COMMENTS TO AMR SEMINAR # 47

CASE NO. 1 – CONTRIBUTED BY DR. ALLEN

Phil Allen: Retiform hemangioendothelioma (Dabska), skin of left heel. My case.

Carlos Bacchi: I agree that the most likely diagnosis in this case is retiform hemangioendothelioma. One differential diagnosis would be the so-called papillary intralymphatic angioendothelioma. In the latter I believe that one has to see prominent intraluminal papillary tuffs. I am curious to hear the opinion of other members of the group who have much more experience with this type of neoplasm.

David Ben-Dor: The architectural features would more neatly fit into the retiform end of the Dabska-retiform hemangioendothelioma spectrum, especially given the patient's age. The lesional vessels are dispersed over a rather large area and I wonder how easy or practical it would be to totally excise this. I also wonder what would have happened if the clinician tried to biopsy this prior to surgery: it's likely he would have landed on what could have looked like edematous connective tissue with mild chronic inflammation and maybe a few strange blood vessels that the average mortal histopathologist (though not necessarily someone as erudite as Phil Allen) would have trouble figuring out what they mean out of context.

Gerald Berry: I agree with the diagnosis of retiform hemangioendothelioma but admit that my experience in these matters is limited. I would defer to the soft tissue pathologists on this one.

Michele Bisceglia: Retiform hemangioendothelioma. Regarding the problematic points you indicated, my current knowledge at this regard is that both retiform hemangioendothelioma and Dabska's tumor are included altogether under the common label of "hobnail hemangioendothelioma". Although it seems that the two types of tumors can be differentiated based on the different clinical setting (childhood in Dabska vs adulthood in retiform hemangioendothelioma) and on the more developed intravascular papillations in Dabska, indeed overlapping cases have been described both in terms of the age of occurrence (several reports of Dabska tumors in young and adults) and histological findings *(Calonje E, et al. Am J Surg Pathol 8:115-25,1994)*. Perhaps, in addition to the more extensive intravascular endothelial papillations, Dabska tumor may be histologically differentiated by the lack of a retiform pattern (no retiform architecture was seen in any of the 12 cases in the series of Fanburg-Smith JC et al. (*Am J Surg Pathol 23:1004-10,1999),* and by the coehistence -in some cases- of lymphangioma or lymphangectasia (*Fanburg-Smith JC, et al. Am J Surg Pathol 23:1004-10,1999; Bisceglia M, Rosai J. G Ital Dermatol Venereol 139 (Suppl. 1 al N.1):91-3,2004; Bisceglia M, et al. Pathologica 97:10-21, 2005; Manivel JC, et al. Hum Pathol 17:1240-4,1986*), and hemangioma or non-descript vascular malformation (*Argani P and Athanasian E. Arch Pathol Lab Med 121: 992-5,1997; Patterson K and Chandra RS. Arch Pathol Lab Med 109:671-3,1985; Quecedo E, et al.* Am J *Dermatopathol 18:302-7,1996*), thus attesting to the derivation of some of Dabska tumors in pre-existing vascular lesions.
Lastly, agree that "hobnail hemangioma" (Guillou L, et al. Am J Surg Pathol 23:97,1999), which includes targetoid hemosiderotic hemangioma (Santa Cruz DJ and Aronberg J. J Am Acad Dermatol 19:550,1988), is a different entity.

Ira Bleiweiss: Benign myxoid vascular lesion. I leave the rest to the soft tissuists.

John Chan: Agree with interpretation of retiform hemangioendothelioma. But I am doubtful if retiform hemangioendothelioma is the same entity as Dabska tumor (which has a different morphology), even though there is some overlap in morphology in some cases.

Tom Colby: Agree with diagnosis. It's nice to actually see something I have heard about but never seen before.

Kum Cooper: Thank you Phil for the lovely example of retiform hemangioendothelioma. Yes, the myxoid stroma is at first a little off-putting! I always believed that hob-nails were part of the morphology of RH; but to equate it to a family of hobnail tumors along with hobnail hemangioma is a quest I will leave to you gurus!

Ivan Damjanov: Retiform hemangioendothelioma. I think that this is a true Dabska tumor.

Otto Dietze: I agree with retiform hemangioendothelioma and believe that the myxoid change is due to the mechanical alteration in this location.

Hugo Dominguez-Malagon: Retiform hemangioendothelioma sounds right, the myxoid stroma is striking, no experience with a case like this.

Vincenzo Eusebi: I suppose that Retiform hemangioendothelioma is correct, but the myxoid stroma is disturbing, and I have no explanation for it/

Giovanni Falconieri: No experience with that matter. I was totally out of track thinking about a soft part (Evan's) myxoid sarcoma. This case underscores again how myxoid changes can compound things in any lesions, especially soft part tumors

Cyril Fisher: Retiform hemangioendothelioma seems a good diagnosis.

Christopher Fletcher: Indeed, the appearances of this lesion fit very well with a retiform hemangioendothelioma. When first describing the lesions, indeed we did not comment on myxoid stromal change – actually, in these slides, it looks as though it may even be stromal edema, although it is hard to be sure. The lesions originally described as Dabska tumor were heterogeneous and included both examples of retiform hemangioendothelioma and what is now known as papillary intralymphatic angioendothelioma. These two groups of lesions actually look quite different – specifically, PILA essentially closely resembles a cavernous lymphangioma, except for the presence of multifocal intraluminal papillary endothelial proliferation. With regard to the biologic behavior of retiform hemangioendothelioma, having now seen another thirty or forty examples since first describing this entity, I have still only seen one tumor which gave rise to lymph node metastasis and none has, to my knowledge, produced systemic metastases.

Andrew Folpe: Spectacular example of a retiform hemangioendothelioma.

Masaharu Fukunaga: Thank you very much for the very interesting case. I agree with your diagnosis of retiform hemangioendothelioma. Myxoid or hyalinized change of the stroma is often observed in cases of retiform hemangioendothelioma and composite hemangioendothelioma. I understand that "hobnail hemangioendothelioma" is a synonym of tagetoid hemosiderotic hemangioma, which is more used clinically.

Thomas Krausz: I agree that this is retiform hemangioendothelioma. This entity may morphologically overlap with papillary intralymphatic hemangioendothelioma (Dabska tumor). As papillae are not prominent in this case, I would not regard it as Dabska tumor. Around the vessels there is sclerosis and perhaps the myxoid change related with the site.

Janez Lamovec: Although there may be some overlap between retiform hemangioendothelioma and endovascular papillary endothelioma (papillary intralymphatic angioendothelioma, Dabska tumor), in their pure forms they appear different. In the WHO blue book they are also separated. Papillary tufts protruding into almost cavernous spaces are quite a typical finding in Dabska tumor and are only rarely and very focally seen in RE. Hobnailing itself may also be a focal feature in a number of endothelial tumors and probably does not represent a specific feature.

Thomas Mentzel: A very interesting case of retiform hemangioendothelioma with unusual stromal changes. Although there are some overlapping features, retiform hemangioendothelioma and so-called Dabska`s tumour, now designated as papillary intralymphatic angioendothelioma, are regarded as two discrete entities. Thanks a lot for mentioning our series of hobnail hemangiomas that are indeed much more common than retiform hemangioendothelioma. We have seen recently (again very rare) cases that have been labeled as "cellular hobnail hemangioma" that could probably represent a "link" between classical hobnail hemangioma and retiform hemangioendothelioma, suggesting a morphological spectrum.

Markku Miettinen: Agree on retiform hemangioendothelioma.

Elizabeth Montgomery: I agree this is retiform hemangioendothelioma/ Dabska family of tumors. Thanks for sharing this around.

Juan Rosai: This is a beautiful example of the vascular tumor that Chris Fletcher and I chose (at his suggestion) to call retiform hemangioendothelioma. It is remarkably similar microscopically to the first case I saw of this entity, which was presented by Elson Helwig at the last meeting of the Arthur Purdy Stout Society (at the time an exclusive "Club" made up of Stout's pupils and protégées) attended by the old man. Helwig proposed the diagnosis of angiosarcoma, and this was accepted by the group as a whole, but only after a heated discussion. That meeting was held on June 1967 at Columbia-Presbyterian Medical Center. Stout died a few months later. Regarding the relationship between retiform hemangioendothelioma and Dabska's tumor, it is perhaps not entirely accurate to say that they are one and the same. We view them as the adult and infantile forms, respectively, of the same basic tumor type. Along similar lines, we regard hobnail hemangioma as the benign counterpart of retiform hemangioendothelioma, and we consider Dan Santacruz's targetoid hemosiderotic hemangiomas as a subset of hobnail hemangioma having a distinctive clinical appearance. Dan thinks that they are the same thing. As a matter of fact, he told me that when he saw our paper on hobnail hemangioma he was a little upset about the proposed change in terminology of "his" entity and thought of writing a letter to the editor about it. He never did, and we remain good friends.

Dominic Spagnolo: I agree with your diagnosis of retiform hemangioendothelioma, Phil. The myxoid stroma is striking ?reaction to trauma, being on the heel; ? a myxoid variant?

James Strauchen: Retiform hemangioendothelioma with myxoid stroma. One of the pictures in the Soft Tissue Fascicle also appears somewhat myxoid with condensation of collagen around the vascular spaces. I always thought of Dabska's tumor as being more papillary and occurring in infants.

Saul Suster: Agree with the proposed diagnosis. I don't think, however, that it is a good idea to equate this lesion with Dabska's tumor, which shows an entirely different morphology (i.e., prominent intravascular papillary tufts). I agree that they all are likely closely related and belong in the same "family" of lesions, but they still their own distinctive character!

Lawrence Weiss: Great case. I did not understand why retiform hemangioendothelioma was separated from papillary intralymphatic angioendothelioma in the WHO book. Is the presence of hyaline papillary cores in the latter so distinctive that it becomes definitional. This case is a case in point, as there are some rare hyaline papillary cores in an otherwise retiform hemangioendothelioma.

Bruce Wenig: I do not have much/any experience with this lesion type but based on the illustrations in Enzinger/Weiss/Goldblum it would appear that this lesion fits best for a retiform hemangioendothelioma, although in that text they appear to separate Dabska from retiform hemangioendothelioma. I am not sure what to make of the myxoid stroma, likely reactive but look forward to read how others in the club interpret the changes seen.

CASE NO. 2 — CONTRIBUTED BY: DR. BACCHI

Phil Allen: . Histologically malignant Leydig cell tumor of the right testis in a one-year-old boy with iso-sexual pseudoprecocity. Thanks for the case and the excellent discussion.

David Ben-Dor: Congratulations on the diagnosis of this fascinating and extremely unusual case. Looking at the slides many of the cells have oncocytic features and I couldn't help but be reminded of the adrenal oncocytic tumor I shared with the group a few years ago and which Michele later incorporated in the series of such cases he published subsequently. In fact Carlos did refer to the similarity between Leydig cell and adrenal tumors, the differentiation relying on anatomy (among other parameters). How about a malignant adrenocortical rest? Strictly speaking though something like this (if it exists) would arise outside the testicle and not in it, as this tumor apparently did.

Gerald Berry: Nice case and excellent discussion. I did not find any Reinke crystals in my case. I was not aware of calretinin reactivity in these tumors.

Michele Bisceglia: Malignant Leydig cell tumor of the testis in a 1 year-old boy with isosexual pseudoprecocity. Agree. In my opinion, this is indeed one of the most clearly presented cases in the history of the club. Thank you very much, Carlos.

Ira Bleiweiss: Agree. Malignant Leydig cell tumor.

John Chan: Agree with diagnosis of malignant Leydig cell tumor, although it is extremely difficult to rule out an adrenocortical carcinoma arising in adrenal rest (which is not uncommon in and around gonads).

Tom Colby: Agree with diagnosis.

Kum Cooper: Carlos, my differential diagnosis was similar to yours: Leydig cell tumor, large cell calcifying Seroli cell tumor and hepatoid yolk sac tumor. Thank you for this exceptional case and was good to renew contact with you in Czech Republic.

Ivan Damjanov: Wow. Incredible, but true. Nice review of the topic, thank you.

Otto Dietze: The first malignant Leydig cell tumour I have seen, thanks for the excellent presentation.

Hugo Dominguez-Malagon: Completely agree with the diagnosis of malignant Leydig cell tumor, nice discussion.

Vincenzo Eusebi: Nice and rare case, I agree with the diagnosis.

Giovanni Falconieri: Excellent case, Carlos. I like the in-depth discussion.

Cyril Fisher: Terrific case, Carlos, and thanks for the useful information.

Christopher Fletcher: Very nice and convincing example of this unusual tumor type.

Andrew Folpe: Difficult case, Carlos. I also wondered about a sclerosing Sertoli cell tumor, especially with the calcification, but your diagnosis seems to fit better. Shared it also with Mahul, who liked it a lot.

Masaharu Fukunaga: Carlos, thank you very much for the beautiful case and detailed comments on criteria of malignancy and immunohistochemical features. I have experience of a couple of cases of Leydig cell tumor of the testis, I assumed they were benign.

Thomas Krausz: In the absence of metastasis, I have always found difficulty in determining whether a Leydig cell tumor is benign or malignant. I agree that using the described criteria this is malignant. Carlos, thank you for the comprehensive discussion.

Janez Lamovec: Malignant Leydig cell tumor. Thank you for your contribution.

Thomas Mentzel: Thank you very much indeed for the beautiful case and for the interesting discussion.

Markku Miettinen: Agree on Leydig cell tumor with significant malignant potential, the tumor has indeed considerable mitotic activity with apparently atypical mitoses also present

Elizabeth Montgomery: Have no better interpretation than malignant Leydig cell tumor. I have not seen such a case. Like Dr. Bacchi, considered adrenogenital syndrome [but the lesion was unilateral] and calcifying Sertoli cell tumor [these usually elaborate estrogenic hormones]. Wild case. Noted that most [save one component] of the isosexual precocity regressed.

Juan Rosai: Very good example of a histologically malignant Leydig tumor. By the way, this case is in press in The International Journal of Surgical Pathology as the youngest patient on record with this entity.

Dominic Spagnolo: Stunning case of malignant Sertoli cell tumor Carlos, and edifying discussion, thank you.

James Strauchen: Malignant Leydig cell tumor (I thought of alveolar soft part sarcoma before I realized it was testis!).

Saul Suster: Wonderful example! Thank you for the educational discussion.

Lawrence Weiss: Great case and great discussion.

Bruce Wenig: Agree with diagnosis of Leydig cell tumor and there appears to be histologic evidence to support the interpretation of malignancy. Very nice discussion; thanks.

CASE NO. 3 — CONTRIBUTED BY: DR. COOPER

Phil Allen: Possible angiomatoid malignant fibrous histiocytoma, retroperitoneum, adhering to the adrenal gland. I am not happy with the diagnosis because of the patient's age, the location, the excessive vascular component and the morphology of the stromal cells with clear cytoplasm and sharply defined cell borders. However, I can't come up with a more convincing suggestion. Incidentally, I think the name change to "angiomatoid fibrous histiocytoma" is unwise. While the original name "angiomatoid malignant fibrous histiocytoma" was never ideal because of the implied relationship to high-grade malignant fibrous histiocytoma of adults, the benign name understates the metastasizing potential and ignores the comparatively high metastasis rate in Enzinger's original paper.

Carlos Bacchi: Was this case positive for desmin? As around 50% of angiomatoid fibrous histiocytoma express this intermediate filament, this also could be of help trying to confirm this diagnosis.

David Ben-Dor: The cystic appearance with the thin septa combined with the chronic inflammation led me to think of adrenal lymphangioma. However there is additional cellularity which could not be explained by this conceptualization. I also wasn't impressed by any particular atypia in the slide I examined.

Gerald Berry: The site threw me off completely from even considering the possibility of angiomatoid fibrous histiocytoma. Thanks for sharing this great case.

Michele Bisceglia: Angiomatoid fibrous histiocytoma. Another rarity. Thank you, Kum.

Ira Bleiweiss: Angiomatoid and inflammatory. I don't know what this is but I don't buy it as histocytic.

John Chan: I am not for a diagnosis of angiomatoid fibrous histiocytoma (despite presence of the characteristic lymphoid rim), which should be a superficially located lesion and which should comprise cells with indistinct cell borders (reminiscent of dendritic cell tumor). Here the cells are ovoid and have distinct cell borders. Some cells are clear or show single clear vacuoles. I think the more likely diagnosis is solid-pseudopapillary tumor of pancreas-type – this tumor can rarely occur outside the pancreas, in the peritoneal cavity or retroperitoneum. The diagnosis can be confirmed or refuted by a beta-catenin immunostain (nuclear translocation). Another crazy thought is a sclerosing hemangioma of pulmonary type (for which a TTF-1 stain would be of interest).

Tom Colby: Agree with diagnosis.

Kum Cooper: My case. The more I look at this case; the more fascinated I become with it!

Ivan Damjanov: Kum, I think that you are right. Also who am I to argue with such consultants, except that in my reading this lesion is supposed to be in children and young adults and on the extremities and not in the adrenal.

Otto Dietze: Although the morphology is convincing, I also would have problems to make the diagnosis in this location.

Hugo Dominguez-Malagon: All cases of angiomatoid MFH I have seen were in soft tissue, never seen one in the abdomen or retroperitoneum.

Vincenzo Eusebi: Angiomatoid fibrous histiocytoma.

Giovanni Falconieri: A difficult example of soft tissue tumor, Kum. I must accept the diagnosis given the *imprimatur* received by the master who reviewed the case.

Cyril Fisher: Looks like angiomatoid FH in exceptional location. Is desmin positive?

Christopher Fletcher: This continues to be the only example of so-called angiomatoid "MFH" that I have personally seen at an intra-abdominal location. In my experience, approximately 40-50% of these lesions show positivity for EMA and/or desmin.

Andrew Folpe: Wow. Kudos to you and Chris. I doubt I would have thought of that in this location, and I'm pretty tuned in to AFH. Really a great pickup.

Jeronimo Forteza-Vila: Agree

Masaharu Fukunaga: Kum, thank you very much for angiomatoid fibrous histiocytoma arising in a unique site, the periadrenal site. I think the histology is typical.

Thomas Krausz: I have never seen an angiomatoid FH that was as richly vascularized in the background as this one. This case has large numbers of genuine blood vessels with adjacent sclerosis. I was even wondering that the dilated angiomatoid spaces are proper vascular ones with endothelial lining or not. Before reading the discussion I was considering some peculiar type of lymphangioma/hemangioma combination. On the other hand there is excess proliferation of "tumor cells", so angiomatoid FH is the most credible diagnosis.

Janez Lamovec: This is a spectacular case! It's really angiomatoid, on low power almost as an aneurysmal cyst of soft tissue. We saw a few cases but they were much more solid.

Thomas Mentzel: Whats for a case ! Did neoplastic cells stain positively for desmin ?

Michal Michal: Amazing case.

Markku Miettinen: Unclassified epithelioid neoplasm ?possible ectopic meningioma, also consider smooth muscle tumors with features of renal capsuloma (usually SMA, Des, ER/PR, HMB45+). Difficult to accept as angiomatoid (malignant) fibrous histiocytoma, considering the location and overall features.

Elizabeth Montgomery: Did not spot that desmin was tried; EMA has been reported in angiomatoid "M" FH. Cannot claim to have an alternative diagnosis to offer, but this lesion is unusual!

Santiago Ramon y Cajal: Extremely difficult case. Thank you. We have to think in these unusual and unclear "fibroblastic" tumors.

Juan Rosai: I find the diagnosis of angiomatoid MFH offered by Chris Fletcher very appealing, even if some features don't fit very well, such as location and EMA positivity . I thought that many of the tumor cells had a "glomoid" look, a feature that I have seen in other cases of angiomatoid MFH and which may be a clue to the nature of the peculiar tumor.

Dominic Spagnolo: I can't think of an alternative to angiomatoid fibrous histiocytoma, despite the extraordinary location. The presence of distinctively grooved nuclei in many areas had me thinking ovarian/transitional/mullerian/renal mixed epithelial/stromal, etc, etc. I note a report by some Japanese authors of an example occurring in the mediastinum (Ann Thorac Surg 2001; 72:283)

James Strauchen: Angiomatoid fibrous histiocytoma in retroperitoneum. I also thought of lymph node lymphangioleiomyomatosis, given the location.

Saul Suster: I'm sorry Kum, but I'm having great difficulty accepting this as an example of angiomatoid fibrous histiocytoma. First of all, the histology is not entirely classical for this entity (many of the cells show spindled hyperchromatic nuclei, rather than the round/oval nuclei with open chromatin), the size of the lesion is out of character for this tumor (17 cm!), the location is bizarre for AFH, the results of the stains are not convincing (how about desmin/CD68 staining?). Granted that you can have "positivity" for almost anything aberrantly in any type of tumor, but focal keratin positivity coupled with convincing EMA positivity does not ring well with AFH. I obviously don't know what this is and have never seen a tumor like this in abdominal location. But I think that AFH is stretching it a bit! The "angiomatoid" features and prominent lymphoid follicles certainly bring to mind some type of lymphangiomatous proliferation, similar to cystic hygromas that can attain large diameters in serosal cavities and still be perfectly well-circumscribed. Could the round/spindle cell proliferation be endothelial in origin (CD31/CD34)???

Lawrence Weiss: Great case for the adrenal file. I didn't know these tumors could be keratin-positive.

Bruce Wenig: Wow, unusual case in and extraordinary unusual locale.

CASE NO. 4 — CONTRIBUTED BY: DR. DAMJANOV

Phil Allen: Atrial myxoma with glandular inclusions. I have not previously seen a case. Thanks for the contribution.

Carlos Bacchi: Very informative case. I hadn't seen a case of myxoma with such rich epithelial elements.

David Ben-Dor: I didn't realize that atrial myxomas could show true gland formation. If these were to embolize, biopsy of a distant implant could cause havoc for the unfortunate pathologist who would have to interpret such a biopsy unless he had the full history (assuming the clinicians themselves were aware of the cardiac lesion).

Gerald Berry: This is the most florid case of epithelial inclusions in an atrial myxoma!

Michele Bisceglia: Atrial myxoma with glandular inclusions. Again a rarity as well as a beautiful case. Was the tumor sporadic or was it part of the myxoma/NAME/LAMB/Carney syndrome?

Ira Bleiweiss: Agree. I vaguely remember seeing a similar case as a resident, too many years ago.

John Chan: Beautiful example of atrial myxoma with glands.

Tom Colby: Agree with diagnosis, spectacular example with frank cysts.

Kum Cooper: Ivan, what is the proposed derivation of these glandular inclusions? A recent study showed atrial myxomas to be calretinin positive supporting the derivation from sensory neurones!

Otto Dietze: I have heard of this rare finding but never seen it before, thank you.

Hugo Dominguez-Malagon: Atrial myxoma with glandular inclusions; spectacular case.

Vincenzo Eusebi: Atrial myxoma with glandular inclusions.

Giovanni Falconieri: A bizarre case. The epithelial cells embedded in the myxoid ground substance are haphazardly arranged in cords and nests and have somehow alarming nuclei. I must confess that a metastatic tumor jumped at my mind.

Cyril Fisher: Atrial myxoma with rare epithelial inclusions, very pretty slide.

Christopher Fletcher: A very pretty and quite convincing case. Do club members truly believe that this represents glandular differentiation? Or, perhaps, could it represent entrapment of mesothelial cells with proliferation? Very remarkably, I recently saw a similar case which, many years after excision, relapsed in the mediastinum – a phenomenon which is difficult to explain.

Andrew Folpe: Terrific example of glandular differentiation in myxoma. Used it for my resident unknown conference and they were suitably impressed. Thanks.

Jeronimo Forteza-Vila: I wonder why glandular inclusions could not be mesothelial inclusions (immunophenotype would be concordant).

Masaharu Fukunaga: Dr. Damjanov, thank you very much for sharing this cellular case. Proliferating cells seem to be perivascular cells to me.

Thomas Krausz: This is the first time I have the opportunity to see an atrial myxoma with glandular component (thank you Ivan). Yes, it looks strangely cellular. Before reading the history/discussion I was considering some type of mixed tumor/pleomorphic adenoma (I have seen a few cases of metastatic pleomorphic adenoma in odd sites and they have always been diagnostically problematic).

Janez Lamovec: We don't get anything from the heart and I didn't know that glandular inclusions may be found in cardiac myxoma. Are they mesothelial in origin?

Thomas Mentzel: To be honest I was surprised to read that we are dealing with a heart neoplasm because the specimen is lined, at least partly, by prismatic cells and goblet cells resembling respiratory epithelial cells. I have never seen an atrial myxoma with so prominent glandular inclusions, many thanks.

Michal Michal: Glandular differentiation in a myxoma of heart. It must be very rare. We have in our files over 50 heart myxomas and none of our cases contain it. It is fascinating what the cardiac myxoma can produce. Not only intestinal differentiation, but even thymomatous differentiation (*D.V.Miller, H.D.Tazelaar, J.R.Handy, D.A.Young, J.C.Hernandez. Thymoma arising within cardiac myxoma Am J Surg Pathol 2005:29:1208-1213*). In fact there are interdigitating cords of epithelium with some lymphoid tissue simulating some properties of thymoma in this fascinating case as well.

Markku Miettinen: Agree on cardiac myxoma, with probable mesothelial inclusions.

Elizabeth Montgomery: This atrial myxoma variant was difficult for me. The phenomenon of the calretinin seems akin to lesions termed "adenomatoid tumors" elsewhere.

Juan Rosai: Myxoma of heart has to be, together with adamantinoma of long bones, one of the most enigmatic types of the seemingly endless repertoire of human tumors. What could those mucin-secreting glands possibly be doing in a tumor which is

otherwise so mesenchymal-looking ? I wonder whether they come from the same source as the epithelial structures of the so-called tumor of the atrioventricular node, i.e., branchial clefts or related atavistic structures.

Dominic Spagnolo: Spectacular cardiac myxoma with heterologous epithelial/glandular elements. Have not seen one so cellular. Many thanks.

James Strauchen: Atrial myxoma with glandular inclusions. Very nice case. We had one some years ago that was misdiagnosed as metastatic adenocarcinoma!

Saul Suster: Great case! We saw a similar case of atrial myxoma with glandular inclusions here a few months ago that was diagnosed by Dr. Wakely. Hard to explain the origin of the glandular inclusions. The lining in this case ranges from low cuboidal epithelium (consistent with mesothelium) to tall columnar and mucinous epithelium. Obviously there is an admixture of cell types that seem to be blending into one another at random, like you would expect in a teratomatous process. Would be of interest to know the results of CK7, CK20, TTF1 and CDX2 in the lining cells of this case!

Lawrence Weiss: Wow. It would be interesting to know which mucins are being produced.

Bruce Wenig: I wasn't aware that these tumors could show this degree of epithelial/glandular differentiation including the presence of ciliated mucin-forming epithelial cells. Thanks.

CASE NO. 5— CONTRIBUTED BY: DR. DIETZE

Phil Allen: Low histological grade, polypoid mixed Mullerian tumor featuring histologically bland tubules, glands and cords; myxoid spindle to stellate shaped mesenchymal cells with occasional mitoses; multiple islands of cartilage with plump chondrocytes; and no squamous elements, arising in the endometrium and infiltrating the myometrium of a female aged 33. I agree that this is quite different from the high-grade malignant mixed Mullerian tumor of older women, nor does it seem to be quite the same as endometrioid carcinomas of the uterine corpus with sex cord-like formations, hyalinization and other unusual morphologic features as described in Am J. Surg Pathol 2005; 29:157-166. Incidentally, the carcinomas in that article do not seem to be terribly malignant. In the present case, the infiltration of the muscle is a cause for concern but this tumour is histologically not wildly malignant.

Carlos Bacchi: I have no alternative diagnosis or any new thoughts in this case.

David Ben-Dor: I agree that it's malignant and that it's low-grade.

Gerald Berry: I am not sure what name to place on this low-grade lesion. I think the emphasis should be placed on low grade.

Michele Bisceglia: Agree on the Mullerian mixed tumor diagnosis. This is not a CHEC (corded and hyalinized endometrioid carcinoma) as described by Murray et al. However, I would consider this tumor as adenosarcoma in the spectrum of Mullerian mixed epithelial-mesenchymal tumors.

Ira Bleiweiss: Agree. Low grade mixed Mullerian tumor- almost a contradiction in terms. An almost endocervical look to the adenoca.

John Chan: Can this be interpreted as a Mullerian adenosarcoma with heterologous element (which is in fact a low-grade malignant Mullerian neoplasm)?

Tom Colby: I don't know what this is but there are probably 20 or 30 examples in Dr. Scully's files. I think it is most likely neoplastic but the heterogeneity of the components and bland features would lead me to get consultative help on this one.

Kum Cooper: This case is tough. The epithelial-stromal architecture does not strike me for a mixed Mullerian tumor; but then again I do not have a better suggestion! I initially wondered about an endometrial polyp with cartilaginous stromal metaplasia. There is also evidence of tubal metaplasia in the epithelial component.

Ivan Damjanov: I could not find any reference to low grade MMT but why not. Makes sense.

Otto Dietze: My case; after hysterectomy no residual tumour was found and after 5 months there is no evidence of metastatic disease. R. Kurman has meanwhile seen this case in consultation and agrees that this lesion is unusual and would hesitate to make a diagnosis of adenosarcoma; he recommends long-term close clinical follow-up.

Hugo Dominguez-Malagon: Low-grade Mullerian mixed tumor seems right, I would also consider the possibility of teratoma.

Giovanni Falconieri: I share your doubts and, in essence, I cannot offer a better interpretation. Were a case like that coming to my attention (and I hope it never comes) I would have a hard time in advising proper clinical management given the young patient age.

Christopher Fletcher: Could this lesion perhaps fit better with adenosarcoma? Are we sure that the epithelial component is definitely malignant?

Andrew Folpe: This is a very strange low-grade Mullerian tumor. I really don't know how to classify this and will be interested in hearing how others would approach this.

Masaharu Fukunaga: Very interesting case! I agree with your diagnosis as a low-grade mixed tumor. The problem is that the glands in this case are very different from those in conventional MMMTs. The glands do not seem to be frankly malignant to me. Some may have myoepithelial cells.

Thomas Krausz: I am not sure about the diagnosis. I agree, this tumor looks strange, and appears too differentiated for an MMT. The glands look benign, focally ciliated. I excluded from the differential diagnosis benign teratoma (no ectodermal differentiation). A variant of adenosarcoma with heterologous cartilaginous differentiation is the best suggestion I can make.

Janez Lamovec: There were previous reports on low grade mixed Mullerian tumors of the uterus (Histopathology 1980; 4: 369-82) and also a very recent one by Zamečnik et al. (Ann Diagn Pathol 2005; 9: 335 -39): The published cases are not quite the same histologically as the one presented but do represent low grade variant of mixed Mullerian tumors of uterus. Your case appears to be one of those. I agree with you that this is a different tumor from those described by Murray et al.

Thomas Mentzel: An interesting example of an obviously low-grade mixed tumour, many thanks.

Michal Michal: Mullerian adenosarcoma with heterologous cartilaginous component. It seems to me that the epithelial component is benign in this case.

Markku Miettinen: Agree on mixed mullerian tumor with heterologous cartilaginous differentiation.

Santiago Ramon y Cajal: I do not know how to call it. First, I was favoring a benign lesion, semi-hamartomatous lesion or a regressive mixed mullerian tumor.

Juan Rosai: I cannot offer a better diagnosis that malignant mixed mullerian tumor, but this lesion sure looks unusual for this entity. I have never seen the cartilaginous component of that tumor type having such an organoid/hamartomatous/malformative appearance as seen here. Perhaps this is the real low-grade variant of MMMT, instead of mullerian adenosarcoma, which probably has nothing to do with it. Or maybe it is an entity which Bob Scully has not described yet.

Elvio Silva: I would favor a benign lesion. It could be that in other slides there is more obvious malignant tumor, but in the slide received I see a polyp with glands with significant tubal metaplasia and cartilagenous metaplasia, but I do not see a malignant lesion. Also,I do not see other elements to call this lesion teratoma. I would call this lesion endometrial polyp with atypical features and cartilagenous metaplasia. I believe that the age of the patient, the glands with tubal metaplasia, and the lack of significant atypia or mitoses do not fit with the diagnosis of MMMT.

Dominic Spagnolo: I have not encountered a similar tumour before. I think your suggestion of a histologically low grade MMMT is entirely appropriate. This tumour is indeed different from the tumours in the report you cite. Thanks for the case.

James Strauchen: I have never seen anything quite like this. There are some case reports of uterine adenosarcomas with cartilage (the epithelial elements strike me as benign).

Lawrence Weiss: I remember seeing a similar case in the files at Stanford during my Fellowship days at Stanford. It had been called an adenosarcoma, with a caveat that it may behave well. I would guess that this is a benign tumor—a funny polyp with metaplasia.

Bruce Wenig: I agree with your diagnosis and cannot suggest an alternative diagnosis.

CASE NO. 6 — CONTRIBUTED BY: DR. EUSEBI

Phil Allen: Right breast tumour resembling the tall cell variant of papillary carcinoma of the thyroid. Am I right in deducing from the 10 years' history that this case is not one of Vincenzo's five published cases?

Carlos Bacchi: This case indeed looks like the variant of papillary carcinoma of thyroid. Amazing case. Thanks for sharing it.

David Ben-Dor: Some of the solid nests look like they're intravascular. I wonder why the lump was left in place for 10 years- was it assumed to be fibroadenoma on the basis of clinic, FNA? One can speculate whether this was originally a benign papilloma which turned bad or a low-grade papillary carcinoma with an unusually indolent course.

Gerald Berry: I agree with the similarity with tall cell variant of papillary thyroid carcinoma. Nice case.

Michele Bisceglia: Breast tumor resembling the tall cell variant of papillary carcinoma of thyroid. This tumor is just oncocytoid as its more famous thyroid counterpart.

Ira Bleiweiss: Apocrine form of papillary carcinoma with invasion. While the cells are tall, I don't think the nuclei really resemble those of papillary thyroid ca. These cells have more consistently prominent nucleoli.

John Chan: Very unusual-looking tumor, which I have not seen personally in my practice. Certainly there is a lot of morphologic resemblance to tall cell papillary thyroid carcinoma, including the oncocytic quality of the cytoplasm.

Tom Colby: Breast carcinoma with oncocytic and papillary features.

Kum Cooper: Thank you Vincenzo for sharing this case from your recently published series.

Ivan Damjanov: Invasive papillary and solid pattern are seen. I thought that this is just one of the papillary carcinomas of the breast, but do not object to the descriptive term you used.

Otto Dietze: Thank you for this case, I was not aware of this entity and thought of a variant of apocrine carcinoma.

Hugo Dominguez-Malagon: It really looks like a tall cell variant of papillary thyroid carcinoma, thank you.

Vincenzo Eusebi: My case. The lady was 74 years old.

Giovanni Falconieri: Nice case Vincenzo. Thanks for submitting this unusual example of breast pathology.

Cyril Fisher: Very rare breast carcinoma, thank you for sharing this case.

Christopher Fletcher: Many thanks for sharing this unusual and educational lesion. I have not previously seen anything similar.

Andrew Folpe: Interesting. I had not heard of that variant of breast carcinoma before. Thank you for sharing this.

Jeronimo Forteza-Vila: There are few cases reported in the literature. We have had the opportunity to see a similar case (submitted for publication).

Masaharu Fukunaga: Interesting lesion. I have never seen this type of breast cancer. Thank you very much.

Thomas Krausz: Never seen anything like this before. The nuclear grooves are striking and it does resemble the tall cell variant of papillary carcinoma. Without the grooves, it also reminds me of neuroendocrine carcinoma of the breast.

Janez Lamovec: This is a very unique case and really resembles tall-cell variant of thyroid papillary carcinoma. In regard to mitochondrion rich cells in breast carcinoma, I am not so sure that this should be such a specific feature. We tried mitochondrion antibody occasionally in different breast carcinoma types and many of them showed a positive and strong reaction and they were not morphologically oncocytic.

Thomas Mentzel: Many thanks for sharing this extraordinary case.

Markku Miettinen: Agree on low-grade papillary carcinoma of the breast; very interesting entity, with resemblance to "tall cell variant of thyroid papillary Ca". Interpretation of invasion is difficult on my slide, but cannot rule it out.

Elizabeth Montgomery: Thanks for allowing the group to see one of your "breast tumors resembling the tall cell variant of papillary carcinoma of the thyroid". Have not seen one before.

Juan Rosai: I hope people enjoyed this case, which was included in the small series of breast tumors resembling the tall cell variant of papillary thyroid carcinoma we reported with Vincenzo Eusebi and the great John Azzopardi (who, by the way, is being honored in his home town, Malta, next May). The morphologic resemblance with the thyroid neoplasm carrying that name is uncanny. I wonder what it means. Perhaps it has something to do with the fact that phyllogenetically the breast is a iodine-concentrating organ. Along those lines, I wonder how many of you knew that the thyroid is an amphicrine (endocrine and exocrine) organ, and that its phyllogenetic precursor is an exocrine structure in the oral cavity known as the endostyle. I found this out myself only a few weeks ago.

Dominic Spagnolo: What an extraordinary tumour of the breast. The nuclei are so distinctively localized in the apical cytoplasm, similar to the oncocytomatous variant of papillary thyroid carcinoma, or even a Warthin's tumor. Thanks for the case.

James Strauchen: Invasive papillary breast carcinoma with tall cell, oncocytic, or acinic features. Was it really present for 10 years?

Lawrence Weiss: Interesting to find out about the metastasis. I was struggling as to whether it was intraductal or invasive.

Bruce Wenig: Cool case. The cells do resemble those of the tall cell variant of thyroid papillary carcinoma, including cells that are twice as tall as wide (although this is entirely dependent on the sectioning as there are cells that are twice as wide as they are tall) PLUS eosinophilic cytoplasm and distinct cell margins. The latter two features help identify the tall cell variant of thyroid papillary carcinoma as "tall cells" can be seen in a wide variety of thyroid lesions. The nuclei seen in the tall cell variant of thyroid papillary carcinoma are among the most classic thyroid papillary carcinoma type nuclei usually demonstrating the full constellation of nuclear

alterations diagnostic for thyroid papillary carcinoma; the nuclei in this breast lesion, however, do not show classic alterations of the nuclei of thyroid papillary carcinoma.

CASE NO. 7 — CONTRIBUTED BY: DR. FISHER

Phil Allen: Biphasic synovial sarcoma with extensive squamous differentiation and SYT-SSX2 fusion gene transcripts, popliteal fossa. I don't think I had ever seen such extensive and convincing squamous differentiation in any of my consultation cases. I would suspect that the incidence of this variant is likely to be less than 1% of synovial sarcomas. Thanks of the contribution Cyril.

Carlos Bacchi: Nice example Cyril of synovial sarcoma with squamous differentiation.

David Ben-Dor: Straightforward case indeed; maybe for you! Was this mass distant enough from the skin and close enough to the joint to make a cutaneous tumor anatomically unlikely? I wonder how much trouble a needle biopsy of this lesion showing the squamous component predominantly could cause unless it fell into the hands of a pathologist with experience in soft tissue tumors or unless the referring orthopedist was sophisticated in pathology (unusual).

Gerald Berry: Beautiful example of synovial sarcoma. I had not seen this much "squamoid differentiation" before.

Michele Bisceglia: Synovial sarcoma with squamous differentiation. Very rare case with extensive squamous differentiation. Of note that no case out of 15 recently published synovial sarcomas of the mediastinum (Suster S, Moran CA. AJSP, May 2005) showed this type of differentiation.

Ira Bleiweiss: Agree. Nice case.

John Chan: Although this case is diagnostically straightforward for the histopathologist, if the lesion had undergone a fine needle aspiration, it must have been misdiagnosed as a "straight-forward" metastatic squamous cell carcinoma!

Tom Colby: Agree with diagnosis.

Kum Cooper: Lovely example Cyril. All we need now to complete our collection is an example with osseus metaplasia!

Ivan Damjanov: Very nice case. No comments

Otto Dietze: Soft tissue pathologists may consider this as a "straightforward" case, I have not seen this before.

Hugo Dominguez-Malagon: Completely agree with synovial sarcoma, the squamous differentiation is unquestionable.

Vincenzo Eusebi: Nice synoviosarcoma with squamous differentiation.

Giovanni Falconieri: Another extraordinary case. Thanks for this submission of this instructive slide.

Christopher Fletcher: Beautiful example of synovial sarcoma with extensive squamous differentiation – in fact more extensive than I can recollect seeing in the past. As Cyril has indicated, this phenomenon, at least in my experience, seems to be somewhat more common in relatively older patients.

Andrew Folpe: Nice example of a BSS with squamous differentiation. This is a particularly florid case of this.

Jeronimo Forteza-Vila: Thank you for this interesting case with molecular confirmation.

Masaharu Fukunaga: I agree. Thank you very much for the beautiful case this type of synovial sarcoma, Chris, thanks you very much. I have never seen this type of lesion.

Thomas Krausz: Extraordinary case (Cyril, thank you very much). I have never seen so extensive squamous differentiation in a synovial sarcoma before.

Janez Lamovec: Thank you, Cyril, for another unusual morphological presentation of synovial sarcoma. We saw this in synovial sarcoma only as a very minor and focal feature.

Thomas Mentzel: Given the prominent squamous differentiation the diagnosis of biphasic synovial sarcoma is quite difficult (at least for me), many thanks.

Markku Miettinen: Agree on synovial sarcoma with keratinizing squamous epithelial differentiation.

Elizabeth Montgomery: Thanks for this great example of squamous differentiation in a synovial sarcoma. Could be dicey on a tiny needle biopsy. The SYT-SSX2 is really interesting as well.

Juan Rosai: This is the most spectacular demonstration of a squamous component in synovial sarcoma I have ever seen. Actually, the event is so rare that I would have questioned the diagnosis were it not for the fact that otherwise the tumor looks quite typical for synovial sarcoma and that the diagnosis was confirmed at the molecular level. I once asked Franz Enzinger how often he had seen good keratinizing squamous epithelium in synovial sarcoma, and he replied "once or twice" (which means that it must be rare indeed!)

Dominic Spagnolo: Beautiful case of synovial sarcoma with extensive squamous differentiation - thanks Cyril. Have not encountered it anywhere near to this degree before.

James Strauchen: Very nice example of synovial sarcoma with extensive squamous metaplasia.

Saul Suster: Spectacular case Cyril! Many thanks for sharing this beautiful example. I had never seen this before.

Lawrence Weiss: Great case.

Bruce Wenig: Great case; I do not recall seeing this extent of squamous differentiation in synovial sarcomas.

CASE NO. 8 — CONTRIBUTED BY: DR. FLETCHER

Phil Allen: Probable variant of nasal chondromesenchymal hamartoma in a male aged 14. I have not previously seen anything like it before and believe that Chris' diagnosis is likely to be correct.

Carlos Bacchi: Great and unusual case. I have never seen anything like this.

David Ben-Dor: The stroma looks more myxoid or myxo-chondroid rather than being frankly cartilaginous. In foci the stromal cells look atypical, but this feature can also be found in antrochoanal polyps, which are pedunculated and arise in the maxillary antrum. There are also small glandular structures lined by cuboidal cells- I don't know if this has been described in chondromesenchymal hamartomas . There are no eosinophils which would be against this being a strange allergic polyp but there are some plasma cells. Given his age the patient would be better off with a chondromesenchymal hamartoma rather than a somewhat bizarre but banal allergic polyp, since in the latter circumstance cystic fibrosis would have to be ruled out.

Gerald Berry: The term nasal chondromesenchymal hamartoma, while awkward seems to encapsulate the lesion perfectly!

Michele Bisceglia: Nasal chondromesenchymal hamartoma. Have no experience: this is the first case I see.

Ira Bleiweiss: New one for me.

John Chan: Very peculiar lesion. No personal experience with similar entity, but agree that "nasal chondromesenchymal hamartoma" would probably be the best fit. I wonder whether the small glands represent part of the process.

Tom Colby: Favor the basically hamartomatous character of this lesion.

Kum Cooper: Thanks Chris I did think of the very same lesion; but sorry no experience with this lesion before.

Ivan Damjanov: I have never seen such a lesion and still do not know whether it is a tumor or hamartoma. "Funny little glands" in the stroma made me think that some morphogenesis is still going on and accordingly I thought that it could be a developmental tumor that are called in the ENT area teratoma (even though they are actually not).

Otto Dietze: I have never seen something similar and despite some immature appearing tissue I believe that it is a benign lesion.

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

Vincenzo Eusebi: Difficult polypoid case, benign. Chondroid material present. Never seen a case like this.

Giovanni Falconieri: Thanks for submitting this unusual case. At least in my experience, nasal lesions resected from youngsters do not receive adequate attention by many surgical pathologists and are quickly signed out as inflammatory polyps, once cancer or other malignancies are ruled out.

Cyril Fisher: Never seen this before but it seems to fit the descriptions. A small series published in APLM 2005; 129:1444-1450 describes EMA and SMA positivity.

Christopher Fletcher: My case. A small series of similar lesions occurring in older patients has recently been published – *Arch Pathol Lab Med* 2005;129:1444-1450 – which gave me some reassurance that perhaps my diagnosis in this case was correct.

Andrew Folpe: I think this fits with nasal chondromesenchymal hamartoma, based on my reading. I had a case that I signed out as this a little while ago, and was going to submit it to the AMR club. However, the more I look at my case, the more I think it is a nasal polyp with variable chondroid metaplasia. I guess one question is "how to tell these two things apart?"

Thomas Krausz: I agree that nasal chondromesenchymal hamartoma is the most credible diagnosis. Additional useful reference: Ozolek JA et al: Nasal chondromesenchymal hamartoma in older children and adults: series and immunohistochemical analysis. Arch Pathol Lab Med 2005, 129:1444-50.

Janez Lamovec: I have never seen it before. No wonder, since the Blue book says there were only 12 reported cases. Thank you for showing us this rarity!

Thomas Mentzel: Many thanks Chris for sharing an example of this rare entity. Just by chance this entity has been reported in older children and even adults most recently (Arch Pathol Lab Med 2005; 129: 1444-1450) and it would be interesting to check if there are morphological differences in cases arising in early childhood and in adult patients

Michal Michal: Nice case. This case seems to be even more interesting by the widespread adenomatous component, which permeates the whole tumor. These tumors may appear in young adults as well (Ozolek et al: Arch Pathol Lab Med 2005:129:1444-1450).

Markku Miettinen: Agree with your designation. Very unusual "developmental tumor". I have no specific experience with these. Could not predict potential with certainty (might recur, if not completely excised).

Elizabeth Montgomery: I am clueless on this case. Looks benign!

Santiago Ramon y Cajal: Difficult case. For me, it looks like a mixed epithelial-mesenchymal tumor, with chondroid metaplasia.

Juan Rosai: Whatever you say!

Dominic Spagnolo: I have not seen anything quite like this before. Aside from the chondroid and spindle cell elements, the respiratory epithelial component, and the proliferation of small glands and nests of epithelial cells (?serous) in the stroma, are very prominent features. Hence, I wonder if this is not more likely a chondro-(osseous) and respiratory epithelial adenomatoid hamartoma (in the REAH spectrum) as described by Adair et al (Mod pathol 1996; 9:100A). This would also be more likely on clinical grounds given the age of the patient. But I agree there are definite similarities to the Dehner cases too. Thanks for the wonderful case.

James Strauchen: Peculiar nasal polypoid proliferation. There seems to be an epithelial component as well with small glandular inclusions in the stroma.

Saul Suster: Never seen or heard of this before! Many thanks Chris for contributing this very unusual but distinctive case.

Lawrence Weiss: Never seen anything like it.

Bruce Wenig: I have had some experience with these unusual lesions and although the histology of this case is not classic, I would agree that it shows diagnostic features for the nasal chondromesenchymal hamartoma. A recent article by Ozolek et al in Archives of Pathology and Laboratory Medicine 2005;129:1444-50, reports a series of 4 such lesions occurring in older children and in adults.

CASE NO. 9 — CONTRIBUTED BY: DR. FORTEZA-VILA

Phil Allen: Idiopathic venous infarction of the cerebral cortex. I would suspect thrombosis of one of the large cerebral sinuses. Apart from the association with sepsis, thrombosis of large cerebral venous sinuses can occur in mountaineers at high altitudes, in AIDS, after lithium therapy and in some hypercoagulopathies.

Gerald Berry: The hemorrhagic lesions raised 2 considerations in my differential diagnosis: 1. cocaine neurotoxicity and 2. cerebral malaria.

Michele Bisceglia: Brain cortical necrosis with fibrin thrombi in small superficial vessels. I do not have any suggestion other than your own one of venous infarction. To support this hypothesis we assume that likely no other organ showed significant abnormalities. Was by chance the patient taking hormones?

Ira Bleiweiss: Pardon my ignorance but.....What is cephalea?

Tom Colby: Nothing to add.

Kum Cooper: Some of the features remind me of cerebral malaria eg. the ring hemorrhages, and possible parasites in red blood cells. The cortical necrosis is not a feature since malaria involves the white matter.

Ivan Damjanov: Some form of hemorrhagic encephalitis, but I am not very good with naming it precisely.

Otto Dietze: Sorry, no suggestion. I think you have done every thing to exclude infectious agents and the thrombosis appears to me as a secondary phenomenon.

Hugo Dominguez-Malagon: Hemorrhagic leucoencephalopathy, there is necrosis of the vessels wall and hemorrhage into Virchow-Robin spaces. I have no idea about the etiology.

Vincenzo Eusebi: It looks like to belong to the group of venous (hemorrhagic) encephalitis (often post influenza).

Giovanni Falconieri: Unfortunately, in my section I only saw some non-specific degenerative changes adjacent to a hemorrhagic focus, or may be (and I guess this is closer to the truth) that I am not able to catch the subtle changes often entailed by most degenerative brain disorders.

Andrew Folpe: I have no idea. Sorry. Another reminder of why I stay away from neuropathology....

Masaharu Fukunaga: I have no idea of its etiology but it is a wonderful case, Dr. Forteza-Vila.

Thomas Krausz: Difficult to reach conclusion. I have similar differential diagnosis: venous infarction versus infection like Rickettsia?

Thomas Mentzel: To be honest I do not have an additional sensitive comment on the etiopathogenesis of the described vascular disorder.

Markku Miettinen: Unfortunately, cannot specify. Viral encephalitis and secondary vascular thrombosis?

Juan Rosai: I pass on this one.

Dominic Spagnolo: I don't have a diagnosis. If infections are reliably excluded, including HIV, and also drug abuse is ruled out, then I wondered if this could be an acute hemorrhagic leukoencephalopathy (Hurst's disease)? However, it seems the changes are mainly cortical, which is not appropriate. I'm afraid this is beyond my area of competence! I look forward to the opinions of those more conversant with medical neuropathology than me. Thanks for the case.

James Strauchen: Cortical thrombosis of ?etiology. Was she on an oral contraceptive? There is a sparse literature on cortical thrombosis in association with oral contraceptives.

Saul Suster: Sorry – have no experience with this type of cerebral lesions.

Lawrence Weiss: Don't ask me.

Bruce Wenig: Looks reactive to me but I cannot suggest a definitive diagnosis.

CASE NO. 10 — CONTRIBUTED BY: DR. LAMOVEC

Phil Allen: Intraductal oncocytic papillary neoplasm of the pancreas. Despite the lack of macroscopically apparent cysts, I agree that this corresponds to the tumour described by Adsay et al in Am J. Surg Pathol 20:980-994, 1996. As in the politics of warfare, the definition of invasion is often hotly disputed. This seems to be a pathologists' cancer discovered by the new breed of organ imagers. Even with the mitotic activity and back-to-back crowding of the tumor cells, there is a good chance the patient will be cured. We will never know if the surgery was unnecessary, unless it metastasizes!!

Carlos Bacchi: Intraductal and invasive papillary-mucinous carcinoma of the pancreas. In the slide I received I didn't find much of the oncocytic appearance.

David Ben-Dor: In some places in my opinion the invasive tumor predominates with foci of poor differentiation. Personally in the slide I examined (which was a bit faded by the time it reached me here, possibly due to the circuitous route it took via Columbus) I wasn't impressed by oncocytic differentiation. A few years ago I saw an oncocytic carcinoma of the pancreas but without the intraductal component as demonstrated here.

Gerald Berry: Nice case. Agree.

Michele Bisceglia: Intraductal and invasive oncocytic papillary-mucinous carcinoma of the pancreas. A comparable case was presented many seminars ago ("Intraductal oncocytic papillary neoplasm of the pancreas": B. Wenig in Seminar 25, case 16). Have personally seen some of such mucinous papillary cases in the pancreas, a couple of which were of oncocytic type. Parenthetically, since you mentioned similar cases described even in the liver, I take this opportunity to say that not more than a week ago a (non-oncocytic) 10 cm sized liver case occurred here of a "multilocular biliary papillomatosis with cystic ectasia of intra- and extra-hepatic biliary ducts

[cystadenomatosis] with extensive intestinal metaplasia and high grade dysplasia in the intrahepatic tract, and low grade dysplasia in the extrahepatic ducts".

Ira Bleiweiss: Agree. Interesting. But does such subtyping in pancreatic cancer really matter?

John Chan: I am not sure if the cells are oncocytic enough to justify the qualifier "oncocytic" in this case.

Tom Colby: I probably would have called this adenocarcinoma with papillary and infiltrating component and microcyst formation. On the basis of this I am not entirely convinced that this is an intraductal neoplasm. Some of the ducts in the adjacent pancreas appear entirely uninvolved.

Kum Cooper: Thanks Janez. I have seen a handful of these tumors but not a combined mucinous and papillary component.

Ivan Damjanov: Agree, although I did not see much merit in calling it oncocytic. Do we really gain from that designation? I must have missed a lot of tumors of this type by calling them just papillary and mucinous.

Otto Dietze: Thank you for this contribution, it is the first tumour of this type in the pancreas I have seen.

Hugo Dominguez-Malagon: Intraductal and invasive papillary mucinous carcinoma of pancreas, excellent case and discussion to learn from, thank you.

Vincenzo Eusebi: I fully agree with the diagnosis. Oncocytes are numerous.

Giovanni Falconieri: Nice case Janez, we have already discussed it at a recent seminar in Ljubljana.

Cyril Fisher: A very rare pancreatic tumor, many thanks for the discussion.

Christopher Fletcher: The cytoplasmic eosinophilia is not so striking in the slide which I received, so I would have had difficulty in recognizing the oncocytic nature of this process.

Andrew Folpe: I'll go with intraductal and invasive papillary mucinous carcinoma. Less convinced on the oncocytic nature, or the need to identify this feature.

Masaharu Fukunaga: Thank you very much for an unusual case of the pancreas, Janez. I did not notice oncocytic cytoplasm.

Thomas Krausz: Beautiful focal oncocytic differentiation (thanks Jan).

Thomas Mentzel: Does it represent a real variant of the growing spectrum of intraductal mucinous neoplasms of the pancreas or a papillary-mucinous carcinoma of the pancreas with oncocytic cellular changes ?

Markku Miettinen: Agree on papillary mucinous adenocarcinoma of pancreas

Elizabeth Montgomery: Neat case. Thanks for sharing.

Juan Rosai: It looks like a good example of papillary adenocarcinoma of the pancreas with both a ductal in situ and an invasive component. I was not too impressed with the alleged oncocytic features of the tumor cells.

Dominic Spagnolo: Agree with your diagnosis of invasive pancreatic adenocarcinoma arising from intraductal papillary mucinous tumour (with a spectrum of intraductal atypia through to cribriform adenocarcinoma-in-situ). The oncocytic features are difficult to appreciate on my slide because of the pallor of the stain, but they are definitely there, albeit forming only a minor component of the proliferation. A very nice case, thank you.

James Strauchen: Unusual pancreatic ductal carcinoma!

Lawrence Weiss: It definitely shows invasion in some areas.

Bruce Wenig: Agree with intraductal and invasive papillary and mucin-producing pancreatic adenocarcinoma but I am not as convinced that there is sufficient oncocytic cytoplasmic change to merit the designation of oncocytic variant.

CASE NO. 11 — CONTRIBUTED BY: DR. MICHAL

Phil Allen: Post hysterectomy prolapse of the fallopian tube with exuberant angiomyofibroblastic stromal response, right side of the vaginal vault. Yet another entity I have not previously recognized.

Carlos Bacchi: Amazing. Very illustrative and educative case. I was leaning to make the diagnosis of aggressive angiomyxoma.

David Ben-Dor: Does this condition usually or always occur following surgery, so that the history- assuming that one is made aware of it- can be helpful in arriving at an accurate diagnosis (as in postop spindle cell tumor of the bladder, for example)? Can the mass be anatomically traced back to the adnexa if the surgeon is astute enough to do so? Fortunately it doesn't look malignant, though one wouldn't want to diagnose aggressive angiomyxoma. In some areas the lesion looks microcystic to me.

Gerald Berry: An important consideration to avoid mistaking this reactive proliferative process for a neoplasm.

Michele Bisceglia: Prolapse of the Fallopian tube with exuberant angiomyofibroblastic stroma. A diagnostic pitfall with noteworthy desmin positivity. Thank you.

Ira Bleiweiss: Agree. Very difficult case.

Kum Cooper: Michal I read the second paper recently from Marissa Nucci; but never thought that I would see a real "live" case so soon. Many thanks.

Ivan Damjanov: Michal, you may be right but I could not find any cilia--most of the cases of tubal prolapse that I have seen have at least some cilia. Could it be an embryonic remnant in the wall of the vagina ? I do not like that explanation either, but do not know how could one prove one way or another.

Otto Dietze: I agree and remember a recent case of angiomyofibroblastic stromal response in a fibroepithelial vaginal polyp, which has also caused some discussion to rule out aggressive angiomyxoma or angiomyofibroblastoma.

Hugo Dominguez-Malagon: Fallopian tube prolapse, it is interesting the resemblance with angio- myofibroblastoma even by IHC, could AMFB represent hamartomatous or metaplastic lesions?.

Giovanni Falconieri: I just see a watery, deciduoid-myxoid stroma with a few hyperplastic glands. In curettage material this may represent a diagnostic pitfall. Gland spacing as well as relation to the abundant stroma should prevent over diagnosis, yet.

Cyril Fisher: Very interesting pseudoneoplastic lesion. The nature of the CD34/desmin positive 'myofibroblasts' is not clearly defined – very few EM studies have been done.

Christopher Fletcher: An interesting and entirely convincing lesion. The presence of entrapped/admixed epithelial structures would make angiomyofibroblastoma an unlikely diagnosis and the cellularity is, for the most part, greater than that seen in aggressive angiomyxoma.

Andrew Folpe: Nice case of fallopian tube prolapse. We see a couple of those every year, and there is usually a bit of head scratching until it dawns on us to think about that diagnosis. Thanks, Michal.

Jeronimo Forteza-Vila: Thank you very much for this interesting case.

Masaharu Fukunaga: Thank you very much for the beautiful case, Michal. I often read prolapse of the fallopian tube, but this is first time I see a case.

Thomas Krausz: I agree, prolapse of fallopian tube often causes diagnostic dilemma. All the cases of tube prolapse I have seen before did show various degree of stromal edema and fibrosis in a richly vascular background.

Janez Lamovec: We have seen prolapse of Fallopian tube presenting in a adenocarcinoma-like appearance. However, the stroma in those cases did not show anything similar to what is seen in this case; it really appears indistinguishable from angiomyofibroblastoma.

Thomas Mentzel: Many thanks for this interesting and misleading case.

Markku Miettinen: The concept of fallopian tube prolapse is interesting. In this case it was difficult to verify fallopian tube origin because of lack of smooth muscle and a clear ciliated columnar epithelium. I would have thought of a benign stromo-epithelial neoplasm, or of a stromal neoplasm with epithelial inclusions.

Elizabeth Montgomery: Prolapsed fallopian tube is a huge pitfall on pap smears as well. I had trouble with this case. Think I found cilia in one area.

Juan Rosai: I guess these could indeed be fimbriae from a prolapsed fallopian tube, but I find it difficult to tell them apart from other displaced mullerian-type epithelium from the region associated with inflammatory and other reactive changes. In any event, it sure looks like a perfectly benign, non-neoplastic process.

Elvio Silva: I would like to know if the entire lesion had the appearance of what is in the slide received or if there were areas where the diagnosis of fallopian tube was more obvious.

Dominic Spagnolo: What a superb case of tubal prolapse with angiomyofibroblastic stroma. A diagnostic trap, particularly in biopsy material. Have never seen a case. Thanks Michal.

James Strauchen: Unusual tubal proliferation. I was unaware of this phenomenon. Thank you!

Saul Suster: Thank you Michal for this terrific case! The myxoid spindle proliferation is certainly a pitfall for the unwary.

Lawrence Weiss: I was clueless, with the brief history.

Bruce Wenig: New one for me. Thanks.

CASE NO. 12 — CONTRIBUTED BY: DR. MIETTINEN

Phil Allen: Round cell liposarcoma with cordlike growth pattern, popliteal fossa. There is no typical myxoid liposarcoma in my slide. I agree with the suggested name change to high grade (dedifferentiated) variant of myxoid liposarcoma. At least that would turn two tumors into one, in the minds of some pathologists.

Carlos Bacchi: Beautiful example of a rare variant of round cell liposarcoma. Thanks.

David Ben-Dor: The resemblance of the small cells to lymphoma is striking but this wouldn't make any sense in the context of the surrounding myxoid neoplasm (which was rather well represented in the slide I received).

Gerald Berry: Agree. Nice Case.

Michele Bisceglia: Round cell liposarcoma. It really mimics other types of round cell tumors.

Ira Bleiweiss: Agree. Excellent example of why you have to look at the entire slide. The myxoid liposarcoma is really hiding off to one side. The vessels even look like angiosarcoma focally.

Kum Cooper: Thank you Markku for this instructive case which I do not recall having seen before! Although round cell liposarcoma was in my differential diagnosis I would have liked to have ruled out sclerosing lymphoma, melanoma and carcinoma. Less likely were the sclerosing epithelioid fibrosarcoma and the nuclear and cytoplasmic changes of the latter are different.

Ivan Damjanov: Yes you are right (as usual).

Otto Dietze: Thank you, a textbook case.

Hugo Dominguez-Malagon: Agree with the diagnosis of round cell liposarcoma, the corded pattern is interesting.

Vincenzo Eusebi: Round cell liposarcoma with associated myxoid liposarcoma. Unusual pattern.

Giovanni Falconieri: A top class lesion which I surely cannot comment on. I shall look forward to reading the club experts' opinion.

Cyril Fisher: Unusual pattern of round cell liposarcoma. The tiny focus of myxoid liposarcoma is quite helpful for the diagnosis.

Christopher Fletcher: Very nice example of high-grade myxoid (round cell) liposarcoma. In my experience, cases such as this with a cord-like growth pattern are sometimes mistaken for epithelioid hemangioendothelioma.

Andrew Folpe: Very nice round cell LPS.

Jeronimo Forteza-Vila: Agree.

Masaharu Fukunaga: I agree. Thank you for a beautiful case. Lipoblasts are easily found.

Thomas Krausz: Very good example with excellent fixation and beautiful morphology.

Thomas Mentzel: A nice case of a high-grade myxoid liposarcoma.

Elizabeth Montgomery: Agree with myxoid/round cell family of liposarcoma. My slide was more "transitional" than round cell.

Santiago Ramon y Cajal: Round cell liposarcoma with cord-like growth pattern. A very attractive look for this liposarcoma.

Juan Rosai: Many of the cells of this tumor look like lipoblasts, and most of their nuclei are round, it is therefore difficult to argue with the diagnosis of round cell liposarcoma. However, it looks very different from the other cases I have seen of the tumor carrying that

name, including those we reviewed with the CHAMP group. I am particularly impressed by the prominence of the fibrohyaline stroma, which I did not think was a feature of this entity.

Dominic Spagnolo: Agree with round cell liposarcoma. I found the hyaline stromal changes unusual as well. Thanks for the case.

James Strauchen: Round cell liposarcoma with "cords". Very nice teaching case!

Saul Suster: Nice case of an unusual morphologic presentation of round cell liposarcoma. I was not so much impressed by the "cording" pattern but rather by the prominent stromal sclerosis and hyalinization. This peculiar pattern of sclerosis (which seems to tightly "warp" around individual cells forming small concentric whorls of collagen) is more reminiscent of some examples of solitary fibrous tumors and epithelioid hemangioendotheliomas I have seen. The similarity with the latter, in particular, is highlighted here by the frequent clear vacuoles scattered throughout. Stromal hyalinization in myxoid and round cell liposarcoma is unusual. Without the benefit of reviewing additional slides showing the more classical features of liposarcoma this would be a singularly difficult diagnosis to make in this case.

Lawrence Weiss: Another example of why we have to look at the whole slide.

Bruce Wenig: Great case; there is a very focal area in my slide of fairly classic myxoid liposarcoma, otherwise I likely would not have considered this diagnosis.

CASE NO. 13 — CONTRIBUTED BY: DR. MIETTINEN

Phil Allen: High-grade jejunal leiomyosarcoma. I wonder if "true" leiomyosarcomas ever develop the KIT or PDGFRA mutations. That would really put the Kit amongst the leiomyoblasts.

Carlos Bacchi: Agree

David Ben-Dor: I was struck by the relatively innocuous (for a high-grade tumor) cytology but there were many mitoses including atypical ones. This case reminds us that you can't automatically assume a spindle cell tumor in the abdomen is a GIST without proving it immunohistochemically though cytologically the cells look very much like smooth muscle.

Gerald Berry: It seems that we need to be reminded of this lesion every once in a while to avoid calling every spindled lesion a GIST! Nice example.

Michele Bisceglia: Leiomyosarcoma of the jejunum. Yes, in the era of GIST, we should not forget that, albeit rare, specific histotypes of stromal tumors do exist other than GIST of both spindle cell (such as schwannoma, leiomyoma and their malignant counterparts) and epithelioid cell morphology. Of note in this regard is the recently described epithelioid cell tumor with clear cell morphology and osteoclast-like cell component (likely a subset of clear cell sarcoma of soft parts) (Zambrano et al. Int J Surg Pathol, April 2003).

Tom Colby: Agree with diagnosis. It's nice to know that we weren't entirely wrong in calling stromal tumors of the intestine leiomyosarcoma many years ago.

Kum Cooper: Good to see that the good old LMS of the GIT still live on!

Otto Dietze: I was hitherto not aware of this peculiar macroscopic presentation, thank you.

Hugo Dominguez-Malagon: Agree with diagnosis of leiomyosarcoma of jejunum.

Vincenzo Eusebi: Nice true leiomyosarcoma.

Giovanni Falconieri: I agree with the interpretation, also based on the confirmatory molecular studies. It is curious that pathologists within the community hospitals are now pushed to over diagnose "mesenchymal" tumors of the GI tract as GIST, even if kit negative. I guess that pathologists of my generation need re-education in this (and not only this) field of pathology. Thanks Dr. Miettinen for submission of this instructive case.

Cyril Fisher: Leiomyosarcoma of jejunum, very nice case. There are subtle morphological differences from GIST.

Christopher Fletcher: Entirely convincing case. The filamentous cytoplasm and discernible cell borders would suggest a smooth muscle neoplasm rather than GIST in the absence of immunohistochemistry.

Andrew Folpe: Agree with true LMS of jejunum. Your many papers in this area have been of great assistance in handling cases such as these.

Jeronimo Forteza-Vila: Our histological diagnosis was GIST, but the immunochemistry profile solves the differential diagnosis.

Masaharu Fukunaga: Thank you very much for sharing this unusual tumor in this location.

Thomas Krausz: I am so pleased to see a real leiomyosarcoma of the intestine, otherwise one would think that GIST is winning all the time.

Janez Lamovec: This appears as leiomyosarcoma and is leiomyosarcoma. However, we see cases that are on H&E similar to this one and we are almost certain they would turn out to be leiomyosarcoma on immuno as well, than we find out they are GISTs.

Thomas Mentzel: Given the advances of immunohistochemistry and molecular pathology, true leiomyosarcomas of the gastrointestinal tract seem to be rather rare today.

Elizabeth Montgomery: Nice classic leiomyosarcoma. No need for IHC on this case!

Santiago Ramon y Cajal: A convincing leiomyosarcoma

Juan Rosai: Straightforward case of leiomyosarcoma, both morphologically and apparently immunohistochemically. But what if it had been positive for CD117? Would it have become a GIST? Or what if it had been positive for HMB-45? Would it have become a PEComa? Just teasing.

Dominic Spagnolo: Have not seen this plaque-like pattern of intestinal leiomyosarcoma before. Also refreshing to see a bona fide smooth muscle tumor rather than a GIST! Thank you.

James Strauchen: A true leiomyosarcoma of the GI tract! Thank you for this rare case.

Saul Suster: Agree 100%! We had one case a year ago that was sternly being defended as an example of GIST with unusually strong muscle marker positivity and negative C-Kit staining. I was forced to send it out to the University of Oregon for the molecular analysis of the c-kit mutation (which was negative) to convince everyone of the diagnosis of leiomyosarcoma.

Lawrence Weiss: Beautiful textbook case.

Bruce Wenig: I am glad that a gastrointestinal tumor that looks like it should be of smooth muscle origin proves to be so.

CASE NO. 14 — CONTRIBUTED BY: DR. SILVA

Phil Allen: Low-grade uterine endometrioid adenocarcinoma associated with undifferentiated carcinoma extensively infiltrating lymphovascular spaces of the myometrium with regional nodal metastases. I hope I haven't missed too many of these in the past.

Carlos Bacchi: It is amazing in this case, at least in the slide we are seeing, that only the undifferentiated component is the one with extensive angiolymphatic dissemination. Great case Elvio.

David Ben-Dor: The undifferentiated component looks intravascular to me in the slide I have. Personally I have difficulty in deciding whether solid areas in endometrioid carcinomas are endometrioid in nature and thus to be used in grading or are really squamoid and are to be ignored for that purpose. I agree that here the solid areas don't have squamous features. Not only is the glandular component well differentiated it looks villoglandular to me, which is supposed to be a rather indolent tumor. Recently I had a rather odd case of a middle-aged woman who had a large mass removed from the mesentery. The mass was adherent to the colon but there was no evidence of colon tumor grossly. Histologically the tumor was a well-differentiated adenocarcinoma. The case was rather puzzling until I was given the history that the woman had a low grade endometrioid adenocarcinoma about 9 years previously which was invasive into the inner half of the myometrium. So low-grade endometrioid tumors can come back to haunt us.

Michele Bisceglia: Dedifferentiated endometrioid adenocarcinoma. My section shows both components and completely agree with your interpretation. Dedifferentiated adenocarcinoma is the right and best term for describing this situation. John Chan described an analogous event in salivary glands and contributed an example of his cases (dedifferentiated adenoid cystic carcinoma of submandibular gland) in AMR Seminar # 34.

John Chan: Nice instructive case!

Tom Colby: This looks like bad cancer to me and the idea of a dedifferentiated endometrioid carcinoma is appealing even though "dedifferentiation" has of late been in the realm of soft tissue pathology.

Kum Cooper: Thank you Elvio. This is a great teaching case from your recent published series. I also enjoyed the paper on undifferentiated carcinoma in Oct AJSP. My questions are: a) how do you grade this tumor: grade 1 or grade 3? and b) how do these behave compared to the "usual" endometriod carcinoma: grade for grade and stage for stage? Was good to talk and spend time with you in the Czech Republic.

Otto Dietze: In endometrioid carcinoma I did not see this before; incredible that you have collected 25 cases!

Hugo Dominguez-Malagon: Nice case, in my slide the two components are seen: an intramucosal well differentiated endometrioid adenocarcinoma and an intramural undifferentiated carcinoma permeating lymph vessels, with no transition between both components. The only problem for me is how to differentiate the solid component of an endometrial carcinoma from the solid areas of the undifferentiated carcinoma?

Giovanni Falconieri: Thanks for this excellent contribution, Elvio. It was nice to see you in the Czech Republic.

Cyril Fisher: 'Dedifferentiated endometrioid endometrial adenocarcinoma", great case. Welcome.

Christopher Fletcher: Thanks for this beautiful and educational case.

Andrew Folpe: Agree with high-grade endometrial carcinoma arising in the setting of a low-grade carcinoma. Less certain whether this is the best use of the term "dedifferentiated".

Jeronimo Forteza-Vila: Thank you very much for the case and comments.

Masaharu Fukunaga: An interesting case. Regarding the submitted slide, I would like make a diagnosis of mixed endometrioid and mucinous carcinoma with prominent lymphatic invasion by solid components. I may hesitate to call it dedifferentiation. Dr. Silva, thank you very much for the informative comments.

Thomas Krausz: Highly educational case. Nuclear grade of the undifferentiated component is not too bad. I am sure many pathologists might diagnose it as grade 2 or 3 endometrioid carcinoma. Excellent/important new data, thank you.

Janez Lamovec: Most interesting and instructing case. The nuclei of a deeper portion of glandular tumor are in some foci not much different from those in the undifferentiated solid component.

Thomas Mentzel: An interesting case of a low-grade endometrioid adenocarcinoma showing foci of a diffusely infiltrating high-grade carcinoma. Given the definition of dedifferentiation, I would prefer the term low-grade endometrioid adenocarcinoma showing progression to high-grade undifferentiated carcinoma instead of dedifferentiated carcinoma (but this is only playing with words, the main message is the poor prognosis of these neoplasms as it has been nicely pointed out).

Markku Miettinen: Agree, apparently extensive lymphatic invasion of undifferentiated carcinoma below a well-differentiated papillary adenoca.

Juan Rosai: Remarkable example of a biphasic tumor of a type I had not seen before. I guess it can be viewed as a form of dedifferentiation or tumor progression.

Dominic Spagnolo: If I understand this correctly, you are making the point that "undifferentiated" carcinoma in any amount implies a worse prognosis than a FIGO/WHO grade III endometrioid carcinoma (the latter based on a combination of an appropriate amount of solid, nonsquamous, nonmorular growth and significant nuclear atypia). Earlier studies have not shown any difference in outcome between grade III endometrioid carcinomas and undifferentiated (nonsmall cell) carcinoma. Your abstract does not provide definitional details in respect of morphology, nor comparative outcome data with FIGO/WHO grade III carcinomas, so I look forward to reading the complete papers. Thank you for the case.

James Strauchen: Nice example of dedifferentiated endometrioid adenocarcinoma as you report! The endolymphatic pattern seems striking. Is this a uniform feature?

Saul Suster: Very unusual case showing striking disparity between the morphology of the initial component and that of the angioinvasive component. Thank you for the helpful abstract.

Lawrence Weiss: I have never seen (or recognized) this before.

Bruce Wenig: Both components are in my slide with the well-differentiated component endometrial related with focal invasion and the undifferentiated carcinoma within the myometrium, including what appears to be angioinvasion. Given the appearance of two noncontiguous and histologically dissimilar appearing carcinomas, one might consider two disparate lesions, including a well-differentiated endometrial adenocarcinoma with myometrial metastasis by undifferentiated carcinoma possibly of non-uterine origin. Thanks for educating me about this entity.

CASE NO. 15— CONTRIBUTED BY: DR. STRAUCHER

Phil Allen: Hepatic MALT lymphoma associated with primary sclerosing cholangitis. Yet another association I have never seen before. Thanks for the contribution.

Carlos Bacchi: Spectacular case!! I have never seen MALT lymphoma in the liver. The lymphoepithelial lesions involving the hepatocytes are really fascinating. Congratulations for sending this case.

David Ben-Dor: The lymphoepithelial lesions involving hepatic parenchyma are dramatic. There are foci of enlarged lymphoid cells containing scattered large cleaved and non-cleaved cells which look to me like germinal centers; I would have thought of follicular lymphoma in the histological differential (maybe because in my own personal experience I've seen a few cases of breast follicular lymphoma where similar logic and expectations could be applicable).

Gerald Berry: Florid hepatic MALToma. Nice example.

Michele Bisceglia: Hepatic MALT-lymphoma associated with primary sclerosing cholangitis. Beautiful case.

John Chan: Unusual case of hepatic MALToma! Instead of forming lymphoepithelial lesions with bile ducts, the lymphoepithelial lesions are formed with the hepatocytes! The lymphoma cells participating in the lymphoepithelial lesions have a monocytoid B-cell appearance.

Tom Colby: Agree with diagnosis. We had a recent case associated with HCV.

Kum Cooper: What a fascinating case! I have never seen hepatic extra-nodal marginal zone lymphoma before; let alone see my concept of lympho-epithelial lesions shattered! Thank you!

Ivan Damjanov: I thought first that this is a T cell (hepatosplenic), but your immuno shows that it is a B cell lymphoma.

Otto Dietze: Very interesting case and not only for hematopathologists. I think that the sclerosing cholangitis has almost progressed to a VBD-syndrome.

Hugo Dominguez-Malagon: Excellent case of hepatic MALT lymphoma.

Vincenzo Eusebi: Impressive "MALT" lymphoma of the liver.

Giovanni Falconieri: I certainly agree with lymphoma. The overall immunoprofile is consistent with marginal B-cell lymphoma.

Cyril Fisher: MALT lymphoma in liver, what a striking appearance. Is this confined to the liver?

Christopher Fletcher: I have not previously encountered MALT lymphoma in the liver – many thanks for sharing this educational case.

Andrew Folpe: Cool case- I'm not sure I can see evidence of PSC in my slide, but the lymphoma is very convincing.

Masaharu Fukunaga: It is very a beautiful and educational case. The lymphoepithelial lesion is prominent. I have never seen MALT lymphoma of the liver. Thank you very much for the comments

Thomas Krausz: Amazing case. Not only me but all my colleagues with liver interests got excited about it.

Thomas Mentzel: An interesting case of hepatic MALT with prominent lymphoepithelial lesions.

Markku Miettinen: Agree on low-grade marginal cell lymphoma of liver.

Elizabeth Montgomery: Fascinating case. Seems like MALT lymphomas can be found in almost any mucosal site.

Juan Rosai: What a beautiful example of MALT lymphoma! It made me reconcile with hematopathology. (I am afraid only temporarily)

Dominic Spagnolo: I can accept this as an extranodal marginal zone lymphoma. The immunophenotype certainly is in keeping with the diagnosis, as it is one of exclusion, and the clinical setting suggests it should be too! But I think the case is harder to prove than in your original paper wherein the lymphoepithelial lesions were clearly bile duct-related in your patient with PBC. I could not convince myself of these lesions in this case (although a keratin might be more definitive). The concept of lymphoepithelial lesions involving hepatocytes is more difficult for me to get my head around. Being the devil's advocate, how can one be sure that one is not simply looking at collections of lymphoma cells distending sinusoids, or even destroying liver cells in the manner of piecemeal necrosis? Intrasinusoidal involvement can occur in different B-cell lymphomas (even to the extent of mimicking hepatosplenic T-cell lymphoma). Further, if both PBC and PSC are autoimmune bile duct destructive lesions, why should one get lymphoepithelial lesions involving bile duct epithelium in one setting, and not in the other (unless I am simply missing them!)? These are just random thoughts that crossed my mind on seeing this one slide. I may be missing key morphological features here, and say again I would not quibble with the diagnosis, but I would appreciate hearing your thoughts about these questions. Thanks for the case!

Saul Suster: Spectacular case – had never seen this before! Truly a collector's item.

Lawrence Weiss: Beautiful case and very distinctive. MALTs in the liver are very characteristic.

Bruce Wenig: Agree with MALT lymphoma.

CASE NO. 16 — CONTRIBUTED BY: DR. WAKELY

Phil Allen: Small inconspicuous nodule of left renal oncocytosis associated with a 3.2 cm ipsilateral renal oncocytoma. If my slide had not been marked, I think I would have missed the small oncocytic nodule. I expect it would have been more clearly outlined in a PAS stain. I will have to make sure that I look for these whenever I have an oncocytoma of the kidney. Thanks for the case and the discussion.

Carlos Bacchi: Great case and discussion.

David Ben-Dor: I would have completely ignored the small dotted focus of (early?) oncocytosis had it not been designated since the cells are fairly similar to those in the surrounding tubules. In the salivary glands oncocytoma as a discrete tumorous lesion and oncocytosis as multifocal smaller lesions are part of the same spectrum by my understanding – could this logic be applicable to the kidney? I suppose that small foci of oncocytosis in the kidney could be overlooked, especially given the similarity of the oncocytes to the lining of the cortical tubular epithelium. The sensitivity of renal tissue to autolysis wouldn't facilitate this. Maybe small foci of oncocytic change would be found in the parenchyma of kidneys with oncocytomas if looked for diligently?

Michele Bisceglia: Renal oncocytosis. Thank you, Paul, for dotting the small focus of oncocytic change on the glass slide. It really could escape a quick search.

Ira Bleiweiss: Agree and thanks for the "dot".

Kum Cooper: Thanks Paul. Now I have my own glass slide of oncocytosis! Was good to spend time with you in Seattle!

Ivan Damjanov: Agree, nice case.

Otto Dietze: Thank you for this contribution, I was not aware of this before.

Hugo Dominguez-Malagon: Nice case and discussion, thank you Paul.

Vincenzo Eusebi: Renal oncocytosis

Giovanni Falconieri: Nice case! Thanks for the dots, otherwise I would have hard time in finding the oncocytic foci. The discussion is also superb, as always, Paul.

Cyril Fisher: Renal oncocytosis, thanks for marking the slide and for the excellent discussion.

Christopher Fletcher: Great case – I suspect that oncocytosis such as this could readily be missed, particularly if one is focusing on the main neoplasm, since these tiny nodules could readily be mistaken for collapsed tubules.

Andrew Folpe: There might be just the tiniest bit of oncocytosis left on my slide. I will have to take your word for this. I've been fortunate enough to see several examples of this very interesting process over the past few years, and to have Mahul Amin around to tell me what I was looking at.

Jeronimo Forteza-Vila: Thank you for the case and comments.

Masaharu Fukunaga: I agree. Thank you very much for sharing this excellent case with us and the informative comments.

Thomas Krausz: Excellent case and discussion.

Janez Lamovec: It was nice of you, Paul, that you marked a minute focus of oncocytosis and thank you for a comprehensive discussion on the phenomenon.

Thomas Mentzel: Thanks for the nice case and especially many thanks for marking the tiny focus of oncocytic cells.

Markku Miettinen: Very nice foci of oncocytosis in my slide, thanks for the markings and description of syndrome, have not seen it before.

Santiago Ramon y Cajal: Very didactic case.

Juan Rosai: I must confess I would have missed the "oncocytosis" in this kidney if the contributor would not have pointed it out. The epithelium of the proximal tubules looks indeed granular and eosinophilic, but I thought that it was the way it was supposed to look normally!

Dominic Spagnolo: Thanks for this rare case of renal oncocytosis, and for the discussion on BHD syndrome.

James Strauchen: Oncocytosis! (I missed this entirely even with your arrow!)

Lawrence Weiss: This is subtle; I had to go back twice to find the lesions (thanks for the dot, which I initially ignored).

Bruce Wenig: Renal oncocytosis; didn't realize how involved/significant these foci can potentially be.

CASE NO. 17 — CONTRIBUTED BY: DR. WEISS

Phil Allen: Large benign multicystic mesothelioma clinically simulating pseudomyxoma peritonei. I thought the histology was typical, even if the clinical presentation was most unusual. I still have not seen one of these in a male, nor one that has dedifferentiated.

Carlos Bacchi: Incredible case considering the size of the tumor, the clinical presentation and even the morphology.

Gerald Berry: Nice example Larry. I don't recall seeing this lesion in a male before. All of our cases have been females.

Michele Bisceglia: Benign multicystic mesothelioma. A huge example. All examples (half a dozen cases) I have personally seen were less or more the size of a lemon.

John Chan: Is there a typo error? Is this multicystic mesothelioma truly calretinin negative?

Tom Colby: Multicystic mesothelioma. Every now and then something that gets called this eventually behaves like a more conventional mesothelioma so I often avoid the word "benign."

Kum Cooper: Multicystic mesothelioma. Do we still use the "mesothelioma" term to describe these indolent tumors?

Ivan Damjanov: Agree, nice case.

Otto Dietze: It is interesting that calretinin was negative in this well differentiated tumor with convincing morphology in the H&E.

Hugo Dominguez-Malagon: Benign multicystic mesothelioma of peritoneum, never seen one as large.

Vincenzo Eusebi: Benign multicystic mesothelioma

Giovanni Falconieri: I agree with the proposed interpretation.

Cyril Fisher: Benign multicystic mesothelioma, rare in a male, very nice case.

Christopher Fletcher: Great example of multicystic mesothelioma. The GYN Pathologists in our department still insist that these should be regarded as multilocular peritoneal inclusion cysts – however, I feel uncomfortable with this, given that these lesions show an undoubted tendency for recurrence, which may be repeated.

Andrew Folpe: Nice example of multicystic mesothelioma. Thanks.

Masaharu Fukunaga: Benign multicystic mesothelioma. I do not know the significance of the positive staining of keratin 5/6, 7.

Thomas Krausz: Nice example. I understand that discussion is still going on in the literature whether benign multicystic mesothelioma is a neoplastic or a reactive condition.

Janez Lamovec: Nice case. We once saw a case of multicystic mesothelioma that showed many hyaline globules that caused some confusion diagnostically.

Thomas Mentzel: A nice example of a rare entity. However, calretinin has been described as negative ?

Markku Miettinen: Agree on multicystic peritoneal mesothelioma. I would be ready to accept this as a neoplasm, but some cases more likely represent non-neoplastic mesothelial cysts.

Elizabeth Montgomery: I am confused by the negative calretinin and the positive WT1 for an interpretation of benign multicystic mesothelioma/peritoneal inclusions cysts. The slide looks like the stated interpretation but the IHC is odd.

Juan Rosai: Nice example of the entity, the unusual aspect being that the patient is a male. I suspect Bob Scully is right in considering this lesion a reactive non-neoplastic process rather than a benign form of mesothelioma, being that he has the annoying tendency to be on the correct side of most controversial gynecologic (and other) issues.

Dominic Spagnolo: Very nice case of benign peritoneal multicystic mesothelioma. Thanks Larry.

James Strauchen: Multicystic peritoneal mesothelioma! Very nice case. The natural history seems to be similar to well differentiated papillary mesothelioma (although some of the latter occurring in the pleura have now been related to asbestos exposure). We have followed one patient here with multicystic peritoneal mesothelioma with multiple recurrences treated with subtotal resection.

Bruce Wenig: Agree with benign multicystic mesothelioma. Nice case, thanks

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

Phil Allen: Primary carcinoma with neuroendocrine features, breast, side not stated, versus metastatic carcinoid tumor, (Arch Pathol Lab Med 127:1373-1375, 2003: and Arch Pathol lab Med 128:292-297, 2004: and page 1810 of the latest edition of Rosai.)

David Ben-Dor: Well-differentiated neuroendocrine carcinoma (a.k.a. carcinoid).

Gerald Berry: It looks like a neuroendocrine carcinoma of the breast to me. I would also exclude a met (although unlikely)

Michele Bisceglia: This looks like a carcinoid tumor of the breast (Cubilla-Woodruff type).

Ira Bleiweiss: Invasive duct carcinoma adjacent to microglandular adenosis.

John Chan: Infiltrative carcinoma, ? neuroendocrine, accompanied by interstitial pigment (? Tatoo)

Tom Colby: Carcinoid tumor or carcinoid-like breast cancer impregnated with what I suspect is India ink.

Kum Cooper: Ductal carcinoma with neuroendocrine features; carbon pigmentation for ? localization.

Ivan Damjanov: Breast carcinoma with neuroendocrine features.

Otto Dietze: Injected dye or colloidal material?

Hugo Dominguez-Malagon: In this breast carcinoma I see two components: an infiltrating part with tubular and cribriform patterns, and a part with solid and nested patterns with recognizable acinar structures, and perhaps neuroendocrine features.

Giovanni Falconieri: Infiltrating carcinoma of usual type admixed with extracellular black, dust-like, probably foreign material.

Christopher Fletcher: This tumor looks remarkably neuroendocrine but appears to be primary at this site, given the multifocal perineural invasion. Is the pigment real? If so, I find it hard to explain/interpret. Is this some type of tattoo?

Jeronimo Forteza-Vila: Sorry, I do not have any suggestion.

Masaharu Fukunaga: Neuroendocrine carcinoma of the breast.

Thomas Mentzel: Histologically, an invasive breast carcinoma with prominent perineural invasion is seen. Did neoplastic cells stain positively for neuroendocrine markers. In addition abundant pigment is noted, that could probably represent foreign pigment (instead of melanin or lipofuscin pigment, which has been reported in mammary carcinoma).

Markku Miettinen: Solid carcinoma, rule out metastasis from another source.

Elizabeth Montgomery: Looks like a carcinoid tumor/ well-differentiated endocrine neoplasm.

Juan Rosai: A remarkable case of well-differentiated neuroendocrine carcinoma involving the breast. It looks so good for a carcinoid tumor of insular type that I even considered a metastasis to the breast from a tumor of the small bowel or some other site. However, it also has areas of in-situ and invasive low-grade ductal carcinoma. I would be curious to know the hormone receptor status of this tumor.

Elvio Silva: I believe it is a carcinoma with neuroendocrine features. The black material maybe was used to find the lesion.

Dominic Spagnolo: Invasive solid papillary carcinoma (?any neuroendocrine differentiation), with a smaller component of well differentiated invasive ductal carcinoma with tubular features, and in-situ DCIS, low grade, cribriform.

James Strauchen: Collison tumor between breast cancer and pigmented carcinoid. The latter may be metastatic, since most reported examples occurred in the thymus or lung!

Bruce Wenig: Carcinoma with neuroendocrine features (carcinoid), including rosette-like structures; neural invasion is present.

Janez Lamovec: My case. This an infiltrating ductal carcinoma with neuroendocrine features. I thought it might be interesting to show another case of a biopsy/tumor with extraneous material in it. The material is a charcoal that has been used and is still used for preoperative localization of nonpalpable (or even palpable) breast lesions.