COMMENTS TO AMR SEMINAR #53

CASE NO. 1 – CONTRIBUTED BY: PHILIP ALLEN:

Carlos Bacchi: Thanks for this beautiful example of benign lymphoepithelial cyst of the head of the pancreas. I have never seen one before.

David Ben-Dor: Dr Allen, nice case. I've seen this in the parotid but not in the pancreas. It seems almost par for the course that some of the unusual cases seen in these seminars were either discovered or the largest series of which was published by one of the members of the club.

Gerald Berry: I agree with the diagnosis of benign lymphoepithelial cyst but must admit that this is the first case that I have encountered.

Michele Bisceglia: Benign lymphoepithelial cyst, head of pancreas. Agree. We had another such case in Seminar #26 contributed by L. Weiss. In my comment to that case, I mentioned having previously seen a case here in a woman who had been earlier operated on for invasive squamous cell carcinoma of the cervix, which in some way raised a few problems.

Ira Bleiweiss: Wow. Never seen this before.

Tom Colby: Agree with diagnosis, lovely case.

Kum Cooper: Thank you. I have seen a couple of these in Africa, and wondered if they were AIDS-defining/presenting as the salivary ones are?

Ivan Damjanov: Agree. Nice example.

Otto Dietze: I have seen this only in the parotid, thank you.

Hugo Dominguez-Malagon: Pancreas and salivary glands have many things in common including lymphoepithelial cyst, did you consider the possibility of AIDS?

Göran Elmberger: Great case. First case for me as well. Noted prominent keratohyaline granules and a relative sparse intraepithelial lymphocytic content - features that would be unusual in a lymphoepithelial branchiogenic cyst of the lateral neck.

Vincenzo Eusebi: Very nice case, never seen one before.

Giovanni Falconieri: My first case as well, Phil. I guess I won't have too many chances to see more cases like this. Thanks for this unusual contribution

Cyril Fisher: Benign lymphoepithelial cyst, excellent slide.

Andrew Folpe: Agree with lymphoepithelial cyst. Very interesting. I have nothing to add.

Christopher Fletcher: Very nice example of this rare and rather enigmatic entity. Since these lesions seem never to be associated with HIV infection (when located in the pancreas), it would be most interesting to know if any similarities could be identified with comparable salivary gland lesions in terms of pathogenetic mechanism.

Jerónimo Forteza Vila: It is a lesion I have not seen before. The amount of keratin draws my attention and makes me think about a teratomatous lesion.

Masaharu Fukunaga: This is my first time to see "benign lymphoepithelial cyst" of the pancreas. Thank you very much for the case and comments.

Thomas Krausz: I have seen only one example of this entity before. Regarding pathogenesis, I think it is similar to those which occur in salivary glands.

Janez Lamovec: I have never seen this lesion in the pancreas, before but it is definitely similar to such cysts elsewhere.

Thomas Mentzel: Many thanks for sharing this rare lesion that probably belongs to the spectrum of acquired multi-cystic reactive conditions as seen in the head and neck area.

Markku Miettinen: Agree on benign lymphoepithelial cyst, and could not find significant atypia suspicious of a well-differentiated cystic metastasis that in other locations might be in the differential.

Liz Montgomery: Very nice example. Thanks for sending it.

Giuseppe Pelosi: This is a very nice case showing a benign lymphoepithelial cyst of the head of the pancreas. This is the first time for me to observe a similar case that is more frequently described in the neck or thymus. I agree with Dr. Allen that this case is interesting and appealing. As far as its pathogenesis is concerned, probably inflammation and secondary dilation changes play some role in the development of this lesion, in keeping with similar occurrences in the neck and thymus. Congratulations on this interesting case.

Santiago Ramon y Cajal: Nice example of lymphoepithelial cyst with a cyst lining of stratified squamous epithelium, organized lymphoid tissue and keratinous content material.

Juan Rosai: Very nice example of so-called benign lymphoepithelial cyst of the pancreas. This lesion, which in all likelihood is non-neoplastic, is very similar to the multilocular thymic cyst and other lesions that Saul Suster and I reported in various places in the head and neck region, most of them related to the branchial arches (Am J Surg Pathol 15: 388-398, 1991). Perhaps the only significant difference is that whereas the lesions in the latter group show a characteristic infiltration of the squamous epithelium by the lymphocytic component, in my experience those located in the pancreas tend to have a very sharp separation between the epithelium and the lymphocytic elements. I still suspect that the pathogenesis is similar, also because both types of lesions occasionally show sebaceous gland differentiation, but it's hard for me to figure out what are branchial arches doing as low as the pancreas.

Joshua Sickel: This case is a nice contrast to the "pseudo-lymphoepithelial" cyst of the pancreas that I submitted for Seminar #54.

Dominic Spagnolo: Beautiful lymphoepithelial cyst of the pancreas. I have only encountered this in the parotid before. Thanks, Phil.

James Strauchen: Didn't know they occurred here! Thanks for this informative case.

Saul Suster: First time I see this in the pancreas! Many thanks for sharing it.

Paul Wakely, Jr.: Very impressive gross image and H&E slide. Best example of lymphoepithelial cyst I have seen.

Lawrence Weiss: Never seen one before. Thanks.

Bruce Wenig: Nice case. I have had the opportunity to see several pancreatic lymphoepithelial cysts. I would be interested in reading Drs. Adsay's and Rosai's views on the pathogenesis of this rare lesion beyond that which Phil provided.

CASE NO. 2 – CONTRIBUTED BY CARLOS E. BACCHI:

Phil Allen: Mastocytosis, probably systemic, retroperitoneal lymph node. I did not recognize the clear cells as mast cells. I would be interested in the results of the Giemsa stain, although I notice on page 445 of the quoted article that the mast cells may contain very few or no metachromatic granules.

David Ben-Dor: Dr. Bacchi, great pickup! I was impressed by the eosinophils at first and didn't think of the diagnosis, and I can't say that I can clearly identify the lesional cells even after reading the explanation. Would a simple Giemsa stain be helpful or is this passé in the age of immunohistochemistry?

Gerald Berry: I always find the presence of eosinophils as a greater prompter to think of the possibility of mast cell lesions. Nice example.

Michele Bisceglia: Mastocytosis. We had a previous case in the spectrum of the same disease in Seminar #36, contributed by O. Dietz. Have seen 2 cases of systemic mastocytosis (abdominal lymph nodes with bowel involvement), and bone lesions (the latter seem to be a consistent finding in systemic disease). A good histochemical stain for mast cells is also Leder stain (naphthol-AS-D-Chloroacetate-esterase), which of course also stains myeloid cells.

Ira Bleiweiss: Another "never seen before".

John Chan: Beautiful case of mastocytosis, superficially resembling marginal zone B-cell lymphoma. As pointed out by Carlos, the accompanying eosinophils and sclerosis provide the clue that the clear cells represent mast cells.

Tom Colby: Agree with diagnosis. Mastocytosis is just unusual enough that it takes me a while to think of it, but once one thinks of it, there is little in the differential.

Kum Cooper: Thank you, Carlos, for this instructional case. The pale clear cytoplasm led me towards the AILD pathway! We have had previous cases in this seminar with more typical morphology but it is always critical to see the morphological variants!

Ivan Damjanov: Agree. Even though all the clues pointing to the right diagnosis are in the slide, I somehow always miss this entity.

Otto Dietze: I agree, the association of eosinophils and sclerosis is a clue to the diagnosis. I nearly routinely use CD 117 staining in cases of eosinophilic colitis and gastritis since I missed this diagnosis several years ago.

Göran Elmberger: Rare case showing classical triad of clear cells, eosinophils and sclerosis. With the characteristic IHC cited, I have nothing to add.

Vincenzo Eusebi: Great case. Eosinophils always tell us something.

Giovanni Falconieri: Pretty difficult, Carlos. I would not have thought about mastocytosis. This lymph node section is also intriguing because of fibrosis and marginal artifactual changes. The interfollicular growth pattern and the capillaries with prominent endothelium may also suggest a peripheral T cell lymphoma. Thanks for this instructive case!

Cyril Fisher: Systemic mastocytosis, great example.

Christopher Fletcher: Very nice case. It could have been of interest to stain this lymph node for CD25, since expression of the latter in mast cell lesions has recently been shown (in two studies from our department) to be quite reliably predictive of systemic mastocytosis, with which your patient is most likely affected, judging by the information which you kindly provided.

Andrew Folpe: Great case of mastocytosis involving a lymph node. This looks exactly like the only other case I have ever seen, one I had as a resident. Thanks.

Jerónimo Forteza Vila: I agree with the diagnosis; when a lesion resembling a low grade B-cell lymphoma is difficult to classify according to histology or to make a first approach with the immunohistochemical study, one of the first diagnostic possibilities is mastocytosis. C-kit and tryptase help to make the final diagnosis. If there is bone marrow involvement or leukemia, hematologists encounter less problems in making a diagnosis than we find.

Masaharu Fukunaga: It is a challenging case. My impression was inflammatory pseudotumor, follicular dendritic tumor (?) Thank you very much for the interesting case and informative discussion.

Allen Gown: Nice example; thanks, Carlos.

Thomas Krausz: Great case. The diagnostic clues discussed by Carlos are very helpful. Was there *KIT* mutation in this case? If there was imatinib, perhaps can be tried as treatment.

Janez Lamovec: The diagnosis of such cases is much easier if lymph nodes are routinely stained by Giemsa.

Thomas Mentzel: For me, it was difficult to recognize the increased number of mast cells on H&E. Did mast cells stain positively for CD25 (a marker that is positive in neoplastic mast cells)?

Markku Miettinen: Agree on mastocytosis, but having limited experience of its nodal presentation would not have been able to diagnose it on H&E; as you say marginal cell lymphoma is a differential, but here pronounced sclerosis may be another clue of mastocytosis.

Michal Michal: To prove the diagnosis in these cases, we found very helpful and easy to perform the typical mutation in the exon 17 mutation in the codon 816 (e17-D816V) of the c-kit gene.

Liz Montgomery: With the GI symptoms, would wonder if the mastocytosis involved with GI tract or just caused diarrhea with systemic modulation. The sclerosis and backdrop of eosinophils are interesting since they are the "flags" to think of mastocytosis. There is some interesting work in skin and GI tract using CD25 :
- Hollmann TJ, Brenn T, Hornick JL. CD25 expression on cutaneous mast cells from adult patients presenting with urticaria pigmentosa is predictive of systemic mastocytosis. Am J Surg Pathol. 2008 Jan;32(1):139-45.
- Hahn HP, Hornick JL. Immunoreactivity for CD25 in gastrointestinal mucosal mast cells is specific for systemic mastocytosis. Am J Surg Pathol. 2007 Nov;31(11):1669-76.

Giuseppe Pelosi: I agree with the diagnosis of mastocytosis growing in a lymph node, but unfortunately I am not experienced in this type of lesion.

Santiago Ramon y Cajal: Thank you for this challenging example of mastocytosis.

Juan Rosai: Very nice case of systemic mastocytosis. The diagnosis is not very easy because of the pale quality of the slide and the fact that the number of mast cells is not very abundant, but the presence of expanses of medium-sized cells with a finally granular or clear cytoplasm surrounded by a sharp cell membrane and accompanied by numerous eosinophils and fibrosis should be a clue to the diagnosis whether the lesion is in the lymph node, spleen or bone marrow (Am J Surg Pathol 7: 425-438, 1993).

Joshua Sickel: We recently had a case of mast cell disease presenting in a colonic biopsy. The patient subsequently was found to have bone marrow involvement. Several years ago I observed a case of chronic myelomonocytic leukemia involving a lymph node which looked very similar to the current case….another potential diagnosis to add to the differential diagnosis.

Dominic Spagnolo: Great case, Carlos. Given the sclerosis and mixed inflammatory infiltrate, inflammatory pseudotumor also entered my differential, but the nodules of clear cells are a give away. Thank you.

James Strauchen: Excellent example of the fact that you can't make the diagnosis if you don't think of it! The Perifollicular involvement is said to be classic. Must be rare, I have seen only one other node like this.

Saul Suster: Totally missed it! Hope I'll keep mastocytosis in the differential next time. Thank you for the contribution and the education!

Paul Wakely, Jr.: Carlos, I have a case of aggressive systemic mastocytosis involving soft tissue and lymph node that I was planning to send to the club. Unlike your case, mine shows obvious cellular features of malignancy.

Lawrence Weiss: Great case. Monocytoid B-cell hyperplasia usually goes with follicular hyperplasia, which is not present in this case. CD25 supposedly stains neoplastic, but not normal, mast cells. With this extensive involvement, the bone marrow (and peripheral blood) should definitely be examined, both for possible involvement by mastocytosis as well as for a myeloid disorder.

Bruce Wenig: By light microscopy, I thought this would prove to be a marginal zone B-cell lymphoma given the clustering of the monocytoid appearing clear cells. Live and learn. Thanks, Carlos.

CASE NO. 3 – CONTRIBUTED BY IRA BLEIWEISS:

Phil Allen: Alveolar soft part sarcoma, posterior chest wall. It is my impression that alveolar soft part sarcoma is more common in the Chinese of Hong Kong than it is in Caucasians in Australia. We hardly ever see this tumor in Australia, but I saw several local cases at the Prince of Wales hospital in Hong Kong over a 5-year-period.

Carlos Baachi: Nice example of alveolar soft part sarcoma. I was looking for something unusual in the lesion but ASPS is unusual by itself.

David Ben-Dor: Dr. Bleiweiss, well I guess cases like this are easy come easy go at Mt. Sinai. The histology does look very typical. Were the intracytoplasmic crystals obvious?

Gerald Berry: Beautiful case. The last one I encountered was in the breast of a young woman.

Michele Bisceglia: Alveolar soft part sarcoma. Nice case. Agree.

Tom Colby: Agree with diagnosis, lovely case. I am not sure I would have been quite bold enough to not have done at least a couple of immunos.

Kum Cooper: Thanks Ira. Great teaching case.

Ivan Damjanov: Agree.

Otto Dietze: Nice case, it's more than a decade ago that I have seen one.

Hugo Dominguez-Malagon: I agree with the diagnosis of ASPS, nice case.

Göran Elmberger: Beautiful and morphologically typical case. Thanks.

Vincenzo Eusebi: Great teaching case.

Giovanni Falconieri: Morphology fits with alveolar soft part sarcoma. I have not had many such cases in my collection yet. I believe this is one of the best I have ever seen. Thanks for this contribution. From a practical point of view, I believe that melanoma, which is suggested by the cell discohesion and some glassy cytoplasms, would be a major differential concern.

Cyril Fisher: Alveolar soft part sarcoma, with solid areas. Nice example.

Christopher Fletcher: Indeed a pretty case. As Ira says, these tumors are indeed very rare, even if we find them easy to recognize – our Sarcoma Clinic here at Brigham/Dana-Farber sees approximately 750 new patients each year (many of them for management of metastatic disease), but we do not seem to see more than a couple of ASPS among this large group each year.

Andrew Folpe: Alveolar soft part sarcoma, principally showing the small nest ("paraganglioma-like") pattern. Nice example.

Jerónimo Forteza Vila: I agree with the approach and diagnosis.

Masaharu Fukunaga: A beautiful case of alveolar soft part sarcoma. Thank you very much.

Allen Gown: While it is probably ASPS, I'm not sure I'd be so cavalier about the diagnosis, particularly in light of the histologic overlap with with Xp11 translocation renal cell carcinomas. I have had cases in which that differential has been brought up, and immunohistochemistry can be helpful, as the renal cell carcinomas generally (but by no means always) express cytokeratins and PAX2.

Thomas Krausz: Classic example. Thank you.

Janez Lamovec: Thank you for showing us this fantastic case!

Thomas Mentzel: Thanks for this nice case of an alveolar soft part sarcoma showing a quite solid growth.

Markku Miettinen: Alveolar soft part sarcoma, fully agree. If one wants a widely available supportive test, then D-PAS stain for cytoplasmic crystals might be one.

Liz Montgomery: Nice "bread and butter" example of alveolar soft part sarcoma. Thank you.

Giuseppe Pelosi: This is a spectacular case of alveolar soft part sarcoma, with classical and diagnostic features for this entity. Very nice and instructive case!

Santiago Ramon y Cajal: Picture perfect example of Alveolar Soft Part Sarcoma with uniform, discohesive cells arranged in an alveolar pattern.

Juan Rosai: Very nice example of alveolar soft part sarcoma (unless it is a metastasis from the type of renal cell carcinoma associated with chromosomal alterations reported by Peter Argani that looks very much like alveolar soft part sarcoma). I remember Dr. Ackerman once made the statement that he didn't believe in the existence of alveolar soft part sarcoma, and that he thought they were all metastases from renal cell carcinomas. I don't think he really believed that, but wanted to provoke Fred Stewart, his Memorial nemesis.

Joshua Sickel: Thanks for this beautiful case for the teaching collection. I don't think I'm brave enough to sign this out without the usual confirmatory special stains!

Dominic Spagnolo: Very nice alveolar soft part sarcoma. I would have wimped and done some immunos!

James Strauchen: Nice case! Didn't know we had it. Surgical Pathology Conference case?

Paul Wakely, Jr.: Nice case. I'm curious if you have seen any examples of FNA smears of ASPS.

Lawrence Weiss: Classic histology in funny location. I must confess that I still would have done immunostains.

Bruce Wenig: Great example of an ASPS.

CASE NO. 4 – CONTRIBUTED BY JOHN CHAN:

Phil Allen: Merkel cell carcinoma with rhabdomyosarcomatous differentiation metastatic to parotid gland from a primary pure Merkel cell carcinoma of the temporal skin. A very convincing and instructive case. Thanks for the contribution John.

Carlos Bacchi: This is really a fascinating case, both by the clinical manifestation of metastatic Merkel cell carcinoma as parotid mass and by the unusual histological appearance with rhabdomyosarcoma differentiation which I had never seen before.

David Ben-Dor: Dr Chan, a few years ago I presented to the club a case of Merkel cell carcinoma in the gingiva, which I assumed metastasized from a primary in the scalp. Afterwards I was told by the oncologist that the patient's scalp was peppered with many small such tumors. So I wasn't sure which of those was the primary. At least in this case there was a known source. Interestingly, I recalled the paper written by you together with Bruce Wenig and Saul Suster which showed that among the cohort of small cell carcinomas, those in the parotid can be CK20 positive. So can you be sure that the tumor in the parotid is the metastasis and not the primary?

Gerald Berry: I think I have seen more variants of Merkel cell carcinoma coming from this seminar group than I have in our institution!!

Michele Bisceglia: Parotid gland –metastatic Merkel cell carcinoma, with rhabdomyosarcoma differentiation (metastatic "Merkel cell carcinosarcoma"). Agree. Nice case. In a case by Fernández-Figueras MT, et. al., you quoted, rhabdomyosarcomatous differentiation was also seen in the metastasis, while it was not seen in the primary (J Cutan Pathol. 2007;34:410-4). In the case by Eusebi, et. al. (case 1 of 3 small cell neuroendocrine carcinoma with skeletal muscle differentiation) the rhadomyoblastic differentiation was seen in the primary, and it was predicted morphologically by the appearance of large plasmacytoid-like cells with abundant eosinophilic cytoplasm (Am J Surg Pathol. 2000;24:223-30). We have seen here also a case which did show rhabdomyoblastic differentiation (desmin and myogenin and other striated muscle markers positive) which was not predicted by cell morphology (monomorphic Merkel cell tumor) and immuno for striated muscle markers was done since the day before we had the same markers positive in an anaplastic medulloblastoma – medullomyobastoma at the protein level - so muscle markers in Merkel were done just to see, for curiosity. Likely all Merkel cell tumors would merit to be studied for striated muscle markers – who knows? You quoted even leiomyosarcomatous differentiation in Merkel cell tumor, and that was also seen in a lymph node metastasis, while it was absent in the primary – Cooper L, et al. Histopathology. 2000;36:540-3.

Ira Bleiweiss: Agree.

Thomas Colby: Agree with diagnosis. I got as far as carcinosarcoma/sarcomatoid carcinoma and the history and immunohistochemistry certainly support Merkel cell carcinoma. With prompting by John's discussion, I did go back and find some cross striations. Amazing! There are two cases in this set where we can find rhabdomyosarcomatous differentiation the old fashion way.

Kum Cooper: Thanks John. Picking up the small cell component and the sarcomatous component was not a problem; BUT metastatic Merkel cell with rhabdomyosarcomatous differentiation...never crossed my mind!!! Great case.

Ivan Damjanov: Agree. No way I would have made this diagnosis without your help and immunohistochemistry. Thanks for teaching me about aberrant differentiation and my apologies to our "ultimate leader" for not reading his 2006 article.

Otto Dietze: Convincing histology from the H&E aspect and a unique case.

Hugo Dominguez-Malagon: Amazing case, this proves that "neuroendocrine carcinomas" are ubiquitous tumors arising from primitive totipotential cells. Merkel tumor and small cell carcinoma of salivary gland can be identical.

Göran Elmberger: Very interesting case. I did find the cross-striations but only after you told me to expect them and with microscope optimized for contrast detection. Given the spatial and temporal relation to the pre-existent Merkel cell carcinoma of the skin, it is natural to interpret the findings as metastases, but I only want to remind you that primary small cell carcinomas of the salivary glands often are CK20 positive.

Vincenzo Eusebi: The usual combination again: neuroendocrine carcinoma and rhabdomyosarcoma. As John has stated, the two components are usually intermingled, with a few exceptions only (1).
Roncaroli F et al. Sarcomatoid carcinoma of the anorectal junction with neuroendocrine and rhabdomyoblastic features. Am J Surg Pathol 1995;19 (2):217-223.

Giovanni Falconieri: Very interesting case demonstrating little known (to me, obviously) polyphenotypic qualities of Merkel carcinoma. Indeed, there is similarity to the lung tumor submitted by Giuseppe Pelosi in AMR52. Thanks for this contribution.

Cyril Fisher: Rhabdomyosarcoma in Merkel cell carcinoma, incredible case.

Christopher Fletcher: Beautiful and very convincing case – it is remarkable that heterologous rhabdomyoblastic differentiation seems to be a particular feature of neuroendocrine carcinomas of all types, as well as squamous cell carcinomas (particularly of skin or upper aerodigestive tract) – but seems much less frequent in other malignant epithelial neoplasms.

Andrew Folpe: Fascinating case. I think I probably would have thought first of metastatic melanoma, and then eventually tipped to the rhabdomyosarcoma. However, since RMS often express cytokeratins and can express neuroendocrine markers, I don't know that I would have thought to run CK 20. Great diagnosis.

Jerónimo Forteza Vila: It is a very exciting case that allows us to speculate from tumor plasticity to cancer stem cells.

Masaharu Fukunaga: What a beautiful case, John! There are two definite cell components, Merkel cell carcinoma and embryonal rhabdomyosarcoma. Thank you very much for sharing this interesting case.

Allen Gown: Interesting case; I have seen one such case myself.

Thomas Krausz: Superb case. I have seen other "crazy" things in association with Merkel cell carcinoma but not rhabdomyosarcoma before. On my slide there is also focal squamous differentiation.

Janez Lamovec: We've never seen this type of Merkel cell carcinosarcoma before. I thought of metastatic small cell neuroendocrine carcinoma with sarcomatous stroma (carcinosarcoma), possibly of pulmonary origin before reading your comment.

Thomas Mentzel: A fantastic case of metastasizing metaplastic Merkel cell carcinoma with rhabdomyosarcomatous differentiation. Interestingly, polyomavirus DNA has been found in the majority number of analysed cases of Merkel cell carcinoma most recently (Science 2008; 319: 1096-1100).

Michal Michal: Must be extremely rare. We have not found a single case of this differentiation in more than 120 cases of Merkel cell carcinoma in our files.

Markku Miettinen: Agree on neuroendocrine small cell carcinoma with a rhabdomyosarcomatous component. As a Merkel cell carcinoma, one might classify this as a small cell carcinoma-like variant.

Liz Montgomery: This is an amazing case. Thanks for reinforcing the point of "plasticity" of Merkel cell tumor as described by Saul.

Giuseppe Pelosi: This is a very difficult case of Merkel cell carcinoma with sarcoma/sarcoma-like component. I never saw a similar cases thus far, but in the general theme of sarcoma differentiation in epithelial tumors, I am collecting some cases of SCLC with sarcoma/sarcoma-like differentiated tumor component, including rhabdomyosarcomatous tumor cells. I congratulate John for this extraordinary tumor, very unusual for me.

Santiago Ramon y Cajal: This is certainly a very difficult case that shows the different morphologic patterns that Merkel Cell Carcinomas can take.

Juan Rosai: Incredible case. I'm quoting Dr. Ackerman again: "Malignant tumors can make anything, and usually do". I have to say that I didn't think that the small cell component in the metastasis was 100% typical of Merkel cell carcinoma because the nuclei seemed to be oval and even spindle rather than round, but we are told that the immunohistochemical profile was typical of this entity. As John Chan kindly pointed out, this tumor fits into the category that we described with Vincenzo Eusebi of small cell neuroendocrine tumor showing skeletal muscle differentiation (Am J Surg Pathol 24:223-230;2000).

Joshua Sickel: Spectacular case. We recently encountered a case of primary Merkel cell carcinoma of the parotid gland (at least we haven't found a primary yet).

Dominic Spagnolo: Another weird Merkel carcinosarcoma. The rhabdo element is stunning. There is focal squamous differentiation too in my slide. Thanks John.

James Strauchen: Didn't know Merkel cells did this!

Saul Suster: Spectacular case, John! This is the first case I see with rhabdomyosarcomatous differentiation.

Lawrence Weiss: A Merkel cell carcinosarcoma—great case.

Bruce Wenig: That is one cool case! Thanks, John

CASE NO. 5 – CONTRIBUTED BY KUM COOPER:

Phil Allen: Metastatic uterine stromal endometriosis with meningothelial-like whorls, retroperitoneum. A most unusual variant. Thanks Kum. Contrary to currently popular thought, I believe this tumor is closer to endometriosis, intravenous leiomyomatosis and benign metastasising leiomyoma than it is to genuine sarcomas. The trouble with the current nomenclature is that clinicians often omit "low grade" when they are talking about a case and some patients end up having high grade sarcoma therapy, sometimes with fatal results. I do not believe that metastases always indicate a carcinoma-like malignant process.

Carlos Bacchi: Nice example of low-grade endometrial stromal sarcoma.

David Ben-Dor: Dr Cooper, the question is to what extent the syncytial meningothelial like whorling isn't an elaboration of the peri-arteriolar whorling seen routinely? I guess that if it's very pronounced and happens to dominate the needle biopsy, it would give rise to interesting conjectures. Was immunohistochemistry done or were the findings too obvious to warrant it? This is because recently I received material which was spontaneously expelled from the uterus and which looked like endometrial stromal neoplasm of some sort (either benign or low grade malignant). Given the odd presentation, I thought it incumbent to at least try and substantiate the diagnosis. However, the immunos were disappointing: CD10 was weak and focal while the desmin was stronger and more prominent. This was not the classical profile though I'm not convinced it ruled the diagnosis out. The question is to what extent the "classical" immunoprofiles are really adhered to in real life?

Gerald Berry: Nice example of ESS.

Michele Bisceglia: Metastatic low grade endometrial stromal sarcoma. Beautiful case. Had not seen before such a whorled pattern in this kind of tumor.

Ira Bleiweiss: Agree, but impossible diagnosis without history. Great case.

Tom Colby: Agree with diagnosis. I have seen that peculiar whirling previously in this tumor.

Ivan Damjanov: Agree. I thought that the tumor looked like a meningioma and entertained the possibility of a PECOMA.

Otto Dietze: I have never seen this pattern before. (Before sending my last case of clear cell AFX to the AMR Seminar, I was not sure whether I should submit a case of low grade stroma sarcoma with endometrioid glands.)

Hugo Dominguez-Malagon: Beautiful case of endometrial stromal sarcoma, I never seen this striking whorled pattern.

Göran Elmberger: Astonishing case. My first thought before reading the location was surely meningioma. The more subtle signs of "starburst" hyalinization and sex-cord-like differentiation might lead your thoughts in right direction. The presentation in retroperitoneal metastases seems not previously described and adds to the diagnostic challenge. Thanks for pointing out this unusual pattern in endometrial stromal sarcoma.

Vincenzo Eusebi: Fortunately this is a slide seminar case. Endometrial stromal sarcoma with whorled pattern. In real life, I am sure I would have done a lot of work-up before reaching the diagnosis.

Giovanni Falconieri: Difficult case, Kum. Without the clinical history, I would have a hard time to put things in the right place! Never seen such meningothelial-like changes in ESS. Thanks for this extraordinary contribution.

Christopher Fletcher: This is indeed an impressive case – in the original small needle biopsy, which Kum had been kind enough to share with me, we had seriously considered the possibility of dedifferentiated liposarcoma, given the whorls and retroperitoneal location.

Cyril Fisher: I have not seen this before in ESS.

Andrew Folpe: Agree with endometrial stromal sarcoma. I kept looking for the well-differentiated liposarcoma, thinking that this was going to be one of those dedifferentiated tumors with meningothelial-like whorls. I don't think I have ever seen this pattern in ESS, but it makes perfect sense once you think about it.

Jerónimo Forteza Vila: Interesting case.

Masaharu Fukunaga: A challenging case without history. My impression was a kind of meningotheilal tumor or dedifferentiated liposarcoma. Thank you very much for the fascinating case, Kum.

Allen Gown: Did this tumor mark as an endometrial stromal sarcoma (i.e. was there CD10 expression, nuclear expression of beta-catenin, etc.?)

Thomas Krausz: Agree with diagnosis. Highly educational case, thanks Kum. Starburst-like hyalinization and sex-cord-like differentiation I have seen before in endometrial stromal sarcoma but the meningothelial-like differentiation is new to me. Before reading the discussion, I was considering dedifferentiated liposarcoma with meningothelial/neural-like whorls.

Janez Lamovec: The whirling pattern is really striking, and given the location of the tumor, in a small biopsy specimen the possibility of a dedifferentiated liposarcoma with similar structures must be entertained. Thank you, Kum, for this extraordinary case.

Thomas Mentzel: Thanks for this difficult case of peculiar low-grade endometrial stromal sarcoma showing a prominent and partly perivascular whorling growth pattern.

Michal Michal: Nice case. In this location it could be easily confused with whorled structures of the primary liposarcomas (A.G.Nascimento, P.J.Kurtin, L.Guillou, Ch.D.M.Fletcher. Dedifferentiated liposarcoma. A report of nine cases with a peculiar neural like whorling pattern associated with metaplastic bone formation, Am J Surg Pathol1998:22:345, J.C.Fanburg Smith, M.Miettinen. Liposarcoma with meningothelial like whorls: a study of 17 cases of a distinctive histological pattern associated with dedifferentiated liposarcoma. Histopathology 1998:33:414).

Markku Miettinen: Agree on endometrial stromal sarcoma. I trust that the tumor was ER and CD10 positive. Incidentally, the "starburst-like" hyalinization has some resemblance to the hyaline rosettes in low-grade fibromyxoid sarcoma variants.

Liz Montgomery: Fabulous example of ESS. Thanks for sharing it.

Giuseppe Pelosi: I agree with the diagnosis of metastatic low-grade endometrial stromal sarcoma for this meningioma-like sarcoma, but I feel that dedifferentiated liposarcoma should also be taken into account on morphological grounds.

Santiago Ramon y Cajal: The whorled pattern is quite prominent in this neoplasm. Thank you for this unusual case of low grade Endometrial Stromal Sarcoma.

Juan Rosai: This case got me. I thought of metastatic endometrial stromal sarcoma but eventually I decided that it looked better for the type of dedifferentiated liposarcoma characterized by neuroid or meningothelial whorls and osseous metaplasia described by Nascimento, Fletcher et al (Am J Surg Pathol 22:945-955;1998). I assume the cells of this tumor were positive for hormone receptors.

Joshua Sickel: Completely missed the diagnosis. I considered de-differentiated liposarcoma with meningothelial like whorls (Oh well, I'm still waiting to make this diagnosis!).

Dominic Spagnolo: What a stunning ESS with meningothelial-like whorls. I have never encountered this before. The meningothelial like structures seem to be miniature versions of the larger, giant collagen rosette formations, as there are gradations in size of the nodules and centrally there are mini-starbursts of collagen. Thanks, Kum.

James Strauchen: Endometrial stromal sarcoma. Unusual "whorls"!

Saul Suster: Very nice case, Kum. Agree completely with your diagnosis. The first time I saw this I completely missed it. I showed the case to John Chan who was visiting us at the time at Ohio State, and he only took one peek at the low power and made the diagnosis (which was confirmed subsequently with immunostains). That was another demonstration of the impressive and already legendary H&E skills of Dr. John Chan. That case was eventually reported by Dr. Wakely and Dr. Chan in the Annals of Diagnostic Pathology.

Paul Wakely, Jr.: Kum, we have seen this tight spiraling of cells in some cases of ESS, and illustrated it in figure 1 of a case published in Ann Diag Pathol 2002;6:312 where John Chan saw the case while visiting here and made the diagnosis.

Lawrence Weiss: I was completely fooled, going after a perineurioma/neural tumor differential.

Bruce Wenig: Agree and do not have anything to add. Out of curiosity, were you able to make the diagnosis on the core needle biopsy?

CASE NO. 6 – CONTRIBUTED BY IVAN DAMJANOV:

Phil Allen: Aggressive, fatal Hodgkin's disease with 11 month clinical course, mediastinal lymph nodes and liver. I defer to the lymphologists.

Carlos Baachi: Hodgkin lymphoma.

David Ben-Dor: Dr Damjanov, I'm wondering whether some of the R-S cells aren't inside lymphoid sinuses with the histiocytic proliferation being sinus histiocytosis. A strange location for R-S cells. Based on this biopsy, the most one can do is to call it mixed cellularity type and leave the prognosis up to the clinicians based on clinical parameters. But of course you don't know what the disease looked like in other foci (not sampled by the mediastinal needle biopsy). In other areas of pathology you can't always predict how a tumor will react based only on the histology: a follicle from a widely invasive follicular carcinoma of the thyroid can look just like a follicle from a follicular adenoma- you would need complementary information to make a correct evaluation. Did the liver nodule look like this or did it show features of progression (i.e. lymphoid depletion if that entity really exists).

Gerald Berry: I agree with the diagnosis of Hodgkin lymphoma. I looked for evidence of a composite lymphoma to possibly explain the aggressive behavior but didn't find evidence of a second malignancy.

Michele Bisceglia: Hodgkin's lymphoma. Have not a clue for the rapid fatal outcome. Just to note the absence of eopsinophils in the background. And am not sure that the lesion was in a lymph node. In some place of the slide, I got the impression that it was in the lung (but of course I am wrong).

Ira Bleiweiss: Agree, but I yield to Jim on this for "our" experience.

Tom Colby: Agree with diagnosis. There are some regions where some might have used the term "reticular subtype" for this case of Hodgkin lymphoma. In my outdated experience, there are occasional cases of Hodgkin lymphoma that just go south quickly for no obvious histologic reason.

Kum Cooper: I suppose the ratio of the increased Hodgkin cells versus the fewer lymphocytes could have been predictive of the "lymphocyte depleted" category; which is a vanishingly rare diagnosis in my experience.

Otto Dietze: I presume that stage 4b and the lymphocytic depletion histology is associated with a bad prognosis.

Hugo Dominguez-Malogon: Because of the sinusoidal pattern, I thought of an anaplastic lymphoma.

Göran Elmberger: Interesting case. Certainly could be Hodgkin's disease with aberrant biology. However, noting the aberrant rapid progress, believe one must consider other diagnostic alternatives. The partly dominating sinusoidal distribution pattern, the relative absence of eosinophilia and plasma cells might point towards the difficult differential diagnosis of anaplastic large cell lymphoma. This dx may also fit well with reported IHC and ISH findings. Any evidence for t(2;5)? Clonality studies performed? The differential diagnosis between anaplastic large cell lymphoma and Hodgkin's disease is known to be difficult. In fact borderline cases in a continuous spectrum as well as secondary development of Ki-1 lymphomas from HD has been described.

Vincenzo Eusebi: I would be reluctant to label this case HD. I would take into consideration anaplastic large cell lymphoma in the first instance.

Giovanni Falconieri: Thanks for submitting a "classic" of surgical pathology.

Christopher Fletcher: The predominantly sinusoidal distribution of tumor in this biopsy would seem to a non-hematopathology expert such as me to be rather unusual, and I would have wondered about the possibility of an unusual case of ALCL. It will be good to hear the opinions of the experts!

Andrew Folpe: High-grade lymphoma is the best I can do off the slide.

Jerónimo Forteza-Vila: Curiously enough, we have seen fulminant liver failure associated with Hodgkin lymphoma (Abdulkader I, Fraga M, González-Quintela A, Caparrini A, Bello JL, Galbán C, Varo E, Diaz-Mediavilla J, Forteza J.: Prolonged survival after liver transplantation for Hodgkin's disease-induced fulminant liver failure. Hepatogastroenterology. 2005 Jan-Feb; 52(61):217-9. PMID: 15783034 [PubMed - indexed for MEDLINE]), and Elaine Jaffe also reported that she has seen cases of Hodgkin associated to fulminant liver failure. The reason for this association is not clear, though it may be an associated viral etiology.

Masaharu Fukunaga: At first it seemed to me that it was a lymphohistiocytic granulomatous lesion. What a kind of subtype is this tumor in Hodgkin's lymphoma? Thank you very much for the interesting case.

Thomas Krausz: In view of the aggressive clinical course I was considering other entities like T-cell/histiocyte-rich large B-cell lymphoma, but histologically I still favor Hodgkin's lymphoma.

Janez Lamovec: Interfollicular/intrasinusoidal growth patterns in this case is striking. I first thought of anaplastic large cell B-cell lymphoma; CD30 positivity would also go along with that. However, with CD15 positivity of RS cells, this is not the case. Cases with massive mediastinal lymphadenopathy may go worse.

Michal Michal: How much different is this tumor from this one:? *AJF Lazar, CDM Fletcher. Distinctive dermal clear cell mesenchymal neoplasm: clinicopathologic analysis of five cases. Am J Dermatopathol 2004:26:273.*

Thomas Mentzel: An unusual case of aggressive Hodgkin's lymphoma arising in an elderly patient. Is the number of immature, blastic cells of prognostic importance?

Markku Miettinen: Agree on Hodgkin lymphoma. Having a relatively small number of lymphocytes (yet abundant histiocytes) this may be close to lymphocyte depletion type. Perhaps a high stage was also a factor.

Liz Montgomery: This looks like Hodgkin's to me though I am no hematopathologist. The horribly aggressive course indeed seems unusual.

Giuseppe Pelosi: This is an interesting case of Hodgkin's lymphoma, especially on the light of the subsequent rapid clinical course. The histopathologic features are diagnostic for this entity, with typical RS cells being observed.

Santiago Ramon y Cajal: I agree that if those atypical cells are CD15 and CD30, the diagnosis is consistent with Hodgkin. We recently have seen two cases of Hodgkin lymphoma with similar clinical features as your case. In our cases, one lymphoma had a marked intravascular component that is clearly unusual in Hodgkin and the other was associated with a hemophagocitic syndrome.

Juan Rosai: I agree with the diagnosis of Hodgkin's disease. For one thing, there are classical Reed-Sternberg cells. They don't make them so nice anymore. There are also areas with a monomorphic proliferation of very atypical cells. The whole thing reminds me of the form called reticular subtype in the Lukes-Collins classification and lymphocyte-depletion in the Rye classification. As a group, the patients were older, with systemic disease and an aggressive clinical course (New Engl J Med 288:751-756;1973).

Joshua Sickel: Reminded me of a autopsy case in residency. Hodgkin's disease involving all abdominal organs with associated granulomatous inflammatory reaction. Patient had died rather suddenly and the diagnosis was unexpected. I don't see anything in this case to suggest a more aggressive clinical course.

Dominic Spagnolo: There are 3 features that strike me about this node. First, there are distended sinuses packed with large foamy histiocytes, some of which show erythrophagocytosis, and I wonder if there is platelet consumption also; could there have been a hemophagocytic syndrome *ab initio* - rare in HL, but does happen (??EBV-related, ??other infection). Second, there is a partly intrasinusoidal distribution of the HL, again uncommon, but happens. Third, in the parenchymal areas of involvement, there is a relatively lymphocyte-depleted background. Whether any of these are predictive of the clinical course here, I don't know, but if there were a hemophagocytic syndrome, this, coupled with the patient's age, would provide 2 adverse factors. What is the frothy eosinophilic material in the background - was Peumocystis excluded? Interesting biopsy and question - thank you.

James Strauchen: I think this would qualify as lymphocyte depleted HD, although some people doubt its existence. Advanced age remains an adverse prognostic factor.

Saul Suster: I suppose conventional wisdom dictates that we accept this as an example of Hodgkin lymphoma, given the RS cells and the immunophenotype. But I suspect our concept of this disease will continue to evolve in coming years. Could it be that the reticular-sclerosing variant (or "lymphocyte-depleted") of the old literature actually corresponds to something else (such as a B-cell anaplastic large cell lymphoma), thus accounting for the marked differences in clinical behaviour? I remember in my old days as a resident the reticular variant of HD was not a rare diagnosis. I haven't seen a case diagnosed as such during the past 10 years at least! Food for thought....

Paul Wakely, Jr.: There are no histopathologic features that I see which would have predicted a rapidly fatal course.

Lawrence Weiss: In this age of modern therapy, there are still about 5% of patients who do not respond to standard treatment, despite having a definite diagnosis of Hodgkin lymphoma. There are no histologic features that predict resistance to therapy. However, there are probably several genetic alterations that may be predictive, and investigators are frantically trying to nail down the specific genes involved as I write this.

Bruce Wenig: Funny looking Hodgkin's, including no eosinophils but if the immunos are supportive, then I agree. Other considerations by light microscopy included (for me) anaplastic large cells lymphoma, true histiocytic lymphoma and a dendritic cell tumor.

CASE NO. 7 – CONTRIBUTED BY OTTO DIETZE:

Phil Allen: Clear cell atypical fibroxanthoma, skin of nose. I have never previously recognized this variant myself. We see lots of cutaneous atypical fibroxanthomas in Australia. Regardless of the immunohistochemical results, I regard them in the same light as squamous carcinomas of the skin. Certainly, the local recurrence and metastasis rates are similar for the two conditions. I also suspect that atypical fibroxanthomas probably "forget" their social standing in the squamous tumor hierarchy, stop producing epithelial markers and assume the disguise of a sarcoma. Whatever the explanation, equating the usual sarcoma-like form of atypical fibroxanthoma with soft tissue malignant fibrous histiocytomas leads to confusion amongst the clinicians, and sometimes to overtreatment.

Carlos Bacchi: Great example of clear cell atypical fibroxanthoma.

David Ben-Dor: Dr Dietze, surprise surprise! I was expecting either a metastatic tumor or maybe a sebaceous carcinoma (some of the cells look a little foamy). I'm glad to know that this lesion stains positively for *something*. The comment about this being an anaplastic squamous cell carcinoma is interesting, but how can you prove it if by definition it loses keratin expression?

Gerald Berry: I also considered a metastasis. The findings seem to fit AFX.

Michele Bisceglia: Clear cell atypical fibroxanthoma. Had not seen this variant before. Thank you.

Ira Bleiweiss: I thought this was a sebaceous carcinoma, but I guess not with the negative keratins.

John Chan: When I looked at this case, I considered balloon cell nevus as my first diagnosis. With the results of the immunostains, I certainly have to agree with the proposed diagnosis of clear cell atypical fibroxanthoma.

Thomas Colby: I can go along with the diagnosis of clear cell atypical fibroxanthoma, but I am not sure I would ever have gotten there by myself.

Kum Cooper: Thank you for this educational case. I was not even aware of a clear cell AFX!

Ivan Damjanov: To me this tumor looked very epithelial and the clear cells made me think that this is a squamous cell carcinoma. But you are most likely right.

Otto Dietze: My case, so far no evidence of recurrence.

Hugo Dominguez-Malogon: Atypical fibroxanthoma, the histology nicely shows the clear cells.

Göran Elmberger: Very interesting case and hypothesis. In cases like this, I always go through the same ddx algorithm including AFX, desmoplastic MM, spindle cell carcinoma, DFSP and leiomyosarcoma. In a clear cell variant as this lesion, I might be tempted to consider sebaceous carcinoma as well. The results of IHC investigations are often helpful in finalizing dx. The location and the evidence of actinic damage – solar elastosis certainly favour some of the above ddx. The relatively benign biology and the location to superficial often sun damaged areas of AFX certainly would make me favour something else than merely a superficial variant of MFH. Against the interpretation as dedifferentiated squamous cell carcinoma is, according to my experience, absence of squamous precursor or component as well as IHC negativity for all epithelial markers including p63. A unique lesion with morphological overlap with MFH?

Vincenzo Eusebi: Nice case.

Giovanni Falconieri: I basically agree with your interpretation; clinical and overall microscopic features fit well. Clear cell changes are striking, indeed. Personally, I have abandoned AFX as a diagnostic term since our physicians often believe that this equates benignity, thus they may convey an excess of reassurance to the patient. I would rather stay adherent to the recent WHO nomenclature that rubricates such lesions under the cutaneous MFH lesions/intermediate malignancy heading.

Christopher Fletcher: If all of the appropriate immunostains are negative (particularly keratins and melanoma markers), then indeed the appearances would seem to fit well with the clear cell variant of AFX, particularly given the smooth deep margin and partial collarette. Since, in clinical terms, AFX is almost invariably benign (and convincing reports of malignancy are vanishingly rare – certainly rarer than in ordinary cutaneous FH), then to regard these as dedifferentiated sarcomatoid squamous cell carcinomas seems somewhat implausible.

Cyril Fisher: Clear cell atypical fibroxanthoma, looks like a relative of clear cell benign fibrous histiocytoma.

Andrew Folpe: Clear cell AFX sounds good. I'd be careful about that "pleomorphic-anaplastic reaction" stuff….

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Agree. The lesion is symmetrical and the lesion will have a benign clinical course.

Allen Gown: Probably the best diagnosis, but a bit surprised that it was CD99- and CD68-negative.

Thomas Krausz: Agree with diagnosis. In general, I still can not make a firm diagnosis of AFX on H&E. For me it is a diagnosis by exclusion – lots of immuno and then consistent with ….

Janez Lamovec: This is to me a malignant tumor, perhaps from the category of AFX but malignant nonetheless. Negative immunohistochemistry in such a pleomorphic tumor is not that unusual, and I would try to exclude a metastasis in this case.

Thomas Mentzel: A wonderful example of rare clear cell atypical fibroxanthoma. Of course you have to exclude poorly differentiated carcinoma in every example of AFX, but AFX represents a distinct clinicopathological entity different from "MFH-like" superficial sarcoma (pleomorphic superficial sarcoma not otherwise specified), and of course different from poorly differentiated squamous cell carcinoma. Typical cases of AFX are characterized by an excellent clinical prognosis (different from superficial sarcoma and poorly differentiated carcinoma) but strict clinicopathological criteria have to be applied!

Markku Miettinen: Fully agree on atypical fibroxanthoma with clear cell features. Seems to be superficial enough to qualify as AFX. If one rules out carcinoma as you did, it is difficult to make a generalization that it is a carcinoma or a reaction to it.

Liz Montgomery: It is interesting how epithelioid the cells look ["atypical epithelioid cell histiocytoma"?]. Since it is small and superficial, should do well following complete excision.

Giuseppe Pelosi: I agree with Dr Dietze that this tumor represents a clear cell atypical fibroxanthoma. The differential diagnosis, in H&E stained sections, may also include renal cell carcinoma or PEComa.

Santiago Ramon y Cajal: Unusual example of an Atypical Fibroxanthoma. I have never seen it before with so much clear cell change. I wonder about CD10 positivity and p63.

Juan Rosai: All I can say about this skin lesion is that it is a malignant clear cell tumor. Obviously, metastatic renal cell carcinoma has to be ruled out before entertaining any other diagnosis (but there are no sinusoidal vessels). It certainly has very little in common with the atypical fibroxanthoma originally described by MacGavran and Kyriakos.

Joshua Sickel: I took the bait and went for metastatic renal cell carcinoma. This is a great learning case. I've seen one case of metastatic RCC involving the nasal sinus, so I figured, why not the skin of nose?

Dominic Spagnolo: Agree with your diagnosis of clear cell AFX. It is identical to the earlier cases also described by Requena (1997) and Crowson (2002), all in J Cutan Pathol. The list of differentials is wide. I recall being shown a similar lesion not so long ago, which I think turned out to be a metastatic renal cell carcinoma deposit. So it is a diagnostic trap. Thanks for the case.
Giuseppe Pelosi: I never saw a solitary fibrous tumor of the prostate and thank Dr Dominguez-Malagon for this opportunity. The morphologic features are characteristic for this entity that has been described everywhere in the body, including unexpected anatomical sites.

James Strauchen: "Clear cell" AFX. The xanthomatized cells supports the relation to MFH rather than SCC.

Saul Suster: Can't argue with the diagnosis.

Lawrence Weiss: If AFX is derived from squamous cell carcinoma, why do we not see more transitional cases?

Bruce Wenig: I agree with AFX, clear cell type. I have seen a number of cases of AFX in and around the ear region; and like this case, were well-circumscribed in their depth and all uniformly behaved in an indolent manner. I had never considered the possibility that this tumor was a "variant" of squamous cell carcinoma. A squamous cell origin seems unlikely, even if keratin expression is "lost" due to dedifferentiation, as the expected biology of a "sarcomatoid" or anaplastic squamous cell carcinoma would be significantly more aggressive than the biology ascribed to AFX. Also, if this were a squamous cell derived neoplasm, then I would expect the epithelium overlying the lesion to show some form of dysplasia (presumably the origin being the surface); even though one of the tissue fragments is ulcerated, the other 2 are not and there is no dysplasia/carcinoma in situ. When dealing with sarcomatoid squamous cell carcinomas of the head and neck, I typically due a broad immunopanel of cytokeratins, as well as p63. I wonder if Dr. Zelger did such a broad panel in suggesting dedifferentiation of a squamous cell carcinoma.

CASE NO. 8 – CONTRIBUTED BY HUGO DOMINGUEZ-MALAGON:

Phil Allen: Mitotically active, 15 cm pelvic tumor involving prostate. The tumor cells look a bit like a monophasic synovial sarcoma. Despite the absence of necrosis, I think the prognosis should be guarded. There is no prostatic tissue in my slide.

Carlos Baachi: Nice example of SFT in an unusual location.

David Ben-Dor: Dr. Dominguez-Malagon, I find it easier to make this diagnosis when I see the staghorn-shaped vessels, much in the same way it's easier to make the diagnosis of pleomorphic adenoma with the cartilage present. But sometimes these features are absent and you have to slog it out- what a pain!

Gerald Berry: Nice example of SFT. It appears no organ is immune for the lesion!

Michele Bisceglia: Solitary fibrous tumor of the prostate. Agree. However, I would alert about the possibility that one can misdiagnose as SFT of the prostate even a trivial spindle cell hyperplastic stromal nodule of the prostate (as seen in nodular hyperplasia of prostate).

Ira Bleiweiss: Agree.

Thomas Colby: Agree with SFT of the prostate.

Kum Cooper: Thank you Hugo. Did you do the CD 117 (c-kit). You mention GIST it in your differential.

Ivan Damjanov: Agree, but only because I could not come up with a better diagnosis. CD34 is the best evidence to support your diagnosis, even though we have had mixed results with two antibodies to CD34 that we have used in parallel.

Otto Dietze: I have never seen SFT in the prostate, thank you.

Hugo Dominguez-Malogon: I have not seen such grade of atypia in FDCS; before I knew the CD21+, I thought it was carcinoma.

Göran Elmberger: Very rare and interesting case. My experience is small. From a pulmopleural perspective, I believe I could accept the tumor as SFT of probably malignant potential (cellularity and high mitotic rate). In prostate, I believe differentiation from tumors of specialized prostatic stroma – STUMP; low-grade stromal sarcoma - is challenging. Birefringent collagen may be indicative of SFT but in my section HPC-like vessels were not prominent. ER?, PgR?, AR?

Vincenzo Eusebi: Solitary fibrous tumour.

Giovanni Falconieri: Agree, spindle cell tumor consistent with SFT. Despite size, a benign course may be expected. Hugo: I would like to thank you once again for your hospitality during our stay in Mexico. The meeting you have hosted was also successful. It was a memorable event, anyway.

Cyril Fisher: Solitary fibrous tumor of prostate. I would call this malignant on published criteria while noting that benign-appearing SFT can recur/metastasize.

Christopher Fletcher: Seems quite convincing for SFT, although I do not see any prostate in my slide.

Andrew Folpe: Agree.

Jerónimo Forteza Vila: Thank you for this interesting case.

Masaharu Fukunaga: This is my first time to see SFT in prostate. Thank you very much for sharing the nice case with you.

Thomas Krausz: Agree with diagnosis. I haven't seen it in the prostate before.

Janez Lamovec: Many of the nuclei of this tumor appear to me cigar-shaped, and fasciculation is also focally pronounced. Did you try SMA and desmin to exclude leiomyosarcoma?

Thomas Mentzel: An interesting case of an atypical malignant spindle cell neoplasm of the prostate containing numerous inflammatory cells. I found it difficult to establish the difference between SFT and STUMP on the given slide.

Markku Miettinen: Agree on solitary fibrous tumor with malignant potential, based on atypia and reported mitotic activity up to 10/10 HPFs. However, it may be difficult to ascertain prostatic origin for a 15 cm-tumor.

Liz Montgomery: Cannot think of a better diagnosis that SFT involving the prostate although there was no prostate tissue on the slide.

Giuseppe Pelosi: I never saw a solitary fibrous tumor of the prostate and thank Dr Dominguez-Malagon for this opportunity. The morphologic features are characteristic for this entity that has been described everywhere in the body, including unexpected anatomical sites.

Santiago Ramon y Cajal: Very interesting case of Solitary Fibrous Tumor of the Prostate.

Juan Rosai: I would go along with the diagnosis of solitary fibrous tumor, although I have a hard time sometimes in distinguishing them from tumors of the specialized prostatic stroma. Actually, I think that the two are closely related.

Joshua Sickel: SFT of the prostate gland. Thanks for sending this instructive case.

Dominic Spagnolo: Nice SFT of the prostate - thank you. I did not get such high mitotic counts in my section. As I understand things, no SFT of the prostate has yet behaved in a malignant fashion?

James Strauchen: SFT of the prostate. Why not

Lawrence Weiss: Nice case. SFT can occur anywhere, but I hadn't seen one in the prostate before.

Bruce Wenig: I guess but it is a rather cellular SFT with a relative absence of the usual vascularity.

CASE NO. 9 – CONTRIBUTED BY VINCENZO EUSEBI:

Phil Allen: Poorly differentiated malignant tumor with immunohistochemical features of follicular dendritic cell sarcoma, left breast. I am always wary of accepting specific diagnoses of poorly differentiated malignant tumors which are based mainly, or only, on immunohistochemistry.

Carlos Baachi: What a case! Based on the morphological ground only I would never guess about the diagnosis of FDC tumor. In most of the cases of FDC tumor that I have seen, they weren't as pleomorphic as this one but there is no reason this couldn't happen.

David Ben-Dor: Dr. Eusebi, phenotypically this looks so much like high grade carcinoma! I could even swear there are glandular spaces here and there. Is immunophenotyping really everything nowadays? - I guess so. How about taking out old medullary carcinomas and re-evaluating them immunohistochemically?

Gerald Berry: The cytologic features appear far more pleomorphic than the cases of FDC than I have seen. I would have ended up at undifferentiated malignant neoplasm.

Michele Bisceglia: Follicular dendritic cell tumor primary in breast. Very rare case. Thank you, Vincenzo.
We – as AMR members- have seen a few such cases from diverse organs (Chris Fletcher contributed such a case in a lymph node). In AMR Register (see website: Archive) under the section of "AMR Seminars per organs," you see that almost all the variants and possibilities concerning with these tumors you mentioned have been contributed by members.

Ira Bleiweiss: My first thoughts were either melanoma or sarcoma, not a carcinoma. What did we do before immuno???

John Chan: This is a brilliant diagnosis of follicular dendritic cell sarcoma. This case shows a much greater degree of nuclear pleomorphism than the average case. If this case comes through routine practice, I might just have signed it out as grade III invasive ductal carcinoma, not bothering to perform any immunohistochemical stains.

Thomas Colby: Agree with diagnosis after reading the details of the evaluation of this case. I confess that I might have called simply high grade carcinoma and not have tumbled onto the fact that there are some subtle peculiarities in this lesion that might be more in keeping with a high grade follicular dendritic cell sarcoma. I will be interested to hear what other members of the group say about this case.

Kum Cooper: Nice pick up Vincenzo! I do recall a previous case from AMR seminar # 23, case 9, which had a more myxoid stroma and more lymphocytes. I saw cases of FDC in Africa (with and without Castleman's) but not in Vermont in 9 years...except for one case in consultation!

Ivan Damjanov: I thought that this tumor has some glandular elements and my diagnosis without your immunohistochemistry was metaplastic carcinoma. But I admit that you might be right.

Otto Dietze: Histology and the immunoprofile is consistent with the diagnosis, I have only seen it in lymph nodes previously.

Hugo Dominguez-Malagon: Extraordinary case, thank you.

Göran Elmberger: Difficult but important case. FDCS is not at the top of my differential. The risk is that a case like this could pass routine examination for a poorly differentiated breast carcinoma. Attention to detail and a high index of suspicion is always of importance. Lack of DCIS and the unusual permeative infiltration pattern with preserved ductular structures might be a tip of in the right direction.

Vincenzo Eusebi: My case.

Giovanni Falconieri: Impossible case, Vincenzo. I would just say poorly differentiated carcinoma. Another gap filled! I have seen FDCS in lymph nodes and they looked differently. As lymphoepithelioma is concerned, I believe that a positive HLA-DR stain may help in discriminating LEC from other breast cancers including medullary carcinoma.

Cyril Fisher: FDCS of breast, very rare and interesting case. Our published case (ref 3), a myxoid tumor, is AMR 23/09. Since then I have seen one or two additional examples.

Christopher Fletcher: The cytoarchitectural features in this case would indeed fit pretty well with FDC sarcoma, although S-100 positivity is relatively uncommon in that context, at least in my experience. The breast is indeed a very unusual anatomic location, albeit Cyril had shared the case which he published with the AMR group some years ago, as far as I remember.

Andrew Folpe: Poorly differentiated malignant neoplasm. I don't really see any histologic features especially suggestive of follicular dendritic cell tumor.

Jerónimo Forteza Vila: I agree that immunophenotype indicates a follicular dendritic cell tumor. Such an anaplastic morphology is not common, but I cannot think of any other option with this phenotype. John Chan already reports that the follicular dendritic cell tumor can simulate anaplastic carcinomas like in this case. Chromatin of some cells is in "salt and pepper" and nuclei have pseudoinclusions. This is consistent with this entity, but I wouldn't have thought about it without immunohistochemistry.

Masaharu Fukunaga: Without history, my impression was high grade angiosarcoma. It is very tough case. This case is also my first time to see it in this location. How about CD35?

Allen Gown: Wow, a spectacular case! Thanks, Vincenzo.

Thomas Krausz: I have difficulty classifying this tumor. Although the immunoprofile and perhaps the lymphocytic infiltrate support the diagnosis of FDC, none of the follicular dendritic cell sarcomas I have seen before were as "primitive" (many mitoses, pleomorphism) as this one. Vincenzo, sorry, I have no "better" diagnosis to offer, so perhaps this is an anaplastic FDC.

Janez Lamovec: This tumor first appeared to me as some type of anaplastic carcinoma NOS. However, with immuno results this may well be FDC although a very anaplastic type. Some sprinkling with lymphocytes as seen in more typical cases of FDC is evident, though.

Thomas Mentzel: Many thanks for this unusual and very difficult case.

Markku Miettinen: Very difficult case, because the odds are overwhelmingly favoring carcinoma and the illusion that some epithelial elements could be part of the tumor. Also, this tumor shows greater atypia and mitotic activity as seen in usual examples of dendritic reticulum cell tumor (as such, this would certainly qualify as sarcoma). As an S100-positive tumor, metastatic melanoma would also be in the differential.

Liz Montgomery: With your immunohistochemical results, FDCS makes the best sense for this lesion although this looks more pleomorphic than some examples. I am afraid I would not have thought to do the CD21 initially and hope I would not have called it a melanoma after the first battery of stains failing to spot the prominent lymphocytes admixed with the large cells.

Santiago Ramon y Cajal: What a bizarre and challenging case! Actually, in my slide my first impression was of a poorly differentiated carcinoma.

Giuseppe Pelosi: This is a spectacular case of follicular dendritic cell tumor of the breast. Differential diagnoses also include metaplastic carcinoma or malignant phyllodes tumor. Thanks again for this very difficult and stimulating case!!

Juan Rosai: Great case. I do not remember having seen before a follicular dendritic cell tumor as pleomorphic and malignant-looking as this, except once at a metastatic site in the lung.

Joshua Sickel: Amazing case.

Dominic Spagnolo: FDC tumor at the anaplastic end of the spectrum. Any other FDC markers thrown at it? EM? Nice difficult case, Vincenzo - thanks.

James Strauchen: Great diagnosis! Wouldn't have thought of it in that location, but in retrospect, it does resemble FDCT with meningothelial-like whorls and scattered lymphocytes. No one really knows how to treat these, as sarcoma or as lymphoma, and surgery is only proven rx. Not clear there is a role for adjuvant chemo rx.

Saul Suster: I suppose the histology is certainly consistent with this diagnosis, albeit a high-grade, pleomorphic and atypical sarcomatous type. What I find out of character for a high-grade and poorly-differentiated tumor such as this is that it should show what I assume is strong (i.e., "beautiful") CD21 positivity. We usually have difficulties getting these tumors to stain with CD21/CD35 even for the more conventional low-grade cases. I am therefore surprised to find that there was convincing positivity in such an atypical case. Could we be missing something here and jumping to conclusions because of the CD21 positivity? After all, basing this diagnosis solely on results of the stains without considering the histology would turn this into an "immunohistochemical" diagnosis....The latter have always made me nervous.

Paul Wakely, Jr.: Certainly fooled me. I was sure I was looking at medullary breast cancer prior to reading your discussion.

Lawrence Weiss: Wow, this is the most malignant appearing FDC tumor I have ever seen. And I have never seen an FDC tumor in the breast before.

Bruce Wenig: Wow! I am not sure what tipped you off to (extranodal) FDC and why CD21 was done (perhaps because everything else was negative). I did not think of FDC and likely would have signed it out as a sarcomatoid (metaplastic) carcinoma (even in the absence of DCIS – at least in the slide I received) or LEC as it certainly has the appearance of a LEC even in the absence of EBV (which I assume was done but was negative). Thanks, Vincenzo.

CASE NO. 10 – CONTRIBUTED BY CYRIL FISHER:

Phil Allen: Presacral (retrorectal) dermoid cyst with Paget's disease of the squamous epithelium in a patient with possible Currarino syndrome. I thought at first that you had excelled yourself with this one, Cyril, until I spotted the dartos muscle in the dermis of the inclusion (fusional) dermoid. In the absence of any testicular elements, we should not regard that minor omission from your scholarly discussion as a balls-up.

Carlos Bacchi: Incredible case. Thanks, Cyril, for teaching me about this entity.

David Ben-Dor: Dr Fisher, this slide seems relatively bereft of adnexae- while there are a few scattered hair follicles; I could find only one sweat gland acinus in the dermis. Does this mean that the stem cells which otherwise would have given rise to normal sweat glands turned malignant instead? Or did all the malignant cells carpeting the basal layer of the epidermis come from that one measly gland? Interestingly, a few of the neoplastic cells contain melanin and there are scattered melanophages in the dermis. Without immuno, how could this be distinguished from in-situ melanoma (asides from perhaps EM or mucin stains)?

Gerald Berry: Agree with the diagnosis. Nice example of a novel lesion.

Michele Bisceglia: Presacral (retrorectal) dermoid cyst with Paget's disease in a patient with possible Currarino syndrome. Not seen before. Did not know about Currarino syndrome (thank you). Something (in some way) similar to this which comes in mind to me, and which I would like to share with all is a case of melanoma in situ arisen in a dermoid cyst of ovary, which we saw here some years ago.

Ira Bleiweiss: Dermoid, obviously, containing Paget's disease, but not so obviously. As the real estate brokers say: location, location, location.

John Chan: Wow! This is a most spectacular case of extramammary Paget disease.

Thomas Colby: Agree with diagnosis. What a fascinating case. Nice discussion about a syndrome that I have never heard of (Currarino syndrome). I find the presence of Paget's disease a particularly interesting feature in this case that seems to be quite rare in this setting.

Kum Cooper: Fascinating case. Did you figure out where the Paget's disease was arising from? Currarino's syndrome? Did you make that up Cyril? (just kidding!)

Ivan Damjanov: Cyril, you are a gentleman and a scholar. Nice case. I was most impressed with your references, even though I flatter myself to be quite informed about teratomas. Currarino syndrome-wow-I was apparently playing hooky the day they taught that in my medical school!!

Otto Dietze: Thank you for this unique case; I have never seen the association of Paget´s disease with teratoma and did not know of Currianos syndrome.

Hugo Dominguez-Malogon: Beautiful deciduoid mesothelioma, thank you.

Göran Elmberger: Great case.

Vincenzo Eusebi: Nice case. Paget's carcinoma is similar to those cases seen in the anus.

Giovanni Falconieri: Very nice case, thanks for this contribution.

Cyril Fisher: My case, now published in AJSP 2008; 32:635-9.

Christopher Fletcher: An extremely impressive case, Cyril – with exotic lesions and syndromes such as this, you will soon be able to relocate to San Giovanni Rotondo!

Andrew Folpe: Wow. The Paget's is obvious, but I hadn't realized the strange clinical scenario when I was looking at the slide. Very interesting- I had not heard of Currarino syndrome.

Jerónimo Forteza Vila: Thank you for this interesting and complex case from the syndrome point of view.

Masaharu Fukunaga: I have not heard about Currarino syndrome. Thank you very much for the beautiful case and informative comment.

Allen Gown: Thanks for teaching me about Currarino syndrome. I wonder if the cells were HER2-positive, as are the vast majority of mammary Pagets.

Thomas Krausz: Currarino syndrome and extramammary Paget's disease in teratomas is new to me, thanks Cyril.

Janez Lamovec: Exceptional case. Thank you, Cyril.

Thomas Mentzel: What's for a combination of rare things, very interesting!

Michal Michal: The only doubt of mine about this amazing case is the teratogenic origin of the lesion.

Markku Miettinen: Fully agree on retrorectal dermoid cyst with Paget's disease (intraepidermal adenocarcinoma). I have not seen this before, but have seen carcinoid in retrorectal (dermoid) cyst several times.

Liz Montgomery: Cyril, this is such a neat case, and I only had heard of Currarino syndrome because I spotted your case report a few months back [Thway K, Polson A, Pope R, Thomas JM, Fisher C. Extramammary Paget disease in a retrorectal dermoid cyst: report of a unique case. Am J Surg Pathol. 2008 Apr;32(4):635-9.]. I imagine this patient will do well.

Giuseppe Pelosi: Presacral (retrorectal) dermoid cyst with Paget's disease in a patient with possible Currarino syndrome. A spectacular case!!.

Santiago Ramon y Cajal: Thank you for this case of Dermoid Cyst and Paget's Disease.

Juan Rosai: Pretty spectacular demonstration of Paget's disease in a pre-sacral dermoid cyst. I never heard of the Currarino syndrome.

Joshua Sickel: Thanks for sharing this unique (once in a lifetime!) case.

Dominic Spagnolo: Spectacular case, Cyril. I had never heard of Currarino syndrome. The Paget's is stunning. Thank you.

James Strauchen: Amazing case!

Lawrence Weiss: Nice discussion.

Bruce Wenig: Cool case. I have seen Paget's in a variety of settings but not in a dermoid cyst. Now I know what Currarino syndrome is. Thanks.

CASE NO. 11 – CONTRIBUTED BY CHRISTOPHER FLETCHER:

Phil Allen: Deciduoid malignant mesothelioma, peritoneal cavity. Looks good to me. Unfortunately, Doug Henderson is away for a few days so I can not get his comments.

Carlos Baachi: Great example of this unusual type of mesothelioma.

David Ben-Dor: Dr Fletcher, would it make any more (or any less) sense to term this *rhabdoid* mesothelioma especially in a male? I wonder whether if a male were pumped up with enough female hormones, a true decidual reaction would result.

Gerald Berry: Agree with the diagnosis.

Michele Bisceglia: Deciduoid malignant mesothelioma. Nice, typical, and educational case. Thank you, Chris.

Ira Bleiweiss: Wow! It looks like alveolar soft part sarcoma, see my case #3 in this seminar.

Thomas Colby: Essentially agree with diagnosis. "Deciduoid" is in the eye of the beholder, and I don't think there are any good criteria to differentiate a mesothelioma with big pink cells from one that is truly deciduoid. This case comes close but to my eye does not have the cohesive appearance that I would like to see but one thing about getting old is that one can quibble and bluster to one's heart's content.

Kum Cooper: Beautiful example, Chris. My differential was obviously much broader! I thought that deciduoid mesothelioma was coming out of flavor?

Ivan Damjanov: Nothing to add, except that this is a very young person for such a tumor. I did not consider PECOMA in the differential diagnosis, but next time I will.

Otto Dietze: Convincing diagnosis with regard to the immunoprofile.

Göran Elmberger: Thanks. Beautiful case of deciduoid MM. I also see some cells that have rhabdoid morphology – another differentiation within the MM spectrum.

Vincenzo Eusebi: Very nice and difficult. Never seen.

Giovanni Falconieri: Quite unusual, never seen such changes in a mesothelioma including glassy rhabdoid cytoplasms, prominent nuclear atypia and melanoma-like discohesion. Thanks for submission of this instructive case.

Cyril Fisher: Beautiful example of mesothelioma with deciduoid change.

Christopher Fletcher: My case.

Andrew Folpe: Spectacular example of deciduoid mesothelioma. Thanks.

Jerónimo Forteza Vila: Thank you for this interesting and complex case from the syndrome point of view.

Masaharu Fukunaga: A beautiful case of deciduoid malignant mesothelioma. Thank you very much, Chris.

Allen Gown: I'm impressed with the number of rhabdoid-looking cells in this lesion, and wonder if any studies looking at INI1 loss were performed.

Thomas Krausz: Great example.

Janez Lamovec: I have seen a couple of those, mostly seminar cases but this one is the most spectacular. Thank you, Chris.

Michal Michal: Typical diffuse deciduoid mesothelioma. I have seen recently a diffuse deciduoid mesothelioma arising from well differentiated papillary mesothelioma.

Markku Miettinen: Agree on malignant epithelioid mesothelioma with deciduoid features, documentation seems unequivocal. Peculiar eosinophilic hyaline globules caught my attention. Perhaps they are derived from erythrocytes (as supposedly in Kaposi sarcoma).

Thomas Mentzel: Thanks for showing this rare variant of malignant mesothelioma.

Liz Montgomery: Thanks so much for sharing this case. It really does look like a PEComa and underscores the value of being humble and confirming things with immunolabeling!

Giuseppe Pelosi: This case illustrates a spectacular deciduoid malignant mesothelioma of the peritoneum. I have observed a few of this mesothelioma variant in the pleura too, inasmuch as I have collected many cases of thoracic tumors. PEComa and epitheliod variant of GIST are certainly differential diagnoses with should be excluded before rendering the final diagnosis.

Santiago Ramon y Cajal: Great case. Thank you very much.

Juan Rosai: Like Chris Fletcher, I originally thought on the basis of the H&E section at the possibility of a PEComa. However, the immunohistochemical profile of this tumor - as he pointed out - is so typical of mesothelioma as to leave no doubts about the diagnosis. Now I fully realize why they thought of giving this variant the qualifier “deciduoid”.

Joshua Sickel: Beautiful case for the teaching collection.

Dominic Spagnolo: Great example of a deciduoid mesothelioma. Have not encountered a "pure" one before - it is spectacular - thanks.

James Strauchen: Deciduoid mesothelioma of the peritoneum. Nice case in a male. Was there a history of asbestos exposure? To account for the latency, it would have to have been in childhood.

Saul Suster: Certainly the most striking example of this type of mesothelioma I have ever seen! Many thanks, Chris.

Lawrence Weiss: Great case. Is it deciduoid change or, more appropriately, rhabdoid change?

Bruce Wenig: My initial thought was PEComa, as well. Nice case.

CASE NO. 12 – CONTRIBUTED BY ANDREW FOLPE:

Phil Allen: Inflammatory fibroid polyp, gastroesophageal junction. I would be reluctant to diagnose a lymphoma on the basis of this slide but would accept the diagnosis if there is unequivocal B-cell lymphoma in the kidney sections, as well as no other cause for the acute renal failure.

Carlos Bacchi: Fantastic case, Andrew! It is so easy to miss the intravascular lymphoma in such an inflammatory florid polyp.

David Ben-Dor: Dr Folpe, you can't be serious about inflammatory fibroid polyps and intravascular B cell lymphoma being "not ... terribly uncommon": this might imply that their occurrence might be of the same order of magnitude, but I wager that even at the Mayo Clinic where you would run into a number of the latter a year, you would see many more of the former. Concentrating on the vessels inside the mass, I would be hard pressed to make the diagnosis, while the vessels outside it are more convincing. I assume the lymphoma was found in sections from other organs (though this is not mentioned specifically)-if it was found only in sections from the polyp, it would be truly remarkable. Of course, you can't make this diagnosis without a biopsy, and I assume there wasn't any indication to perform one on the patient antemortem or maybe it was counter indicated due to her general condition.

Gerald Berry: I always find collision tumors fascinating and this one is no exception!

Michele Bisceglia: Intravascular large B-cell lymphoma involving an inflammatory fibroid polyp. Nice and difficult case. Other analogous cases were presented in previous seminars (e.g. by J. Forteza-Vila in Seminar 13 - Neoplastic angioendotheliomatosis plus progressive multifocal leukoencephalopathy of the brain; and by J. Strauchen in Seminar 31 -Angiotropic B-cell lymphoma). Have seen 2 such cases in other educational seminars (in a percutaneous renal biopsy – in

glomeruli – case of Dr. G. Monga from Turin, now in Novara – Italy; and in a prostate biopsy – case of G. Frizzera). In our file we have 2 cases here, one was in trephine bone marrow biopsy. And probably I had also the opportunity to see a case in a skin biopsy (likely a case of David Ben Dor, who kindly showed it to me on my request).

Ira Bleiweiss: Great case of evil lurking within.

Thomas Colby: Agree with diagnosis. I actually found more intravascular lymphoma in the sub mucosa than in the polyp.

Kum Cooper: Wow, Andrew, that does take some careful scrutiny. My dermatopathologist just this week showed me a case with involvement of subcutaneous vasculature. I have also seen this lymphoma involving the blood vessels of the adrenal gland, brain and salivary glands.

Ivan Damjanov: I missed those lymphoma cells but they are there no question.

Otto Dietze: An important argument to perform post mortems with histology.

Hugo Dominguez-Malogon: I missed the intravascular lymphoma cell, nice case.

Göran Elmberger: Wonderful case. Two for one. Reminds me of a great teacher recently passed away – Sixten Franze'n. He was the Scandinavian father of FNA and he had a strong interest in haematology as well. He always made an interpretation of the peripheral blood component of an FNA and on more than one occasion diagnosed an haematological malignancy or anemia in addition to a somatic carcinoma in one smear.

Vincenzo Eusebi: Another difficult case. I have missed the neoplastic intravascular cells.

Giovanni Falconieri: Thanks for this unusual case. Looking carefully, I could finally notice the atypical lymphoid cells sitting in the vessels.

Cyril Fisher: Subtle lymphomatous infiltrate. Great case.

Christopher Fletcher: Great case – certainly validates the role of the autopsy!

Andrew Folpe: My case. Hope you liked it.

Jerónimo Forteza Vila: Very nice case.

Masaharu Fukunaga: Without history, I paid attention only to the SMT and did not notice the intravascular lesion. Thank you very much for the educational case, Andrew.

Allen Gown: Maybe it was my slide, but the intravascular lymphoid cells looked a bit small for DLBCL.

Thomas Krausz: What a coincidence. I have never seen this combination.

Janez Lamovec: Intravascular lymphoma of stomach submucosa and in Vannek's tumor – what a curiosity!

Thomas Mentzel: Again, an interesting and "easy to miss" combination, because atypical lymphoid cells are present in few vessels only.

Markku Miettinen: Very unusual combination, but well-documented. I suppose intravascular lymphoma was disseminated being incidentally present in this polyp.

Liz Montgomery: Wow, Andrew, you are really slick. Inflammatory fibroid polyp seems the best dx for the submucosal gastric polyp but the intravascular lymphoma is sneaky! I hate to wonder whether I would have spotted the IV lymphoma prospectively in this were it a prospective gastric polyp biopsy.

Giuseppe Pelosi: Intravascular large B-cell lymphoma involving an inflammatory fibroid polyp: very intriguing case that may be very difficult to recognize. Diagnostic clues are the atypical cells inside the vessel lumina!!

Santiago Ramon y Cajal: Beautiful case that shows the validity of post-mortem examination.

Juan Rosai: Great case. The last intravascular large B cell lymphoma I saw was in the breast. It looked like a perfect high-grade intraductal carcinoma. It was shown at a seminar of the Penrose Cancer Hospital and most people (including myself) called it comedocarcinoma.

Joshua Sickel: Great case.

Dominic Spagnolo: You're kidding! What an amazing coincidence of 2 uncommon lesions - to be filed under esoterica. Thanks, Andrew.

James Strauchen: Amazing case! Vessels in adjacent normal mucosa were more involved on my slide.

Saul Suster: Very subtle, indeed. In the excitement of recognizing the inflammatory fibroid polyp, I totally missed the atypical cells within the vessels! Congratulations for the great pick-up!

Lawrence Weiss: I got the inflammatory fibroid polyp, but missed the lymphoma. I should change specialties.

Bruce Wenig: Cool case (not for the patient).

CASE NO. 13 – CONTRIBUTED BY JERONIMO FORTEZA VILA:

Phil Allen: Splenic marginal zone lymphoma progressing to a diffuse B-cell lymphoma in a cervical lymph node and bone marrow, with over-expression of MYC. This is too hard for me.

Carlos Baachi: Agree with the diagnosis of splenic marginal zone lymphoma with progression to a DLBCL.

David Ben-Dor: Dr. Forteza-Vila, cytologically in the slide from the later specimen, there seems to be a variation between large cells as in large cell lymphoma, medium sized cells as in Burkitt like, and small cells as in the original neoplasm as seen in the spleen. Hard to say to what extent this might be due to fixation artifact.

Gerald Berry: Agree with the diagnosis.

Michele Bisceglia: Splenic marginal zone lymphoma with progression to a diffuse B cell lymphoma with overexpression of MYC. Nice case, and beautifully followed up. Had a case with similar problems recently: and -just to stay on simple markers, if I am not wrong (and this would be of help) - Burkitt-like lymphoma does not express BCL-2 molecule.

Thomas Colby: Agree with diagnosis on the spleen. The recurrence 3 years later still appears to show a background of (somewhat) small lymphocytes in some regions (or else there is some fixation artifact) in addition to foci with larger cells and increased mitotic activity.

Kum Cooper: Is this not the lymphoma that used be call splenic lymphoma with villous lymphocytes?

Ivan Damjanov: Agree, even though with MYC translocation, we would have called it Burkitt-like lymphoma.

Otto Dietze: Richter transformation of a small cell B lymphoma; I cannot comment whether YC translocation is part of this process or there is another interpretation, e.g. another lymphoma.

Hugo Dominguez-Malogon: Should this be called “dedifferentiated” MALT?

Göran Elmberger: Interesting case.

Vincenzo Eusebi: Marginal cell lymphoma.

Giovanni Falconieri: I have found this case very difficult. I cannot say more than large B cell lymphoma and, frankly, did not note much difference among the different cell populations although many cells in both slides have plasmacytoid features. Thanks for this challenging contribution.

Andrew Folpe: Um, one of those lymphomas that begins with an “M”?

Masaharu Fukunaga: Agree. Thank you very much for the impressive case.

Thomas Krausz: Agree with diagnosis. Highly educational case.

Thomas Mentzel: Whereas section B shows obvious features of high-grade malignant lymphoma, I’ve found it very difficult to establish this diagnosis on section A.

Markku Miettinen: Agree on splenic marginal cell lymphoma with a Burkitt-like transformation.

Liz Montgomery: No comment.

Santiago Ramon y Cajal: Nice example of Marginal Zone Lymphoma progressing to Diffuse B Cell Lymphoma.

Giuseppe Pelosi: I agree with the diagnosis of splenic marginal zone lymphoma with progression to a diffuse B cell lymphoma. Interesting and difficult case!

Juan Rosai: Very nice demonstration of a marginal zone lymphoma of the spleen which is progressing to a diffuse large B cell lymphoma.

Joshua Sickel: I favored transformation to Burkitt's lymphoma. We just had a case marginal zone lymphoma with large cell transformation in a lymph node.

Dominic Spagnolo: Agree with both interpretations. Ideally, one would need to show clonal identity between the 2 lymphomas to establish that there has been progression from the splenic MZL, rather a second *de novo* aggressive DLBCL harboring a *MYC* translocation. I am not aware that MYC has been studied in the published cases of transformed splenic MZL. The cases I have seen have not shown this aggressive Burkitt-like histology. The presence of the *MYC* translocation is an indicator of aggression whether there are Burkitt-like features or not. Thanks for the case.

James Strauchen: SMZL with large cell transformation! Unusual, but well documented to occur. The c-myc translocation is also well documented to occur in a subset of diffuse large B-cell lymphoma. Over expression of bcl-2 favors DLBCL over Burkitt or Burkitt-like lymphoma in this case.

Lawrence Weiss: Great case. I would also interpret the case as a high-grade transformation of the previous low grade lymphoma.

Bruce Wenig: Agree; not much to more to offer.

CASE NO. 14 – CONTRIBUTED BY ALLEN GOWN:

Phil Allen: Sertoliform adenoma of the rete testis. Thanks for the case. I had never even heard of it before, but I agree with the diagnosis.

Carlos Baachi: I agree with the diagnosis of Sertoliform adenoma of the rete testis.

David Ben-Dor: Dr. Gown, it's interesting to note that the nodule is *outside* the testicle. I would have thought the location to be consistent with adenomatoid tumor. Wouldn't inhibin be positive in a sertoli cell tumor?

Gerald Berry: This is the first example of this lesion that I've seen. The "bi-directional" phenotype is interesting.

Michele Bisceglia: Sertoliform adenoma of the rete testis. Had no idea of this. Thank you for teaching.

Ira Bleiweiss: A new one on me.

John Chan: Rete testis adenoma is certainly an excellent suggestion.

Tom Colby: A new entity for me.

Kum Cooper: Allen, the only other thought was a juvenile granulosa cell tumor where I would have liked inhibin and calretinin to be positive in addition to the MART-1. Also JGCT is mitotically active.

Ivan Damjanov: Sounds good- I am embarrassed, but I do not know anything about this entity and must accept your diagnosis.

Otto Dietze: From the H&E aspect, my diagnosis would favor Sertoli cell tumor. However, the immuno phenotype was inconclusive and I very much appreciate your and Dr. Amin´s diagnosis.

Hugo Dominguez-Malogon: I agree, before the immuno, I called it Sertoli.

Göran Elmberger: Rare case. No experience. Sounds reasonable.

Giovanni Falconieri: Extraordinary case. I did not know the entity. Thanks for this submission.

Christopher Fletcher: I have never seen such a case and cannot come up with any better suggestion.

Cyril Fisher: Sertoliform adenoma of rete, very rare case.

Andrew Folpe: Very interesting case. I really wasn't aware of sertoliform adenoma of the rete testis, but the pictures seem to fit. I shared it with Rafael Jimenez, an excellent GU pathologist who recently joined us, and he agreed with that diagnosis.

Jerónimo Forteza Vila: I agree. Thank you for this interesting case.

Masaharu Fukunaga: My impression was Sertoli cell tumor without history. I have never seen this type of tumor. Thank you very much for sharing the rare tumor with you.

Allen Gown: My case. No additional comments.

Thomas Krausz: I have no "better" diagnosis. Before reading the discussion, I was considering a variant of Sertoli cell tumor and adenomatoid tumor.

Janez Lamovec: This appears as a benign tumor – adenoma but I would not be able to go any further.

Thomas Mentzel: I've never seen a lesion like this, many thanks.

Markku Miettinen: Thank you for raising my awareness of Sertoliform adenoma, I would have considered this histologically a variant of Sertoli cell tumor.

Liz Montgomery: Hmm. This just looks like a Sertoli cell tumor to me, and I would not have bothered with the IHC! I showed it to Jon [Epstein] and he had the same views. Is "sertoliform adenoma of rete testes" a hair splitting variant of sertoli cell tumor?

Giuseppe Pelosi: Sertoliform adenoma of the rete testis: I agree with the diagnosis, but I would also consider a well-differentiated Sertoli-Leydig cell tumor.

Santiago Ramon y Cajal: I guess I agree with you.

Juan Rosai: I'll buy the diagnosis of Sertoliform adenoma, although it still looks like there is a true stromal cell component, as also suggested by the positivity of Mart-1. What about calling it an adenoid Sertol cell tumor?

Joshua Sickel: Sertoliform adenoma sounds like a great idea.

Dominic Spagnolo: The morphology seems fine for Sertoliform adenoma/cystadenoma of the rete testis, and I don't have an alternative. The negative inhibin and calretinin seem unusual though. I have never seen this before. Thanks for the case.

James Strauchen: Setoliform adenoma of the rete! Thank you for this instructional case!

Saul Suster: Never heard of this before! Thanks for the education!

Paul Wakely, Jr.: This entity is a "first" for me.

Lawrence Weiss: I never heard of the entity, and have never seen a similar case—I just assumed it was a Sertoli cell tumor. Now I have.

Bruce Wenig: Given my vast experience with this lesion (this is my first such case), I would tend to agree with the stated diagnosis, and cannot suggest an alternative consideration.

CASE NO. 15 – CONTRIBUTED BY JANEZ LAMOVEC:

Phil Allen: Anaplastic oligoastrocytoma, left frontal lobe with postoperative glioblastoma metastasis in left femur. This is the first case I have seen. Thanks for the contribution.

Carlos Baachi: Without any history, this case would be really difficult to diagnose. Nice example of metastatic glioblastoma. I always wanted to see a metastatic GBM.

David Ben-Dor: Thanks, Janez, for taking the trouble to have this unusual bone biopsy recut for us. I think the most one could say without having knowledge of the previous history would be poorly differentiated malignant tumor. At least it was the GFAP positive astrocytic element that sent the metastasis which enabled one to get a handle on this (provided

the thought arose to have it done). Though not a brain tumor, an example of an *intracranial* tumor which can give rise to bone metastases outside the cranium is angioblastic meningioma (as I learned a few years ago).

Gerald Berry: I have seen these lesions metastasize to the lung. This is the first example of a metastasis to the bone that I have seen.

Michele Bisceglia: Metastatic glioblastoma to bone. Have never seen one, despite the fact that in the last 16 years (since our Neurosugical Division was set up here) we have seen more than 7 hundred glioblastomas. I only recall 3 remote metastases from glial tumors: one in the striated lumbar muscles of a patient (malignant oligodendroglioma of brain) which likely arrived there by CSF dissemination, and 2 ependymomas (lymph nodes of neck).

Ira Bleiweiss: Wow. Never seen this happen before.

Thomas Colby: Agree with diagnosis. Fortunately the occurrence is sufficiently rare that seeing a metastasis in the absence of any prior clinical history would indeed be unusual.

Kum Cooper: Thank you, Janez, for this unfortunate case. Did you obtain 1p19q del by FISH? We do this routinely since even the oligoastrocytoma is supposed to portend a better response to adjuvant therapy with this cytogenetic abnormality.

Ivan Damjanov: Excellent case.

Otto Dietze: An interesting case with regard to histology and the patient's course.

Hugo Dominguez-Malogon: I agree with metastatic glioblastoma, thank you Janez.

Göran Elmberger: Valuable reminder of unusual biology. Great case.

Vincenzo Eusebi: Thank you, Janez.

Giovanni Falconieri: Thanks, Janez, for submitting this rare case of metastatic glioblastoma. Although we have a very active neurosurgical team, I do not have memory of metastatic gliomas outside the CNS during my past 6 years of service here. I believe that the brain tumor is glioblastoma. On the bone fragment, I am not sure what it is: the cellularity is abnormal, yet it does not seem fully comparable to that of the primary tumor, also because of some desmoplastic reaction, a phenomenon which is not observed in the CNS due to the lack of lymphatics; spindle cells in meningothelial whorl arrangement are also present. In essence, I agree that this may represent metastatic glioblastoma. I presume that phenotypic changes in metastases of glioblastoma might reflect the change of milieu where tumor cells implant.

Cyril Fisher: Glioma metastatic to bone, a remarkable rarity, many thanks, Janez.

Christopher Fletcher: Impressive case, Janez! I have only personally encountered 2 or 3 examples of GBM with distant metastasis – one of which was shown to me as a frozen section not long after I moved to Boston – and of course, at least for some minutes, we did not have the relevant prior history!

Andrew Folpe: Metastatic GBM. This is one of those things you read about, but never see. Thanks very much, Janez.

Jerónimo Forteza Vila: I agree with the diagnosis provided that previous information is known.

Masaharu Fukunaga: Thank you very much for the unusual case and the detailed discussion, Janez.

Allen Gown: Thank you; I've never seen a metastatic glial tumor to bone before!

Thomas Krausz: I agree that it would be very difficult/impossible to diagnose the tumor in the bone without the previous history and pathology.

Thomas Mentzel: Many thanks for sharing this very rare case of metastasizing glioblastoma.

Markku Miettinen: The bone involvement looks like a convincing example on a peripheral metastasis of glioblastoma. Perhaps there is also primitive neuroepithelial-like differentiation.

Liz Montgomery: This is an amazing case, and I am surprised the poor woman is still alive. We have large files of brain tumors because P Burger is here and I think we have only 2 cases of GBM metastatic to bone in our archives.

Santiago Ramon y Cajal: Thank you very much for this interesting case, which reminds us once again of the importance of adequate clinical information.

Giuseppe Pelosi: Metastatic glioblastoma to bone: great and very unusual case. I do not have specific comments to the case.

Juan Rosai: If the GFAP was truly positive, I would have to agree with the proposed diagnosis of this very unusual case.

Joshua Sickel: Rare case and great discussion. I've seen only one example of this phenomenon several years ago.

Dominic Spagnolo: You're right about the difficulty without the benefit of the history and previous histology. I would have had a hard time classifying the brain recurrence also and would have even considered a high grade neuroepithelial element. Thanks for this rare case, Janez

James Strauchen: Metastatic glioblastoma! Wild case! I never would have gotten the diagnosis on the bone biopsy without the history or thought of getting GFAP. The survival seems surprisingly long, since one might have expected a rapidly downhill course with so aggressive a tumor. The prolonged survival supports an oligo component. Was any cytogenetics done?

Saul Suster: Wow! I've seen few cases of extracranial metastases of gliobastoma but this is the first one I see in bone!

Lawrence Weiss: Extraordinary case. Actually, in areas is reminiscent of a glial neoplasm.

Bruce Wenig: Another cool case for us but unfortunately not for the patient. I agree that in the absence of a known intracranial neoplasm (perhaps an unlikely event in the setting of metastatic disease), it would be challenging (an understatement) to consider the metastasis as originating from a high-grade glial malignancy.

CASE NO. 16 – CONTRIBUTED BY MICHAL MICHAL:

Phil Allen: Oncocytic papillary renal cell carcinoma. This looks pretty convincing to me. I am astounded that the American Journal of Surgical Pathology took more than 6 months to reject the paper. They require reviews to be returned electronically within 14 days and they send electronic reminders. It looks like a bad slip-up.

Carlos Baachi: Great case.

David Ben-Dor: Dr, Michal, to me the image in the recent 4th series AFIP kidney fascicle (fig. 2-59, p. 129) illustrating type II papillary carcinoma of the kidney looks pretty similar to this case. If the unique feature of this case is the genetics, then I apologize for not being able to figure this out on my own!

Gerald Berry: Agree. Nice case.

Michele Bisceglia: Oncocytic papillary renal cell carcinoma. Very nice and fully studied case. Thanks. Michal.

Ira Bleiweiss: Agree.

John Chan: The diagnosis of papillary renal carcinoma (oncocytic) is easy to make from slide a, with papillary architecture and psammoma bodies. Diagnosis from slide b is more difficult – with the packeting and tubular patterns, and admixed partially clear cells, the eosinophilic variant of chromophobe carcinoma also enters into the differential diagnosis.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Thank you, Michal, for this instructive case. Recently, there have been papers suggesting that both papillary and chromophobe RCC should not be Fuhrman graded. Do you subscribe to that as well?

Ivan Damjanov: Agree. Michal, those who know about the history of your contribution give you full credit and those who do not…..just forget about them.

Otto Dietze: I agree with the diagnosis, a good teaching case with regard to the performed investigations.

Hugo Dominguez-Malagon: Completely agree. This proves that "oncocytoma" is a phenotype and not an entity.

Göran Elmberger: Important case. Thanks for pointing out points of importance in differentiating from other oncocytic renal tumors. Especially the solid pattern in slide b was difficult. I guess psammomatoid calcific concretions, nuclear grade and necrosis are alarming findings.

Vincenzo Eusebi: Oncocytic papillary renal cell carcinoma.

Giovanni Falconieri: Nice case, Michal. Renal oncocytic tumors are always a source of diagnostic difficulties. I believe that the size of the lesion is such to raise the index of suspiciousness about cancer, although I have memories of unusually large oncocytomas. Thanks for the discussion**.**

Cyril Fisher: Oncocytic papillary renal carcinoma, excellent example.

Christopher Fletcher: An entirely convincing case.

Andrew Folpe: Agree with oncocytic papillary renal cell carcinoma.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: My impression without history was chromophobe carcinoma. Thank you very much for sharing the wonderful case, Michal.

Allen Gown: Thank you; nice correlation with molecular findings.

Thomas Krausz: Diagnostically challenging case. The high nuclear grade is helpful to distinguish it from oncocytoma. I assume one needs the cytogenetics to make a firm diagnosis of oncocytic papillary renal cell carcinoma. The story about the publication is so sad.

Janez Lamovec: In areas lacking papillary formations, this tumor is almost impossible to distinguish from oncocytoma or even from chromophobe cell carcinoma.

Thomas Mentzel: Thanks Michal for presenting a case of this interesting variant of papillary carcinoma of the kidney.

Michal Michal: This is my case.

Markku Miettinen: Agree on papillary oncocytic carcinoma. Your selection for tumor name is good.

Liz Montgomery: Very beautiful case.

Giuseppe Pelosi: Oncocytic papillary renal cell carcinoma: interesting case!.

Santiago Ramon y Cajal: Good example of Oncocytic Papillary Renal Cell Carcinoma.

Juan Rosai: Nice case, but I would have called it an oncocytoma with papillary features.

Joshua Sickel: We had a similar case at South Bay Pathology Society a few months ago.

Dominic Spagnolo: Terrific case of oncocytic papillary renal cell carcinoma. Thanks, Michal.

James Strauchen: Oncocytic papillary RCC (with the chromosomal abnormalities!). Priority in the literature and fame are fleeting!

Saul Suster: Great case, Michal. Oncocytic tumors of the kidney are very complex and I don't believe they have been nicely sorted out yet. Please keep working on this, Michal.

Lawrence Weiss: Thanks for the great example. Don't get me started on reviewer stories—I have my own collection.

Bruce Wenig: Nice case.

CASE NO. 17 – CONTRIBUTED BY MICHAL MICHAL:

Phil Allen: Primitive small cell tumor with epithelial, gangliocytic, neuroendocrine and mesenchymal differentiation, bifurcation of left carotid artery. Thanks for the contribution. I have not seen one like this before.

Carlos Bacchi: What a difficult case to classify!

David Ben-Dor: Dr. Michal, this could serve as an all purpose immunohistochemistry control (along the lines of the "spring roll" proposed by John Chan years ago) since it has everything in it.

Gerald Berry: A very interesting case. Could this represent an unusual multidirectional differentiation/maturation of a neuroblastoma?

Michele Bisceglia: Primitive small cell tumor with epithelial, gangliocytic, neuroendocrine and mesenchymal differentiation. Fascinating case.

Ira Bleiweiss: Something bad and blastic.

John Chan: This is a curiosity! Probably a blastomatous form of paraganglioma (paraganglioblastoma).

Thomas Colby: Remarkable case and the diagnosis is appropriately descriptive. I was not aware of the prior report of these tumors.

Kum Cooper: Fascinating tumor, Michal. Thanks for the education!

Ivan Damjanov: Intriguing tumor I do not even pretend to understand what it is or try to offer an explanation.

Otto Dietze: Very good example of this rare entity, you can really distinguish the whole spectrum of differentiation from one H&E slide.

Hugo Dominguez-Malogon: Wow! What a case, thank you.

Göran Elmberger: Michal, where do you find all unique cases? Certainly not the typical glomus tumor even if location and morphological findings seem to support your suggested diagnosis of extra-adrenal paraganglioblastoma.

Vincenzo Eusebi: Whatever you say Michal. Multidirectional small cell tumour.

Giovanni Falconieri: Impossible case. Beside the fact that we do not see pediatric tumors (except CNS ones), I believe that this case has a number of phenotypic and immunohistochemical features making microscopic interpretation hard for the average surgical pathologist. It has a vague alveolar arrangement of tumor cells, in fact – looking at the glass slides without knowing the history; I considered the possibility of a strange paraganglioid tumor with gangliocytic differentiation.

Cyril Fisher: No experience of this extraordinary entity, a remarkable case.

Christopher Fletcher: A very remarkable case – when seeing this combination of features, one might even need to consider the possibility of metastasis from a germ cell tumor.

Andrew Folpe: Fascinating primitive tumor. I like the idea of some relationship to paraganglioma. I must read your paper.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: It is very interesting and challenging. Thank you very much for the detailed comments.

Allen Gown: What a strange and wonderful tumor! Thank you, Michal.

Thomas Krausz: I haven't seen this type of tumor before; however, some of the features remind me of a ganglioneuromatous paraganglioma of the cauda equina with extensive keratin expression (Human Pathology, 2005, 36:444)

Thomas Mentzel: An interesting case of a polyphenotypic small cell neoplasm.

Michal Michal: This is my case.

Markku Miettinen: Seems to be an unique case and entity. Your descriptive name is good. One could also think of some kind of "blastoma". However, not easy to fit into teratoma.

Liz Montgomery: This is amazing. In places, it looks like a germ cell tumor. Thanks for educating us on this type of lesion.

Giuseppe Pelosi: Primitive small cell tumor with epithelial, gangliocytic, neuroendocrine and mesenchymal differentiation: great case, I never saw this tumor type before!!

Santiago Ramon y Cajal: Beautiful case and description.

Juan Rosai: Never seen anything like it.

Joshua Sickel: Great case. Thanks for the discussion.

Dominic Spagnolo: Totally weird, impossible case, Michal. I was not aware of your paper, which I have now read.

James Strauchen: Looks like a blastoma of some sort! I have never seen anything exactly like it.

Saul Suster: This is a new one for me! Many thanks for sharing it.

Lawrence Weiss: Unbelievable. Where do you get these cases?

Bruce Wenig: Agree with primitive small cell tumor with mixed cell differentiation as indicated. What is the expected outcome for patients' with this tumor? Do they respond to treatment? What is the proposed treatment?

CASE NO. 18– CONTRIBUTED BY MARKKU MIETTINEN:

Phil Allen: Extraskeletal osteosarcoma, arm. I agree with the diagnosis. I don't think it is an ossifying fibromyxoid tumor, and I also believe it is a high grade sarcoma.

Carlos Bacchi: Osteosarcoma?

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Extraskeletal osteosarcoma. Fully agree with your diagnosis.

Ira Bleiweiss: Agree with extraskeletal osteosarcoma.

John Chan: Agree with interpretation of extraskeletal osteosarcoma.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Great case Markku. I have not seen a case since my days as a resident in Africa!

Ivan Damjanov: Agree.

Otto Dietze: The few cases of extraskeletal osteosarcoma I have seen were aggressive tumors with high grade histology, and I believe that this one belongs into this category.

Hugo Dominguez-Malogon: I wonder if some of extraskeletal osteosarcomas may represent a dedifferentiation of other tumors (including nodular fasciitis).

Göran Elmberger: No other opinion from me. Thanks for rare example of EO! The tumor is seemingly of high malignant potential with LVI growth in close association with pseudocapsule in spite of well circumscription.

Vincenzo Eusebi: This case to me looks like an osteosarcoma.

Giovanni Falconieri: I am not very familiar with bony lesions yet I do not see an alternative to extraosseous OS. Thanks for this submission.

Cyril Fisher: Extraskeletal osteosarcoma vs. malignant OFMT (favor the latter supported by the encapsulation).

Christopher Fletcher: Given the prominent trabecular component of epithelioid or more ovoid cells with variably eosinophilic or clear cytoplasm, then I would also have considered the possibility of a malignant myoepithelial tumor but clearly immunostains would allow such a distinction to be made.

Andrew Folpe: Agree with osteosarcoma. I don't see any areas in this one slide that are especially suggestive of ossifying fibromyxoid tumor.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: It is an interesting case. How about the immunostaining of myoepithelial markers? It seems to be also malignant myoepithelioma. There are areas of sheet-like arrangements of atypical cells.

Thomas Krausz: The trabecular and focally nested growth of rather bland epithelioid cells are rather unusual for an osteosarcoma. In my experience, on extensive sampling many of the extraskeletal osteosarcomas turn out to be something else (dedifferentiated liposarcoma, MPNST, synovial sarcoma and malignant mixed tumor). I assume epithelial and neuroendocrine markers are negative in this case.

Janez Lamovec: Extraosseous osteosarcoma, agree with a diagnosis.

Thomas Mentzel: Thanks for this unusual case of extra skeletal osteosarcoma with a prominent osteocartilagenous differentiation. Usually cases of rare extra skeletal osteosarcoma show only focal malignant osteoid and are mainly composed of a high-grade, "MFH"-like sarcoma.

Elizabeth Montgomery: Very nice case with lovely osteoid.

Giuseppe Pelosi: This is a high-grade neoplasm that has been diagnosed as extraskeletal osteosarcoma. I concur with this interpretation for the presence of malignant osteoid and cartilage. A differential diagnosis also includes sarcomatoid carcinoma especially in the setting of particular clinical presentations, such as in the breast, lung or female genital tract.

Santiago Ramon y Cajal: I agree with you that this case corresponds to extraskeletal osteosarcoma closer to high than to low grade.

Juan Rosai: Nice case. Some areas raise the differential diagnosis with myositis ossificans and others with metastatic carcinoma, but there is plenty of malignant osteoid and cartilage.

Joshua Sickel: Classic case for the teaching collection.

Dominic Spagnolo: Agree with soft tissue osteosarcoma, and with your comment about the unusual morphologic patterns. Also considered malignant OFMT but difficult to prove here.

James Strauchen: Agree with extra skeletal osteosarcoma.

Saul Suster: I can certainly see the resemblance with ossifying fibromyxoid tumor. If such, it would have to correspond to the malignant variant of it. On the other hand, the cells look too uniform and too bland for a conventional extraskeletal osteosarcoma.

Lawrence Weiss: It does have an "ossifying fibromyxoid tumor-like" feel, but I think it is probably just an "ordinary" osteosarcoma.

Bruce Wenig: Based on the provided information, I agree with extraskeletal osteosarcoma. Any history of radiation to this area? I do not identify any foci indicative of OFT. As compared to the case Markuu has provided, the few examples of this entity I have previously seen histologically appeared more like an undifferentiated pleomorphic sarcoma.

CASE NO. 19– CONTRIBUTED BY CESAR MORAN:

Phil Allen: Multicystic myxoid lesion with unidentified stromal cells, right lung. I can't recognize this as endometriosis nor can I see any convincing lung in my section. I don't know what it is. As previously mentioned, our lung expert, Doug Henderson, is away so I can't show it to him.

David Ben-Dor: Dr. Moran, this seems to be a highly unusual presentation for this entity. We are given no explanations or commentary- is there a history? Endometriosis elsewhere? This reminds me of the crazy case that Falconieri showed us of an endometrial stromal tumor (or was it granulosa cell tumor?) showing up in the lung decades after the primary was removed and summarily forgotten. (Paul Wakely also showed us something in the same vein). Is the septate appearance germane to the lesion itself secondary to cystic change or is it merely the lesion infiltrating into the alveolar septate? I don't see any glands- shouldn't this then be endometrial stromal tumor?

Gerald Berry: Agree. I have seen a number of clinical cases where the diagnosis was suspected but never proven with tissue. This is a terrific teaching case.

Michele Bisceglia: Endometriosis of the lung. Cesar, I am a bit embarrassed in saying that not only I did not make the correct diagnosis "blind" without knowing yours, but I cannot make it not even after reading your own diagnosis. I am worried of and for myself: in fact, I thought of a malignant biphasic tumor (?synovialsarcoma – mitoses in the stromal component are misleading).

Ira Bleiweiss: Beautiful case, Cesar. Amazing amount of endometrial stroma. Did she have monthly hemoptysis? I recently had a case of incidental endometriosis at the tip of the appendix, nothing quite so dramatic I'm afraid.

John Chan: I favor a diagnosis of metastatic low grade endometrial stromal sarcoma over endometriosis. There is too extensive stromal cell proliferation for endometriosis. Even the epithelial cells lining the cysts and clefts may not be endometrial epithelium, but might represent pneumocytes. Perhaps a TTF-1 immunostain may help.

Thomas Colby: I would include metastatic endometrial stromal sarcoma in the differential. It would be nice to document that there were epithelial elements present in the lung that had an immunohistochemical staining pattern (i.e. ER/PR positive) consistent with endometrial glands and that they were TTF negative.

Kum Cooper: Cesar, I am astounded! Never seen a case before! Did you do a CD10 and ER?

Ivan Damjanov: In my slide, I did not find glands and most of the mass was composed of spindle cells—could it have been some leiomyomatosis or lymphangioleiomyomatosis or endometrial stromal lesion?

Otto Dietze: Thank you for this nice contribution, we have seen this in a small biopsy two years ago and could not make the diagnosis without a reference center.

Hugo Dominguez-Malogon: Sorry, in my slide there is a cystic lesion that does not resemble endometriosis.

Göran Elmberger: Difficult case. Without characteristic endometrial glands and hemosiderin deposition, I would need more evidence such as a positive IHC reaction for ER and PgR before being able to make such an unusual diagnosis. Right sided and subpleural location supports dx.

Giovanni Falconieri: Instructive case, never seen such a case of pulmonary endometriosis except conventional examples of pleural/diaphragmatic locations.

Cyril Fisher: Endometriosis of lung, very uncommon.

Christopher Fletcher: I wonder if I am being very stupid – in the slide which I have, there is no lung tissue (although this may possibly be pleura), and I do not see either endometrioid epithelium nor any evidence of hemorrhage – I am perplexed....."

Andrew Folpe: Nice case – thanks.

Jerónimo Forteza Vila: Thank you for this interesting surgical pathology case.

Masaharu Fukunaga: It is a wonderful educational case. The stroma shows focally sex-cord like arrangements.

Thomas Krausz: Before reading the diagnosis, I considered metastatic endometrial stromal sarcoma entrapping alveolar epithelium (the epithelium does not look endometrioid type). I assume the epithelial cells are TTF1 negative.

Janez Lamovec: Very difficult case to diagnose. I must admit I didn't get it.

Thomas Mentzel: Many thanks for this nice example of pulmonary endometriosis.

Elizabeth Montgomery: This case is difficult for me to diagnose as endometriosis, and I considered other entities including ESS, various entities with smooth muscle differentiation, and even synovial sarcoma [though not quite right for SS]. The epithelial part is completely flattened so I had trouble recognizing it as endometrial and there is no hemosiderin. I would have needed to work this up a bit.

Markku Miettinen: Agree on gynecological stromal proliferation. I suppose the epithelial elements were ER/PR-positive. Also, the possibility came to mind that some stromal elements are gyn-type smooth muscle.

Giuseppe Pelosi: Endometriosis of the lung. Great case! I remember a case I saw in consultation several years ago, in which a bifocal pulmonary endometriosis had been misdiagnosed as pulmonary blastoma and the patient should have undergone pneumonectomy!!!

Santiago Ramon y Cajal: Quite extensive picture of endometriosis of the lung.

Juan Rosai: What about metastatic endometrial stromal sarcoma?

Joshua Sickel: I thought this was a metastatic endometrial stromal sarcoma, completely missed the glandular component. Thanks for this amazing case.

Dominic Spagnolo: A man of few words, Cesar! Wonderful case of pulmonary endometriosis.

James Strauchen: Pleural endometriosis! Stroma only. Wild! Catamenial pneomothorax is the classic presentation

Lawrence Weiss: Nice Case.

Bruce Wenig: Yes it is.

CASE NO. 20– CONTRIBUTED BY JAMES STRAUCHEN:

Phil Allen: Angiotropic metastatic malignant melanoma, lower lobe of right lung. Angiotropism is fairly common in desmoplastic malignant melanomas. Moreover, this metastatic tumor looks just like a desmoplastic melanoma of the face.

Carlos Bacchi: Nice case.

David Ben-Dor: Dr. Strauchen, angiotropic (not *angioinvasive*) metastatic spread – never heard of it and never would have thought of it. Assuming I thought of melanoma (not guaranteed) given the spindle cell proliferation, I would think that this would fit nicely with the desmoplastic type (unless the spindle cells are really fibroblasts- would need immuno). Based on H and E, I have trouble making out the intimate association between the tumor cells and blood vessels- double immunostaining for CD34 and S100 would be helpful. What is truly remarkable is the fact that, glancing at the recent reference in Advances, this mechanism was suggested close to 100 years ago and apparently overlooked or ignored until it was recently resurrected. I wonder how many other gems are hidden in the old musty volumes (and not in English)? This case is truly educational. Am I to assume that if I get melanoma, I should come to Mt Sinai rather than Memorial?

Michele Bisceglia: Angiotropic metastasis of malignant melanoma. Have never noted this pattern before.

Ira Bleiweiss: Amazing what melanoma can do.

John Chan: Difficult case without knowing the history of melanoma. Morphologically, I also considered the possibility of epithelioid hemangioendothelioma.

Thomas Colby: Agree with diagnosis. I have seen a couple other spindle melanomas metastasize to the lung and the histology was similar.

Kum Cooper: I had metastatic melanoma in my differential, but did not appreciate the angiotropism at first go! Thank you for demonstrating this unusual pattern.

Ivan Damjanov: Consistent with angiotropic malignant melanoma—tough diagnosis.

Otto Dietze: I agree, angiotropic growth of MM is probably more frequent if we look to this phenomenon.

Hugo Dominguez-Malogon: A new one for me, thank you.

Göran Elmberger: Very interesting phenomenon. Thanks.

Giovanni Falconieri: Very interesting, thank you, Dr. Strauchen for contributing this example of unusual melanoma spreading.

Cyril Fisher: Extraordinary appearance which does indeed resemble EHE.

Christopher Fletcher: I can see bundles and nests of cells that certainly look like metastatic melanoma, set within a dense collagenous stroma, but I am having difficulty recognizing the angiocentricity, at least in the slide which I received, although there do appear to be one or two large vessels which are occluded by neoplastic cells.

Andrew Folpe: Metastatic melanoma involving a blood vessel wall.

Jerónimo Forteza Vila: Thank you for this interesting case.

Masaharu Fukunaga: My impression without history was inflammatory myofibroblastic sarcoma. This is my first time to see “angiotrophic metastasis of malignant melanoma”.

Thomas Krausz: This case certainly illustrates why angiotropic malignant melanoma is under appreciated as without special stains it is difficult for me to see the angiotropism of the tumor cells.

Janez Lamovec: It is difficult to appreciate all that infiltrated vessels. The tumor appeared more like desmoplastic malignant melanoma to me.

Thomas Mentzel: An interesting phenomenon of infiltration in malignant melanoma that is probably seen more frequently in melanoma metastases than in primary neoplasms.

Elizabeth Montgomery: This is amazing. The metastatic lesion appears deceptively bland so thank goodness you had the history. Over time it seems we all learn to fear bland melanomas and always list melanoma in the ddx of just about everything!

Markku Miettinen: Agree on metastatic melanoma, would be almost impossible without immunostains.

Giuseppe Pelosi: This is an interesting case of angiotropic metastasis of malignant melanoma. I do not have specific comments to this case.

Santiago Ramon y Cajal: Once again, your interesting case highlights the importance of pertinent clinical information.

Juan Rosai: It looks more desmoplastic than neurotropic to me.

Joshua Sickel: Agree with diagnosis.

Dominic Spagnolo: It looked very much like metastastic desmoplastic melanoma to me. The angiotropic nature escaped me (and still escapes me). I see the superficial resemblance to an epithelioid vascular tumor, even to the extent of nested invasion ("angiocentricity") of large vessel walls, but this is not my understanding of extravascular migratory metastasis, where tumor ostensibly binds to endothelium via this purported matrix-based angiotumoral complex. I don't doubt the phenomenon occurs locally at the primary melanoma site, but I find it a quantum leap to accept that this mechanism may account for remote metastasis, e.g. to brain, rather than intravasal spread. At least with neurotropism (including in local recurrences), one actually sees the tumor around nerves, distant from the main primary focus - why with this extravascular phenomenon does it typically stop at the advancing edge (or at least in close proximity to it) of the melanoma? More questions than answers for this Luddite at the moment.

Lawrence Weiss: This is unbelievable. I couldn’t but my finger on what was going on. I am glad I saw this case, so I don’t miss it when it counts.

Bruce Wenig: Metastatic malignant melanoma.

CASE NO. 21– CONTRIBUTED BY PAUL WAKELY, JR.:

Phil Allen: Decidual reaction in the cervix. I cannot see any embryonal rhabdomyosarcoma in this material.

Carlos Bacchi: Great case. It is really focal the presence of rhabdomyosarcoma.

David Ben-Dor: Dr. Wakely, this case truly makes me feel humble if not inadequate. Thanks for having mercy at least on my soul by placing the dot. If I understood correctly what you pointed out, then this lesion seems to be diffusely infiltrating through the cervix (tracking along the vessels as in the angiotropic spread proposed in the last case) rather than forming a mass? I think it takes a lot of guts to make this diagnosis which is truly remarkable. For this kind of case, it might be helpful to attach a photo with a legend of the histology and the immunostains.

Gerald Berry: Beautiful example of a lesion that can be easily overlooked.

Michele Bisceglia: Embryonal rhabdomyosarcoma of the uterine cervix. Thank you, Paul. I did not notice before all those observations.

Ira Bleiweiss: Thanks for the dot. I would have totally missed it. Very humbling.

John Chan: I favor an interpretation of Mullerian adenosarcoma (with rhabdomyosarcomatous component). The deep seated glands cannot be readily explained by a rhabdomyosarcoma.

Thomas Colby: Agree with diagnosis.

Kum Cooper: Paul, this is ever so subtle! No, I do not have any RMS of the cervix in Vermont; but saw a handful in Africa where the diagnosis was much more obvious!

Ivan Damjanov: No way would I have made this diagnosis without your help.

Otto Dietze: I cannot offer a similar observation from my own material, but I know from a college who had the same misfortune, when he missed a RMS within a lesion from the external ear, which was believed to be a granulation polyp.

Hugo Dominguez-Malogon: I agree with ERMS, thank you Paul.

Göran Elmberger: Very difficult case. No wonder dx was delayed. Awareness of cervical presentation in teenagers and young adults and clinical presentation seems important tip-off. Thanks for sharing.

Vincenzo Eusebi: I hope the immuno is consistent with clear cut rhabdo differentiation. Cambium layer is indicative of botryoid subtype.

Giovanni Falconieri: Difficult case, Paul; indeed I think it is quite easy to overlook the diagnostic clues; were it not for the dot I could not recognize the small foci of malignant small round cells. The deciduoid changes secondary to pill also confound the matter. If I saw something previously, I missed it for sure.

Cyril Fisher: Amazing case. Thanks for marking the slide, Paul.

Christopher Fletcher: This is a subtle but convincing case. In my experience, cartilaginous differentiation in this clinically distinctive subset of embryonal RMS is a relatively frequent finding (even in the absence of prior therapy). It is very hard to understand why these tumors are associated with a very much better prognosis than comparable lesions in the pediatric age group at other locations.

Andrew Folpe: That's a very hard case, Paul. I can see why the small foci of ERMS were missed in that background. I've seen a few cases of cervical RMS- they were all much more obvious than this. The issue tends to be whether one is dealing with a pure RMS or some type of Müllerian tumor with a RMS component.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: It is very difficult to find the RMS element. I am afraid that I would sign out as "a benign polypoid cervical lesion". Thank you very much for the great case and the detailed comments

Allen Gown: Thanks for this example and the case description.

Thomas Krausz: Paul, I am glad you put the green dot on the slide, otherwise I also would have missed it.

Janez Lamovec: I understand that these small foci of RMS could be overlooked on cursory examination. A very dangerous mistake.

Thomas Mentzel: A very difficult diagnosis and many thanks for the green dot!

Michal Michal: Why not to call the lesion as Mullerian adenosarcoma with RMS differentiation?

Elizabeth Montgomery: You were very clever to spot this and evaluate it further with myogenin labeling.

Markku Miettinen: Thank you for the dots – still difficult to identify it histologically as rhabdomyosarcoma, but your documentation seems convincing. One could easily think endometrial stromal type of differentiation, but lack of CD10, ER and PR would disprove this in a rhabdomyosarcoma. In an older woman, one could wonder if this is related to/part of MMMT, especially with the cartilage.

Giuseppe Pelosi: Embryonal rhabdomyosarcoma of the uterine cervix. I have seen at least three cases of this tumor type growing as endocervical polyps that had been misdiagnosed as benign lesions. Therefore, it is very important to accurately scrutinize endocervical polyps in young people, in order to avoid missing these deceptive lesions that sometimes are very hard to be recognized.

Santiago Ramon y Cajal: Thank you for your beautiful case and description of Embryonal Rhabdomyosarcoma of the uterine cervix.

Juan Rosai: Very difficult case. I assume that the alleged skeletal muscle differentiation was confirmed with desmin, skeletal muscle actin and- in particular - myogenin stains.

Joshua Sickel: I misinterpreted this as mullerian adenosarcoma with rhabdo component.

Dominic Spagnolo: A treacherous and challenging case, Paul. I somehow doubt that this is endocervical in origin. To me it looks as if it's arising in endometrium, involving the isthmic region and "prolapsing" down into cervix pushing squamous mucosa ahead of it. Much of the polyp looks benign, and has benign endometrial stromal and fibroblastic (and ?myoid) components, though I agree there are malignant foci in the stroma and also subepithelially, that turn out to be rhabdomyosarcoma. Am not sure how I would call this, but am not convinced it is a primary endocervical rhabdomyosarcoma.

James Strauchen: Missed this one entirely!

Lawrence Weiss: I can certainly understand how the diagnosis was initially missed. It is surprising that it took an additional 6 months to rebiopsy. Any longer follow-up on the case?

Bruce Wenig: What a case. I found another small focus of malignant small round cells elsewhere in my slide. Thanks.

CASE NO. 22– CONTRIBUTED BY LAWRENCE WEISS:

Phil Allen: Metastatic mature cystic teratoma with sarcomatous component (embryonal rhabdomyosarcoma), retroperitoneal lymph node. Thanks for the case and the reference, Larry.

Carlos Bacchi: Nice example of germ cell tumor with sarcomatous component.

David Ben-Dor: Dr. Weiss, I realize that these cases are organized in purely alphabetic order without any ulterior motive but here the rhabdomyosarcoma is as (blatantly) obvious as it wasn't in the previous case (rhabdomyosarcoma of the cervix). To see this tumor in such unusual contexts might otherwise take a lifetime but here I'm seeing this twice in one sitting.

Michele Bisceglia: Mature cystic teratoma with sarcomatous component (embryonal rhabdomyosarcoma). Agree. Thank you. This is a finding that sometimes can be seen.

Ira Bleiweiss: Agree.

Thomas Colby: Agree with diagnosis; and cross striations are readily found.

Kum Cooper: Thank you, Larry. I have a similar case on file with testicular mixed germ cell tumor and a PNET component in the metastasis to the retroperitoneum.

Ivan Damjanov: Agree.

Otto Dietze: Thank you for this contribution, the RMS differentiation is very good to be seen on H&E.

Hugo Dominguez-Malogon: Very illustrative case, thank you for the nice comments on our paper Larry.

Göran Elmberger: Very interesting case.

Vincenzo Eusebi: Nice case and typical features of embryonal rhabdomyosarcoma.

Giovanni Falconieri: Great case, thanks Dr. Weiss for this contribution.

Cyril Fisher: Rhabdomyosarcoma arising in teratoma, a rare event indeed.

Christopher Fletcher: Beautiful and convincing case – I assume that the outcome will most likely be poor.

Andrew Folpe: Rhabdomyosarcoma arising in association with teratoma. Very nice case.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Thank you for the beautiful case, I agree.

Allen Gown: I guess rhabdomyosarcomas "win" in AMR 53 - three of them! Thanks, Larry, for this nice example of this rare tumor.

Thomas Krausz: Yes, it is great to see this case especially in view the recent publication on this topic.

Janez Lamovec: Fantastic case! Thank you.

Thomas Mentzel: A wonderful case of a mature teratoma with a rhabdomyosarcomatous differentiation (showing in the given slide some features of spindle cell rhabdomyosarcoma).

Elizabeth Montgomery: Thanks for sharing this case.

Markku Miettinen: Agree on rhabdomyosarcomatous differentiation in metastatic cystic teratoma.

Giuseppe Pelosi: This is an example of mature cystic teratoma with sarcomatous component (embryonal rhabdomyosarcoma) of the testis. Interesting and well documented case. I remember a few mediastinal teratomas with secondary malignant changes consisting in rhabdomyosarcoma component, which usually run a very aggressive clinical course despite medical treatment.

Santiago Ramon y Cajal: Nice example of Mature Cystic Teratoma with rabdo-sarcomatous Component. Thank you!

Juan Rosai: Spectacular example of rhabdomyosarcomatous differentiation in a teratoma. It reminds me of the cases we reported many years ago of spermatocytic seminoma of the testis associated with sarcoma, including rhabdomyosarcoma (Am J Surg Pathol 12: 75, 1988).

Joshua Sickel: Beautiful and rare case. Never seen this before.

Dominic Spagnolo: A very nice case of mature cystic teratoma with embryonal rhabdo – thanks, Larry.

James Strauchen: Sarcoma in mature cystic teratoma following therapy of non-seminomatous GCT. Nice example!

Saul Suster: Agree completely with diagnosis.

Bruce Wenig: Yet another cool case and back-to-back (sort of) cases of embryonal RMS, although this one with a bit more obvious RMS than Paul's case.

FOLLOW-UP COMMENTS TO AMR SEMINAR # 52

CASE NO. 8 – CONTRIBUTED BY GIOVANNI FALCONIERI:

Ira Bleiweiss: Thanks, Falco for sending me a slide. This case is just what I expected based on your description and have seen a few times in the past. I think it should be classified as a malignant phyllodes tumor with the usual cautions of non-predictable behavior.