focal collections of foamy macrophages and osteoclasts, make a good fit.

Dominic Spagnolo: I really can't add anything without having more clinicopathological and radiologic detail. I must say osteosarcoma was not at the top of my list – rather I was considering some other malignant "epithelioid" neoplasm composed of granular cells. Could it be a fibrohistiocytic lesion rather than osteoblastic? I agree the bone all looks reactive, but after reading your discussion and going back on the section, there may very well be some matrix deposition occurring although I found it hard to assess on this section. Look forward to the answer Vincenzo.

James Strauchen: Would have considered the 1996 original as benign and the metastasis as metastatic giant cell tumor.

Saul Suster: Both the original and the lymph node lesion are cytologically benign and I would be unable to call either one osteosarcoma. I think that what we are seeing here is analogous to the phenomenon described as "benign metastasizing giant cell tumor of bone". Lung metastases from "benign metastasizing giant cell tumors" look equally bland as the original, and characteristically contain metaplastic, benign-appearing bone. I have seen one previous case in which a histologically typical and benign GCTB "metastasized" to lymph node. A similar phenomenon has been described for other histologically "benign" tumors, including "benign metastasizing leiomyoma" of the uterus, and now the "benign metastasizing dermatofibroma of Bisceglia".

Bruce Wenig: What a case. Just looking at the 1996 case despite the cellularity of the lesion the overall constituent cells look benign including bony spicules that appear reactive, The overall appearance of the lesion falls within the spectrum of giant cell reparative granuloma rather than a giant cell tumor. The tumor within the axillary lymph node (2004 slide) is histologically identical to the 1996 condyle lesion including the presence of "benign-appearing" bony spicules, and at this time I would also favor a diagnosis of metastatic osteosarcoma originating from the 1996 condlye lesion. Even in retrospect I find it difficult to consider the 1996 lesion as malignant and confronted with a similar appearing condyle lesion now I would still consider it to be benign although with the experience of the current case I may add a comment that the aggressive biologic behavior cannot be excluded.

Lawrence Weiss: Osteosarcoma did not even cross my mind on the original specimen. I was thinking of some crazy exogenous substance deposition in histiocytes. However, the lymph node looks like a metastasis and there is bone in it, so I guess it must be an osteosarcoma, no matter how benign the bone looks.

CASE NO. 8 — CONTRIBUTED BY: DR. FISHER

Phil Allen: Multiple metastases, implants or recurrences with two perforations, sigmoid colon, of the giant cell mural nodule component of a borderline mucinous cystadenoma of the left ovary removed two years previously. I think prognosis in this case should be guarded because of the multiplicity of the implants or metastases.

Carlos Bacchi: This is really a fantastic case. I was only able to diagnose giant cell tumor and I thought this could be primary from the intestine wall.

David Ben-Dor: It was curious to see this case right after looking at the immediately preceding one in which the issue of a bone giant cell lesion was raised. In fact I think this could fit nicely with a true giant cell tumor of bone and given some of the ectatic vessels the thought of aneurysmal bone cyst even came to mind; neither of these would be expected on the serosal surface of the colon but given the nature of the cases presented to this forum anything can be expected. This lesion looks rather bland. Was the fact of the mural nodule in the previous ovarian tumor known to the pathologist(s) who worked up the colon or was it discovered only after a very laborious and circuitous process?

Michele Bisceglia: Giant cell tumor involving sigmoid colon. It seems likely that this lesion is related to the mural nodule of the previous ipsilateral ovarian mucinous tumor.

Ira Bleiweiss: Also strange in much the same way as case 7. Never seen anything like this happen either.

Tom Colby: Agree with diagnosis. Spectacular case!

Kum Cooper: What a fascinating case Cyril! Jaime Prat reviewed a series recently in Am J Surg Path. I agree that it fits best into the "sarcoma-like" nodule group.

Hugo Dominguez: Fascinating case, should the ovarian tumor be called mixed mesodermal tumor?

Giovanni Falconieri: Great case, Cyril. Unfortunately, I have no clue to a better name.

Christopher Fletcher: What a remarkable and unusual case – I agree entirely that this must represent spread of the sarcoma-like mural nodule identified in this patient's prior ovarian mucinous neoplasm. In the absence of such a history, diagnosis in this case would be extremely difficult.

Andrew Folpe: What a strange case. By itself, I would call this a soft tissue giant cell tumor (of the bone type). They've been reported in location such as the pancreas, under somewhat different names. I have never seen or heard of one arising in association with an ovarian mucinous tumor. I'd even wonder whether the ovarian tumor could represent a collision tumor or tumor-to-tumor metastasis, rather than a mesenchymal mural nodule.

Jeronimo Forteza-Vila: It seems a giant cell tumor and not only a highly exuberant reactive lesion.

Masaharu Fukunaga: Very interesting. I agree. I presume that the colon lesion is a metastatic one from the left ovarian tumor. In the colon, vascular invasion is observed.

Thomas Krausz: I agree, the invasion of the bowel wall looks aggressive/destructive and mitotic activity is brisk. Should I have seen a nodule like this in the wall of an ovarian borderline mucinous cystadenoma I probably would have called it giant cell rich sarcoma-like mural nodule and expected benign behavior. I feel that the tumor involving the bowel wall is more likely to represent a metastasis than an independent primary, even though giant cell rich GISTs and variants have been described. On retrospect, I would also consider the possibility of a giant cell rich "real" sarcoma, like leiomyosarcoma, in the wall of the ovarian mucinous tumor.

Thomas Mentzel: What an unusual case ! Does the lesion show features of multinucleated giant cell tumor as it has been described in the omentum (Ultrastruct Pathol 1996; 20: 89-99) ?

Elizabeth Montgomery: What a bizarre case. This lesion must be related to the prior ovarian one but certainly unusual.

Cesar Moran: Nice example in the G.I tract.

Joshua Sickel: Spectacular case, Cyril! When you mentioned the ovarian tumor, I thought to myself, "You must be kidding!?". Thanks for submitting this rarity.

Dominic Spagnolo: What an extraordinary occurrence. It emphasizes the difficulty of predicting the behavior of some of these mural nodules occurring in mucinous ovarian neoplasms. Even on the histological appearances of the colonic lesion you submitted, I would not have confidently predicted metastatic potential, but would not have ruled it out either. Like you, I am assuming the 2 lesions must be related, and given the history, it appears that metastasis is most likely.

James Strauchen: Giant cell tumor versus sarcoma or sarcomatoid carcinoma with giant cells. These also occur in the pancreas.

Saul Suster: This slide seminar is definitely dedicated to vexing and weird giant cell lesions! Don't know what this is, never seen anything like this, have no clue, etc.

Bruce Wenig: Back-to-back unusual cases of tumors with giant cells behaving badly neither one of which I have seen previously. Thanks.

Lawrence Weiss: Great. I agree that the current tumor probably represents spread from the ovary.

CASE NO. 9 — CONTRIBUTED BY: DR. FLETCHER

Phil Allen: Undifferentiated large round cell tumor, subcutis, left knee region with t(11; 22) (q24; q12) translocation and EWS gene rearrangement by FISH in female aged 52. I would have been tempted to believe the fashionable interpretation of the cytogenetics and FISH studies if it were not for the patient's advanced age and the subcutaneous location. I doubt that this is the same tumor as Ewing's sarcoma of bone and deep soft tissue of young individuals.

Carlos Bacchi: Great teaching case for all of us! It is good that now we have molecular biology to confirm or rule out some of our diagnoses.

David Ben-Dor: My first thought was Merkel cell tumor. Can't argue with the final diagnosis.

Michele Bisceglia: Extraskeletal Ewing's sarcoma/PNET. I take the liberty of reporting here excerpts from one of the Excerpta/Entities (*EWS of the skin and superficial soft tissues*) which has been very recently published in Pathologica (April, 2005): *<<EWS/pPNET comprises around 1% of soft tissue tumors in general; the most common location are the deep soft tissues of the lower extremities (including the periosteal tissue), the paravertebral region, the retroperitoneum, and the intraabdominal cavity (pelvis, peritoneum, diaphragm). Rare visceral locations are also on record (kidney, pancreas, uterus, larynx). Very rarely it occurs in the skin and subcutaneous tissues (superficial EWS/pPNET) with forty-five cases of primaries reported so far (1-17). …… Children and young people are usually affected (13,14,16), but less often superficial EWS/pPNET also occurs in adulthood with six such total cases on record (1,4,7-9,13,17). Congenital cases may also be encountered (MB, unpublished personal observation of two cases). Both sexes are affected. In order of frequency, anatomic locations include lower limbs, trunk (chest and abdomen) and pelvis, head (mainly the scalp) and neck, and upper limbs (13,14,17). A case of EWS/pPNET of the breast is also on record (18)>>.* Of course the numbers in brackets refer to the references (review of the literature) which are quoted in that source.

Ira Bleiweiss: Agree.

Tom Colby: Malignant tumor with genetic translocation characteristic of Ewing's sarcoma. Genetic definitions of tumors will probably cause us to be "astonished" many more times in the future.

Kum Cooper: Thank you Chris for sharing your "archival esoterica" with us. I do not see too many of these here cases here in VT!

Hugo Dominguez: Interesting case, Independently of the cytogenetic finding the phenotype is of an embryonal sarcoma with divergent differentiation.

Giovanni Falconieri: Another impossible case.

Cyril Fisher: This is a very instructive case that shows the necessity for molecular genetics without which the correct diagnosis would not be made.

Andrew Folpe: Great case- thanks for submitting it, Chris. We are just about to submit our manuscript about histologic and immunohistochemical diversity in ES/PNET, and I would certainly echo your comments about how the morphologic spectrum of this tumor is broader than usually appreciated. We did not have one exactly like this, but a couple of different cases contained similar elements.

Jeronimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: PNET, very educational case, thank you very much. The immunoprofile of the stromal cells in this case is very interesting. I sometimes wonder if a tumor represents a PNET or a neuroendocrine carcinoma (tumor).

Allen Gown: The case does demonstrate the value of detecting the presence of t(11;22)(q24;q12) in lesions in which the differential diagnosis includes PNET/ES, which we now routinely perform via FISH in our laboratory. Immunos are suboptimal for identifying this entity owing to the great variability in immunophenotype, as exemplified by this case.

Thomas Krausz: Extraordinary case. Before reading the discussion because of the cystic spaces lined by tumor cells and the varied "stroma" I was even considering a PNET-like variant of poorly differentiated synovial sarcoma. The rich immuno-profile reflects the full neuroectodermal potential (especially the chromogranin) and matches well with the varied histology.

Thomas Mentzel: Many thanks Chris, for showing us such a broad spectrum of MPNET. To be honest and knowing the immunohistochemical findings, I was not thinking on this diagnosis.

Elizabeth Montgomery: This is fascinating and underscores that there is a small (thankfully) minority of cases for which we really need molecular support to make the correct diagnosis. We, too, have recently encountered a similar case. It will be interesting to see Andrew's comments since he has recently studied a series of such cases with molecular confirmation and a host of morphologic patterns.

Cesar Moran: Nice example.

Joshua Sickel: I remember a case of Ewing's (post-treatment), which had a peculiar cystic and alveolar pattern.

Dominic Spagnolo: I thought the stromal element was the most intriguing part of this PNET/Ewing's – I don't think I have seen this reticular myxoid (and even somewhat myxochondroid) appearance to this extent before, and the immunophenotype in these areas is intriguing. Do you think the stromal element has any particular significance in this context? I shall heed the admonition to consider PNET/Ewing's more often with these weird small cell tumors.

James Strauchen: PNET with unusual morphology. Also considered neuroendocrine carcinoma.

Saul Suster: thank you Chris for sharing this unusual case. I had never noticed this peculiar reticular myxoid stroma in these tumors before. I guess we'd better brace ourselves to accept cytogenetic translocations as the next "gold standard" for soft tissue tumor diagnosis!

Bruce Wenig: My immediate consideration was that of a neuroendocrine neoplasm such as a Merkel cell carcinoma. Agree diffuse areas look good for Ewing's sarcoma/PNET; other histology is unusual and outside my previous experience with Ewing's/PNET. Thanks. Out of curiosity it may be interesting to do p63 and calponin staining to see if the foci showing cytokeratin, S100 protein and GFAP positivity but absence of CD99 reactivity are p63 and calponin positive. If yes, perhaps there is a myoepithelial component to this tumor (even though the histology of these cells are not quite those of myoepithelial cells).

Lawrence Weiss: What a wild case—a PNET progressing to a M (maturing) NET.

CASE NO. 10 — CONTRIBUTED BY: DR. FORTEZA VILA

Phil Allen: Micronodular thymoma with B cell lymphocytes. I cannot see any germinal centres in the lymphoid tissue, which is not unduly prominent. In this case, I would refer unto Caesar what is Cesar's and Saul's (Am J. Surg Pathol 23: 955-963, 1999).

Carlos Bacchi: Great case. I have never seen this type of thymoma before.

David Ben-Dor: The WHO classification of thymic tumors is arcanely talmudical verging on the kabbalistic. It's easier to use the Suster-Moran approach and call it thymoma. But I guess for those willing to invest the time and effort, the intricacy of the former provides an intellectual challenge with its own satisfactions.

Michele Bisceglia: Micronodular thymoma with lymphoid stroma. Nice case. Thank you also for the beautiful panel of pictures.

Ira Bleiweiss: Agree.

Tom Colby: Agree with diagnosis, I guess (Saul and Jeronimo, please educate me about the amount of nuclear atypia that one can accept in a thymoma. It seems to me that if I saw these nuclei in a number of other contexts I might say that cytologic features of malignancy were present).

Kum Cooper: I have not seen the micronodular variant before...thank you.

Hugo Dominguez: Nice case of lobular thymoma, the photographs are superb.

Giovanni Falconieri: Agree with micronodular thymoma.

Cyril Fisher: Thymoma, very nice case.

Christopher Fletcher: Seems a very convincing case of micronodular thymoma, which I had previously not seen before – many thanks.

Andrew Folpe: Agree with thymoma. I tend to lose track of all the classification systems. I'm not sure I had heard of this variant-thanks for educating me.

Masaharu Fukunaga: I have never seen micronodular thymoma. Thank you very much for sharing this very rare lesion.

Thomas Krausz: Agree with diagnosis.

Thomas Mentzel: Thanks for sharing this rare variant of a rare entity.

Cesar Moran: This is a subject from which I would like to stay away (i.e., don't get me started….!!!)

Joshua Sickel: Beautiful example. I pray that I will never make the same mistake of calling this lymphoma

Dominic Spagnolo: Nice example of micronodular lymphoma with prominent B-lymphoid stromal hyperplasia – thank you.

James Strauchen: Unusual thymoma.

Saul Suster: Agree; typical example of micronodular thymoma. Although we were not mentioned by name in the WHO book, this variant of thymoma was actually described by Dr. Moran and I (Am J Surg Pathol 23:955-962, 1999). In our original description of this tumor, we regarded this as an unusual morphologic variant of spindle cell thymoma (WHO type A). Other than for avoiding a misdiagnosis of lymphoma on a small biopsy, there is no clinical difference between this tumor and conventional spindle cell thymoma. Prognosis depends on the status of capsular integrity, as with all other thymomas. Interestingly, two of the other "special type" thymomas entered as separate categories from the "A-B-AB-C" types in the new WHO book include two other rare variants also described by Dr. Moran, the "metaplastic" thymoma with pseudosarcomatous stroma, and hyalinizing thymoma. In the next edition these shall be reclassified as types D, E and F.

Bruce Wenig: This tumor is identical to the pictures of the micronodular thymoma with lymphoid stroma shown in the recent WHO book. Was the tumor invasive or non-invasive? Completely resectable or not?

Lawrence Weiss: Beautiful example. It has everything but the germinal centers.

CASE NO. 11 — CONTRIBUTED BY: DR. LAMOVEC

Phil Allen: Large (8.5 cm), undiagnosed, histologically indeterminate, CD34 positive mesenchymal tumor with multiple microcysts, subcutis, nape of neck. I don't think I have seen one like this before. I doubt that it is a solitary fibrous tumor or a variant of cutaneous histiocytoma.

Carlos Bacchi: I have no idea how to call this but I believe that it is benign.

David Ben-Dor: The Lord who in his infinite wisdom created complicated soft tissue tumors to behold in awe and wonder was also kind and merciful in creating soft tissue pathologists capable of explaining them to us (and maybe to Him). I personally don't understand what a "fibroblastoma" is, since the texts I consulted (Enzinger-Weiss and the AFIP fascicle) refer either to desmoplastic fibroblastoma or giant cell fibroblastoma. The latter could fit histologically but is generally seen in young children and not in the neck. But who am I to argue with authority and experience, especially when Dr. Fletcher has taught me that what is canonized in the authoritative texts does not necessarily jive with what one actually sees under the microscope on a day to day basis.

Michele Bisceglia: Aneurysmal type of SFT / pericytoma-like fibroblastoma. Agree on the concept of a morphological continuum in the spectrum of these neoplasms.

Ira Bleiweiss: ????

Tom Colby: Don't know what this is. Aneurysmal as an adjective applied to whatever this is seems descriptively appropriate.

Kum Cooper: Wow Janez - this is way beyond my league! Thank you for sharing the case.

Hugo Dominguez: I would call it a solitary fibrous tissue, angiomatoid.

Giovanni Falconieri: Don't know how to call it, yet it looks benign despite the size.

Cyril Fisher: I would have called this SFT with myxoid, cystic and angiomatoid features.

Christopher Fletcher: This lesion remains very difficult to classify and, when Janez sent the case to me in early 2000, I could not make a specific diagnosis. However, the immunophenotype as well as the morphologic appearance in some more solid areas was very SFT-like. Pericytoma-like fibroblastoma was a term that Juan Rosai, Jim Woodruff and I had discussed and used tentatively in the late 1990s for lesions which I would nowadays regard as cellular examples of SFT as well as fat-forming SFT (so-called lipomatous hemangiopericytoma). However, although the current case may perhaps represent an unusual microcystic variant of solitary fibrous tumor, the appearances are not absolutely convincing in that regard. I suppose, if I were to see this for the first time today, I would likely label this lesion descriptively as an 'atypical fibroblastic neoplasm with microcystic features' – such is progress!

Andrew Folpe: Unclassified mesenchymal tumor, probably benign. I don't see much here that brings to mind a solitary fibrous tumor. I'm not sure what the immunos necessarily add, either. Not everything has a name (yet?).

Jeronimo Forteza-Vila: My diagnosis was SFT.

Masaharu Fukunaga: Janez, thank you very much for a great case and photo. I would like to call this atypical solitary fibrous tumor.

Allen Gown: I've come to call cases like this "CD34-omas", and I'm sure the CD34 expression is telling something about the nature of the tumor, but I'm not sure exactly what!

Thomas Krausz: Not sure either. I would consider a variant of SFT ("microcystic SFT") or a "fibroblastoma" variant of myxoid DFSP (giant cell fibroblastoma without giant cells which has never been described). Cytogenetics might help.

Thomas Mentzel: Numerous enlarged cells with enlarged nuclei and scattered multinucleated giant cells are present. What about an intermediate form" between solitary fibrous tumor and giant cell angiofibroma ?

Elizabeth Montgomery: Looks like a variant of SFT.

Cesar Moran: This tumor looks fibrohistiocytic to me.

Joshua Sickel: Defer to the soft tissue experts. I considered a low grade myofibroblastic sarcoma. Doesn't remind me of SFT.

Dominic Spagnolo: Weird thing – my thoughts were SFT/PHAT/giant cell angiofibroma-like, but have never seen anything quite like this before. It isn't right for any of the above, but they were the thoughts I had before reading your comments. The angiectactic and pseudoangiectic features I found more striking than an essentially hemangiopericytic nature, but I can appreciate what Chris is saying.

James Strauchen: I think this is some variant of solitary fibrous tumor (supported by the immuno). I also considered hemangioblastoma of peripheral soft tissue.

Saul Suster: Don't know what this is and don't have a name for it. The number of cases that we see on a regular basis that I have never seen before and are unable to find in the books continues to surprise me. Obviously there is still a future in the name-giving

business in soft tissue pathology. I would suggest we be on the outlook for additional cases and triage them to Janez so that this can be formally reported (deservingly as a "new entitity") in the literature.

Bruce Wenig: I am definitely in the category of not knowing what this tumor is. I have recently seen two sinonasal lesions with similar prominent blood filled cystic spaces that proved to be sinonasal-type hemangiopericytomas, but the histology in this case does not quite fit for that tumor type although some of the IHC findings does fit. I look forward to seeing what other members felt this tumor represents.

Lawrence Weiss: I have no idea what this is. I am not sure that I like the "pericytoma-like fibroblastoma" idea. What we need is a paper on this entity (with a better name).

CASE NO. 12 — CONTRIBUTED BY: DR. MICHAL

Phil Allen: . Low-grade trichoblastic carcinosarcoma of the skin. The circulated section restores one's faith in the potential for published photomicrographs to exactly recapitulate what one sees in a slide. The published pictures are superb and are a great credit to Michal and the publisher. Unfortunately, I don't think I have ever seen another example, but it looks as though it is a definite entity. Thanks for the contribution.

Carlos Bacchi: I only could tell that is a carcinosarcoma.

David Ben-Dor: This is really a fascinating case brilliantly analyzed (and I'm not saying this because Michal will be my host in two months!). I found at least one focus showing the neoplastic epithelium curving around the mesenchyme in a ball and socket fashion very reminiscent of a hair follicle. Other than that the stroma looks rather primitive and blastlike (as in Wilm's tumor) at least in proximity to the epithelium. In most places the epithelium looks like it is retracting from the stroma, but I thought that here and there these components seem to be blending. Given that the stroma is intrinsic to a conventional basal cell carcinoma even if not itself considered malignant, maybe we should call it a "basal cell carcinofibroma"?

Michele Bisceglia: Low-grade trichoblastic carcinosarcoma of the skin. Never seen a case like this tumor. Thank you for the contribution.

Kum Cooper: Michal, I like your notion of a "true" carcinosarcoma of the skin!

Hugo Dominguez: Spectacular case, I do not remember one like this. Only one question: why to call it "low grade" if both components look so atypical?

Giovanni Falconieri: Another challenging microscopic entity I was not aware before. Thanks Michal for this contribution

Cyril Fisher: Terrific diagnosis.

Christopher Fletcher: This is indeed a remarkable and apparently unique case. It might have been of interest to stain the stromal component with a range of additional cytokeratin antibodies, before being certain that these were mesenchymal in nature.

Andrew Folpe: As always, a great case from you, Michal. I agree it is a carcinosarcoma, and it does seem trichoblastic, so why not "trichoblastic carcinosarcoma"? It would be interesting to look for the hair-specific "hard" keratins in these sorts of lesions. For some reason those markers haven't been applied at all in dermatopathology.

Jeronimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: Thank you very much for a rare case and comments, I have never seen it before. Michal.

Allen Gown: Wow! This is an interesting case and one that I've never seen before. Thanks, Michal.

Thomas Krausz: Fantastic case. I haven't seen a trichoblastic tumor like this before.

Thomas Mentzel: Many thanks for sharing this extraordinary case. As discussed with Dmitry, I would probably classify the neoplasm as a metaplastic trichoblastic carcinoma. On the other hand you are absolutely right, that a clear biphasic neoplasm is present, and this neoplasm represents probably a true carcinosarcoma given the mentioned histogenesis of hair follicles (probably similar to Wilms tumor).

Cesar Moran: I have never seen a similar case. Thanks for this interesting case.

Joshua Sickel: Fantastic case! It may be difficult convincing a clinician that a carcinosarcoma will behave in a low grade fashion.

Dominic Spagnolo: Thanks Michal for this beautiful and unique "Michaloma". I have not encountered a similar lesion before. My first impression of the large, anastomosing epithelial islands was that they looked poromatous, but the smaller nests at the peripheral edge of the lesions do absolutely look like follicular germinal epithelium.

James Strauchen: Trichoblastic tumor. I think our gyn people have a similar case in the vulva.

Saul Suster: Thank you Michal for sharing this unique and exotic case with us. I have never seen anything like this before and I believe the designation you propose is as good as any other and makes good sense. Congratulations on another "first" in surgical pathology.

Bruce Wenig: In my experience with mucosal upper airway lesions, carcinosarcoma is becoming (if not already) a vanishingly rare diagnosis, especially knowing that the sarcomatoid component in those mucosal lesions may be cyokeratin negative and reactive for mesenchymal markers (e.g., vimentin, others). Given the intimate relationship between the differentiated epithelial component and the spindle cell "mesenchymal" component in this lesion even in the absence of confirmatory IHC staining I would still be more inclined to consider this tumor to be a spindle cell sarcomatoid carcinoma. Perhaps p63 staining should be done as p63 has been shown to be helpful in upper aerodigestive tract spindle cell squamous carcinomas that are cyokeratin negative.

Lawrence Weiss: Holy cow. I have certainly never seen anything like this before.

CASE NO. 13 — CONTRIBUTED BY: DR. STRAUCHEN

Phil Allen: Abdominal angiostrongylosis due to Angiostrongylus costaricensis. A superb case. Thanks for the contribution.

Carlos Bacchi: I agree with the diagnosis.

David Ben-Dor: Obviously understanding the geographic distribution of disease is of paramount importance in understanding the case.

Michele Bisceglia: Abdominal angiostrongylosis. Thank you for this exotic intestinal helminthiasis. A similar case was contributed in AMR seminar n. 21 by Dr. H. Molina-Hirsch (case 13).

Tom Colby: Agree with diagnosis. Spectacular case. The inflammatory infiltrate rich in eosinophils with associated granulomas is similar to basidiobolomycosis but obviously the organisms differ and allow a diagnosis.

Kum Cooper: I have NOT seen this critter in Southern Africa! The closest I came to was Strongyloides!.

Hugo Dominguez: Nice case of angiostrongylosis. The disease is endemic in south-east Mexico. I remember a striking case of generalized "hyperinfectant" disease in a patient with immunosuppression.

Giovanni Falconieri: Thanks for this exotic contribution

Cyril Fisher: Great case. Fantastic addition to the parasite collection.

Christopher Fletcher: Many thanks for sharing this impressive case which is totally outside my prior experience.

Andrew Folpe: The case of the seminar! What an awesome slide. Thanks very much for sending it.

Jeronimo Forteza-Vila: Nice case. I agree with the diagnosis. Thank you for such an illustrated case.

Masaharu Fukunaga: I have never encountered angiostronglyus, thank you very much for the excellent slide.

Allen Gown: Thank you for submitting this fascinating case and one that is not a soft tissue tumor! We don't see very much parasitic disease in the States so this is a treat.

Thomas Krausz: Never seen it before. Very educational. Thanks for submitting it.

Thomas Mentzel: Many thanks, and I was lucky, because intravascular worms were present on my slide.

Elizabeth Montgomery: Thanks so much for this educational case.

Cesar Moran: Most of the cases that I have seen of this entity have been in the appendix. Interesting case.

Joshua Sickel: Magnificent teaching case. Thank you!!

Dominic Spagnolo: Wow!! Thanks for this amazing case, which I'm never likely to encounter here.

Saul Suster: Thank you for the exotic case; great example for the collection.

Bruce Wenig: Great case. Thanks.

Lawrence Weiss: Another case for the worm files. Great section with the organisms in the vessels!!!!

CASE NO. 14 — CONTRIBUTED BY: DR. WAKELY

Phil Allen: . Poorly differentiated malignant tumor with rhabdoid features, probably sarcoma, presumably primary, mediastinum. I don't believe that extrarenal rhabdoid tumors are a genuine entity. It seems likely to me that the mediastinal tumor is the primary. I don't think I have previously seen a tumor with this histological appearance in the mediastinum but I think it is more likely to be a sarcoma than a carcinoma.

Carlos Bacchi: Malignant undifferentiated tumor with rhabdoid features.

David Ben-Dor: Not knowing the immunohistochemistry results the cells look very hematolymphoid to me. Some of the cells almost look like Reed Sternberg cells. Can you absolutely rule out a granulocytic sarcoma with your immunos? I assume it would be superfluous to do chromogranin in light of the keratin negativity even though it is mentioned that the tumor extends from the thyroid (without making specific mention as to whether the two are connected on imaging).

Michele Bisceglia: Extrarenal rhabdoid tumor. Agree with the interpretation of the case.

Ira Bleiweiss: Rhabdoid tumor

Tom Colby: Malignant tumor with rhabdoid phenotype, NOS. These tumors can turn up in a variety of places and determining a primary site probably depends more on the radiology than any fortuitous immunostains that may be positive. I don't know what significance to apply to the chromosome 22 abnormality. I am not sure how many extrarenal rhabdoid tumors have been looked at genetically and thus don't know of the specificity of that abnormality.

Kum Cooper: Paul, I wondered about a plasmablastic lymphoma. Cases have ben described outside of the oral cavity. They are also usually CD 20 negative. CD 79a is positive

Hugo Dominguez: The best I can do is "undifferentiated sarcoma with rhabdoid phenotype"

Giovanni Falconieri: Nice case, Paul. I totally agree with your assessment.

Cyril Fisher: Undifferentiated rhabdoid neoplasm, could be malignant rhabdoid tumor though the absence of CK is unusual.

Christopher Fletcher: I would simply label this as a poorly differentiated epithelioid malignant neoplasm with rhabdoid features. I believe that this cytomorphology may be shared by a wide variety of different tumors in adult patients. Nowadays, for practical purposes, extra-renal rhabdoid tumor in adults is no longer regarded as a discrete entity, since none of these lesions have the characteristic abnormalities of chromosome 22 identified in pediatric lesions. I think that your suggestion that this may prove to be a metastasis from some sort of renal neoplasm (possibly even carcinoma) is a good one. Irrespective of what tumor type leads to this ultimately undifferentiated morphology, it seems that all such lesions in adults with this rhabdoid phenotype are associated with a very aggressive clinical course.

Andrew Folpe: I can't do any better than "malignant neoplasm with rhabdoid phenotype" on this slide. Given that the patient has a large renal mass, I very much wonder whether this may represent a metastatic renal cell carcinoma, with an undifferentiated, rhabdoid phenotype. I don't think this has any relation to the pediatric rhabdoid tumors, so the cytogenetics result seems quite appropriate.

Jeronimo Forteza-Vila: I think that an extrarenal rhabdoid tumor or a carcinoma that has lost its differentiation are good options.

Masaharu Fukunaga: It is a very interesting and tough case. It is not a typical case of rhabdoid tumor immunohistochemically and ultrastructurally. I can not but call it an undifferentiated malignant tumor, unknown origin. Thank you very much, Paul.

Allen Gown: Rhabdoid tumors still are a wastebasket term, and given the absence of cytokeratin expression I'm not sure how to ultimately classify it.

Thomas Krausz: I would still consider the possibility of metastasis from a rhabdoid variant of renal cell carcinoma (described in the last few years and is distinct from rhabdoid tumor of kidney).

Thomas Mentzel: I do not have a better idea than sarcoma with rhabdoid features.

Elizabeth Montgomery: I would have assumed it was one of the many faces of metastatic renal cell carcinoma (or of renal rhabdoid tumor).

Cesar Moran: I cannot offer a better alternative.

Joshua Sickel: I agree with extrarenal rhabdoid tumor. Perhaps this patient has a concurrent RCC or metastasis to the kidney? Aren't the vast majority of renal rhabdoid tumors diagnosed in very young children?

Dominic Spagnolo: I too have called these undifferentiated sarcomas with rhabdoid features, expressing only vimentin after exhaustive immuno panels (vimentinomas) and ultrastructural scrutiny. I am surprised that there was a paucity of intermediate filaments ultrastructurally. I have never seen this presentation in the mediastinum however. The last case I saw was in November 2004 in a 50 year male with a mass invading left neck soft tissue with direct infiltration of nodes. He has had at least one local recurrence, and no other primary site has been found.

James Strauchen: Extarenal Rhabdoid tumor.

Bruce Wenig: I considered an anaplastic plasmacytoma but in the absence of CD138 staining that diagnosis is doubtful (although it may be worth doing CD79, EMA, kappa and lambda might be helpful). I would think it important to know what the solid renal tumor represents.

Lawrence Weiss: I've never seen this before in the mediastinum, but it fits my histologic definition of an extrarenal rhabdoid tumor.

CASE NO. 15— CONTRIBUTED BY: DR. WEISS

Phil Allen: . Inflammatory pseudotumor of the adrenal. Larry's conflict can easily be resolved by transposing this entity into a neoplastic key, the major one of which is benign and the minor, malignant (inflammatory fibrosarcoma). I trust this is music to your ears, Larry.

Carlos Bacchi: I also would call this pseudoinflammatory tumor.

David Ben-Dor: I see many dispersed plasma cells and occasional eosinophils in a dense fibrotic matrix. I assume the former would be polyclonal (if you bothered to perform the stains). Can't think of anything better. Why did the patient have such extensive surgery?

Michele Bisceglia: Inflammatory pseudotumor of the adrenal gland. Agree. But I have never previously seen such an occurrence.

Ira Bleiweiss: Agree

Tom Colby: Agree with diagnosis.

Kum Cooper: Larry the closest I have seen resembling this process in the retroperitoneum is retroperitoneal fibrosis, which I submitted as a case to the seminar.

Hugo Dominguez: It certainly looks like inflammatory pseudotumor to me.

Giovanni Falconieri: I do not have better alternatives.

Cyril Fisher: Inflammatory pseudotumor seems reasonable. Are SMA/desmin positive?

Christopher Fletcher: Recognizing the inherent weakness of the term 'inflammatory pseudotumor', in that the latter subsumes a wide variety of different lesional types, many of which have proved to be truly neoplastic, nevertheless, it is hard to come up with a better designation for this very unusual case. Since most examples of inflammatory myofibroblastic tumor in adults are ALK-negative, then it is very hard to prove the latter diagnosis in adult patients unless there is a more obvious cellular, fascicular component.

Andrew Folpe: Agree with inflammatory pseudotumor. Thanks for submitting this case, Larry, and thanks for your recent hospitality.

Jeronimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: Inflammatory pseudotumor, I agree. Thank you very much for this unique lesion in the adrenal glands.

Allen Gown: Never seen anything like it. Curious what the other members have to say.

Thomas Krausz: Agree with diagnosis.

Thomas Mentzel: Did non-inflammatory cells stain positively for actins (inflammatory myofibroblastic tumor) ?

Cesar Moran: Very nice example. I do not think I have seen one of these cases in the adrenal.

Joshua Sickel: Great case, Larry! The first one I've ever seen.

Dominic Spagnolo: I agree with your diagnosis of inflammatory pseudotumor. I have not personally encountered one before. John Chan mentions one in his paper on ALK expression in IMTs (AJSP 2001; 25:761), and there was a report of a calcifying fibrous pseudotumor in the radiology literature (Br J Radiol 2001; 74:452).

James Strauchen: Inflammatory pseudotumor. I have never seen one in the adrenal!

Bruce Wenig: I felt this is a myofibroblastic dominant lesion of the adrenal (residual cortical tissue seen compressed along the periphery). I have vague recollection from my AFIP days of seeing 1 or 2 similar adrenal cases (I/we did not report them). In the absence of ALK-1 staining a diagnosis of inflammatory myofibroblastic tumor as opposed to pseudotumor would appear less appropriate.

QUIZ CASE NO. 1 — CONTRIBUTED BY DR. DOMINGUEZ:

Phil Allen: Monophasic synovial sarcoma, right kidney, to be confirmed by the FISHmonger .

Michele Bisceglia: Monophasic synovial sarcoma, Wilms' tumor (which can occur in adulthood with an incidence of 1 case per million people), and EWS/PNET are my favourite diagnostic possibilities.

Tom Colby: Malignant tumor, NOS. Sadly I think I would need some immunos to exclude things like melanoma, poorly differentiated carcinoma, synovial sarcoma, et al.

Kum Cooper: PNET vs PDSS. IHC and cytogenetics to resolve.

Hugo Dominguez: Sporotrichosis?

Giovanni Falconieri: Synovial sarcoma.

Christopher Fletcher: Considerations in differential diagnosis might include small cell carcinoma, poorly differentiated synovial sarcoma, a metastasis from elsewhere or, least likely, a very poorly differentiated transitional cell carcinoma. I believe that this lesion is almost impossible in the absence of immunostains.

Andrew Folpe: High-grade malignant neoplasm- r/o PNET, r/o poorly differentiated synovial sarcoma.

Jeronimo Forteza-Vila: Rule out synovial sarcoma.

Masaharu Fukunaga: Poorly differentiated synovial sarcoma, most likely and the second choice is PNET.

Thomas Mentzel: A small round/plump spindled cell malignant neoplasm with vascular invasion – Ewing`s sarcoma/MPNET of the kidney ?

Michal Michal: It has some features of primary synovial sarcoma of the kidney.

Joshua Sickel: Endometrial low grade stromal sarcoma? Synovial sarcoma?

Dominic Spagnolo: Malignant small cell tumor of the kidney, favor PNET/Ewing's, but need to exclude others with appropriate work-up.

James Strauchen: Round cell sarcoma, adult blastemal Wilms versus PNET.

Paul Wakely: Primitive peripheral neuroectodermal tumor of kidney, primary.

Hugo Dominguez: Primary synovial sarcoma of the kidney. Immunohistochemical stains were positive for cytokeratin, vimentin, bcl-2 and focally positive for CD99. They were negative for S100, desmin, chromogranin and CD45. In situ PCR for the fusion transcripts of SYT-SSX was positive.

Lawrence Weiss: Poorly differentiated synovial sarcoma

QUIZ CASE NO. 2 — CONTRIBUTED BY DR. WAKELY:

Phil Allen: Necrotizing granulomatous inflammation, hilar lymph node, presumably histoplasmosis. I can't find the picture of the GMS stain.

Michele Bisceglia: Mycotic disease. Probably a combination of fungal infections: (?) Nocardia spp. (branched filaments) plus (?) candidiasis or histoplasmosis (blastospores or yeast cells).

Tom Colby: Hamazaki Wiesenberg bodies. The GMS stain does not look like it came from the center of a necrotic granuloma. Were any organisms present in the granulomas? The H-W bodies are seen in histiocytes in the sinuses.

Kum Cooper: Histoplasmosis.

Giovanni Falconieri: Granulomatous lymphadenitis

Andrew Folpe: Granulomatous inflammation secondary to yeast (? Histoplasma?)

Jeronimo Forteza-Vila: Fungal granulomatous lesion.

Masaharu Fukunaga: Epithelioid granuloma with central necrosis. Tuberculosis?

Thomas Mentzel: Granulomatous lymphadenitis with the evidence of caseating granulomas (acid fast staining ?).

Joshua Sickel: Histoplasmosis.

Dominic Spagnolo: Necrotizing granulomatous lymphadenitis (infective), with numerous Hamazaki-Wesenberg bodies. I think it is the latter showing up on the silver stain. The background does not look like a granuloma, and the shapes and sizes of the silver positive structures mirror the H-W bodies present in the node. I would have TB at the top of my list as possible infectious agents.

James Strauchen: Necrotizing granulomatous lymphadenitis. I think the GMS stain represents artifact.

Saul Suster: The reason why I suggested to Paul that he send this in as a Quiz case is because of the fortuitous association of Hamazaki-Wesenberg bodies with the granulomas, thus enhancing the potential for confusing these structures with fungal organisms.

Paul Wakely: I presented this case recently at our daily peer review conference, and Saul suggested I send it in to the group as a quiz case. This is a hilar lymph node from a 40 y/o woman who also had a wedge resection of a mass in the right lower lobe of her lung that turned out to be a necrotic granuloma. There is an attached photo of a GMS stained image of this node.
Diagnosis: Hamazaki-Wesenberg bodies.
Comment: H-W bodies are also called yellow-brown bodies because of their appearance in the H&E stain. A photo of the Gomori methenamine silver stain of this node is included because the only practical reason for presenting this case is the potential for confusing these bodies as fungal yeast organisms (which parenthetically was done by several faculty members at our conference). This is particularly so if the node contains granulomas as this one does. You will note that on your H&E slide H-W bodies are primarily within the sinusoids of the node, not within the granulomas. The literature states that these bodies represent large residual bodies/ giant lysosomes composed of lipofuscin pigment. They are not specific for sarcoid, but found in a variety of conditions.
References: Ro JY et al. Yellow-brown (Hamazaki-Wesenberg) bodies mimicking fungal yeasts. Arch Pathol Lab Med 1987; 111:555; Sieracki JC, Fisher ER. The ceroid nature of the so-called "Hamazaki-Wesenberg" bodies". Am J Clin Pathol 1973;59:248.

Lawrence Weiss: Small yeast, ? histoplasmosis, but I do not see true budding

FOLLOW UP COMMENTS:

AMR SEMINAR #39, CASE 19, SUBMITTED BY SAUL SUSTER:

Phil Allen: These latest circulated sections of the second pelvic recurrence are similar to the previously circulated slide (AMR number 39, Case 19) except that there are numbers of syncytial type or multinucleate cells, possibly due to the radiotherapy. Mitoses are very hard to find and I cannot see any necrosis. I can not see any typical features of stromal endometriosis (low-grade endometrial stromal sarcoma) but the cells look like the old-fashioned epithelioid smooth muscle cells. The relationship between benign metastasizing leiomyoma, intravenous leiomyomatosis and stromal endometriosis is close, with transitional cases occasionally being observed. I think Saul is right and this is a variant of stromal endometriosis (low-grade endometrial stromal sarcoma) with epithelioid cells of the type seen in epithelioid smooth muscle tumors of the uterus. The primary lesion may have been one of the uterine "leiomyomas," although a primary retroperitoneal Mullerian tumor is also possible.

David Ben-Dor: For endometrial stromal sarcoma I would expect the cells to be smaller, and more spindly; also I have trouble delineating the spiral arterioles. Why couldn't the "leiomyomas" in the original hysterectomy have been stromal tumor nodules, possibly the intravenous variant?

Thomas Colby: I like your idea Saul. I think the cytology and the stromal change would fit with low grade ESS. The presence of epithelial elements can also be explained. This case has some peculiar giant cells, the significance of which is not clear to me.

Andrew Folpe: ESS seems like a reasonable diagnosis, although the histology isn't perfect. CD10 has turned out to be "the vimentin of the new millennium", so I wouldn't place too much weight on it either way.

Masaharu Fukunaga: Thank you very much for the follow up slide. I could not find residual endometrial tissue in the previous slide. It seems to me low-grade stromal sarcoma with sex-cord-like differentiation. Interestingly, the histology of this one and the previous one is basically same, but it is different immunohistochemically on CD10. Is CK is positive in this one? I had a case of uterine tumor resembling ovarian sex cord tumor that metastasized to the iliac bone. The metastatic lesion was positive for CK and initially a diagnosis of "adenocarcinoma, metastatic" was rendered. The original diagnosis of the uterine tumor was "cellular leiomyoma"

Dominic Spagnolo: I still find this difficult, but I would agree with your interpretation now that this is most likely a low grade ESS, with epithelioid features. Thanks for the follow-up.

Lawrence Weiss: Agree with low-grade endometrial stromal sarcoma

FOLLOW-UP COMMENTS:

AMR SEMINAR #41, Quiz Case 3, SUBMITTED BY PAUL WAKELY, JR:

Phil Allen: The recurrence is not as obviously endothelial as the originally distributed lymph node lesion and there are still not many mitoses, although the nuclei are alarming. I note that Chris Fletcher thought the original was a metastatic angiosarcoma whereas John Chan favored polymorphous hemangioendothelioma, metastatic angiosarcoma to be excluded. On the basis of the relatively long follow-up, the lymph node lesion is probably the primary. It looks as though polymorphous hemangioendothelioma is not as harmless as I thought it was.

Andrew Folpe: I guess fortuitously the first high power field I came down on had two mitotic figures. That finding, the cytology, and the infiltrative growth pattern lead me to agree that this should be considered at least low grade malignant and I would probably favor intermediate grade. Anecdotally the last time I was in Rochester, Tony Nascimento was showing me another case that he thought represented a metastatic polymorphous hemangioendothelioma.

Christopher Fletcher: Indeed I think that there is no question that this recurrent mass shows features of angiosarcoma, high grade. My recollection is that I favored angiosarcoma when Paul first submitted this case. Either way, with the passage of time, it seems that quite a few of the lesions which we originally diagnosed as polymorphous hemangioendothelioma have ultimately behaved as angiosarcomas – this was one of the reasons that we did not include polymorphous hemangioendothelioma in the new WHO classification (2002), given the increasing concerns that this may not be a discrete entity.

Thomas Colby: Well, I thought the original case was convincing for a polymorphous HE, but there aren't very many cases of it yet. The current material seems to be behaving like a low-grade malignant vascular tumor. Perhaps we will discover that this is the natural history of polymorphous HE. Thanks for giving us this follow-up.

Masaharu Fukunaga: The previous one seems polymorphous hemangioendothelioma and this time, it looks angiosarcoma, low to intermediate grade. Thank you Paul, for sharing this very interesting case.

Dominic Spagnolo: This recurrence is very different and monomorphous compared to the original polymorphous cytoarchitecture. I agree with calling it angiosarcoma but would not know whether it is likely to now behave in an aggressive manner or not, low mitotic activity notwithstanding. Thanks for the follow-up.

Lawrence Weiss: Recurrent hemangioendothelioma (low grade angiosarcoma)