COMMENTS TO AMR SEMINAR #58

CASE NO. 1 – CONTRIBUTED BY VOLKAN ADSAY:

Phil Allen: Large (18 cm), subsynovial, ?intra-articular, myxoid sarcoma with inflammatory cells, right posterior knee. I don't think this is a described entity but I am pretty sure I have seen two similar cases before, both just over 20 years ago. Both were intra-articular and subsynovial in the knee joint. One was excised arthroscopically and there was no tumor apparent on follow-up arthroscopy a few months later. Despite the alarming appearances, the arthroscopic findings suggested to the clinicians that it was benign. In a burst of enthusiasm, I wrote both cases up as a new benign entity and submitted the paper to Virginia LiVolsi, who was then Editor of the now-defunct journal, "Surgical Pathology." As she was rejecting the paper on the grounds of inadequate follow-up, the tumor recurred. I withdrew the paper and I eventually heard that both patients died with metastases. I still haven't written them up.

Carlos Bacchi: What a case!

David Ben-Dor: No differential? that's mean. Is the loss of INI-1 supposed to imply that this is an epithelioid sarcoma?- doesn't look like one. Just looking at the histology- looks like a true synovial lesion, if I had to vote I wouldn't call it malignant.

Gerald Berry: In light of the strong diffuse CAM5.2 staining I would have to settle on epithelioid sarcoma. That said I was not thinking along this track based solely on the histological findings.

Michele Bisceglia: 17-year-old male with leg mass. Malignant tumor (sarcoma-NOS, myxoid, spindle/ epithelioid in my view). Hi, Volkan: very pleased to meet you in Istanbul. In regard to this case, since you ask us about the diagnosis, I would categorize this case in the Archive of the Club as a Quiz case.

Tom Colby: Not sure what this is. There appears to be a background of a vascular abnormality but I am not sure that squares with the fact that most of the lesion was solid. At any rate, it would be of interest if there is a vascular malformation as there is marked vascularity to this process. I shared this case with a colleague who noted that it looked chordoid and I would probably make a descriptive diagnosis, including the terms "chordoid features" and say I wasn't sure what this was and that I would share it with esteemed soft tissue colleagues in the AMR society so that they could "pull my you know what out of the fire." Hopefully the lesion was entirely resected.

Kum Cooper: Thank you Volkan for the wonderful meeting/visit in Turkey. You were an excellent host. The cytokeratin and INI IHC point to a proximal-type epithelioid sarcoma. What about EMA and CD34?

Ivan Damjanov: Malignant rhabdoid tumor of soft tissue? Could this be a synovial sarcoma? Not quite sure what to make out of this slide and these data.

Otto Dietze: Proximal type epitheloid sarcoma (vs. extrarenal rhabdoid tumor).

Hugo Dominguez-Malagon: The immunologic profile and loss of INI1 fits for epithelioid sarcoma. However the lesion has a cystic appearance and some "zoning" phenomenon and inflammatory changes that could correspond to a reactive process. Even with the INI1 loss I am not sure that this is a neoplastic process.

Göran Elmberger: Background changes pigmented synovitis without giant cells. Could possibly be classified as malignant giant cell tumor of tendon sheath with few giant cells. INI1- in favour of CERT/proximal myxoid epitheloid sarcoma variant... Rhabdoid cells present.

Giovanni Falconieri: Difficult case, I can find convincing clues. Hemosiderin incrustation in an 18 cm sized mass suggests a longstanding lesion, if this matches the clinical history I am inclined to consider a low grade soft tissue tumor, yet this is something I would defer to the soft tissue gurus.

Franco Fedeli: Sarcoma, not otherwise specified, with focal chordoid features. Look forward to your diagnosis on this leg mass in a 17-year-old male.

Christopher Fletcher: Despite the unusual cystic appearance, the tumour cell morphology and immunophenotype suggest that this may represent epithelioid sarcoma. It would be interesting to know the results of staining for EMA and CD34.

Andrew Folpe: Sarcoma with loss of INI-1 expression. I'd favor a myoepithelial tumor (40% of which may be INI-1 negative) over anything related to epithelioid sarcoma or rhabdoid tumor.

Jerónimo Forteza Vila: Nice case. Our first possibility is an epithelioid sarcoma.

Masaharu Fukunaga: Pigmented villonodular synovitis (diffuse type giant cell tumor) with low malignant potential.

Thomas Krausz: The cystic change and the focal myxoid matrix together with the granulation tissue obscuring the neoplastic infiltrate causes differential diagnostic dilemma. It would be important to see the solid part of the neoplasm, however in the light of the immunohistochemical and molecular data I favor the diagnosis of epithelioid sarcoma rather than soft tissue myoepithelial tumor or a variant of extraskeletal myxoid chondrosarcoma.

Janez Lamovec: ?Unusual epithelioid sarcoma, ?malignant mixed tumor of soft tissue.

Thomas Mentzel: Given the reported findings, the differential diagnosis includes epithelioid sarcoma and myoepithelioma.

Markku Miettinen: Malignant epithelial neoplasm with myxoid matrix, most consistent with epithelioid sarcoma variant. Large tumor size and young patient age would seem to support epithelioid sarcoma, along with the INI/SMARCB1-loss.

Liz Montgomery: What a peculiar cystic/myxoid appearance. With that immunolabeling pattern it seems best to regard it as epithelioid sarcoma with an area with the odd changes. You note that the rest was solid so perhaps it appeared more classic?

Santiago Ramon y Cajal: Phenotypically, this neoplasm is remarkable for its prominent vascularity as well as for areas of spindle and reticular morphology.I would favor a spindle cell hemangioendothelioma. In the differential I would consider synovial sarcoma and rhabdomyomatous tumors.

Dominic Spagnolo: Not sure – need more stains. Favor myoepithelial carcinoma (but SMA negative; these can show INI loss). Dediiff'd extraskeletal myxoid chondrosarc (also can lose INI but shouldn't be so strongly keratin+ and EWS not involved). Don't like it for synovial sarcoma. Looks weird for epithelioid sarcoma. Epithelioid MPNST can lose INI but shouldn't be keratin+ and frankly doesn't look like one. Am obviously missing something!

James Strauchen: Epithelioid sarcoma with cystification. The INI loss is consistent with epithelioid sarcoma, however, the cystification is striking.

Saul Suster: Don't know what this is – my first impression was benign. I don't think I trust all these stains anymore – I don't feel comfortable making "immunohistochemical" diagnoses on things that don't make sense on the H&E.

Eduardo Zambrano: At least some of the cysts appear to be vessels infiltrated by tumor cells. Given the apparent angiocentric or angioinvasive nature of this rather myxoid spindled to epithelioid tumor, the possibility of epithelioid hemangioendothelioma crossed my mind. However, the absent CD31 expression makes this possibility less likely, while the loss of expression of INI1 places it in the epithelioid sarcoma/rhabdoid tumor category.

CASE NO. 2 – CONTRIBUTED BY DAVID BEN-DOR:

Phil Allen: Gastrointestinal stromal tumor in a core biopsy from the prostatic region. The section that I have seen seems to be the same as those reported by Herawi, Montgomery and Epstein in Am J Surg Pathol 2006;30:1389-1395. I hope it responds to imatinib.

Carlos Bacchi: Good case of GIST. Thanks for the excellent discussion.

Gerald Berry: Agree with the diagnosis of GIST. The lesion learned is the need for liberally staining spindled cell lesions for CD117!

Michele Bisceglia: What a nice review on the topic of "rectal-prostatic" GIST. Of course no question on the diagnoses which were rendered. Thank you, David, for underlining this issue. Two notes: i. speaking of the most unusual GIST locations certainly everyone noticed the recent publication of the first case of a supradiaphragmatic GIST – a pleural-based GIST (Long KB, Butrynski JE, Blank SD, Ebrahim KS, Dressel DM, Heinrich MC, Corless CL, Hornick JL. Primary extragastrointestinal stromal tumor of the pleura: report of a unique case with genetic confirmation. Am J Surg Pathol. 2010;34:907-12.). ii. the differential diagnosis of rectal-prostatic GIST includes also prostatic solitary fibrous tumor (Herawi M, Epstein JI. Solitary fibrous tumor on needle biopsy and transurethral resection of the prostate: a clinicopathologic study of 13 cases. Am J Surg Pathol. 2007;31:870-6).

Ira Bleiweiss: Histologically benign spindle cells - best I can do.

Tom Colby: Submitted as a GIST of the prostate. A few of these have turned up in the chest and presenting as a prostate mass in the pelvis would not be entirely surprising. That's gist the way it is.

Kum Cooper: Thank you David for sharing this precious case/slide with us. I have only read about this in the prostate and this is the first I am seeing it. They may also present in the vulva (still awaiting for that to pop up !). I love the "tourists in Istanbul" comment! Watch out for my "man from Istanbul" in AMR 58!

Ivan Damjanov: GIST in an unusual site, but without immunohistochemistry we would have called it a smooth muscle cell tumor.

Otto Dietze: I have recently seen a histologically malignant case from the uterus with diffuse strong positivity in spindle cell areas as well in pleomorphic cells.

Hugo Dominguez-Malagon: My diagnosis was of a sarcoma, non-classified, however as you said if this case were located in the GI tract GIST would be the first choice.

Göran Elmberger: Great case and great story. Reminds me of my first 2 weeks in FNA clinic at Karolinska. I had the great fortune to join the now 50 year old leading Karolinska unit to learn about FNA cytology at 1993 when I returned from a residency training period at UNMC Nebraska. The first two weeks we held the traditional international FNA course under Torsten Löwhagen and that became my introduction to cytology. After the course our acting chair Lambert Skoog wanted to test me. He showed me a unique once in a lifetime case of benign metastasizing pleomorphic adenoma to the iliac crest and to his surprise I got it immediately right. I was so inexperienced I did not even recognize I was in Istanbul! I believe the IHC and molecular findings of an activating mutation would be defining in this case. From a strict morphological perspective I believe schwannoma is to be ruled out.

Giovanni Falconieri: Excellent discussion on a very intriguing case. I need an extra-trip to the Bosphorus to reinforce the Istanbul concept.

Franco Fedeli: Very nice description and very important point you addressed either the prostatic GIST in your cases and those in the literature were primary or secondarily involving the prostate. However going through the literature one can find histogenetic explanation for GIST primarily arising outside the gastrintestinal tract: the interstitial cells of Cajal (i.e., interstitial Cajal-like cells) have been identified also in prostate (Shafik A, Shafik I, el-Sibai O. Identification of c-kit-positive cells in the human prostate: the interstitial cells of Cajal. Arch Androl. 2005;51:345-51. Nguyen DT, Dey A, Lang RJ, Ventura S, Exintaris B. Contractility and Pacemaker Cells in the Prostate Gland. J Urol. 2010 Nov 13.), Fallopian tube and uterus (Popescu LM, Ciontea SM, Cretoiu D. Ann N Y Acad Sci. Interstitial Cajal-like cells in human uterus and fallopian tube. 2007 Apr;1101:139-65), and bladder (Johnston L, Woolsey S, Cunningham RM, O'Kane H, Duggan B, Keane P, McCloskey KD. Morphological expression of KIT positive interstitial cells of Cajal in human bladder. J Urol. 2010;184:370-7.

Cyril Fisher: Convincingly documented GIST in unexpected location. Thanks for good discussion. Results of mutational analysis would be of interest.

Christopher Fletcher: GIST spindle cell type, likely arising in periprostatic soft tissue. Indeed it is easy to forget this diagnosis in this location.

Andrew Folpe: Agree with GIST. Interesting presentation.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Thank you very much for the description. This is the first time I see GIST in the prostate.

Thomas Krausz: David, thank you for the philosophical discussion. Without the immuno, it would be difficult. I would add cellular schwannoma also to the differential diagnosis.

Janez Lamovec: Without immuno it would be difficult to get the right diagnosis. I thought it was some kind of myofibroblastic tumor, STUMP or low grade MPNST.

Thomas Mentzel: Many thanks for sharing this interesting and rare case !

Markku Miettinen: GIST of colon/rectum.

Liz Montgomery: What a fun case of a GIST appearing on a "prostate" biopsy. In the beginning, Jon would bring those cases to me because they were like "elephant in a tree" but now he is totally onto them (in contrast I still have to bring him "is this actually prostate cancer crawling into this colon biopsy" cases). By chance, he had already shared this cute case with me! What a hoot. He is sent such a high volume of prostate and "prostate" biopsies that he seems to have an example of all entities known to humankind that show up on prostate and "prostate" biopsies!

Santiago Ramon y Cajal: Thank you for this interesting case and for the review on stromal tumors in the prostate.

Juan Rosai: I think we will have to accept this case as a GIST involving the prostate, although that was certainly not the first diagnosis that came to my mind when looking at the H&E sections. Maybe we should accept the fact that any tumor type can occur anywhere. I appreciate Dr. Ben-Dor quoting Dr. Ackerman's "Man from Istanbul" story.

Dominic Spagnolo: Nice case of GIST masquerading as a prostatic neoplasm, and informative discussion. I have not encountered such a lesion on TRUS biopsies. Looking at it blind I was thinking smooth muscle neoplasm first. Thanks David.

James Strauchen: GIST in an unusual location. Also thought of leiomyoma or prostatic stromal tumor.

Saul Suster: Agree with GIST. Unusual location.

Eduardo Zambrano: Very nice summary, David. Thank you! I confess I was in favor of a smooth muscle neoplasm, but will try not to miss the man in Istanbul next time I see him.

CASE NO. 3 – CONTRIBUTED BY OFER BEN-ITZHAK:

Phil Allen: Gastritis from selective internal radiation therapy (SIRT) with yttrium impregnated microspherules. I think I have seen this before in the liver but not in an accidentally infused stomach. Thanks for the discussion and references.

Carlos Bacchi: Amazing and very interesting case of Ittrium gastritis. I have never seen these microspheres before. Thanks for instructing me.

David Ben-Dor: Nope, never saw it. I hope that if I did I wouldn't dismiss the spheres as artifact (maybe I already have?). Beautiful demonstration- if I do see it henceforth I won't have any excuse not to pick it up.

Gerald Berry: I have seen this pattern once or twice before. It is always worthwhile seeing it again and again.

Michele Bisceglia: Yttrium associated gastritis. Nice case and thorough presentation. Never seen one.

Ira Bleiweiss: Wow! Are the slides radioactive?

Tom Colby: Agree with diagnosis of Yttrium-associated gastritis. I have seen this before and recognized the microspheres but could not for the life of me remember the name.

Kum Cooper: Wow! thank you very much for this slide. I recognized these microspheres instantly from the recent color photographs in publications in the literature. Yttrium-associated gastritis....so cool!

Ivan Damjanov: We had a case recently that really "scared" us because it contained fewer of the spherules and showed much more cellular atypica induced by radiation.

Otto Dietze: Thank you, I belong to those who did not see this before.

Hugo Dominguez-Malagon: Never seen a case like this, very illustrative discussion, thank you.

Göran Elmberger: Beautiful case. Never seen this here even though Yttrium has a very interesting history being discovered 1787 by Arrhenius just outside Stockholm in Ytterby mine at Resarö. Ytterby means "outer village" in Swedish. In that mine 7 basic elements all belonging to the group of lanthanoids were discovered.

Giovanni Falconieri: Great case and discussion, Ofer. I cannot recall seeing this before. Another gap filled! Thanks

Franco Fedeli: Yttrium associated gastritis. Never seen one. This case with its opaque microspheres reminds me of a case I saw some years ago of an hepatocellular carcinoma resection specimen which had previously been treated with doxorubicin-eluting-bead embolization (DEB) and then resected. Aside from the large ischemic zone with complete tumor necrosis one could well notice lots of black microspheres, the ones which are overloaded with the drug in point at the time of injection (here is a good reference dealing with the working mechanism of this treatment as well as showing illustrations of the dry form of Quadrasphere microspheres used in DEB which I refer to: Lee KH, Liapi EA, Cornell C, Reb P, Buijs M, Vossen JA, Ventura VP, Geschwind JF. Doxorubicin-loaded QuadraSphere microspheres: plasma pharmacokinetics and intratumoral drug concentration in an animal model of liver cancer. Cardiovasc Intervent Radiol. 2010;33:576-82.).

Cyril Fisher: Wow, what a striking appearance! Great slide.

Christopher Fletcher: This is indeed an amazingly distinctive appearance, although I have only personally seen this once before because I look at very few GI biopsies (thankfully !).

Andrew Folpe: Fascinating. I got as far as "granulomatous response to something that looks spherical", but I have never seen Yttrium before.

Jerónimo Forteza Vila: I agree with your diagnosis. We deduce that the contrast medium travelled along blood vessels and got stuck in the lung.

Masaharu Fukunaga: Thank you very much a wonderful case. I have never seen Yttirum associated gastritis.

Thomas Krausz: Ofer, thank you very much. I haven't seen Yttrium associated gastritis before. Very interesting.

Janez Lamovec: I have never seen this before. Thank you.

Thomas Mentzel: Many thanks ; I`ve never seen this before.

Markku Miettinen: Embolization material and ulcer. Could the embolization itself play a role in the ulcer (ischemic damage?)

Liz Montgomery: Lovely case of SIRS yttrium spheres. We see a lot of them in our consult material because the radioactivity can produce terrible changes that appear similar to dysplasia so the unwary who are not onto the black particles can be fooled.

Santiago Ramon y Cajal: Very nice slide. Thank you very much. I've never seen these microspheres before.

Juan Rosai: Cases don't get as cute and spectacular as this very often. It would make a good candidate for the "Images in Pathology" section of a pathology Journal.

Dominic Spagnolo: Thank you for this spectacular case of Yttrium induced gastritis and for the nice discussion. There is quite remarkable foveolar hyperplasia in the mucosa flanking the ulcer my section.

James Strauchen: Yttrium microspheres. I have seen a case of this here as well. Another disease of progress!

Saul Suster: Spectacular histology! I have never seen this before!!! Thank you, Ofer, for sharing this case with us.

Eduardo Zambrano: Very interesting! I had not seen this before. Recognizing the gastritis and the particles was the easy part, but I had no idea what the particles actually represented.

CASE NO. 4 – CONTRIBUTED BY GERALD BERRY:

Phil Allen: Medullary carcinoma with glandular/cribriform pattern, right lobe of thyroid.
Thanks for this very convincing example.

Carlos Bacchi: Nice case of medullary carcinoma of thyroid with organoid, glandular/cribriform pattern.

David Ben-Dor: Medullary carcinoma can also mimic anaplastic carcinoma. Years ago, shortly after starting my present job a sad looking woman presented herself to the department and explained that she had a thyroid mass removed a few years previously in our hospital which was diagnosed as anaplastic carcinoma. As a result she underwent very intensive chemotherapy. I was able to find the glass slides (but not the blocks) and I told her that given that she was alive meant that that diagnosis was erroneous- the tumor did show severe atypia but it was limited to the thyroid and didn't seem to invade outside it. I deduced from all of this that she really had a form of medullary carcinoma but unfortunately not having the blocks available I couldn't have the immunos done to prove it (when her initial diagnosis was made I don't think that immunohistochemical staining for calcitonin was available). The cribriform areas really have a striking resemblance to carcinoid tumors.

Michele Bisceglia: Medullary carcinoma with glandular/cribriform pattern. Agree on all your assertions, Gerry. Recall that, several years ago, had a cytological case of a metastatic lymph node in a patient who had undergone previous thyroidectomy in another institution due to a "follicular carcinoma" in pre-immunhistochemistry era. FNA showed cytologic features suggesting medullary carcinoma (along with some fluffy material resembling amyloid). We revised the previous histological slides and requested some unstained slides: the tumor showed diffuse glandular follicular growth pattern and was immunopositive for calcitonin and negative for thyroglobulin. Amyloid was not seen in the primary, but was histologically confirmed in the metastatic neck lymph node.

Ira Bleiweiss: Medullary carcinoma. Some areas even look meningiomatous.

Thomas Colby: Agree with diagnosis of medullary carcinoma.

Kum Cooper: Thank you Gerry for the reminder of the morphological heterogeneity of medullary carcinoma of the thyroid. On low power the "Zellballen" pattern is quite striking and does bring paraganglioma into the differential diagnosis. However, the glandular differentiation along with the calcitonin clinches the diagnosis. A "back-door" marker in the context of MEN is also mCEA which is positive in medullary carcinoma.

Ivan Damjanov: The periphery shows more of the typical features—I had the impression that the other changes are fixation artifacts.

Otto Dietze: I have seen glandular patterns in several other endocrine tumors but not in c-cell-carcinoma.

Hugo Dominguez-Malagon: In my slide there is a nice cribriform pattern, however, occasionally medullary carcinoma can be "amphicrine" and display follicular structures.

Göran Elmberger: Interesting case. Mimicker due to varied architectural patterns. Wonder if these structures are true glandular or possible true neuro rosettes... Villin? CEA? EMA?

Giovanni Falconieri: Nice case, the cribriform pattern is clearly recognizable. Perhaps there is some hyaline material suggesting amyloid.

Franco Fedeli: Medullary carcinoma with glandular/cribriform pattern. From the morphological point of view, insular carcinoma of the thyroid is the main consideration.

Cyril Fisher: Unusual variant pattern of medullary carcinoma. Many thanks.

Christopher Fletcher: Beautiful example of medullary carcinoma with focally pseudoglandular features.

Andrew Folpe: Interesting medullary carcinoma variant. Thanks for submitting it.

Jerónimo Forteza Vila: I agree with your diagnosis. The pattern for paraganglioma could be considered with the differential diagnosis.

Masaharu Fukunaga: I initially thought that was a poorly differentiated carcinoma. Thank you very much for the beautiful case.

Thomas Krausz: Very nice example.

Janez Lamovec: We've just reviewed some of our MTC cases and had a few of them with lobular/insular variants very similar to this one. Some of them were pure, some admixed with other patterns.

Thomas Mentzel: An interesting case of medullary carcinoma showing centrally and focally a glandular growth pattern.

Michal Michal: I saw a similar case some 20 years ago.

Markku Miettinen: Agree on medullary carcinoma.

Liz Montgomery: Medullary carcinoma makes great sense and it certainly immunolabeled appropriayely. This was hard for me and my slide shows solid nests and there was no/minimal amyloid to clue me in!

Santiago Ramon y Cajal: Interesting and unusual phenotype for medullary carcinoma. Could be misleading in a biopsy.

Juan Rosai: I know that carcinoid tumors and medullary thyroid carcinomas can be paraganglioma-like, but this is too much. Actually, this is one of the best examples of the paraganglioma "look" I have seen in a long time. Therefore, before accepting the diagnosis of medullary thyroid carcinoma, I'd like to be told that there are no S-100 protein-positive sustentacular cells and that the tumor cells are positive for TTF1 and keratin.

Dominic Spagnolo: Nice example of medullary thyroid carcinoma with glandular/cribriform architecture. Thanks Gerry.

James Strauchen: Medullary carcinoma of the thyroid with an unusual glandular/cribriform pattern.

Eduardo Zambrano: Medullary carcinoma of the thyroid was on the top of my differential, certainly requiring IHC confirmation. I have never seen this cribriform variant.

CASE NO. 5 – CONTRIBUTED BY MICHELE BISCEGLIA (# 146141-7)

Phil Allen: Phosphaturic mesenchymal tumor, subcutis, right heel. Thanks for the case and the extensive discussion, Michele. It was lucky he put his foot in the machine.

Carlos Bacchi: Thanks for the case.

David Ben-Dor: What a case and what a discussion!! I was impressed by the bluish quality of the matrix which reminded me of elastin- is this the calcified lattice like matrix? - very unusual looking.

Gerald Berry: Phosphaturic mesenchymal tumor. I must admit that I was not aware that we are now subclassifying these lesions!

Michele Bisceglia: Phosphaturic mesenchymal tumor, mixed connective tissue type. My case (previously presented in Istanbul on June 2010).

Ira Bleiweiss: Never seen this before.

Tom Colby: Agree with diagnosis of phosphaturic mesenchymal tumor.

Kum Cooper: Thank you Michele for this beautiful example of PMT. As you are aware we published two cases that were not associated with any biochemical abnormality.

Ivan Damjanov: I have now seen more of these tumors through the AMR than I will ever see for the rest of my life. Would I recognize them? Most likely not without the story. Thanks Michele.

Otto Dietze: Except for the seminar cases, I have no personal observation of a similar case.

Hugo Dominguez-Malagon: Thank you Michele for this beautiful case of PMT, a collector´s case.

Göran Elmberger: Fascinating entity. I wonder what the precursor cell in the soft tissues is and what is the physiological role of FGF-23? Why does the calcific debris precipitate locally?

Giovanni Falconieri: Spectacular case Michele. As always, nothing to add to your discussion.

Franco Fedeli: Phosphaturic mesenchymal tumor, mixed connective tissue type. Michele, I well recall you lecturing in Istanbul about this issue. Thanks for giving me the opportunity to look again at this nice case. If it were in bone, chondromyxoid fibroma might be a suggestion.

Cyril Fisher: Phosphaturic mesenchymal tumor, nice example. Thanks, Michele.

Christopher Fletcher: This is a beautiful and very characteristic example of phosphaturic mesenchymal tumor with lots of 'grungy' calcification, as described by Andrew. This particular pattern seems to me quite reproducible in morphologic terms and, as such, can sometimes be recognized in the absence of the biochemical syndrome.

Andrew Folpe: Nice PMT. We have a paraffin section RT-PCR assay for FGF23, by the way, if anyone has similar cases that they would like evaluated for this hormone.

Jerónimo Forteza Vila: Nice case. We interpret this is a paraneoplastic lesion associated with the mesenquimal tumor.

Masaharu Fukunaga: Agree. Thank you very much for the excellent case and description.

Thomas Krausz: Very nice example with great discussion. The first example of phosphaturic mesenchymal tumor I diagnosed many years ago was intracranial.

Janez Lamovec: I remember this one; you presented it in Istanbul. As usual, in depth discussion.

Thomas Mentzel: A very nice example of phosphaturic mesenchymal tumour showing nicely prominent flocculent calcifications.

Michal Michal: PMT with typical slate-colored amorphous matrix.

Markku Miettinen: Phosphaturic mesenchymal tumor. Degenerating chondroma-like features, as usual.

Liz Montgomery: What a great phosphaturic mesenchymal tumor, complete with Andrew's "grungy material".

Santiago Ramon y Cajal: Phosphaturic mesenchymal tumors are intriguing entities, challenging for the clinician, radiologist and pathologist. The location in this case makes its detection even harder. Great discussion, Michele, as usual.

Juan Rosai: This looks to me like a good example of the phosphaturic mesenchymal tumor. It certainly has the combination of myxochondroid areas, multinucleated giant cells and hemangiopericytoma-like foci that are described in this entity. I should add, for what is worth, that I don't like very much naming tumors according to the paraneoplastic features they may be associated with, because sooner or later somebody will find some examples that look just the same but don't have the association. Think of the hypercalcemic small cell tumor of the ovary as one of the many examples.

Dominic Spagnolo: Thanks Michele for a typically in-depth discussion of this beautiful case of phosphaturic mesenchymal tumor of mixed connective tissue type

James Strauchen: Phosphaturic tumor. I always miss these. The calcific "grunge" should have a clue.

Saul Suster: Very nice example of phosphaturic mesenchymal tumor, an entity described based only on very humble H&E observations made by one of our former AMR Club members, Dr. Noel Weidenr, together with a good friend of many of us, Dr. Daniel Santa Cruz.

Paul Wakely: Wonderful summation Michele. Thank you.

Eduardo Zambrano: Great example of phosphaturic mesenchymal tumor, mixed connective tissue-type. I enjoyed the presentation Michele gave of this case in Istanbul.

CASE NO. 6 – CONTRIBUTED BY MICHELE BISCEGLIA:

Phil Allen: Eventually fatal sporadic lymphangioleiomyomatosis, retroperitoneal paraaortic lymph nodes and lung. Thanks for the discussion Michele.

Carlos Bacchi: Agree on lymphangioleiomyomatosis.

David Ben-Dor: A Bisceglia triple- header! Remarkable cases accompanied by thorough and erudite discussions- what more could a pathologist want? (I'm sorry if this sounds like a movie review).

Gerald Berry: LAM with nodal involvement. Nice case.

Michele Bisceglia: Sporadic systemic lymphangioleiomyomatosis involving both lymph nodes (histology shown) and lung (HRCT diagnosis). My case - previously presented in Istanbul on June 2010. After Istanbul, this case was published in Adv Anat Pathol for the section of Selected Cases from AMR Seminars.

Ira Bleiweiss: Great case. Stumped me.

Tom Colby: Agree with diagnosis of lymphangiomyoma/lymphangioleiomyomatosis involving lymph nodes. One can see how Stout's original name for these lesions: lymphangiopericytoma, was descriptively appropriate. Whenever I have seen this lesion involving lymph nodes (and not presenting as a mass lesion) in the retroperitoneum, there has been associated pulmonary lymphangioleiomyomatosis. When these lesions present as a mass lesion (lymphangiomyoma) the vast majority, but not all, have pulmonary LAM.

Kum Cooper: Thank you for sharing this LAM with us.

Ivan Damjanov: Very nice and instructive case.

Otto Dietze: I had another case of LAM in the following seminar with only tiny infiltrates in several lymph nodes without evidence of other organ involvement.

Hugo Dominguez-Malagon: Excellent case of LAM, I also enjoyed the discussion in Istambul.

Göran Elmberger: Beautiful case. Very peculiar and characteristic look which enables us to recognize the entity. I remember my first case in a young woman presenting with an axillary node in FNA! What are the melanosomes doing in a perivascular epithelioid cell?

Giovanni Falconieri: I agree with LAM. I would have hard time to consider this possibility on a frozen section.

Franco Fedeli: Sporadic systemic lymphangioleiomyomatosis in abdominal lymph node. A few years ago while examining under the microscope a hysterectomy surgical specimen which came due to endometrial adenocarcinoma in an adult lady, one of the accompanying lymph nodes (iliac lymph node) was the site of involvement by (what we thought was) LAM. As far as I subsequently knew, the patient had no stigmata of LAM – thus according to the classification you used in your scholarly description - that case would be best categorized as lymphangioleiomyoma.

Cyril Fisher: Lymphangioleiomyomatosis, convincing case. Thanks for the detailed discussion.

Christopher Fletcher: Perfect example of lymphangioleiomyoma(tosis). Probably the chylous ascites was the main clue to this case being systemic, since most localized retroperitoneal examples of LAM are sporadic and not associated with lung disease.

Andrew Folpe: Intranodal LAM. Nice write-up (where do you find the time?!!?)

Jerónimo Forteza-Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Angiomyolipoma, thank you, Michele for the detailed description.

Thomas Krausz: Very nice example with great discussion. I hope that one day I will understand the partial melanocytic differentiation of PEComas/LAMs much better.

Janez Lamovec: Another Istanbul case. The hemangiopericytoid pattern is most pronounced. Erudite discussion again.

Thomas Mentzel: Many thanks for this beautiful example of rare lymphangioleiomyomatosis !

Markku Miettinen: Lymphangiomyoma type PEComa, involves lymph node.

Liz Montgomery: Beautiful case of another member of the PEComa clan.

Santiago Ramon y Cajal: Thank you very much for bringing up this very interesting entity. Reviewing this clinical history one should remember to investigate thoroughly (or to recommend thorough investigation) in patients with respiratory conditions that worsen with or after pregnancy, especially if clinical findings do not quite fit together.

Juan Rosai: Very good example of lymphangioleiomyomatosis as part of the PEComa spectrum. A piece of trivia: This tumor was first named lymphangiopericytoma by Stout at one of the Seminars of his Society (at the time a Club) and published as such by Enterline soon thereafter.

Dominic Spagnolo: Excellent discussion of LAM Michele – thanks!

James Strauchen: Lymphangioleiomyomatosis. Very nice example of lymph node involvement.

Saul Suster: Very nice example of nodal LAM. Thank you Michele for the nice and thorough discussion!

Eduardo Zambrano: Lymphangioleiomyomatosis. Thanks for the update summary, Michele.

CASE NO. 7 – CONTRIBUTED BY MICHELE BISCEGLIA:

Phil Allen: Undiagnosed, biologically low grade malignant tumor, left kidney with pulmonary metastases and 11 year survival as at 2010. I don't think there is enough evidence to justify a diagnosis of solitary fibrous tumor. The only thing I can suggest would be to check for estrogen and progesterone receptors and to consider giving the patient a trial of progesterone anti-estrogens and other drugs used for treating so-called low grade endometrial stromal sarcoma.

Carlos Bacchi: Sarcoma, NOS.

David Ben-Dor: This case still looks like a synovial sarcoma to me, despite the contrary evidence. It looks very monomorphous and doesn't seem to show any of the architectural variegation noted in SFT, though the gaping blood filled spaces seen at the periphery of slide 7C could be reminiscent of the hemangiopericytoma type vessels seen in that condition (but here they are lined by tumor and not endothelial cells).

Gerald Berry: Based solely on the histological features I would not have favored SFT. If the CD34 is convincingly positive then malignant SFT seems to be a reasonable diagnosis.

Michele Bisceglia: Unclassified non-pleomorphic renal sarcoma – probably *de novo* malignant SFTK. My case (not presented in Istanbul). Now I notice that one of these circulated slides shows a focal area of nuclear pleomorphism, a finding which was not seen in the original slides. At a most recent follow-up the tumor was found in progress. Look forward to your opinions.

Ira Bleiweiss: Don't know what to call this except malignant. I don't think it looks like SFT

Thomas Colby: Agree with diagnosis. I have seen a few cases in the chest with this degree of heterogeneity, including the microcystic areas and the very epithleioid-appearing areas. Slides 7A and 7B have areas that are quite recognizable as SFT with the stubby spindle cells. Obviously synovial sarcoma can produce many of these patterns (as may endometrial stromal sarcoma).

Kum Cooper: I morphologically also thought that this was synovial sarcoma.

Ivan Damjanov: I could not classify this tumor.

Otto Dietze: We have a recent case of metastasizing renal sarcoma, we called it undifferentiated / high grade, a reference centre favoured due to focal positivity for HMB-45 for Pecoma.

Hugo Dominguez-Malagon: I also thought that it was a synovial sarcoma of the kidney, the proposed diagnosis of SFT is reasonable.

Göran Elmberger: Difficult case. Basically I agree with your diagnostic suggestion even if I feel some uncertainty given the absence of benign SFT component, the rarity of the lesion and the relatively non-specific staining results. Dr Arganis diagnostic suggestion seems well verbalized... Have we excluded the entity of translocation negative SS from our thinking??

Giovanni Falconieri: Great case Michele, of course I agree to the assessment and I have no point in favor of either options. High-grade sarcoma remains the diagnostic opinion I would also agree upon. I have learnt that SFT and SS may share a number of immunophenotypical features. As far as my limited experience may count, I suspect that there are cases in which further distinction suffer from irreducible bias especially in cases where molecular investigations do not dispel the matter. Did you try calponin? According to Fisher article in Histopathology in 1998, calponin is positive in virtually all SS.

Franco Fedeli: Unclassified non-pleomorphic renal sarcoma – probably de novo malignant SFTK. Very difficult case to discern. Sarcoma-NOS is my diagnosis. Speaking of malignant SFT in visceral locations, have previously observed one malignant SFT of the liver which gave rise to bone (femur) metastasis: that case had clear-cut areas of benign SFT.

Cyril Fisher: I cannot add to the thorough analysis but would also be uncomfortable with the diagnosis of malignant SFT in the absence of a benign component.

Christopher Fletcher: While it is conceivable that this may represent malignant SFT, it would be extremely difficult to prove or justify that diagnosis, given the morphologic appearances in these slides and in the absence of any recognizable component of more benign-appearing SFT. Instead, like Pete Argani, I would be stuck with unclassified renal sarcoma.

Andrew Folpe: Undifferentiated sarcoma of kidney with metastasis to lungs. Not synovial sarcoma. Not SFT.

Jerónimo Forteza Vila: It remains is more of a synovial sarcoma in spite of the negativity of the molecular tests.

Masaharu Fukunaga: My first impression was synovial sarcoma. It is very difficult to make a diagnosis of SFT on H&E only.

Thomas Krausz: Sorry, Michele, I could not reach a specific diagnostic conclusion on this case. Malignant solitary fibrous tumor is a possibility.

Janez Lamovec: I thought as you did of synovial sarcoma. By the way, there are other reports on CD34 positivity in synovial sarcoma of lungs (Mikima et al. Path Res Pract 2003; 199: 827-33; Pelmus et al. Am J Surg Pathol 2002; 26: 1434-40).

Thomas Mentzel: I think as well that the diagnosis of a unclassifiable sarcoma with features of malignant solitary fibrous tumour is the best idea.

Markku Miettinen: Malignant solitary fibrous tumor seems to be the most logical explanation.

Liz Montgomery: It is great to have a slide of this. Pete shared it with me when it came in and at least to me it did not look right for synovial sarcoma, especially since the cells were too pink and had too much cytoplasm. We did not feel 100% confident about malignant SFT but it was the best we could come up with!

Santiago Ramon y Cajal: I first thought of synovial sarcoma. Then after reading the discussion, I agree with you that TFS would be the best diagnosis.

Juan Rosai: I would go along with the diagnosis of mesenchymal tumor compatible with malignant solitary fibrous tumor, especially after the scholarly considerations of Dr. Bisceglia, but I don't think I can rule out some of the obvious alternatives.

Dominic Spagnolo: I can't argue against a malignant SFT Michele. I also considered SS, sarcoma NOS, and anaplastic clear cell sarcoma but the CD34 would be against this.

James Strauchen: Unclassified renal sarcoma possibly malignant solitary fibrous tumor.

Saul Suster: My first thoughts when looking at this without the history were those of a clear cell sarcoma of kidney or a metastatic malignant melanoma. The pseudoalveolar growth pattern seen in slides 7A and 7C would be quite unusual for a solitary fibrous tumor or a monophasic synovial sarcoma. The results of the stains and other techniques are, as often happens with these problem cases, more confusing than helpful. I don't know what this tumor is and would favor the terminology of "spindle cell sarcoma, NOS".

Paul Wakely: Looking at these 3 slides cold before reading the history and discussion, I thought I was looking at the pediatric entity of clear cell sarcoma of kidney with focal anaplasia.

Eduardo Zambrano: Interesting renal tumor; difficult (if not impossible) to classify. For the sake of expanding your differential diagnosis, I would include clear cell sarcoma of the kidney. Although, by and large, that is fundamentally a pediatric renal tumor, according to the AFIP fascicle, patients as old as 54 years of age have been described. The cells in this case are separated by optically clear spaces, which may arguably contain the mucopolysaccharide-rich material seen in those tumors. CCS is CD34-negative, though, which would argue against that diagnosis in this case.

CASE NO. 8 – CONTRIBUTED BY THOMAS COLBY:

Phil Allen: Fatal massive pulmonary embolic foreign material consistent with microcrystalline cellulose, associated with pulmonary hypertension and right ventricular hypertrophy in a patient with no known history of IV drug abuse. Thanks for the case and the very instructive discussion, Tom.

Carlos Bacchi: Amazing case Tom. I have never seen such a case before.

David Ben-Dor: Together with Ofer's case, this is another beautiful example of an iatrogenic pathology (though here the material was self-administered). Did this unfortunate patient have to resort to self-administration of pain killers because the medical system was insufficiently sensitive to her needs in this regard? This type of finding is also seen in heroin addicts. What caused her pain, was it related to the underlying condition? Was the PTH entirely related to her intravenous administration of pain killers?- if so she must have been doing it for a while. This reminds me of the story which was publicized in the press of a fireman who was a 9/11 responder and who died several years afterward. An autopsy was performed in a suburban hospital where the local pathologist found foreign body giant cells in his lungs from which he concluded that the patient acquired occupational lung disease consequent to his actions then. However the family desiring to press further claims against the government sent the slides to the NYC medical examiner, Charles Hirsch (who authored one of the articles included in the references), who having had more exposure to this pathology, noted that the giant cells were congregating around blood vessels, and said that the man besides being a hero was also a drug addict.

Gerald Berry: Agree with diagnosis. I had a similar case a number of years ago although the patient was lost to follow-up (AMR #34).

Michele Bisceglia: Massive embolic foreign material consistent with microcrystalline cellulose. Thank you Tom. Never seen one before in my practice. Another case, which had some clinicopathologic similarities with this case, was contributed by Gerry Berry in Seminar 34 ("Microcrystalline pulmonary intravascular material secondary to intravenous injection of oral Vicodin tablets").

Ira Bleiweiss: Agree.

Thomas Colby: My case of intravenous talcosis.

Kum Cooper: Thank you Tom for sharing these varieties of foreign body giant cell reaction in the lung.

Ivan Damjanov: Crystalline birefringent material—I accept your diagnosis, and agree that it is really florid.

Otto Dietze: Thank you, I have seen this previously only in association with talc.

Hugo Dominguez-Malagon: Very impressive case, it is incredible how many things that are injected intravenously.

Göran Elmberger: Florid case with interesting description of pathogenesis. The few cases I have seen had the more classical primary drug addict history rather than the "iatrogenic" IBD background.

Franco Fedeli: Massive embolic foreign material consistent with microcrystalline cellulose. Never seen one before in my practice.

Giovanni Falconieri: Quite bizarre case, Tom. We see once in a while foreign material microembolism (in IVDA, for example) but not to the spectacular extent as in this slide. Thanks for the thorough discussion.

Cyril Fisher: What a distinctive picture. Great slide. Thanks for the additional images.

Christopher Fletcher: Given the prominence of the giant cell reaction, does this imply that the patient must have injected (or was injected with) this material on multiple occasions with cumulative effects? I have no personal experience of this type of process.

Andrew Folpe: Very cool- glad to have an example in my collection. Thanks, Tom.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: A wonderful case. Thank you, Thomas for the interesting descriptions. It is very informative.

Thomas Krausz: Dramatic histology. I haven't seen this type of foreign material in the lung before.

Thomas Mentzel: What a strange behaviour of the patient !

Markku Miettinen: Agree on cotton/cellulose granulomas related to IV drug abuse.

Liz Montgomery: This is truly horrifying to see all the foreign material and the patient's respiratory death with these ruined lungs with all this foreign material must have been awful.

Santiago Ramon y Cajal: Striking case. Thank you.

Juan Rosai: Another spectacularly photogenic case, worth of inclusion in "Images in Pathology".

Dominic Spagnolo: Very nice case of microcrystalline cellulose granulomatosis – thanks Tom.

James Strauchen: Fabulous example of embolic foreign material! There was a case in New York of a 9/11 victim whose family sought compensation for interstitial lung disease but the medical examiner ruled that the foreign material was intravascular and, therefore, a manifestation of IV drug abuse rather than 9/11.

Saul Suster: Great example! Thank you, Tom.

Eduardo Zambrano: Remarkable histology of a very florid embolic process.

CASE NO. 9 – CONTRIBUTED BY GORAN ELMBERGER:

Phil Allen: Erdheim-Chester disease, fronto-temporal meninges and long bones in a 59-year-old male with congenital aortic insufficiency. This is quite a common disease, but only in the files of the AMR seminars.

Carlos Bacchi: Difficult case to diagnose without seeing the bone lesion.

David Ben-Dor: Did you make the diagnosis of this condition based on this biopsy alone? Then you're a genius. This is otherwise an extremely difficult diagnosis in the absence of any clinical history.

Gerald Berry: Agree. I suspect your list of references captured every known case of Erdheim-Chester disease!

Michele Bisceglia: Pseudotumoral intracranial Erdheim-Chester disease in a patient with sclerotic bone changes. Very interesting case, Goran. Also interesting in your case are the findings of "coated aorta" and that of perirenal fibrosis in themselves, which I believe are the least cited manifestations of the disease in the literature. Regarding the relationship of Chester-Erdheim disease with Langerhans cell histiocytosis, an issue that you addressed and also quoted in your list of references, I would like to say that have seen one such case. This case is case 2 of the two cases contributed in AMR Seminar # 28. Around two years after the contribution in AMR Seminar, that case (which was published in Advances in cooperation with Saul Suster and Tom Colby, who also contributed in AMR Seminars their own cases with lung and pleural involvement) presented with diffuse manifestations of LCH of the skin. I contributed some kodachromes of the histology of LCH associated with Chester-Erdheim disease in Seminar # 35, and published it in a minor Italian journal of dermatology. Subsequently the patient died for brain complications (hypothalamic-hypophyseal axis involvement by Chester-Erdheim disease).

Ira Bleiweiss: Agree.

Thomas Colby: Agree with diagnosis of Erdheim-Chester disease. This case is particularly photogenic with all of the foam cell change and intervening sclerosis. The multinucleated cells are also quite pretty.

Kum Cooper: Thank you Goran. The AMR seminar has over the years taught me to recognize Erdheim-Chester disease! Tom Colby also presented a great example in Mexico City.

Ivan Damjanov: Agree, nothing to add. Wow, you really reviewed the literature! Thanks.

Otto Dietze: Nice case, I remember one personal observation some years ago, published by our radiologists.

Hugo Dominguez-Malagon: Agree with the diagnosis of ECD, CNS tumor-like manifestations should be very rare, thank you for the case and nice discussion.

Göran Elmberger: This is my case. Looking forward to your comments. One of the cases I presented at the 4'th AMR slide symposium in Istanbul 2010.

Giovanni Falconieri: Another great example of CED, to be added to the cases which have already circulated during the past years. Thanks, Goran, also for the thorough discussion.

Franco Fedeli: Pseudotumoral intracranial Erdheim-Chester disease in a patient with sclerotic bone changes. Rare disease in a rare location. Touton cells along with absence of emperipolesis I understand are probably the morphologic clue to this diagnosis. Touton cells are also a clue for (juvenile) xanthogranuloma, an entity which has been well found in adults and occasionally in the CNS. I recall Michele emphasizing in Istanbul one of his cases which initially he believed was Erdheim-Chester involving a cranial nerve and that at the end (also considering the absence of systemic involvement – mainly bone & lung) it was concluded as (juvenile) xanthogranuloma of cranial nerve. To Michele: I could not find in the literature any case of juvenile xanthogranuloma of the cranial nerves, instead could find a paper dealing with two cases of (juvenile) xanthogranuloma of the peripheral nerves (George DH, Scheithauer BW, Hilton DL, Fakhouri AJ, Kraus EW. Juvenile xanthogranuloma of peripheral nerve: a report of two cases. Am J Surg Pathol. 2001;25:521-6). Maybe you have to publish your case affecting the cranial nerve (?VII cranial nerve).

Christopher Fletcher: Indeed the appearances of this predominantly xanthomatous lesion fit very well with Erdheim-Chester disease, as supported by the radiologic findings in bone in your patient.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Andrew Folpe: Agree with Erdheim-Chester. Very nice example.

Masaharu Fukunaga: Thank you very much for the wonderful systemic case. Goran. I have never made a diagnosis EC disease myself.

Thomas Krausz: Agree with diagnosis, very nice example.

Janez Lamovec: What a case! I have seen some cases in AMR seminars before and only one case (bone, lungs) here but this is spectacular. One meningeal case was presented by Michele (AMR#28, case 3).

Thomas Mentzel: Many thanks for sharing this rare manifestation of Erdheim-Chester disease !

Markku Miettinen: Fibroxanthomatous infiltration, seems to fit in Erdheim-Chester by associated findings with bone lesions. It is a clinicopathologic constellation diagnosis only.

Liz Montgomery: Fantastic case. Thanks for reminding me to always keep Erdheim-Chester in my differential diagnosis of peculiar histiocytic lesions.

Santiago Ramon y Cajal: Thank you for this remarkable case of Erdheim-Chester disease.

Juan Rosai: Very nice case of a xanthogranulomatous lesion compatible with Erdheim-Chester disease. This disease seems to be getting very popular these days, to the point of eclipsing RD disease, and I don't like it!

Dominic Spagnolo: Have not encountered intracranial Erdheim-Chester disease – thank you for the case and in-depth discussion.

James Strauchen: Another case of Erdheim-Chester disease! Thank you for the fabulous bibliography!

Saul Suster: Would have not ever been able to make this diagnosis in the absence of the history and the radiologic findings. Thank you, Goran, for sharing this spectacular case!

Eduardo Zambrano: Xanthogranulomatous lesion, consistent with Erdheim-Chester disease. Another example of this pathogenetically enigmatic disorder.

CASE NO. 10 – CONTRIBUTED BY GIOVANNI FALCONIERI:

Phil Allen: Well differentiated papillary malignant mesothelioma, left pleura with no recurrent tumor 11 months after an apparent complete excision. Our local mesothelioma guru, Doug Henderson, is presently on tour in Outer Mongolia so I can't obtain his opinion. I expect that this tumor will eventually recur and behave more aggressively.

Carlos Bacchi: I will leave the case with the experts but I believe this is a well-differentiated epithelioid malignant mesothelioma.

David Ben-Dor: In honor of this case I cracked open the latest fascicle from the AFIP. The topic of "mesothelioma in situ" is discussed theoretically along with "atypical mesothelial proliferation". The photos of the lesions used to illustrate these concepts show mostly surface proliferations much more localized than what is seen in this case. Further a drawing reproduced from Tom Colby's and Churg's article which appeared in the AJSP in 2002 showing the parietal pleura markedly thickened by tumor is considered to be "usually malignant"; those tumors which infiltrate into the fat were termed "almost always malignant" (you can't get more definite than that, right?) (I assume the same logic holds for lesions of the visceral pleura overlying the lung). Also isn't there lymphatic invasion? I vote for malignant (if only on points and not a knock-out).

Gerald Berry: Malignant mesothelioma. ? Localized type.

Michele Bisceglia: In my opinion this case is epithelial mesothelioma, invasive, seemingly clinically localized. Thanks, Falco, for sharing this case with us.

Ira Bleiweiss: Mesothelioma.

Thomas Colby: I would go with localized (malignant) mesothelioma in this case. The only “benign” mesothelial lesion we recognize in the chest is adenomatoid tumor and those are vanishingly rare (and best diagnosed only at autopsy where there is no risk of follow-up disrupting your impression). In theory one could postulate a benign localized mesothelioma as a counterpart of a malignant localized mesothelioma but in practice most cases like this are put into the latter category. The benign (to date) follow-up is not surprising.

Kum Cooper: Well differentiated papillary epithelioid mesothelioma. Has focal deciduoid changes too. These have been described in the paratesticular region with an excellent prognosis; and more recently described in the pleura as well. They do however have strict criteria with regard to diagnosis (e.g. size, pattern and differentiation). Look forward to lung/soft tissue expert views.

Ivan Damjanov: I thought this is a mesothelioma.

Otto Dietze: A really good interpretation of an unusual tumor, I would have probably favoured malignancy.

Hugo Dominguez-Malagon: I would probably would have signed this lesion as a mesothelioma, the polygonal cells are arranged in solid sheaths, even without necrosis and scarce mitosis there is some nuclear atypia with visible nucleoli.

Göran Elmberger: Falco. Pleural based lesion seemingly invading lung tissue. IHC – mesothelial.? I would suspect localized malignant mesothelioma –deciduoid variant? Maybe extensive IHC utilizing full mesothelioma panel supplemented with pneumocyte markers such as TTF1 and Napsin A would be helpful in establishing this unusual dx. FISH for homozygous 9p21 deletion may also strengthen the case. Prolonged follow-up may ultimately reveal diffuse malignant mesothelioma...

Giovanni Falconieri: My case, the more I look at it the more convinced I am that this is mesothelioma, yet the patient is fine and all instrumental investigations keep to be negative. Is it possible that mesothelioma may behave so indolently, and for so long? Should I have any news I'll let you know.

Franco Fedeli: In my opinion this case is epithelial (localized) mesothelioma with invasion. Very rare entity, Falco. Thanks for sharing it with us.

Cyril Fisher: Consistent with Erdheim-Chester disease, nice slide.

Christopher Fletcher: The appearances certainly fit very well with a mesothelial neoplasm – was there any deeper invasion? Certainly a strange case.

Andrew Folpe: I don't see how you can avoid calling this malignant mesothelioma.

Jerónimo Forteza Vila: I agree with your diagnosis. This tumor shows more malignancy in the architectural pattern than in the histology.

Masaharu Fukunaga: I favor the deciduoid mesothelioma.

Thomas Krausz: I think that the extent of the mesothelial proliferation is too much for a reactive lesion (there is extensive stratification of the tumor cells forming tumor nodules, also papillae with stratification). I would favor the diagnosis of malignant mesothelioma epithelioid type. On the other hand, not to have a recurrence for 11 months is quite unusual.

Janez Lamovec: Falco, we discussed this the other day. I told you that I would have problem to call this mesothelioma benign, in spite of follow-up data. I mentioned to you that we had somewhat similar lesion years ago on which two topnotch experts in the field differed in opinion – benign vs malignant. The patient had recurrence after quite a long time and succumbed to disease.

Thomas Mentzel: Given the morphological and immunohistochemical findings I would sign out this case as well as a mesothelioma with slight atypia and scattered mitoses.

Michal Michal: Deciduoid mesothelioma.

Markku Miettinen: Would call it localized malignant mesothelioma with tubulopapillary and "deciduoid" features (localized pending through clinico-radiologic staging).

Elizabeth Montgomery: Could this be a tiny deciduoid mesothelioma???? I found a case report of one that was indolent. konkwo A, Musunuri S, Diaz L Jr, Bedrossian C, Stryker S, Rao S. Deciduoid mesothelioma: a rare, distinct entity with unusual features. Ann Diagn Pathol. 2001 Jun;5(3):168-71

Santiago Ramon y Cajal: I don´t know. According to IHC I would agree with your diagnosis, however with the oncocytic morphology and the clinical presentation I would be very cautious in ruling out a metastatic origin (adrenal???)

Juan Rosai: I believe that this tumor is a mesothelioma. It seems to be pretty well circumscribed and well differentiated. However, I would not call it benign. I have seen several morphologically similar examples recur locally and eventually become diffuse. I would rather call it localized well-differentiated mesothelioma, and I would be very cautious about the prognosis.

Dominic Spagnolo: Had this been a diffuse pleural involvement, I would have called it malignant mesothelioma . As it is localised, I guess I have to call it localised malignant mesothelioma, though I would not quibble with your appellation. As I understand it, so-called localised malignant mesotheliomas are often "curable" with adequate local resection.

James Strauchen: ? Localized malignant mesothelioma. Seems too large to be an adenomatoid tumor.

Saul Suster: I guess this case qualifies for a diagnosis of localized malignant epithelioid mesothelioma. We probably need longer follow-up to make sure this has been "cured".

Paul Wakely: Falco, I was certain that I was looking at a malignant mesothelioma with deciduoid morphology, but I guess the 11 month duration without any untoward morbidity goes against that consideration.

Eduardo Zambrano: I would favor a deciduoid mesothelioma. Antonio Nascimento and Chris Fletcher published the first series in a peritoneal location in 1994, and since then some examples have been published involving the pleura. I'll be interested to see what others think. Nice case, Falco!

CASE NO. 11 – CONTRIBUTED BY FRANCO FEDELLI:

Phil Allen: Primary mucinous carcinoma, skin of scalp. I think I saw one of these about 40 years ago but have seen no others until this one. Thanks for the contribution and discussion.

Carlos Bacchi: Agree. Nice case for a slide collection.

David Ben-Dor: I enjoyed very much meeting with you in Istanbul and look forward to interacting with you as part of the group's activities. Your region of Italy is indeed lovely (as is the entire country). After seeing the slide I wasn't surprised to learn about the neuroendocrine reactivity, and as you said, the same association between neuroendocrine differentiation and mucinous carcinoma is also seen in the breast. Another homology between the tumors seen at these sites (according to the old saw that the breast is in fact a large sweat gland). Notwithstanding the elegant proof you submitted of this being primary (the focal finding of myoepithelial cells) I still think the best way to separate a primary from metastatic mucinous carcinoma in the skin is still clinical.

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Mucinous carcinoma of the skin. Ciao, Franco. Wellcome to the Club. Beautiful and rare case, with also beautiful images appended in internet (CK5/6 highlights very well the myoepithelial layer attesting to the fact the tumor is primary of the skin). According to Kazakov et al, that you quoted, 140 cases have been reported up to 2004 in the literature to which Kazakov et al added a series of 37. Kazakov emphasised several homologies of this cutaneous colloid carcinoma with its mammary counterpart, including hormone receptors expression and neuroendocrine differentiation, as in your case. I have personally seen 2 such cases (1 on the face [included in Kazakov's series] which occurred and locally recurred in an old patient and 1 on the nape of the neck in a young adult woman). As in general, in both cases the course was very indolent (probably due to fact that they have almost always a large *in situ* component – the same explanation Dr. Rosai gave for the colloid carcinoma of the breast in previous editions of his textbook – e.g. 7th edition).

Ira Bleiweiss: Agree. I've seen a few of these.

Thomas Colby: Agree with diagnosis of mucinous carcinoma of the skin.

Kum Cooper: Welcome aboard Franco. Agree with mucinous carcinoma. I would nevertheless add a comment that metastatic carcinoma (e.g. from the breast) should be ruled out.

Ivan Damjanov: Agree, although first I thought that it was a metastasis.

Otto Dietze: Thank you, convincing case and diagnosis.

Hugo Dominguez-Malagon: Agree with mucinous carcinoma of the skin (similar to breast) with neuroendocrine features.

Göran Elmberger: Great case Franco. I enjoyed the comments on IHC and importance of finding myoepithelial cells as sign of skin primary in this mucinous eccrine carcinoma. We do see an analogue tumor in salivary gland.

Giovanni Falconieri: Mucinous carcinoma with in-situ component. I fully agree with your microscopic interpretation Franco. Thank you for the discussion as well. I understand that the distinction from a metastatic breast cancer can be made on a clinical basis only due to the indistinguishable morphologic and

immunophenotypic profiles. This is not new in adnexal skin tumors, with cases of eccrine carcinoma being often positive for ER. Good start my friend, and welcome to the club!

Franco Fedeli: Mucinous carcinoma of the skin. My case. Forgot to indicate that few immunos had been attached to be put in the website.

Cyril Fisher: Mucinous carcinoma in skin, a rare case. Thanks for useful discussion.

Andrew Folpe: Mucinous carcinoma of the skin.

Jerónimo Forteza Vila: I agree with your diagnosis. It should be considered as a possibility a breast cancer metastasis.

Masaharu Fukunaga: Colloid carcinoma of the skin. A beautiful case. Welcome, Dr. Fedeli.

Thomas Krausz: I agree: histologically it is very similar to mucinous breast carcinoma.

Janez Lamovec: Indistinguishable from the one in the breast. Difficult to spot an in situ lesion without immuno.

Thomas Mentzel: A rare case of cutaneous mucinous carcinoma. Despite the presence of a focal in-situ component a metastasis has to be excluded very carefully.

Markku Miettinen: Agree on primary mucinous carcinoma of the skin (with appropriate clinical correlation).

Liz Montgomery: This case really resembles metastatic breast carcinoma although presumably a colloid breast cancer would not be likely to spread to the scalp! Thanks for sharing this with the group.

Santiago Ramon y Cajal: Diagnosing primary mucinous carcinoma of skin is quite challenging and warrants a thorough clinical work-up. Very interesting. Thank you!!

Juan Rosai: Very nice example of so-called mucinous carcinoma of the skin, the tumor type which some authors call (I believe unwisely) adenocystic carcinoma. The main interest of the case is the presence of neuroendocrine features; a similar phenomenon was documented many years ago in the breast by Capella, Eusebi, Mann and Azzopardi (powerful team!) and has recently been evaluated in the skin by Mihm's group (Am J Surg Pathol29:1330-1339,2005).

Dominic Spagnolo: Welcome to the club Franco! A nice case of primary cutaneous mucinous carcinoma – thank you.

James Strauchen: Primary mucinous carcinoma of the skin.

Saul Suster: Beautiful example of mucinous carcinoma of the skin! Thank you, Franco, for the contribution.

Eduardo Zambrano: Challenging case. Primary mucinous carcinoma of the skin sounds good to me. Welcome to the Club, Dr Fedelli!

CASE NO. 12 – CONTRIBUTED BY MASAHARU FUKUNAGA:

Phil Allen: Hyalinized cotylenoid dissecting leiomyoma with adipose metaplasia, uterus and pelvis, female aged 56. The few other cases I have seen have not been as hyalinized as this one nor have I previously seen adipose metaplasia in this condition. Thanks for the contribution.

Carlos Bacchi: Thanks for showing this unusual type of leiomyoma that I have never seen before.

David Ben-Dor: I think the key to recognition is awareness of the lesion and the ability to identify it macroscopically. In that context, I'm not sure how a frozen would help except to rule out some high grade malignancy. Very nice slide of a very interesting entity.

Michele Bisceglia: Cotyledonoid dissecting leiomyoma of the uterus (Sternberg tumor). Beautiful case. Thank you, Masa, also for the gross pictures. A similar case was contributed by John Chan in AMR Seminar #32.

Gerald Berry: Leiomyoma with degenerative features.

Ira Bleiweiss: New one on me.

Thomas Colby: Great case. Who can argue with such a lovely name as "cotylenoid dissecting leiomyoma of the uterus?"

Kum Cooper: Thank you Masa for reminding us of this unusual leiomyoma. The gross cotyledonoid appearance is a great clue to the diagnosis. I have seen about 3 or 4 of these over the years; since recognition following the Sternberg paper. I am surprised that the h-caldesmon is negative! Before looking at the gross description, I also entertained endometrial stromal sarcoma with stromal hyalinization (and your CD 10 is positive too!). (Int J Gynecol Pathol. 1999 Oct;18(4):310-9). It was great to see you in Brazil.

Ivan Damjanov: Leiomyoma, I like your fancy name.

Otto Dietze: I agree; the diagnosis is primarily based on macroscopy.

Hugo Dominguez-Malagon: Beautiful case of cotyledonoid leiomyoma, thank you Masaharu.

Göran Elmberger: Interesting and impressive gross. Sheep in wolf's clothes!

Giovanni Falconieri: Nice case, Masa. I recall a similar case contributed a few years ago by Dr. Chan.

Franco Fedeli: Cotylenoid dissecting leiomyoma of the uterus (Sternberg tumor). From the gross pictures one can derive why this tumor can be misinterpreted as malignant due to its pseudoinfiltrative features.

Cyril Fisher: Cotylenoid dissecting leiomyoma, rare example.

Christopher Fletcher: Very convincing example of cotyledonoid dissecting leiomyoma – as you say, the gross appearances are key to the diagnosis.

Andrew Folpe: Very interesting and distinctive leiomyoma variant. Thanks for sharing this case.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Thomas Krausz: Very nice example. I have seen a more cellular example before.

Janez Lamovec: One of those was submitted before by John Chan (AMR#32, case 3) – interesting case. Thank you.

Thomas Mentzel: Thanks for this interesting case containing abundant hyalinised stroma.

Markku Miettinen: Leiomyoma, Mullerian type, with sclerosing and lipoleiomyoma patterns.

Liz Montgomery: What a fantastic case of a cotyledon dissecting leiomyoma. Thanks so much.

Santiago Ramon y Cajal: Impressive case of cotyledonoid dissecting leiomyoma of the uterus. Thank you very much! It's the first case I have seen.

Juan Rosai: Nice example of cotyledonoid dissecting uterine leiomyoma (Sternberg tumor). I gather the features of this lesion are more impressive grossly than microscopically, because at the latter level the lesion (to quote again Dr. Ackerman) "is not very romantic". As a piece of trivia, it is called Sternberg's tumor not after the Steve Sternberg of the Surgical Pathology book and The American Journal of surgical Pathology we all know and love, but after his older brother, the late William Sternberg, who was a distinguished gynaecologic pathologist at Tulane. His paper on "The morphology, androgenic function, hyperplasia and tumors of the human ovarian hilus cells" (Am J Pathol 25493-521, 1949) is a classic.

Dominic Spagnolo: Spectacular cotyledonoid dissecting leiomyoma – thanks!

James Strauchen: Weird leiomyoma of the uterus!

Saul Suster: I remember reading the paper in the Am J Surg Pathology on the "Sternberg tumor" many years ago. Don't recall ever having grossed one myself. My son is now a student at Tulane – this should give me an excuse for checking out one of the original examples of this lesion housed in their magnificent gross specimen collection in their museum at the Medical School.

Paul Wakely: Absolutely lovely example Masaharu. Though I was aware of the entity, I never thought I would see one. Thanks much.

Eduardo Zambrano: I favored some type of (hyalinizing) uterine leiomyoma, but was not aware of this cotyledonoid dissecting variant.

CASE NO. 13 – CONTRIBUTED BY THOMAS KRAUSZ:

Phil Allen: Focal mucosal ischemic necrosis after Kayexalate treatment for hyperkalemia. I did not recognize the basophilic angulated crystals. I don't know if they use Kayexalate here at Flinders Medical Centre but if they do, I will be now be able to confound them with my AMR acquired knowledge. Thanks, Thomas, for the contribution.

Carlos Bacchi: Amazing case.

David Ben-Dor: My mother was hospitalized twice for severe hyperkalemia brought on by an over dosage of blood pressure medications given her by her treating physician for otherwise mild hypertension. Fortunately she survived his best attempts to poison her to death and is now hale and hearty and past ninety. She was treated with dialysis on an emergent basis- I don't know if she got kayexalate and if she did I'm grateful that she didn't develop this additional complication which might have finished her off, especially since she was in acute renal failure at the time, and from the discussion it appears that the latter would have compromised the colon even more. Was this patient's hyperkalemia related to her plethora of chronic conditions? Or to the polypharmacy? In my slide I saw foci of mucosal necrosis with the features of pseudomembranous colitis- the volcanic type eruptions of exudate. Without the revelation in the discussion I doubt whether I would have picked up the non- birefringent basophilic crystals (though with polarized light I did see a small amount of birefringent material in the exudates. I pity this woman's health insurer (if she has one)!

Gerald Berry: Agree.

Michele Bisceglia: Colon with focal transmural ischemic necrosis following Kayexalate treatment for hyperkalemia. Never seen such a case before. Very educational case, and elegant and through discussion. Thank you, Thomas.

Ira Bleiweiss: As my teenage son would say (or text) - OMG!

Thomas Colby: Spectacular example of ischemic necrosis associated with (and indeed demonstrating) Kayexalate. My GI pathology colleague literally wet his pants over this case.

Kum Cooper: Yes, the basophilic crystals are a great "give-away" for drug medication. Thank you for sharing this non-neoplastic entity with us!

Ivan Damjanov: Instructive—worth remembering the appearance of these basophilic rhomboid particles.

Otto Dietze: I agree, the diagnosis is preliminary based on macroscopy.

Hugo Dominguez-Malagon: Never seen a case like this, thank you.

Göran Elmberger: New to me. Better take care next chewing gum...

Giovanni Falconieri: Spectacular case, Thomas! Thanks for this contribution and the excellent discussion.

Franco Fedeli: Colon with focal transmural ischemic necrosis following Kayexalate treatment for hyperkalemia. I think this is and extraordinarily rare condition. Have seen a case in a slide seminar with esophageal involvement.

Christopher Fletcher: Thanks for the valuable education Thomas – I had never seen such as case and was not aware of this complication of kayexalate medication.

Andrew Folpe: I hadn't realized that Kayexelate could cause bowel ischemia. Thanks for educating me, Thomas.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Transmural ischemic necrosis following Kayexalate treatment for hyperkalemia is very new to me. Thank you very much for the detailed description, Thomas.

Thomas Mentzel: Many thanks for this interesting case and the detailed discussion.

Markku Miettinen: The changes look like ischemic, perhaps this is part of the Kayexalate injury pathogenesis?

Liz Montgomery: What a perfect example of Kayexalate-associated ischemic disease.

Santiago Ramon y Cajal: Very illustrative case showing the adverse effects of Kayexalate in the g.i. tract.

Juan Rosai: Another exotic type of iatrogenic colitis. Beautiful slides.

Dominic Spagnolo: Have not seen kayexalate induced ischaemic necrosis for a while. I remember one spectacular colonic case many years ago (at another institution) which, if I recall correctly, resulted in a pseudotumoral mass. Thanks for the case.

James Strauchen: Kayexalate necrosis. Very informative case!

Saul Suster: Another deeply-blue staining foreign material! Thanks for sharing this unusual case with us – had never seen this before!

Eduardo Zambrano: I again recognized the intestinal ulcers and the purple crystals, but did not know what they represented. Great teaching case.

CASE NO. 14 – CONTRIBUTED BY THOMAS MENTZEL:

Phil Allen: Microcystic / reticular schwannoma, deep soft tissues, right forearm. I thought it was neural but did not recognize it. I don't think I have seen one of these before. This is another entity to be added to the list of myxoid tumors. Thanks for the contribution.

Carlos Bacchi: Very classical example of reticular schwannoma.

David Ben-Dor: I vaguely remember Tom Krausz submitting a case of this previously. Despite that I didn't think of that possibility when I looked at the slide - myxoid liposarcoma came to mind. This makes me a repeat offender.

Gerald Berry: Spectacular case. I have read about this pattern of schwannoma but this is the first convincing case. A potential trap but for the S100 stain.

Michele Bisceglia: Reticular schwannoma. Thank you, Thomas, for addressing this issue. This entirely (diffuse) reticular form of schwannoma is likely related to the focally reticular schwannoma described by

Kazakov et al in 2006 (Kazakov DV, Magro G, Yu Orlov A, Shelekhova KV, Matsko DE, Spagnolo DV, Michal M. Benign schwannoma with perineurioma-like areas: A clinicopathologic study of 11 cases. Int J Surg Pathol. 2006;14:320-5).

Ira Bleiweiss: Wow. I never would have thought of schwannoma for this.

Tom Colby: I guess I agree with a diagnosis of reticular schwannoma. Would it be gauche for a non soft tissue pathologist to ask why this isn't a neurofibroma?

Kum Cooper: Thank you Thomas for sharing this instructive (?scary) case of variant schwannoma with us. It is always great to see these new entities on glass slides.

Ivan Damjanov: Never seen one. Thanks.

Otto Dietze: Convincing histology and IHC.

Hugo Dominguez-Malagon: Agree with diagnosis of reticular schwannoma, however many cells have a granular appearance, EM study would be interesting in this case.

Göran Elmberger: Thanks for sharing this unique case. Not easily recognized as schwannoma variant unless you are familiar with the entity...

Giovanni Falconieri: Another phenomenal case! My (totally wrong) idea was something in the adipose realm ... thanks for this extraordinary contribution.

Franco Fedeli: Reticular schwannoma. Nice case. Regarding the gastrointestinal location, recently an additional paper appeared in Annals of Diagnostic Pathology illustrating this same variant in the stomach (Chetty R. Reticular and microcystic schwannoma: a distinctive tumor of the gastrointestinal tract. Ann Diagn Pathol. 2010 May 6.). Furthermore, do not know if this variant has something to share with another variant Saul reported also in Annals a couple of years ago (Tozbikian G, Shen R, Suster S. Signet ring cell [myxoid] gastric schwannoma: report of a new distinctive morphological variant. Ann Diagn Pathol. 2008;12:146-52.)

Cyril Fisher: Reticular schwannoma, very nice case. Thank you, Thomas.

Christopher Fletcher: Thomas, I have to say that this lesion looks rather different from the reticular/ microcystic schwannomas which we described. This lesion seems to be much more distinctly spindled and to have less well-defined microcystic spaces. However, given your finding of strong S-100 protein positivity as well as the presence of some vessels with thick hyaline walls, then it does seem reasonable to assume that this is some kind of myxoid schwannoma. Certainly a remarkable case.

Andrew Folpe: Extensively myxoid schwannian tumor. I guess "reticular schwannoma" is a good name for this.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Retiform schwannoma, this is the first time I see it. I might have been overlooking this type of tumor. Thank you, Thomas.

Thomas Krausz: Agree with diagnosis. Interestingly the tumor cells are smaller than those of conventional schwannoma and phenotypically more similar to those of neurofibroma.

Janez Lamovec: Typical case. We have seen some of them over the years.

Markku Miettinen: Difficult to accept as a schwannoma. Unusual "none-of the above"- type nerve sheath tumor? Diffuse mild atypia also, although not easy to find mitoses. Cannot exclude low-grade malignant behavior.

Liz Montgomery: Another lovely variant nerve sheath tumor. Thanks so much, Thomas.

Juan Rosai: I guess I will have to buy the diagnosis of microcystic/reticular schwannoma, although it sure looks different from the bona fide schwannoma of our youth.

Dominic Spagnolo: Pretty example of reticular schwannoma – thanks.

James Strauchen: Unusual Schwannoma!

Saul Suster: I am not sure I am able to identify the "reticular" pattern in my slide. The two things that stand out for me in this lesion are the stellate shape of the cells and the vaguely myxoid background. I think that given the histology and the results of the markers, this lesion most likely falls in the group of peripheral nerve sheath tumors (schwannoma-neurofibroma), only this one displays an unusual variation in morphology. Reticular, however, would have not been a term that would have first come to mind to describe it.

Eduardo Zambrano: I favored some type of myxoid reticular nerve sheath tumor, but did not have a name for it. Did not quite look like reticular perineurioma. Thanks for teaching me about this unusual variant of schwannoma!

CASE NO. 15 – CONTRIBUTED BY ELIZABETH MONTGOMERY (#S09-43545):

Phil Allen: Fibrous hamartoma of infancy, back, male aged 17 months. I have found that the main diagnostic difficulty with this entity, originally described by the Australian pathologist Douglas Reye of Reye's syndrome fame, occurs in those cases that are mainly keloid-like.

Carlos Bacchi: Beautiful example of fibrous hamartoma of infancy.

David Ben-Dor: I don't see pediatric cases so this was new to me. The proliferation is infiltrative and looks rather ill-defined: are margins and possible recurrence an issue here?

Gerald Berry: Agree. Nice case.

Michele Bisceglia: Fibrous hamartoma of infancy. Beautiful case.

Ira Bleiweiss: ?

Thomas Colby: Agree with diagnosis, lovely example.

Kum Cooper: Thank you Liz for this fine example. I saw many more in Africa; but they seem to be rare here in Vermont.

Ivan Damjanov: Nice example.

Otto Dietze: Thank you. I can only remember one personal observation more than 20 years ago.

Hugo Dominguez-Malagon: It is really a classic case of fibrous hamartoma of infancy, a collector´s slide.

Göran Elmberger: Thanks. Certainly filled a gap in my collection files...

Giovanni Falconieri: Beautiful case, thank you for submitting this "classic" of surgical pathology. Perfect specimen orientation and excellent sectioning!

Franco Fedeli: Fibrous hamartoma of infancy. Location and age all is perfect. The "crop" of hair surprised me. I am not sure it was previously reported. From my early studies in Medicine I learned that quite often such findings ("crop" of hair) may represent a stigma for an underlying occult disease, usually dysraphism of vertebral column and even spinal cord.

Cyril Fisher: Very pretty FHI with the components nicely displayed.

Christopher Fletcher: Interesting case indeed. While fibrous hamartoma seems an entirely reasonable diagnosis, it is quite unusual for the primitive 'component' to be quite so cellular and so fascicular, at least in my experience.

Andrew Folpe: Classic FHI. Thanks for the recut, Liz.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Fibrous hamartoma of infancy. A beautiful case, thank you, Beth.

Thomas Krausz: One of the most beautiful examples I have ever seen.

Thomas Mentzel: Many thanks for this classical case!

Markku Miettinen: Nice fibrous hamartoma of infancy. All three components are present.

Santiago Ramon y Cajal: Very nice slide for the collection. Thank you very much!

Juan Rosai: Finally, a prototypical case of a rare entity.! I had not seen one for years. Nice discussion, although I was a little sad to see Enzinger's name in the text or among the references.

Dominic Spagnolo: I don't see much paediatric stuff so it was nice to see such a classic fibrous hamartoma of infancy.

James Strauchen: Fibrous hamartoma!

Saul Suster: Great case of fibrous hamartoma of infancy Liz – many thanks. This is the first one I see with actual epidermis overlying it – most of the cases I saw in the past were more deep seated. I'm sure we must have many like this here in our Children's Hospital pediatric pathology division.

Eduardo Zambrano: Nice example of fibrous hamartoma of infancy. I saw a few examples of this entity in my previous life as a pediatric pathologist.

CASE NO. 16 – CONTRIBUTED BY SANTIAGO RAMON Y CAJAL:

Phil Allen: Histologically malignant (grade 2), recurrent chondroid tumor, now in soft tissues of right biceps (?brachii, ?femoris). Primary soft tissue chondrosarcomas hardly ever resemble the common chondrosarcomas of bone. I don't think I have ever seen a primary soft tissue chondrosarcoma that looks like this present case but I have seen soft tissue seedings from peripheral bone chondrosarcomas arising in osteochondromatous exostosis. If we can exclude the possibility of a previously excised osteochondroma or a central chondrosarcoma of bone, I would accept this is a most unusual, recurrent, primary atypical cartilaginous tumor of soft tissues. The fact that it has recurred is worrying and that, coupled with the histology, suggests that further recurrences are likely. The tumor may even metastasize, particularly if it dedifferentiates in a recurrence.

Carlos Bacchi: The presence of binucleation, areas of hypercellularity, some cellular atypia and mitotic figures would go along with at least low-grade cartilaginous neoplasm. Chondrosarcoma?

David Ben-Dor: It doesn't look like it could metastasize at this point even if it were malignant. The issue might be whether it could continually recur and possibly undergo frank malignant degeneration. And if that is conceivable, what would you do differently than what is already being done? More extensive surgery? Amputation? There is a rabbinical maxim which goes something along the line of "the gift of prophecy is given to fools".

Gerald Berry: I think the metastatic potential of this lesion is extremely low. It appears to have a recurring potential.

Michele Bisceglia: You are right, Santiago. Atypical chondroma (at least) in my view. Nuclear atypia (binucleation and multinucleation, large nuclei, hyperchromatic nuclei, focal hypercellularity, focal spindling, myxoid cartilage, and several mitotic figures). These features are not appropriate for a benign chondroma even in the soft tissue (uncertain malignant potential would be good).

Ira Bleiweiss: Chondroma.

Thomas Colby: Well-differentiated cartilaginous neoplasm NOS. Based on the histology and the history of recurrence I would not want to label this lesion as benign and based on the histology would favor chondrosarcoma.

Kum Cooper: Thank you Santiago for this challenging case. The atypia, cellularity and mitotic activity make me concerned for a low grade sarcoma (the soft tissue chondromas I have seen have atypia but this seems too excessive to me at least!). The question is what does one call this tumor: ? chondrosarcoma or malignant myoepithelioma. I defer to the STT gurus.

Ivan Damjanov: I thought that this is a chondroma of soft tissue, but the most important thing is that it has recurred and that the margins are still involved. It will probably recur but I doubt that it would metastasize. On the other hand we had a benign enchondroma of the finger that we thought was benign but metastasized.

Otto Dietze: In my opinion recurrence favors at least "unknown malignant potential", if you would not even go further.

Hugo Dominguez-Malagon: Extraskeletal chondroma can recur in 15% of cases, re-excision is usually curative.

Göran Elmberger: Sadly I have no personal experience with this lesion. I was pretty impressed with the cellular atypia when I blindly reviewed the case even if the atypia partly had a degenerative virocyte-like touch. Proliferation rate on MIB-1? We do know that some tumors behave differently depending on organ context. One example is adenoid cystic carcinoma in salivary glands and in breast described as a case of Dr. Jekyll and Mr. Hyde... The fact that this tumor recurred is worrisome to me and I would be in favour of unknown malignant potential – at least...

Giovanni Falconieri: Chondroid tumors make me always nervous, no matter the degree of circumscription and differentiation that they show. I fully agree with your points: in a young adult patient with a recurrent tumor I am sure I would not call this benign, though I do not have better insights to offer. Thanks Ramon for this real-life case problem.

Franco Fedeli: Tumor of uncertain malignant potential in my view. Although in some place some pathologic conditions of cartilaginous nature (tenosynovial osteochondroma, synovial chondromatosis, laryngeal chondromas, submucosal chondromas of the palate) may have histological worrying features which do not confer worse prognostic significance, in this case of soft tissue chondroma I would be guarded in my diagnosis because of the atypical findings.

Cyril Fisher: The behaviour would suggest low grade chondrosarcoma.

Christopher Fletcher: The history of recurrence, the striking multinodularity and the degree of hypercellularity in this case would lead me to wonder whether this might represent something such as chondrosarcoma arising in synovial chondromatosis in the adjacent shoulder joint (or a related bursa). Was radiologic information from the time of the primary excision available?

Andrew Folpe: Very interesting case. I'm really not sure whether we should call this a chondrosarcoma, perhaps arising in soft tissue chondroma. I think most people would err on the side of calling this benign. It probably doesn't matter very much if you get clean margins on it.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: I would like to call it a soft tissue chondroma. I want to hear the experts' opinion...

Thomas Krausz: Difficult, but I am wondering whether this is a recurrent tenosynovial (extraarticular) chondromatosis (benign).

Janez Lamovec: As the classical teaching has it, morphological features that define low grade chondrosarcoma in long tubular bone or pelvic/shoulder girdle bones do not mean much in small tubular

bones and in extraosseous tumors. As you, I always wondered why is that so, and don't have an answer to that. Yes, something is missing.

Thomas Mentzel: Great case ! I have no experience with the long-term follow-up of these cases of chondromas with slight atypia and scattered mitoses arising in proximal soft tissues.

Michal Michal: If the lesion was not in connection with the bone, I would call it chondroma.

Markku Miettinen: Chondroma of soft parts with atypia.

Elizabeth Montgomery: This lesion was not so distal as ones in which we'd dismiss the nuclear changes and cellularity. In my unschooled opinion it is reasonable to continue to do so in finger cases since there is no point in labeling the patient as a cancer patient for something likely to recur only if the excision is incomplete. For this one, it would probably be important to glorify it a bit more to encourage proper excision but I defer to those with more experience with cartilage tumors.

Juan Rosai: I would go for a soft tissue chondroma. I realize there is some atypia but we have always been told that this does not matter as much as for the cartilaginous tumors located within the medullary region of a long bone.

Dominic Spagnolo: How large was this thing? The proximal location is unusual for soft tissue chondroma, and there is impressive "atypia" although the nuclei appear smudgy and degenerate. Despite the location, and the fact that this is already a recurrence, I do still think this is a soft tissue chondroma. As to whether one should call something with this appearance and location as being of uncertain malignant potential, I don't know. I have not seen enough of these to offer an informed opinion.

James Strauchen: Tissue chondroma. According to WHO 15-20% recur but never transform to chondrosarcoma.

Saul Suster: Santiago, this is indeed a problem case! If it were in bone I would be very nervous; but if the lesion is in soft tissue and has been removed with an adequate free margin, I would only recommend observation. The slide you submitted, however, shows tumor that is too close to the margins for comfort. I have no strong opinion on the name you give it as long as the surgeon understands that he needs a complete excision with good clear margins.

Paul Wakely: The hypercellularity in one of these nodules is disconcerting Santiago, but I'm not convinced we should be calling these "of undifferentiated malignant potential". I would certainly like to know what happens to this patient say 5 years from now.

Eduardo Zambrano: I agree with Santiago. If this tumor were associated with bone, the degree of atypia, cellularity, mitotic activity and myxoid change would warrant a diagnosis of chondrosarcoma. However, these atypical changes are accepted in so-called soft tissue chondromas, a lesion which has potential for local recurrence but with (to my knowledge) no reported instances of metastatic disease, pointing to an inherent benign biological behavior even in the presence of "atypical" features.

CASE NO. 17 – CONTRIBUTED BY JOSHUA SICKEL:

Phil Allen: Clear cell adenocarcinoma associated with dermoid cyst with striking verrucous hyperplasia and virocyte-like cells, left ovary. I too have never seen or read about anything like this before. Amazing!!.

Carlos Bacchi: Never seen that type of combination before.

Gerald Berry: Agree. Nice case.

David Ben-Dor: I agree that the squamous proliferation looks very strange in this location- it looks very reminiscent of linear epidermal nevus (here's your paper if you can't call it a condyloma!). I'm glad that you took the possibility of a yolk sac tumor seriously enough to rule it out with immuno- that was my first impression. Where are the hobnail cells?

Michele Bisceglia: Clear cell adenocarcinoma arising in association with a dermoid cyst with striking verrucous hyperplasia. Indeed this is a very rare type of epithelial malignancy arising in the context of ovarian teratoma.

Ira Bleiweiss: Agree.

Kum Cooper: Thank you for this interesting case. Ye, YST was also on my first differential diagnosis.

Ivan Damjanov: Clear cell adenocarcinoma –it does not look like a yolk sac carcinoma.

Otto Dietze: I have not seen this association in a dermoid cyst (but melanoma and papillary thyroid carcinoma).

Hugo Dominguez-Malagon: I would regard this case as a somatic transformation (adenocarcinoma with a follicular-papillary pattern and clear cells) in a mature cystic teratoma, not necessarily ovarian clear cell carcinoma because the hobnail cells and nuclear atypia are lacking. Suggest additional immunostains including thyroglobulin, TTF1, A1-AT, and p53.

Göran Elmberger: No, I did not see this myself. Regarding HPV I had a beautiful case of HPV HR related BAC like mucinous lung tumor that proved to be a late metastases from a remote adca in endocervix. Case presented originally as unilateral mucinous cystic ovarian tumor 3 months before cervical adca was detected. All three tumors shared same HR HPV-type, viral load (quantitative PCR) and same insertional DNA site! To me evidence of primary endocervical carcinoma with metastases to ovary and lung. Off course one could also consider other relationships but I believe evidence is for clonal origin in my case. Could the verrucous hyperplasia be part of a linear epidermal nevus or some kind of hamartoma developing in a teratoma?? ip12 status of clear cell carcinoma? Somatic malignancy in teratoma or collision tumor?

Giovanni Falconieri: Great case, Josh. Needless to say it, I have not seen this before. Thanks for this contribution.

Franco Fedeli: Clear cell adenocarcinoma arising in association with a dermoid cyst with verrucous hyperplasia. Never encountered such an occurrence and was not aware of this possibility either. Of course the teratogenic nature of a dermoid cyst may well give rise to any kind of tumor. Oligodendroglioma arising in one such dermoid cyst was the most unusual combination that I've seen.

Andrew Folpe: Wow. I was sure this would be YST. Never seen anything quite like this combination.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: A very interesting case. I agree. Thank you very much for sharing the case.

Thomas Krausz: Very interesting, unusual combination. I am also wondering whether the epidermal hyperplasia/papillomatosis is "induced" by the underlying (abnormal non-dermal type) mesenchyme.

Janez Lamovec: Again something I haven't seen before; very unusual.

Thomas Mentzel: I do agree that the verrucous epithelial proliferation on top of the clear cell adenocarcinoma resembles viral induced changes – what a pity that HPV was negative!

Markku Miettinen: Clear cell carcinoma variant, somatic evolution of teratoma? with HPV-like changes in the squamous component of teratoma.

Liz Montgomery: Lovely case. I have zero experience with such a thing.

Santiago Ramon y Cajal: In my first impression I thought of a germ cell tumor instead of clear cell carcinoma. The verrucous configuration in the dermoid cyst is quite striking; however, I have no experience whatsoever in HPV as a possible etiology of primary ovarian neoplasms.

Juan Rosai: Nice example of combined mature cystic teratoma and clear cell carcinoma. Looking at the latter, one may understand why Schiller put together clear cell carcinoma and yolk sac tumor into his mesonephroma bag.

Dominic Spagnolo: I don't recall seeing this degree of verrucous change in the squamous epithelium of a dermoid. I may have missed it or ignored it!

James Strauchen: Clear cell carcinoma of ovary associated with a dermoid cyst with striking verrucous hyperplasia. Did you try staining it for HPV?

Saul Suster: Not see this before.

Eduardo Zambrano: Very interesting! I have not seen this before.

CASE NO. 18 – CONTRIBUTED BY DOMINIC SPANGOLO:

Phil Allen: Multilocular thymic cyst, anterior mediastinum. This looks very similar to the lymphoepithelial cyst of the pancreas that I submitted to the club several seminars ago and which will be appearing as an AMR case in an upcoming issue of Advances in Anatomical Pathology. Thanks for the submission and the discussion, Dom.

Carlos Bacchi: Agree with the diagnosis of acquired thymic multilocular cyst.

David Ben-Dor: I could appreciate only the florid lymphoid hyperplasia in my slide- the epithelial proliferation wasn't present. But the lymphoid tissue on its own gives enough food for thought- obviously given the size of the lesion one would be concerned about not overlooking an early low grade lymphoma. If I had this case (especially if there was only a small biopsy of it) I would want someone as thorough and as skilled as Dominic to look at it.

Gerald Berry: Agree. Acquired multilocular cyst.

Michele Bisceglia: Acquired thymic multilocular cyst with epithelial hyperplasia and prominent lymphoplasmacytic and follicular lymphoid hyperplasia. Totally agree, Domenico. Do not see any thymoma herein or extranodal marginal zone lymphoma. Parenthetically Jeronimo contributed a case of "micronodular thymoma with lymphoid stroma" in AMR Seminar # 45. Again parenthetically, would like to say that I have seen a case (now in your hands for further investigations) of extranodal marginal zone lymphoma of the thymus associated with pulmonary amyloidosis, a very rare clinicopathologic condition with only few cases reported in the literature.

Ira Bleiweiss: Agree.

Thomas Colby: I am concerned by both the lymphoid tissue here and the degree of epithelial proliferation. I look forward to comments by the thymic contingent. It seems as though lymphoproliferative disease and in-vogue entities such as IgG4 disease have been reasonably excluded. I am concerned by the size of this lesion and the degree of epithelial proliferation although it does appear to be organized into a thymic-like arrangement.

Kum Cooper: Thank you Dom. I fully agree with your interpretation. Nice discussion.

Ivan Damjanov: Thymic cyst. I thought that the adjacent changes are remarkable but do not change the diagnosis.

Otto Dietze: Thank you, I have known this hitherto only from the literature.

Hugo Dominguez-Malagon: Multilocular thymic cyst seems reasonable.

Göran Elmberger: Pretty much lacking my own experience I find your diagnosis appealing. Something must be going on with your patient's immune system recognizing the synchronous engagement of submandibular gland and eye lesion – lacrimal gland? Maybe after all some subtle rheumatoid disease will appear... Maybe some minor or temporary immunodeficiency state? I can not see any evidence for thymoma or MALT lymphoma but maybe I would have "FISHED" or PCR'd harder for MALT associated translocations particularly the t(14;18) recognized in ocular adnexa/orbit and SG lesions since PCR would be a more sensitive tool than clonality analysis in this setting.

Giovanni Falconieri: Difficult case, Dom. Of course, I agree with the conclusion and have nothing to add or comment on further. Your description is very accurate and focuses on all the points that, in my opinion as well, matter in this particular case. Thanks for this contribution.

Franco Fedeli: Acquired thymic multilocular cyst with epithelial hyperplasia and prominent lymphoplasmacytic and follicular lymphoid hyperplasia. In my view you are completely right.

Christopher Fletcher: Beautiful and very convincing case!

Andrew Folpe: Seems like a multilocular thymic cyst to me. Interested in hearing the comments of others.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: This is my first case of multilocular thymic cysts with epithelial and lymphoid hyperplasia. Thank you very much for the case and the detailed description.

Thomas Krausz: I agree with thymic cysts. In view of the presence of numerous lymphoid follicles with germinal centers I am surprised that the patient had no symptoms of myasthenia gravis.

Janez Lamovec: Agree with the diagnosis. The experts in the club will give relevant comments.

Thomas Mentzel: In my slide there is a prominent lymphoid infiltrate and cystic spaces lined by uniform epithelial cells but no medullary epithelial proliferation is seen.

Markku Miettinen: Thymic cyst and follicular lymphoid hyperplasia.

Liz Montgomery: Beautiful case. I am afraid I would have been naïve and thought of thymoma together with the cyst but defer to Juan and Saul and look forward to their views.

Santiago Ramon y Cajal: On these sections, I would favor a benign cystic lesion.

Juan Rosai: Spectacular example of the lesion that Saul Suster and I reported many years ago as multilocular thymic cyst. I don't know about Saul, but I still like the idea that the primary event is the lymphoid hyperplasia, which induces cystic dilatation of the squamous epithelium, sometimes associated with pseudoepitheliomatous proliferation.

Dominic Spagnolo: My case. Saul, thanks for your opinion ahead of time on this.

James Strauchen: Multilocular thymic cyst. The epithelial hyperplasia is reminiscent of the epimyoepithelial islands of benign lymphoepithelial lesions of salivary glands.

Saul Suster: I had the opportunity to review this case before submission to the seminar. I believe this is a classical example of acquired multilocular thymic cyst, and entity whose concept was contributed and entirely delineated by Dr. Rosai (I just happened to be the lucky resident whom he gave the project to). I certainly sympathize with Dominic's uneasiness regarding the prominent epithelial hyperplasia, which stands out even more on keratin stains. But I have seen such changes repeatedly in a variety of benign (non-thymomatous) processes and I guess by now I'm already used to it and regard it as part of the normal spectrum in these lesions. Although a couple of cases reported in the original series recurred locally, the majority of these tumors are cured by simple excision. I am not worried for thymoma, lymphoma, or any other type of malignancy in this lesion.

CASE NO. 19 – CONTRIBUTED BY PAUL WAKELY, JR.:

Phil Allen: Metanephric adenoma, superior pole, left kidney. I have to confess a profound ignorance of renal tumors. I would be in an even worse position were it not for the AMR seminars. Thanks for the contribution.

Carlos Bacchi: Metanephric adenoma.

David Ben-Dor: Nice case-. In the context of renal papillary tumors I get worried about mixing this up with papillary carcinoma. The WT-1 is discriminatory in this situation. The foamy macrophages seen in papillary carcinoma are missing here, and the cells are compact regular and monotonous, as befits a benign lesion, despite their being "blue".

Gerald Berry: Metanephric adenoma.

Michele Bisceglia: Metanephric adenoma in adult. Nice case, Paul. Parenthetically 2 previous metanephric adenomas have been circulated in the AMR Seminars, both were contributed by John Chan in AMR Seminars # 2 and # 20, respectively. Again parenthetically, the term metanephric adenoma was coined in 1992 by an Italian group of pediatric pathologists from Gaslini Children's Hospital in Genoa; citation from their original paper "*In a recent survey of more than one hundred childhood renal tumors in our Laboratory files, we identified a unique case characterized by an unusual degree of differentiation and cell maturity…… The term metanephric adenoma is suggested for this tumor, which may represent the benign counterpart of Wilms' tumor*." (Ref. Brisigotti M, Cozzutto C, Fabbretti G, Sergi C, Callea F. Metanephric adenoma. Histol Histopathol. 1992;7:689-92). Getting back to your case, it was WT1 positive and of course this is appropriate. In our immunohistochemical study, in cooperation with dr. Rosai on the expression of TTF1, WT1 and CD56 in a series of nephroblastoma (AJSP 2009; 33:454-461) we also included 5 cases of metanephric adenomas (MA). In regard to MA: 1 of 5 MA was negative for WT1, and all cases were negative both for CD56 and TTF1. [*Opposite to MA, nephroblastoma was CD56 positive in over 95% of cases [this finding in accordance with previous study by Muir et al (AJSP 2001;25:1290-1296) and TTF1 positive in one sixth of cases, i.e. in 8 of 48 cases which were investigated*]. Lastly, would like to say that several years ago had the opportunity to look at a case that a friend of mine showed me. A well circumscribed renal tumor with microtubular and focally papillary growth pattern in an adult lady. My first (immediate) diagnosis was "metanephric adenoma". Then he showed me a strongly positive thyroglobulin immunostain relevant to the same case. At the time. the pathologists who were dealing with that cases, knew that the patient had never been operated on the thyroid, so they thought of an ectopic thyroid tumor in the kidney (around that time in the literature there were papers claiming the exhistence of a primary papillary thyroid carcinoma of the kidney [Angel et al. Urology 1996;48:632-635], but there were also strong opponents against this hypothesis [Heffner DK, letter to the Editor, Urology 1997; 50:485-486]. After some time I called my friend to know which was the end of the story with his case and he told me that also another pathologist (over the ocean) made the same diagnosis as I did, before looking at the immuno. The true end of the story was that finally they knew that indeed the patient had been operated for a thyroid nodule 35 (thirty-five) years earlier. That case was then published (Insabato L, Di Vizio D, De Rosa G, Prezioso D, Corcione F, Terracciano LM. Renal metastasis from thyroid carcinoma 35 years after detection of the primary tumor. Tumori. 2003;89:99-101). The message is: metanephric adenoma sometimes need to be distinguished not only from nephroblastoma and other primary renal tumors, but also from solitary metastatic tumors with tubular or tubulo-papillary growth pattern.

Ira Bleiweiss: Agree.

Thomas Colby: Agree with diagnosis of metanephric adenoma.

Kum Cooper: Thank you Paul for this instructive case. The papillary structures certainly in this age group entertains a papillary carcinoma. The small tubules (on re-examination) are clearly there within the papillary structures. great case!

Ivan Damjanov: I still have problems distinguishing metanephric adenoma from solid papillary carcinoma, but I accept you diagnosis.

Otto Dietze: I agree, seems to me a typical example of this tumor.

Hugo Dominguez-Malagon: A classical example of metanephric adenoma, thank you Paul.

Göran Elmberger: Papillary predominant lesion. Guess the WT-1 settles the dx, but still papillary RCC type I in the differential. FISH CEP 7 & 17? IHC panel PAX8, CD15, CD57, AMACR? WT1 after all positive in 10 % of RCC papillary type.

Giovanni Falconieri: Nice case of a "book entity" which – at least in my experience – may be overlooked and misinterpreted as a malignancy, Thanks Paul for this contribution.

Franco Fedeli: Metanephric adenoma in adult. Thank you for contributing this case. My experience with this entity is limited to just one case dating back to several years ago, when I asked Rosai and dr. Reuter for help.

Cyril Fisher: Metanephric adenoma with prominent papillary pattern. Association with angiomyolipoma is interesting.

Christopher Fletcher: Many thanks for this classic example !

Andrew Folpe: Great example of metanephric adenoma.

Jerónimo Forteza Vila: Nice case. I agree with your diagnosis.

Masaharu Fukunaga: Metanephric adenoma, thank you the beautiful case, Paul. The differential diagnosis includes papillary renal cell carcinoma and Xp translocation renal cell carcinoma.

Thomas Krausz: Very nice example. Similarly to you I also would have done the immuno to confirm it.

Janez Lamovec: Very characteristic example of metanephric adenoma. Thank you, Paul.

Thomas Mentzel: Many thanks for sharing this rare benign renal tumour!

Michal Michal: Metanephric adenoma. But very strange-a papillary variety. I do not remember seeing a similar case among our nearly 50 cases of metanephric adenomas.

Markku Miettinen: Agree on metanephric adenoma of kidney.

Liz Montgomery: This is a beautiful case. What a treat.

Santiago Ramon y Cajal: Beautiful case. Thank you. I was wondering of the possibility of a genetic syndrome in this patient.

Juan Rosai: Very nice example of so-called metanephric adenoma.

Dominic Spagnolo: Great example of metanephric adenoma.

James Strauchen: Metanephric adenoma.

Saul Suster: Nice example.

Eduardo Zambrano: Metanephric adenoma.

QUIZ CASE #1 – CONTRIBUTED BY JOSHUA SICKEL:

Phil Allen: Myospherulosis, left breast.

Michele Bisceglia: Myospherulosis. Thank you very much, Josh, for giving us the answer in advance!. Myospherulosis was first contributed in AMR Seminar by John Chan in AMR Seminar # 19.

Thomas Colby: Myospherulosis is not exactly in my sphere of practice these days but is what the cytologists are describing in fine needle aspirations from fatty sites similar to the myospherulosis debunked by one of our members (see Rosai in AJCP 1978;69:475-481).

Otto Dietze: Sorry, I would have missed this diagnosis.

Hugo Dominguez-Malagon: Agree with myospherulosis, nice example.

Göran Elmberger: Agree. Nice pictures.

Giovanni Falconieri: Impossible case, Josh. I congratulate you for your sharp eye!

Franco Fedeli: Myospherulosis

Masaharu Fukunaga: Myosphrulosis, it is new to me. Thank you very much for the impressive slides.

Dominic Spagnolo: Nice example of myospherulosis.

James Strauchen: Myospherulosis. The original cases were ENT and related to petrolatum based dressings.

QUIZ CASE #2 – CONTRIBUTED BY SAUL SUSTER:

Phil Allen: The best I can do is ossifying fibromyxoid tumor without bone, right thumb, but it is not a good match and the patient is young (13 years)

Gerald Berry: Given the age and location I would favor aponeurotic fibroma. That said it is missing both the calcifications and the giant cells.

Michele Bisceglia: I think this lesion is in the spectrum of low-grade fibromyxoid sarcoma, although I acknowledge that the anatomical location in this case is not typical of low-grade fibromyxoid sarcoma. Whatever the tumor in point is, I take the opportunity to list herein several soft tissue entities that can more often occur on acral sites (Pathologica 2006;98:239-298). The list, herein modified, is taken from Table XIX in that publication: Rudimentary supernumerary digit; Acquired digital fibrokeratoma; Koenen's periungual fibroma (so-called angiofibroma of TSC); Myxoid cyst; Xanthoma tuberosum; Infantile digital fibromatosis; Superficial acral fibromyxoma; Acral myxoinflammatory fibroblastic sarcoma; Cellular digital fibroma; Giant cell tumor of tendon sheath – localized-type; Glomus tumor; Sclerosing perineurioma; Hybrid schwannoma-perineurioma tumor; Calcifying aponeurotic fibroma; Chondroma; Fibroosseous pseudotumor of the digits; Lipofibromatous hamartoma of the nerve (with or without macrodactyly); Nora's lesion; Fibroma of tendon sheath; Fibromatosis (palmar: Dupuytren's disease; plantar: Ledderhose's disease); Pyogenic granuloma; Epithelioid hemangioma & epithelioid hemangioendothelioma (acral variant); Congenital & infantile fibrosarcoma; Clear cell sarcoma; Epithelioid sarcoma (conventional or "distal" type).

Ira Bleiweiss: Glomus tumor.

Thomas Colby: If the immunos exclude a variant of glomus then I would have to go back to square 1.

Ivan Damjanov: Myofibroblastoma.

Otto Dietze: Perineuroma (?).

Hugo Dominguez-Malagon: Sclerosing perineurioma.

Göran Elmberger: Superficial low-grade fibromyxoid sarcoma with giant collagen rosettes.

Giovanni Falconieri: No good idea, perhaps no idea at all. I guess it is benign.

Franco Fedeli: Mesenchymal tumor with myxoid features of low grade malignancy. Those collections of round to polygonal cells occasionally centered by some early hyalinization could suggest some sort of giant rosettes or higher grade areas. Look forward to the answer.

Christopher Fletcher: This is a tough case to diagnose in the absence of any immunostains. Possibilities I would consider would include low-grade fibromyxoid sarcoma with hypercellular areas and perhaps either some type of nerve sheath or myoepithelial lesion.

Andrew Folpe: Low-grade fibromyxoid sarcoma with (early) collagen rosettes.

Jerónimo Forteza Vila: We think of the possibility of a solitary fibrous tumour or a low grade fibromyxoid sarcoma.

Masaharu Fukunaga: Glomus tumor.

Janez Lamovec: ?Giant cell tumor of tendon sheath (without giant cells).

Thomas Mentzel: The unencapsulated neoplasm is composed of relatively uniform spindled and plump cells set in a collagenous stroma. Despite the lack of atypia, mitoses are easy to find. Neoplastic cells are arranged at least partly in nests and whorls. Did neoplastic cells stain positively for EMA ?
- sclerosing perineurioma ?

Markku Miettinen: Low-grade fibromyxoid sarcoma.

Liz Montgomery: To me it looks like a low grade fibromyxoid sarcoma caught in the act of turning into a hyalinizing spindle cell tumor with rosettes.

Dominic Spagnolo: Favor myopericytoma. Rule out peripheral nerve sheath tumour (?hybrid).

James Strauchen: ? Myoepithelioma.

Saul Suster: My Case. This was a consult case I received from a local community hospital. I had the same kind of difficulties as everyone else with this case and that was the reason I submitted it as a Quiz case – to get a sense for the degree of difficulty and "rarity" of this lesion. My diagnosis was non-committal: "low grade spindle cell sarcoma" consistent with either a low-grade myxofibrosarcoma or a low-grade malignant solitary fibrous tumor. We ran a panel of IHC here and obtained negative results for AE1/AE3, EMA, S-100, SMA, MIB-1, Glut-1, p63 and CD68. The only stain that was strongly positive in the spindle cells (other than vimentin) was bcl-2. I agree that the best fit for this tumor is a low-grade myxofibrosarcoma, although, admittedly, it is not the most classical and the clinical presentation is also unusual for this entity. The hypercellular areas are definitely unusual – they do not quite make if for "hyalinizing rosettes" but they certainly look distinctive. Perhaps some new variation on the theme?