

COMMENTS TO AMR SEMINAR #54

CASE NO. 1 – CONTRIBUTED BY VOLKAN ADSAY:

Phil Allen: Large (11 cm), poorly differentiated, vimentin and SMA positive, angio-invasive, malignant mesenchymal tumor resembling a glomus tumor, right kidney. Comment: I am very cautious about labeling tumors like this malignant glomus tumors.

Carlos Bacchi: Considering the morphological findings only, I was unable to go further than just classify this case as sarcoma, NOS. On the other hand, with the help of reticulum staining and expression of SMA and type IV collagen (around individual cells), malignant glomus tumor is really a nice pick up. Great case, especially with the presence of thrombus extending into the atrium.

David Ben-Dor: At first glance, I was impressed by the sheet like proliferation of rather small monotonous cells to the point that I thought of lymphoma. My compliments- I wouldn't have come up with the possibility of glomus tumor. Actually, in one focus I found a small focus of hyaline material surrounded by tumor mimicking a follicle!

Gerald Berry: I agree with the diagnosis of malignant glomus tumor (glomangiosarcoma). I haven't seen one in the location but the histology and immunoprofile fits.

Michele Bisceglia: Malignant Glomus Tumor (Glomangiosarcoma). Dr. Adsay, welcome to the Club. Agree with your diagnosis. The first case of malignant glomus tumor (with visceral metastases) we had in the Seminars was by Saul (contributed in Seminar n. 14). Another malignant visceral example (in the stomach) was contributed by Markku Miettinen in Seminar 40.

Ira Bleiweiss: Agree, but only after you told me the answer, amazing case.

John Chan: I agree with the interpretation. But for argument's sake, can this be alternatively interpreted as malignant juxtaglomerular cell tumor, which is also a glomus-like tumor?

Tom Colby: Agree with diagnosis of glomangiosarcoma.

Kum Cooper: Thank you Volkan. Never seen one of these in the kidney before, let alone a malignant glomus tumor! At the periphery of my slide, the more bland looking foci does show the typical architecture with distinct cytoplasmic borders.

Ivan Damjanov: Agree. Very interesting case. No doubt that it is malignant. I first thought that this might be a malignant JG cell tumor, or a hemangiopericytoma, but accept your diagnosis of glomangiosarcoma.

Otto Dietze: Impressive case, I have not seen something similar before.

Hugo Dominguez-Malagon: Glomangiosarcoma is an excellent possibility, I also considered synovial sarcoma on morphology.

Göran Elmberger: Great case. I basically go along with your diagnosis of malignant glomus tumor. However, I find it conceptually difficult to delineate this rare and recently described tumor type from the juxtaglomerular cell tumor. The juxtaglomerular cell is a relative of the glomus cell and has a definitive role and histological counterpart in kidney as opposed to the glomus cell. Malignant and non-functional variants have been described. IHC-pattern, microcystic pattern could go along with juxtaglomerular differentiation. Lack of large vessels and absence of hypertension history indirectly support dx of glomus tumor. Renin IHC? Hypertension? EM?

Vincenzo Eusebi: Difficult case. Immuno makes the diagnosis of glomus tumour plausible. I do not know how malignant it would be.

Giovanni Falconieri: "Malignant small round cell tumor". That's all I can say. It entails a broad differential diagnosis including poorly differentiated carcinoma or melanoma. Stretching my imagination I could recognize some conventional glomoid area. Thanks for contributing this extraordinary rare and challenging case. I am looking forward to read Michal and Michele's comments who have both gained extra-experience with renal tumors.

Cyril Fisher: Malignant glomus tumor seems a good diagnosis.

Andrew Folpe: Too cool. I wish I could say that I had thought of that! It's obviously malignant, and I would have had to work it up. I hope I would have thought to do SMA. In retrospect, it fits perfectly with a malignant glomus tumor, of the "de novo" type.

Christopher Fletcher: A beautiful and entirely convincing example of malignant glomus tumour arising in the kidney. I can recollect seeing just one case such as this in the kidney in the past.

Jerónimo Forteza Vila: I agree with the diagnosis. It is necessary to remember glomus tumour must be included inside the tumours of small and round cells.

Masaharu Fukunaga: A typical beautiful case of malignant glomus tumor. Thank you very much for the case and comments.

Allen Gown: Wonderful case!

Thomas Krausz: Diagnostically challenging case. Before reading the discussion, I was considering poorly differentiated synovial sarcoma round cell type and mesenchymal chondrosarcoma without the cartilaginous component. In conjunction with the immuno-result, I agree with the diagnosis.

Janez Lamovec: I thought that this was a clear cell sarcoma in adult but with immuno results this is obviously not. Thank you, Volkan.

Thomas Mentzel: Many thanks for this outstanding case. Given the overlapping features of perivascular myoid neoplasms, I would label this case probably as a malignant myopericytoma. Although rare malignant glomus tumor may be composed predominantly of atypical round cells, in many cases a spindle cell morphology is seen.

Michal Michal: Most probably malignant glomus tumor. In the kidney, an appearance identical to glomus tumor can be seen in juxtglomerular tumor. I would try to make EM to exclude rhomboid crystalloids.

Markku Miettinen: Agree on malignant glomus tumor; too many mitoses, although maintains glomus tumor appearance.

Liz Montgomery: This is fascinating. With the IHC you relate and the proclivity to grow in association with [as well as inside!] vessels, a glomus cell lesion seems the best dx. Maybe this is the real "hemangiopericytoma" if one thinks of the "true" HPC as a member of the family of glomangioma, glomangiomyoma, myofibroma, et al, as nicely reviewed a few years ago by Drs. Gengler and Guillou. [Solitary fibrous tumor and haemangiopericytoma: evolution of a concept. Histopathology. 2006 Jan;48(1):63-74. Review.]

Santiago Ramon y Cajal: Morphologically, this renal mass is striking for being quite monomorphic with sheets of cells with scant cytoplasm and abundant vasculature. With the IHC profile described a diagnosis of glomangiosarcoma is quite sound.

Juan Rosai: Very nice case. I don't know of any reported case of glomangiosarcoma of the kidney either. Victor Reuter's group wrote a nice paper on 3 cases of glomus tumor of the kidney and reviewed the literature on the subject (Am J Surg Pathol 31:585, 2007), but none of them were thought to be malignant. Going back to Volkan's case, one could argue about the nomenclature used. If I remember well, Enzinger originally described glomangiosarcoma as a tumor combining features of classic glomus tumor with those of an obvious sarcoma, whereas he reserved the term malignant glomus tumor for neoplasms that looked like a glomus tumor throughout but had malignant features. If one were to accept this distinction (and I am sure it is valid), Volkan's case would fit better as a *malignant glomus tumor*.

Another comment I wanted to make is that – for the sake of completeness - it may be worthwhile to do a stain for renin or an EM study to rule out the alternative possibility of a juxtglomerular cell tumor. This lesion does not really look like one, but since juxtglomerular cells are modified smooth muscle cells and juxtglomerular tumor may have a hemangiopericytoma-like or glomus tumor-like appearance, it would not be unreasonable to evaluate this tumor along those lines.

Joshua Sickel: Thank you for contributing this once in a lifetime case!

Dominic Spagnolo: Pretty spectacular case of glomangiosarcoma, which I did not consider in my differential. Thank you.

James Strauchen: Malignant glomus tumor of the kidney! Fabulous case.!

Saul Suster: Quite extraordinary case! I have never seen a glomus tumor in the kidney, let alone a malignant one. I do agree that this tumor is malignant, and I also agree that given the immunophenotype and monotonous round cell morphology with prominent vasculature it would fit nicely for a malignant glomus tumor. But given that this is a quite unusual location and diagnosis, I do think it would benefit from closer scrutiny. In particular, E.M. to rule out a juxtglomerular cell tumor would be of value.

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

Volkan Adsay: I think it's a great case of this phenomenon. However; I've also seen metastatic well differentiated endocrine neoplasia (with morphologically similar primaries in the pancreas, GI tract, and one medullary thyroid carcinoma) that elicited ductular proliferations and stromal changes, closely mimicking this entity (or perhaps they were metastasis to a hamartoma to begin with, hard to be sure). Since then, I recommend screening of the patient for a primary, just to make sure. For this case, though, I really think the distribution and cytology is in keeping a benign endocrine proliferation. I agree.

Phil Allen: Bile duct adenoma with neuroendocrine proliferation. I agree with the diagnosis. I don't remember reading O'Hara's article nor can I remember ever seeing or hearing about a similar case.

Carlos Bacchi: Interesting case David! I was also debating with myself if this tumor could behave as neuroendocrine tumor or just as bile duct adenoma with neuroendocrine features. I also thought about the unlike possibility of a metastatic NET into a bile duct adenoma. Close clinical correlation could help in this regard but as you rightly said it is probably irrelevant at this point.

Gerald Berry: I agree with bile duct adenoma with a neuroendocrine proliferation. I think it is probably a neuroendocrine lesion arising in the adenoma. However, I don't think a collision tumor can be entirely excluded and a work-up of the pancreas, small bowel, etc might be considered.

Michele Bisceglia: Bile duct adenoma with neuroendocrine proliferation. Agree. To be honest, I would have likely not been able to notice the neuroendocrine proliferation if you had not indicated it. Thank you, David.

Ira Bleiweiss: Agree. Must have been a tricky frozen.

John Chan: I think the neuroendocrine cell proliferation is striking enough in this case to merit a designation of carcinoid tumor (focally, there are even tumor islands lying in lymphovascular spaces), in addition to bile duct adenoma.

Tom Colby: Agree with diagnosis. The cytoplasmic features of the cells are also reminiscent of zymogen granules.

Kum Cooper: Thank you David. I would still prefer the surgeon to rule out a metastatic well differentiated neuroendocrine tumor from the pancreas. My slide also has focal perineurial invasion. Could this be a metastasis to a bile duct adenoma? As a similar phenomenon has been described in meningiomas.

Ivan Damjanov: Agree. There is no question that the lesion shows neuroendocrine differentiation, but one does not see what one does not know and I would have missed it.

Otto Dietze: The growth pattern of the neuroendocrine proliferation seems to be rather aggressive.

Hugo Dominguez-Malagon: Bile duct carcinoma. I also considered the possibility of pancreatic choristoma.

Göran ElMBERGER: Very interesting and rare case. I completely agree with the diagnosis as well as Dr Portman's concerns about the malignant potential of the lesion with regard to perineural and perivascular growth. I have no problems in accepting Dr. Bhatia's arguments for reclassifying these tumors as peribiliary (did you have access to reported antibodies), but I assume that the classification as hamartomas vs. adenomas is a little more problematic. In standard textbooks, the differential between benign neoplasm and hamartomas is regarded as sometimes arbitrary (Rubin Farber). The classification as hamartomas implies that the lesion is of developmental nature and thus present at birth. This could be the case in our lesion given the subcapsular localization and the juxtaposition to a large bile duct. The conceptualization as hamartoma might accommodate for the perineural and perivascular growth pattern as well.

Vincenzo Eusebi: Very interesting case. Histologically, it looks like a minute insular (argentaffin/ Masson Fontana positive) carcinoid. A metastasis from the gut is a distinctive possibility. Two vessels in my section contain tumour cells.

Giovanni Falconieri: Nice case, David. I fully agree with your careful assessment. I believe that the microscopic entity you are alluding to is likely underreported. Speculatively, because of the neuroendocrine features (nests and cords of low grade tumor cells; artifactual retraction from surrounding stroma; salt and pepper quality of chromatin within fairly oval to round nuclei) one may wonder whether the appellation of adenocarcinoid/well differentiated neuroendocrine carcinoma might be better applied. In this case the biliary proliferation might be just reactive. I also believe that this is independent from the stomach tumor. Great discussion.

Cyril Fisher: Looks like neuroendocrine. Difficult to think this is not a neoplasm. I can see why Bernard Portmann suggested consideration of metastasis. Beautiful slide, many thanks.

Christopher Fletcher: This is a truly remarkable lesion, the like of which I have not personally seen (or in truth even heard of...) previously. The neuroendocrine component certainly has quite worrisome morphology which, in other circumstances, might well make one worry about a metastasis.

Andrew Folpe: Fascinating. I had not heard of bile duct adenoma with neuroendocrine proliferation, but it makes perfect sense. I was wondering about some sort of pancreatic heterotopia, but, of course, it lacks exocrine cells.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: My impression was a neuroendocrine or acinar cell proliferation. How about the possibility of ectopic pancreatic tissue? Thank you very much for the interesting case and informative discussion.

Allen Gown: Thanks for this most interesting case.

Thomas Krausz: Histologically the islands of neuroendocrine cells look like islets of pancreas, so why not ectopic pancreas in the liver?

Janez Lamovec: Agree with diagnosis. I have never seen this before.

Thomas Mentzel: Thanks for sharing this interesting and rare neoplasm.

Markku Miettinen: Agree on neuroendocrine (? Paneth cell-like) differentiation in bile duct adenoma.

Michal Michal: Nice case. I would just rethink the name "hamartoma". It looks to me like a regular tumor. Maybe bile duct "neuroendocrine tumor" -or "carcinoid" would be a more fitting name. It seems to me that it grows in quite infiltrative way. In one spot the tumor seems to show angioinvasion.

Liz Montgomery: The bile duct adenoma part is easy. Like you, I am not sure how we know whether the endocrine component is not a met from a well-differentiated endocrine neoplasm. My slide has a component that has gastric type mucin which also is peculiar. Too bad we will never know in light of the patient's more serious neoplasm. Thanks for your nice discussion of this process. Will enjoy learning Dr. Miettinen's views.

Santiago Ramon y Cajal: This hepatic lesion is well circumscribed with bland looking bile-duct like and neuroendocrine structures. I agree that it is an incidental finding unrelated with the carcinoma for which the procedure was being performed. Is it a Bile Duct Adenoma with Neuroendocrine Proliferation or could it possibly be Pancreatic Heterotopia?

Juan Rosai: Very elegant case. I suppose an alternative terminology could have been *adenocarcinoid tumor* of the liver, in the sense that it has an amphicrine composition, analogous to appendiceal tumors that carry name (not to be equated with goblet cell or signet ring carcinoid).

Joshua Sickel: Unusual case...I haven't seen this before.

Dominic Spagnolo: I have not personally encountered this before. I can accept the explanation provided but have to say I could not find a single bile ductule containing any endocrine cells (at least with the same cytological features as the stromal neuroendocrine nests), which I might have expected if they had a ductular origin. Perhaps it is simply a sampling issue that my slide does not show any obvious relationship between the 2 elements. At any rate, it is a beautiful case, and will make me look harder at my next peribiliary hamartoma. Thanks David.

James Strauchen: Carcinoid tumor in bile duct adenoma. I was unaware of this association. The existence of primary hepatic carcinoid is of course controversial since metastatic carcinoid is much more frequent.

Saul Suster: Very unusual case. I think the interpretation of this being a neuroendocrine proliferation superimposed in a bile duct hamartoma is a very logical and convincing one, but I would first want to rule out a metastasis from another organ. Neuroendocrine tumors seem to have a strong predilection for spreading to the liver and I would want to make sure that is not the case here first.

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

N. Volkan Adsay: Great case.

Phil Allen: Massive, congenital, histologically benign, infiltrating melanocytic tumor, skin and muscle of left side of face and scalp, midline over the nose, left and right orbits, left sphenoid bone and outer plate of left temporal bone. I have no personal experience with any other similar cases. At the moment, it seems to be benign but I agree that future malignant change is possible.

Carlos Bacchi: What a difficult case to diagnose by the time the first biopsy was performed! Although I thought about the possibility of melanoma, I was particularly impressed by the rarity of mitotic figures. At this point, with follow-up information, the designation of congenital melanocytic tumor is an appropriate one. Thanks for the excellent discussion.

David Ben-Dor: I'm not sure whether pathology is as much of a science as it is the study of probabilities based on morphology. With that in mind, there is a saying in Hebrew which goes something to the effect of: "prophecy is given to fools" (parenthetically this can apply to the prognostications of the geniuses on Wall Street). This case shows that in some instances only time will tell. Even if the child develops metastatic disease in the future, it won't necessarily imply that the lesion was malignant to begin with, since it is known that large congenital melanocytic lesions are prone to develop into malignancies.

Gerald Berry: I think the epithelioid appearance and infiltrative arrangement of the tumor suggest a congenital melanoma. That said, I would have sought the help of our dermatopathologists!

Michele Bisceglia: Congenital melanocytic tumor of the face, scalp and orbit. Difficult case. Several types of congenital tumors have unexpected biologic behavior and should not be viewed in the same light under which we see similar lesions in adulthood. This is indeed an educational case. Many thanks.

Ira Bleiweiss: Don't know anything about these, but it certainly looks like a melanoma.

John Chan: I have no idea how best to call this tumor. Perhaps this exemplifies the sometimes benign behavior of some malignant-looking neoplasms in the pediatric age group. For this age group, I have been taught that, if there are uncertainties about the nature of the tumor or the malignant potential, it is best to just wait and see.

Tom Colby: Agree with diagnosis.

Kum Cooper: Fascinating! I am amazed that you have the follow-up to support the low-grade growth of this tumor!

Ivan Damjanov: I vote for melanoma.

Otto Dietze: The low proliferative activity seems to me in keeping with a benign course.

Hugo Dominguez-Malagon: This is a difficult case, I thought it was a malignant melanoma but the clinical course goes with a benign lesion.

Göran Elmberger: Interesting case. Given the absence of atypia, necrosis, mitoses and low proliferation rate, I would be reluctant to sign out the case as melanoma. The 3-year follow-up with no signs of progression lends further support to the benign nature of this tumor. Thus, I agree with your descriptive dx of congenital melanocytic tumor. At the time of diagnosis, one might add of uncertain malignant potential but retrospectively melanocytoma might be another description. I had a similar diagnostic problem with a laryngeal melanocytic tumor in an infant. Opinions of expert pathologists spread from frank melanoma to uncertain malignant potential but follow-up 12 months without signs of recurrence.

Vincenzo Eusebi: Case impossible. I am inclined to go along with the diagnosis of congenital melanocytic tumour. The cells are epithelioid and are similar one to another. Pseudovascular spaces are more common in benign naevi¹. Therefore, I am not convinced that this lesion has metastatic potential, but I am on the side of benign lesion. (Collina G, Eusebi V. Naevocytic navel with vascular-like spaces 45. *Br J Dermatol.* 1991;124:591-5).

Giovanni Falconieri: Great case, Ofer. I share all your doubts. Melanocytic lesions in youngster, and in kids in particular, are a source of distress at the microscope inasmuch as managing of large lesions in peculiar sites may further compound the matter for cosmetic reasons, such the one at hand. As long as my opinion may bear any importance I think that this case should be labeled as "atypical melanocytic tumor", at best; in the circulating slide I could see sheets of discohesive, non-proliferating, yet atypical melanocytes (nucleolar prominence; irregular nuclear membrane) often with rhabdoid quality and perhaps some pyknotic changes. I am afraid that this is melanoma, yet in children. As many accountable experts of the art say, it is likely that in this baby things may pursue a better course. The relatively good follow-up seems to support this further.

Cyril Fisher: Very difficult case. I guess the outcome is the diagnostic determinant here.

Christopher Fletcher: As Dr. Ben Itzhak knows, I was the second of the so-called 'experts' and did not have the courage to call this lesion benign, despite acknowledging that the outcome might well be good... I am therefore very happy for the patient and his parents to know that the child has done so well to date.

Andrew Folpe: Very strange case. Neurocristic hamartoma?

Jerónimo Forteza Vila: I agree with the diagnosis. We don't know this entity.

Masaharu Fukunaga: It is a challenging case. I hesitate to call it histologically malignant melanoma despite of aggressive behavior. Thank you very much for the detailed information and a very interesting discussion.

Allen Gown: Thank you for this interesting case and write-up.

Thomas Krausz: Frightening clinical picture and histology. Mitotic activity is relatively low, but that does not exclude melanoma. However, I still follow a basic rule, not to diagnose definite melanoma in a newborn. Suggest complete excision of smaller lesions and follow-up with re-biopsy a year later for giant ones (they usually show maturation), so I agree with your second expert (behavior of atypical melanocytic lesions cannot always be predicted on histologic ground in an infant)

Janez Lamovec: This really appears more like melanoma than pigmented neuroendocrine tumor of infancy although a benign course would be more consistent with the latter possibility. However, I wouldn't have courage to call this a benign melanocytic lesion despite the low mitotic activity.

Thomas Mentzel: Given the clinical features and the presence of an atypical melanocytic neoplasm with cytologic atypia and rare mitoses, it is hard to call the shown lesion a congenital nevus. Otherwise, mitoses are very hard to find and nuclear atypia is not so prominent. Neoplastic cells stain positively for HMG-45, and probably the diagnosis of an atypical epithelioid blue "nevus" could be discussed.

Markku Miettinen: Melanocytic neoplasm of uncertain biologic potential, would not dare to predict with certainty.

Liz Montgomery: Another amazing case. It is good that the child is attending school and doing so well. With the lack of mitotic activity [and knowing the outcome] and the spindly areas, one wonders about a strange melanocytic epithelioid nerve sheath tumor, but I certainly would not have the guts to call this lesion benign prospectively and would still hesitate to make any guarantees now.

Santiago Ramon y Cajal: This is a very difficult case with a differential of congenital nevus vs melanoma. Retrospectively one would be tempted to call it congenital nevus; however, morphologically it is very difficult to commit one way or the other. Perhaps a hint would be the lack of significant mitoses in the primary neoplasm.

Juan Rosai: I have seen several cases like this, all in neonates, located in the head, and often combining cutaneous and intracranial components. I think they are congenital "borderline" melanocytic lesions exhibiting greater evidence of their neural ancestry than the more common acquired nevi. A case I saw, involving the periauricular region and the meninges, ended up as a typical melanoma. A closely related tumor is the "neurocristic hamartoma" and the malignant melanotic "neurocristic tumor" arising from it, as described by Pearson et al (Am J Surg Pathol 20:665, 1996). I must confess I have trouble in fully understanding this paper.

Joshua Sickel: Bizarre congenital melanocytic tumor simulating melanoma. I encountered a similar case several years ago. A 2 year old girl with a large congenital nevus developed a deep nodular lesion. Histologic sections showed typical features of congenital nevus superficially, with abrupt transition to a nodular proliferation of atypical, mitotically active melanocytes extending into the subcutis. The case was seen by several expert dermatopathologists. Diagnoses ranged from congenital nevus with focal proliferation (benign) to malignant melanoma. Several years have passed and to my knowledge, the patient is doing well. My impression is that the traditional histologic criteria for melanoma go out the window in this age group.

Dominic Spagnolo: A fascinating case. I was considering a congenital melanoma, but mainly because of the clinical scenario, I would have been reluctant to call it melanoma, thus congenital melanocytic tumor seems a reasonable rubric without making a judgment as to likely biological behavior!

James Strauchen: Congenital melanocytic nevus with atypical melanocytic proliferation ("melanocytic hamartoma").

Saul Suster: Very difficult case. I've always had problems with these lesions in children, and the literature has not been terribly helpful either. Despite the 3 year uneventful follow-up, I still would not be prepared to call this benign or a run-of-the-mill congenital nevus. For the patient's sake I'm hoping this will continue to "mature" and behave as a benign neoplasm, but I would still have to label it as a melanocytic tumor of at least uncertain malignant potential. This looks ugly!

CASE NO. 4 – CONTRIBUTED BY GERALD BERRY:

N. Volkan Adsay: Beautiful case.

Phil Allen: Large, (5.3 cm), fatal, congenital, immature teratoma, left atrium involving left coronary artery. As anticipated, I enjoyed this case.

Carlos Bacchi: Great case for a teaching set. Thanks.

Michele Bisceglia: Intracardiac teratoma (left atrium). This is the first time I've seen such a case in this particular anatomic location. Thank you, Gerry.

Ira Bleiweiss: Wow. Everything's here except the proverbial kitchen sink.

Thomas Colby: Agree with diagnosis. Dramatic example.

Kum Cooper: Thank you Gerry. I submitted a cardiac fibroma to the AMR # 29 case 3.

Ivan Damjanov: Immature teratoma.

Otto Dietze: A teratoma like from a textbook in this rare location!

Hugo Dominguez-Malagon: Beautiful case of cardiac teratoma, never seen one before, thank you.

Göran Elmberger: Thanks for the unique case.

Vincenzo Eusebi: Nice case of intracardiac immature teratoma.

Giovanni Falconieri: Usual tumor but bizarre location! Thank you for this extraordinary contribution, a valuable teaching case.

Cyril Fisher: Teratoma from left atrium, nice case.

Christopher Fletcher: What a beautiful and very rare case

Andrew Folpe: Congenital immature teratoma of the heart. Another routine AMR case (not!).

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: This is my first time to see cardiac teratoma. The case contains immature components. Thank you very much for the beautiful case.

Thomas Krausz: I haven't seen primary teratoma in the heart before. Thank you for the great example.

Janez Lamovec: What a rarity! Thank you.

Thomas Mentzel: Many thanks for this rare case.

Markku Miettinen: Agree on immature teratoma, with a major neuroepithelial component.

Liz Montgomery: Gallery of the weird! Cannot claim to have ever seen a cardiac teratoma.

Santiago Ramon y Cajal: This is a very nice case of intracardiac teratoma with a very nice slide for the teaching set. Thank you!

Juan Rosai: Nice case of immature teratoma. Its location confirms the fact that nearly all intrathoracic teratomas are either thymic or intrapericardial. The large amount of immature neural elements reminds me of what one often sees in sacrococcygeal teratomas. As in the latter, neural immaturity should not be equated to clinical malignancy, the way it is done in the ovary.

Joshua Sichel: Amazing case!

Dominic Spagnolo: Very nice cardiac teratoma, thanks. Not something we encounter in our practice here.

James Strauchen: Immature cardiac teratoma.

Saul Suster: Spectacular case – never seen this before!

Paul Wakely, Jr.: Beautiful example of an immature teratoma. Some of the best discussions on teratomas that I have read are by Dr. Rupert Willis, 1962 edition The Borderland of Embryology and Pathology, and the 2nd series AFIP fascicle Extragenital Teratoma by Gonzalez-Crussi. Amazing how a benign entity can still kill.

CASE NO. 5 – CONTRIBUTED BY MICHELE BISCEGLIA:

N. Volkan Adsay: Very impressive.

Phil Allen: Fatal systemic air embolism after endoscopic retrograde cholangiopancreatography (ERCP) for removal of bile duct stones, associated with ascending cholangitis, cirrhosis of the liver and chronic lymphatic leukemia. I was not aware of this rare complication of ERCP. Thanks for the contribution, Michele.

Carlos Bacchi: Congratulations once more for the discussion in this illustrative case.

David Ben-Dor: In this case, the slide is less complicated than the story. Besides from the air bubble, the liver looks totally wrecked. I wonder if these complications have any connection with the previous surgical alterations of normal anatomy.

Gerald Berry: A nice reminder that seemingly routine cases can go awry! Beautiful images.

Ira Bleiweiss: Autopsy material in AMR. That's new in itself.

Tom Colby: Agree with diagnosis. Unusual example where we can actually appreciate air emboli.

Kum Cooper: Suppurative ascending cholangiohepatitis. I last saw this as a resident in darkest Africa! Michele, are the spaces in the liver tissue air?

Ivan Damjanov: Agree. As usual, Michele is a great presenter.

Otto Dietze: Very well documented teaching case, especially for those of us who have to deal with forensic questions.

Hugo Dominguez-Malagon: I thought it was an infection by gas producing anaerobic bacteria.

Göran Elmberger: Thanks for very an interesting and educative case. Something like interstitial emphysema in thorax? Air bubbles secondary to gas-forming bacteria? These might be additional possible mechanisms for finding.

Vincenzo Eusebi: Instructive case.

Giovanni Falconieri: A valuable and instructive case. Nothing to add to the peculiar aspect of your case, Michele. Just to comment once again that reiterated ERCP is, by itself, a risk factor especially in a patient with ancient gastro-duodenal resection. Years ago I was involved in a malpractice claim where the patient died of post-operative hemorrhage following the 4th ERCP (within a lapse of 40 days). The endoscopist was initially accused of excess of interventionism as long as indication to a repeated procedures was not justified by the clinical evidence of jaundice of undetermined origin, but at the end of the story he was found not guilty.

Christopher Fletcher: As always, an astonishing case from Michele ! Given the remarkable lesions which he consistently finds in San Giovanni Rotondo, I often wonder what the rest of us are missing....

Cyril Fisher: Striking appearance!

Andrew Folpe: Interesting case, thanks.

Jerónimo Forteza Vila: The definitive diagnosis that endures this case is the air presence in the heart in the radiology and in the autopsy. Very demonstrative the histological images of the liver. It is a very rare complication of air embolism.

Masaharu Fukunaga: Michele, thank you very much for the wonderful case, detailed information and images.

Allen Gown: Great presentation!

Thomas Krausz: Highly educational case.

Thomas Mentzel: What's for a dramatic complication !

Michal Michal: Nice case Michele. Again, one of the "Padre Pio" Cases.

Santiago Ramon y Cajal: Nice autopsy case showing not only the air bubbles related to the embolism, but the prominent microabscesses in the liver which explain the relevance of the ERCP performed.

Juan Rosai: Good case and scholarly discussion. Too bad we cannot confirm the diagnosis by performing an immunohistochemical stain for air!

Joshua Sickel: Congratulations on solving this mysterious case. I was not aware of this unfortunate complication of ERCP. At our hospital, I'm sure this autopsy would have been sent to the medical examiner's office because of the medicolegal ramifications.

Dominic Spagnolo: A typically meticulously studied case, Michele. Thanks for the education.

James Strauchen: Iatrogenic air embolism! Wild case. A reminder that every undertaking has a particle of risk!

CASE NO. 6 – CONTRIBUTED BY THOMAS COLBY:

N. Volkan Adsay: It does indeed show many similarities to what we see in autoimmune pancreatitis, showing duct-centric plasma-lymphocytic infiltrates associated with periductal expansion and a distinctive, delicate sclerosis. I've always thought that the paucity (or often, total lack) of conventional granulomas and giant cells is a peculiar and interesting feature of this phenomenon, (considering the presence of vasculocentric and ductcentric inflammation in other conditions). I would like to caution the group that, perhaps not too surprisingly, we are beginning to see prominent IgG4+ plasma cells in non-specific inflammations, on occasion. The overall histologic pattern is important to identify this entity.

Phil Allen: Hyper IgG4 disease, lung. I was not aware of this condition. Thanks very much for the case and discussion, Tom. I have shown the lung section to Doug Henderson, who does not think he has previously seen a case. The histology is very striking and one would think, unforgettable.

Carlos Bacchi: I initially thought this case was just a non-specific inflammatory infiltration in the lung. On the other hand, I was impressed by the infiltration of plasma cells and lymphocytes of airways and vessels, including the vessel walls. Thanks for teaching me about this entity, which I wasn't aware of.

David Ben-Dor: Thanks for the masterful summary of the clinical and pathological aspects of this disease, and for sharing with us your ongoing thoughts concerning the pattern of pulmonary involvement, which is a work in progress.

Gerald Berry: A great example of a "renamed" entity. I had IMT in my differential diagnosis but hadn't seen this pattern. Nice case.

Michele Bisceglia: Histologic changes consistent with so-called hyper IgG4 disease. Tom, I like the concept that lymphoplasmacytic sclerosing lesion in a given organ in this immunopathologic context is part of a IgG-4-related systemic disease. For sure, lymphoplasmacytic sclerosing pancreatitis is the most common lesion of the disease (have just seen a personal case last month). Lung is likely the least common involved organ. In fact, in a very nice paper on the subject (Zamboni et al. Virchows Archiv 2004; 445:552-563) dealing with 53 resection specimens of such cases plus 9 biopsy specimens, no lung disease is on record.

Ira Bleiweiss: Interstitial lung disease is very difficult. I'm glad there are others who are experts.

John Chan: Yes, we are now seeing IgG4-related sclerosing disease involving more and more body sites – recently we have encountered cases involving the breast or skin. This lung lesion is a bit unusual in that the infiltrate also involves the arteries – while typically only veins are affected in IgG4-related sclerosing disease. But perhaps the vasculature in the lung is different from the systemic circulation.....

Tom Colby: My case. Some additional follow-up: 8 months after the initial lung lesion was identified, there was a radiologic recurrence in the same region.

Kum Cooper: Wonderful Tom! The vascular component is striking. John Chan has also described this in the lachrymal gland; and with the emergence of MALT type lymphoma. We just recently saw our first case with BOTH cardiac and renal lesions!!

Ivan Damjanov: Agree. We learned to recognize this disease in the pancreas and liver and now we must expand it to other organs as well.

Otto Dietze: Thank you for this very timely contribution and the excellent presentation.

Hugo Dominguez-Malagon: Impressive case of IgG4 disease, involvement of the lung must be a rare event.

Göran Elmberger: Very interesting case. Thanks for pointing out the possible localization of hyper IgG4 disease in the lung. The lesion would certainly be difficult to squeeze into the present established classification. It is amazing when new insights change our diagnostic work. In the H&N area, chronic sclerosing sialoadenitis (Kuttner tumor) has been suggested to belong to the same group of diseases when generations have attributed the disease to sialolithiasis etc. I will keep my eyes open for this new entity in pulmonary pathology.

Vincenzo Eusebi: Very instructive. I would have missed the diagnosis.

Giovanni Falconieri: Needless to say that I totally ignored the topic you are addressing. Looking at the case as an "unknown" slide, I would say that there is a diffuse chronic interstitial pneumonia, pattern III, with alveolar desquamative changes and pleural involvement. Simply impossible to move further

Cyril Fisher: Hyper IgG4 disease involving lung, great slide, many thanks.

Christopher Fletcher: This is a beautiful and entirely convincing case. I recently saw a similar lesion in the stomach, which also seems to be a novelty in the setting of IgG4 disease – but maybe people with expertise in GI pathology are entirely familiar with such lesions.

Andrew Folpe: Great discussion. A very striking picture in the lung. We are getting tons of requests to do IgG4 on retroperitoneal fibrosis, sclerosing mesenteritis, etc. I wonder how meaningful some of these results really are, since we've never really examined clearly reactive lesions, like post-traumatic mesenteric fat necrosis for IgG4 (+) plasma cells.

Jerónimo Forteza-Vila: I agree with the diagnosis.

Masaharu Fukunaga: This is the first time I see hyper IgG4 lung disease. The discussion is well organized and very informative. Thank you very much.

Allen Gown: Thank you for this fascinating case.

Thomas Krausz: Before reading your discussion, I was considering plasma cell leukemic infiltrate in the lung. Permeation of the wall of numerous blood vessels including subendothelial spaces and airways is striking. Thank you very much for the thought-provoking discussion.

Janez Lamovec: Thank you for educating us on IgG-4 sclerosing disease. If I saw a case like that, I would have probably called it an inflammatory pseudotumor.

Thomas Mentzel: Many thanks for the excellent teaching on this "new" disease!

Liz Montgomery: In the pancreas, the analogous process spares the arteries and really affects the veins and ducts [we see the pancreas cases a lot since there are so many Whipple operations here]. That seems the trend in the lung as well; the veins and airways are far more damaged than the arteries. This pattern can also be encountered in a subset of cases currently diagnosed as sclerosing mesenteritis, which, like the pancreas lesions, tends to be tumefactive. Interesting that your patient has had some success with steroid treatment. However, I suspect some reports of finding a lot of IgG4 in various lesions might reflect a very non-specific phenomenon.

Santiago Ramon y Cajal: Very interesting case of the so called entity Hyper IgG4 Disease. Anyway, our first impression was autoimmune disease with prominent vasculitis after ruling out a neoplastic process. It would be helpful to be able to group many poorly defined autoimmune entities in a common pathogenesis as would be Hyper IgG4 Disease. Please let us know what you think of the orbital lesion after reviewing the slides.

Juan Rosai: Wow! I thought it looked like a "Liebow's entity", but I did not know which, although the idea of lymphomatoid granulomatosis crossed my mind. Tom says that he tried to sell me one or two of these cases as Rosai-Dorfman's disease, but he does not say whether I bought it or not. I found in my consults file a case he tried to sell me as Rosai-Dorfman's disease and another he was pushing for angiolymphoid hyperplasia with eosinophilia, but I was not sure of either. The other comment I wanted to make is that a diagnosis of hyper IgG4 disease sounds very sophisticated, but that one should be careful with defining entities on the basis of a single immunohistochemical or molecular criterion. Most of them do not hold in the long run.

Joshua Sickel: Almost identical to a case Tom submitted to a recent South Bay Pathology Society meeting. I hope I recognize this disease when the next one comes along! I'm currently working up a case of chronic sclerosing sialadenitis (Kuttner's tumor) which is probably another example of hyper IgG4 disease.

Dominic Spagnolo: I agree, the findings would be consistent with systemic hyper IgG4 disease. Were the serum IgG4 levels known? I, retrospectively, stained up a couple of autoimmune pancreatitis cases and Kuttner tumors recently, and

have found the number of IgG4 cells, while typically abundant, quite variable within any one histological section, and have used the ratio of IgG/IgG4 cells as a guide to aiding diagnosis, as suggested by others. I have also been staining unrelated mundane inflammatory lesions in different sites with plasma cell rich infiltrates, and have found the number of IgG4 cells in some of these can be quite high (though typically low), and can outnumber 20/hpf in selected fields. As you say, we still have a way to go in assessing the range of IgG4 plasma cell numbers in various diagnostic settings. We probably have more to learn about serum levels too, specifically if and how they may vary during the disease course.

James Strauchen: IgG4 sclerosing disease of the lungs! The angiocentricity of the plasma cell infiltrates is striking.

Saul Suster: I thought of Rosai-Dorfman disease at first, but the concentric fibrosing pattern with plasmacellular infiltrates is quite distinctive! Thank you for sharing this truly educational case for me!

Paul Wakely, Jr.: The "lifting" of the endothelium by mononuclear cells is very striking, and reminds me of the endothelialitis seen in acute vascular rejection.

CASE NO. 7 – CONTRIBUTED BY GÖRAN ELMBERGER, M.D.:

N. Volkan Adsay: Interestingly just last week in the California Path Society Meeting, Stacey Mills showed a similar case, also occurring in the oral cavity. Curiously, the intraluminal acidophilic secretions were very prominent in his case as well.

Phil Allen: Microcystic adnexal carcinoma of the tongue (Ebner's glands derived tumor). Comment: Looks pretty good to me but I have never previously seen a similar case, and I can't find any recent references to the condition. Thanks for the discussion.

Carlos Bacchi: I totally agree with Göran's interpretation in this case. I don't think this case has the morphological features of adenoid cystic carcinoma, mucoepidermoid carcinoma or low-grade polymorphous adenocarcinoma, all carcinomas in the differential diagnosis.

David Ben-Dor: The tumor looks very syringoma-like and in places seems deceptively bland. This may be one of those stealthily and widely infiltrating tumors in which the specimen margins are hard to define and thus, along with the widespread neural invasion, resist surgical removal, leading to multiple recurrences (reminiscent of desmoplastic melanoma).

Gerald Berry: We have recently had an identical case here. I ended up calling it low grade adenocarcinoma, NOS because it didn't have the cytologic or architectural features of tubular variant of adenoid cystic carcinoma. I didn't think of microcystic adnexal carcinoma because of the intraoral location.

Michele Bisceglia: Microcystic adnexal carcinoma of the tongue (MAC): A tumor derived from Ebner's glands. Agree, Goram. Thank you. This is my first.

Ira Bleiweiss: Thanks. Never seen a case before.

Thomas Colby: Agree with diagnosis even though I have never heard of Ebner's glands. I thought the histology fit with that seen in microcystic adnexal carcinoma at other sites.

Kum Cooper: I have only seen this tumor on the eyelids and it certainly looks similar in morphology. Much thanks for sharing this case, Goran.

Ivan Damjanov: I am an old-fashioned pathologist, and I would have signed it out as adenoid cystic carcinoma, but would not argue with your diagnosis.

Otto Dietze: I agree with the diagnosis, infiltration pattern is even more pronounced than in several adenoid cystic carcinomas.

Hugo Dominguez-Malagon: No suggestions, this extraordinary case really resembles microcystic adnexal carcinoma of the skin, never heard of one in the tongue and of Ebner Glands.

Göran ElMBERGER: My case. Looking forward to your comments.

Vincenzo Eusebi: Very nice case. This is a syringoid-like carcinoma that wherever is localized (skin, salivary gland, breast) changes its name. The common feature to all sites is the fact that it is locally widely invasive wherever it appears. The localization in the tongue is really exceptional.

Giovanni Falconieri: Never seen MAC before, so I cannot add to the entity discussion. Very bland cytology, no? I must admit I have had some trouble in getting the right clues to the case however the infiltrating tentacular pattern at the periphery and perineurial invasion are convincing that this is malignant, beyond question. It would be nice to have follow up information once available. Thanks, Goran, for submitting this instructive and rare case.

Christopher Fletcher: Certainly this lesion looks like a perfect example of microcystic adnexal carcinoma – but I would not personally feel comfortable (or competent) to speculate about the cell/site of origin.

Cyril Fisher: This resembles microcystic adnexal carcinoma of skin and seems a good diagnosis.

Andrew Folpe: Why isn't this a pseudoglandular squamous cell carcinoma?

Jerónimo Forteza Vila: I agree with the diagnosis and is typical the perineurial infiltration.

Masaharu Fukunaga: It is great to meet you at Mexico City in June. I have never seen microcystic adnexal carcinoma except as a skin appendage tumor.

Allen Gown: Thank you for this interesting case.

Thomas Krausz: I agree with the diagnosis.

Janez Lamovec: This tumor is really histologically identical to syringomatous carcinoma or WHO microcystic adnexal carcinoma. I was not aware of its possible occurrence outside the skin, and I have also first heard of Ebner's glands. Thank you for education!

Thomas Mentzel: A very interesting neoplasm that shows indeed striking similarities to MAC (sclerosing sweat duct carcinoma) of the skin. Did neoplastic cells stain positively for cytokeratin 15, a marker that is supposed to be positive in MAC ?

Markku Miettinen: Agree on microcystic adnexal carcinoma.

Liz Montgomery: Nice case. Very infiltrative. Must be a nightmare for the surgeon to get good margins.

Santiago Ramon y Cajal: It looks like a Microcystic Adnexal Carcinoma.

Juan Rosai: This tongue tumor sure resembles microcystic adnexal carcinoma of skin, but if it really arises from Ebner's glands (never heard of them before), it may not be a good idea giving it the same name, being that MAC of skin is a type of skin adnexal (and specifically sweat gland) tumor.

Joshua Sichel: Agree with diagnosis. I will be interested to hear Bruce Wenig's comments.

Dominic Spagnolo: I can't think of a better designation than microcystic adnexal carcinoma - have never seen this before in the tongue. Thanks for the case.

James Strauchen: Fascinating case! The neurotropism is striking. I was previously unaware of Ebner's glands!

Saul Suster: This is certainly identical in pattern of growth and morphology to microcystic adnexal carcinoma of the skin. Had never seen one in the tongue before!

CASE NO. 8 – CONTRIBUTED BY GIOVANNI FALCONIERI:

Phil Allen: Large atypical schwannoma with scattered mitoses, nasal sinuses. I agree with Falco that this is probably benign but the large size, the mitoses, and the pleomorphism are worrying. I agree that follow-up should be vigorous.

Carlos Bacchi: Nice case of benign schwannoma in an unusual location.

David Ben-Dor: I haven't seen one either- yet.

Gerald Berry: Agree. Nice case.

Michele Bisceglia: Sinonasal schwannoma. I think you are right, Falco, but I am a little worried with the mitotic rate present here. Look forward to others' opinions.

Ira Bleiweiss: Agree.

Thomas Colby: Agree with diagnosis. Favor benign even though it is a little cellular.

Kum Cooper: Thank you Falco. Looks a little "cellular" without the lymphoid aggregates.

Ivan Damjanov: Agree, to me it looks benign.

Otto Dietze: Rare location but typical morphology, I agree that it looks benign.

Hugo Dominguez-Malagon: Completely agree with the diagnosis of sinonasal Schwannoma.

Göran Elmberger: Thanks. As you stated, very uncommonly seen in SN tract submucosal. Agree with dx. Add to list of differential though farfetched glial heterotopia.

Vincenzo Eusebi: Thank you very much for this case.

Cyril Fisher: The diffuse S100 protein positivity supports sinonasal schwannoma which is typically non-encapsulated.

Christopher Fletcher: Indeed a very nice example of sinonasal schwannoma, of which we published a small series some years ago (Hasegawa et al, *Mod Pathol* 1997; 10:777-784). The consistent lack of encapsulation of schwannomas in this anatomic region can sometimes make distinction from a malignant tumour, particularly in the setting of hypercellularity, more difficult.

Andrew Folpe: Agree with schwannoma. Most of the ones in the nose aren't encapsulated, like SFT's in this location. It hadn't occurred to me that they were that rare. I'm sure we have quite a few if anyone feels like writing a series up.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Agree. I have never seen sinonasal Schwannoma, thank you, Falco.

Thomas Krausz: Beautiful example. I have seen similar examples without capsule at other mucosal sites (esophagus, stomach).

Janez Lamovec: Agree with the diagnosis. Nice case.

Thomas Mentzel: Thanks for the nice case. It has been reported that schwannomas in this anatomic location lack a capsule what may cause diagnostic problems (*Mod Pathol* 1997; 10: 777-784), and it has been speculated that schwannomas in this location as well as in the gastrointestinal tract may arise from autonomic nerves (*Histopathology* 1995; 27: 355-360).

Markku Miettinen: Mucosal cellular schwannoma with mitotic activity, probably benign.

Liz Montgomery: Nice example of upper aerodigestive tract schwannoma said to be infiltrative. They seem under-recognized but probably not rare. I guess other group members will have additional comments (Hasegawa SL, Mentzel T, Fletcher CD. Schwannomas of the sinonasal tract and nasopharynx. *Mod Pathol.* 1997 Aug;10(8):777-84).

Santiago Ramon y Cajal: From a morphologic point of view, it looks like a Schwannoma.

Juan Rosai: What a relief! Finally a typically, easily recognizable example of a familial tumor! The location is unusual, but well documented (*Mod Pathol* 10:777-784, 1997; *Arch Pathol* 127:1196-1199, 2003). This case shows nicely a feature emphasized by Chris Fletcher, i.e., that schwannomas of the upper aerodigestive tract are usually unencapsulated, in contrast to their counterparts in the usual places.

Joshua Sickel: Agree with diagnosis. I've seen a case of solitary fibrous tumor in this location, but never schwannoma!

Dominic Spagnolo: Nice example of a sinonasal schwannoma, Giovanni. I saw a cellular variant in 2006 which presented as a nasal polyp. As is typical in this site, it too was unencapsulated.

James Strauchen: Schwannoma. The histology seems typical even if the location is not. I have never seen one in the sinus before, although we recently had a similar lesion in the mouth.

Saul Suster: Agree with the diagnosis. Andrew, I think you should indeed take this as a project for one of your fellows. You could pull these cases from your files (which I'm sure are numerous) and ask AMR members to contribute theirs too. This appears to be an unusual location for these tumors and a large series might shed some new insights or reinforce known concepts on these lesions at this site.

CASE NO. 9 – CONTRIBUTED BY MASA HARU FUKUNAGA:

N. Volkan Adsay: Excellent example.

Phil Allen: Mesonephric adenocarcinoma of the uterine cervix with typical and atypical mesonephric hyperplasia. An excellent case. Thanks for the contribution, Masa.

Carlos Bacchi: Thanks for the case. It is interesting to see the mesonephric hyperplasia side by side with the adenocarcinoma.

David Ben-Dor: Thanks for sharing with us an example of a tumor which is referred to often. I'm not totally certain as to where the benign and atypical portions begin and end, but is there anything specific about the malignant portion that should make one think of mesonephric carcinoma in the absence of the connection with the benign portion? Most recently, I had a provocative encounter with this topic in a routine bilateral salpingo-oophorectomy from a middle aged woman for ovarian cyst. A random section from the contralateral adnexa showed a structure which reminded me of epididymis. After puzzling over this for a while, it occurred to me that this could be a mesonephric rest from the broad ligament which are known to occur and which apparently developed more than usual to the point of forming an organoid structure. It was a pleasure seeing you and your lovely family again in Mexico.

Gerald Berry: Agree. Beautiful example.

Michele Bisceglia: Mesonephric adenocarcinoma of the uterine cervix with mesonephric hyperplasia. Beautiful example, Masa. Thanks for contributing this rare tumor. I also agree on the spectrum of the mesonephric duct proliferation in this case.

Ira Bleiweiss: Definitely looks mesonephric.

John Chan: Beautiful case illustrating the spectrum of changes from mesonephric hyperplasia to atypia to adenocarcinoma.

Thomas Colby: Agree with diagnosis. Very nice demonstration of carcinoma associated with its presumed tissue of origin.

Kum Cooper: Lovely example, Masa, with the beautiful background of hyperplasia and atypia! Pity that the CD10 was not positive.

Ivan Damjanov: Agree with both diagnoses

Otto Dietze: Convincing diagnosis on basis of morphology and IHC.

Hugo Dominguez-Malagon: Beautiful case of mesonephric adenocarcinoma of the cervix, very well documented.

Göran Elmberger: Beautiful case. Certainly worth keeping in the differential diagnosis. Believe as you that there is risk of under recognition.

Giovanni Falconieri: Invasive, poorly circumscribed adenomatoid tumor with architecture pleomorphisms and malignant cytology. Looks nasty. Hope for the patient that this tumor has read the books.

Cyril Fisher: Looks like what you say!

Andrew Folpe: Agree with mesonephric adenocarcinoma. Very nice case.

Jerónimo Forteza Vila: I agree with the diagnosis.

Thomas Krausz: This is the most convincing example I have ever seen. Thank you very much.

Janez Lamovec: Beautiful case! Adenocarcinoma appears almost blastoid. The adjacent mesonephric remnant and foci of mesonephric hyperplasia are spectacular. Thank you, Masa, for this case.

Thomas Mentzel: Thanks for this wonderful case showing the mentioned three “components”.

Michal Michal: This is the most persuasive case of mesonephric adenocarcinoma I ever saw!

Santiago Ramon y Cajal: This is a very beautiful case of mesonephric adenocarcinoma, especially valuable for the teaching set because it shows typical and atypical mesonephric hyperplasia.

Juan Rosai: Very nice demonstration of mesonephric gland hyperplasia combined with mesonephric gland adenocarcinoma. The areas of hyperplasia are particularly noteworthy because of their cystically dilated quality and their inspissated eosinophilic thyroid-like content.

Joshua Sickel: We have seen a few mesonephric adenocarcinomas in our department. Thanks for the great teaching case.

Dominic Spagnolo: Spectacular case of mesonephric carcinoma – thanks, Masa.

James Strauchen: Mesonephric carcinoma of the uterine cervix arising in mesonephric hyperplasia. Wow! Are these related to FATWO (female adnexal tumor of probable Wolffian origin)?

CASE NO. 10 – CONTRIBUTED BY THOMAS KRAUSZ:

N. Volkan Adsay: I thought it was going to be SFTBP mutation case (just kidding). Fascinating case

Phil Allen: Chronic pneumonitis of infancy due to *abca3* gene mutation. Thanks for the contribution, Thomas. These genetic disorders causing neonatal morphologic pathology are too hard for old adult pathologists like myself.

Carlos Bacchi: Thanks for the comprehensive and informative discussion.

David Ben-Dor: Thomas, you are a true renaissance man – I didn't know that your protean interests include the pathology of congenital neonatal disorders. The genetics is involved and beyond me. One aspect I'm curious about: I went over the slide before reading any of the printed materials- the slide looked like the lung, but I was puzzled over the absence of bronchial cartilage. Is this due to my not seeing lung sections from infants often enough or is this part of the disorder?

Gerald Berry: Nice example and discussion.

Michele Bisceglia: Chronic pneumonitis of infancy due to *abca3* gene mutation. Difficult case, Thomas. Congratulations. Excellent diagnosis mainly based on morphological findings.

Ira Bleiweiss: ???

John Chan: Many thanks for sharing this most instructive case! Never heard of ABCA3 mutation before.

Thomas Colby: Organizing acute lung injury consistent with ABCA 3 gene mutation.

Kum Cooper: Thank you, Thomas, for the education on this rare entity.

Ivan Damjanov: Agree. There is no point in arguing with data which are quite convincing! I would have signed it out probably as some type of chronic pneumonitis/bronchopulmonary dysplasia. Only God knows how many cases of this type did I miss and assign to some pulmonary dysmaturity

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

Hugo Dominguez-Malagon: No experience with *abca2* gene mutation and pneumonitis, very illustrative case, thank you.

Göran Elmberger: Thanks for this great case. We have ECMO centre here so I have been fortunate to see a few surfactant protein B deficiency/mutations. As you write, the histopathology seems to be rather non-specific with one case presenting with classical alveolar proteinosis pattern. Also recommend work-up including IHC, EM and molecular mutation analysis.

Vincenzo Eusebi: Thank you very much for this instructive case.

Giovanni Falconieri: My slide features a fragment of partially collapsed lung consistent with term pregnancy, so there is at least evidence of tissue immaturity for a 5 wk-old baby. Some alveoli are filled with granular material and desquamated cells with bland nuclei and granular cytoplasm. And that's the best I can say looking at the "unknown" slide. The rest is impossible Thanks, Thomas, for providing this challenging case.

Cyril Fisher: Pneumonitis. No comment.

Christopher Fletcher: Thank you, Thomas, for introducing me to this condition of which I was not previously aware.

Andrew Folpe: I'm totally out of my league on this one.

Jerónimo Forteza Vila: Very interesting and elaborated case.

Masaharu Fukunaga: Very unusual case. Thank you, Thomas for the slide, beautiful EM figures and informative description.

Allen Gown: Thank you for this informative case!

Thomas Mentzel: Many thanks for the excellent teaching on this rare disorder.

Santiago Ramon y Cajal: Thank you for this very interesting case of chronic pneumonitis of infancy caused by abca3 gene mutation.

Juan Rosai: This is all news to me. Thanks for keeping me updated.

Joshua Sickel: Thanks for submitting this rare and unusual case. I learned a great deal from your excellent discussion.

Dominic Spagnolo: Thank you for the education, Thomas - I was not aware of this. I got as far as chronic pneumonitis. ??cause.

James Strauchen: A new one for me! Thank you for this fascinating case.

Saul Suster: Abracadabra mutation? Now you've really made me feel like an "old-geezer pathologist"! Thank you for the update!!!

CASE NO. 11 – CONTRIBUTED BY THOMAS MENTZEL:

N. Volkan Adsay: It would be interesting to know the genetic makeup of the two components and how these mixed types behave.

Phil Allen: Liposarcoma with mixed lipoma-like and myxoid patterns, voluntary muscle, upper anterior right thigh. I expect this will behave as a myxoid liposarcoma, i.e., it is likely to have considerable metastasising potential over time. I am personally cautious about interpreting, or over-interpreting, the FISH results.

Carlos Bacchi: Nice case.

David Ben-Dor: Dedifferentiated liposarcoma would seem reasonable to a non-soft tissue aficionado.

Michele Bisceglia: Liposarcoma, mixed type. Agree, Thomas. Fully investigated.

Ira Bleiweiss: Myxoid liposarcoma.

Thomas Colby: Agree with diagnosis. 30 years ago I saw a liposarcoma in Saudi Arabia that was half again larger than the size of a rugby ball. I recall it had every histologic pattern of liposarcoma that I recognized at that time, including myxoid, round cell, sclerosing, well differentiated, and pleomorphic. Needless to say, cytogenetics was hardly a twinkle in anyone's eyes at that time (according to Goggle, rugby balls must be between 280 and 300 mm in length with an end-to-end circumference of 740-770 mm, and width of 580 and 620 mm).

Kum Cooper: Thank you, Thomas, for this well documented example of mixed liposarcoma-both morphological and molecular. I have seen an example of well-diff/dediff retroperitoneal liposarcoma with interspersed areas of myxoid liposarcoma. Interestingly the dediff areas were low-grade in character. This tumor has already recurred about three times over the last few years.

Ivan Damjanov: Agree. Nice demonstration.

Otto Dietze: Rare tumor, well documented, thank you.

Hugo Dominguez-Malagon: I assume that this is the first genetically proven case of a mixed liposarcoma, congratulations.

Göran Elmberger: Beautiful case with fairly classical lipoma like atypical lipomatous tumour and myxoid liposarcoma. I note that as late as 2002 in the WHO blue book fascicle on soft tissue chapter on myxoid liposarcoma, the lack of genetic evidence to support the concept of mixed type liposarcoma is still expressed. This case and the one you cite in your description certainly seem to bear hard evidence. The interpretation of the genetical findings is not so clear to me. Does not really seem to support clonal evolution-dedifferentiation. Collision tumor?? Common precursor lesion – divergent clonal evolution? Any ideas?

Vincenzo Eusebi: Very nice and unusual case of intramuscular mixed myxoid /well differentiated liposarcoma.

Giovanni Falconieri: Thank you for submitting this unusual variant of LPS.

Cyril Fisher: Mixed type liposarcoma, very rare case, thanks, Thomas

Christopher Fletcher: Thanks for this interesting and apparently quite unusual case. The morphology alone would likely have led me to diagnose this as a myxoid liposarcoma with some morphologically well-differentiated areas as one quite often sees – and, even in these well-differentiated areas, the lesion has more prominent myxoid stroma and delicate thin-walled blood vessels than in conventional ALT. Can we be sure that amplification of MDM2 and CDK4 did not occur as a consequence of the (12;16) translocation? It would be very interesting to know if you could detect the (12;16) translocation in microdissected well-differentiated areas – I have a strong suspicion that this might be the case.

Andrew Folpe: This looks like a conventional myxoid liposarcoma with some mature fat to me. My understanding, from talking with Andre Oliveira, is that mdm2 amplification can be seen in a variety of sarcomas, including conventional myxoid liposarcoma. There is a report in Diagn Mol Pathol 2004; 13: 92 of a conventional myxoid LPS with mdm2 amplification.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: A beautiful case of liposarcoma, mixed type, which was also analyzed by molecular studies. Thank you very much.

Allen Gown: Lovely case!

Thomas Krausz: The “well differentiated liposarcomatous” component does not show classic “bizarre stromal cells”

Janez Lamovec: We see quite a number of liposarcoma cases here but I don't recall to have seen a convincing case of mixed type of liposarcoma.

Markku Miettinen: Myxoid liposarcoma, with a well-differentiated liposarcoma-like component. Certainly it is an interesting possibility that there would be dual molecular changes. Also it would be of interest whether myxoid liposarcoma CHOP gene rearrangement is absent in the well-differentiated component.

Liz Montgomery: My slide seems only to have the myxoid liposarcoma component although in areas it has matured into something lipoma-like punctuated by capillaries and myxoid material but no large hyperchromatic cells as one usually expects in WD LPS/ALT. It seems unusual to have negative MDM2 IHC and have amplification by FISH but of course I would not have done any of the molecular because it all looks like myxoid liposarcoma to me!

Santiago Ramon y Cajal: The two components of this mixed type liposarcoma are very well defined. It is very interesting to have the molecular confirmation.

Juan Rosai: Great case, which demonstrates conclusively that mixed myxoid-well-differentiated liposarcoma exists, and that its two components have their respective molecular markers. When we wrote a series on liposarcomas with the CHAMP group (Am J Surg Pathol 20: 1047, 1996; 20: 1182, 1996) we included a few cases that we thought represented mixed tumors of this kind, but we were criticized with the argument that they were well-differentiated liposarcomas with prominent secondary myxoid changes. Interestingly, in the classic paper by Enzinger on liposarcoma (Virchows Arch 335: 367, 1962), mention is already made about the fact that in some well-differentiated liposarcomas of adult type (which today would be called atypical lipomatous tumors) “the mucoid matrix was sometimes abundant and the pattern approached that of a more mature myxoid form”.

Joshua Sickel: Beautiful composite tumor. Thanks for the great discussion.

Dominic Spagnolo: A beautifully studied rare mixed liposarcoma - thank you. Perhaps these may be more common than we think?

James Strauchen: Myxoid/round cell liposarcoma and atypical lipomatous tumor/well differentiated liposarcoma. Since the two components have distinct molecular abnormalities is this simply a collision tumor?

Saul Suster: Very nicely documented case of mixed liposarcoma. We saw several examples like this from the files at Ohio State University. Obviously these cases go against current dogma that "requires" a specific set of cytogenetic abnormalities to classify lipomatous tumors. I think Dr. Rosai's suggestion that morphologic complexity is likely to be mirrored by molecular and cytogenetic complexity is true – unfortunately these tumors not only refuse to read the surgical pathology books but the molecular-genetic ones also! Our quest for rigid Aristotelian categorization of everything continues to be foiled by nature.

CASE NO. 12 – CONTRIBUTED BY ELIZABETH MONTGOMERY:

N. Volkan Adsay: Some areas reminded me of palisaded myofibroblastoma with amianthoid fibers and giant rosette formation. Focal schwannoma like features and a groin location would have been good for that entity too.

Phil Allen: Histologically bland, S100 negative, neuroid/ependymoid spindle cell tumor with amianthoid fibers and metaplastic bone - ?intranodal hemorrhagic spindle cell tumor. I don't know what this is. The partial shell of metaplastic bone raises the possibility of an ossifying fibromyxoid tumor but that diagnosis fits no better than the other suggestions. It seems to me to be closer to Saul's intranodal haemorrhagic spindle cell tumor than to anything else. I will be interested in Saul's opinion.

Carlos Bacchi: I would favor palisaded myofibroblastoma of the lymph nodes but I would rather wait for the experts' opinions.

David Ben-Dor: Where would it come from?

Gerald Berry: I think that ectopic ependymoma fits best although the location is certainly odd.

Michele Bisceglia: ? Ectopic ependymoma. I would have thought of intranodal palisaded myofibroblastoma, but I am not sure of what this lesion is. Cannot explain GFAP positivity. Look forward to others' opinions.

Ira Bleiweiss: I would have thought this was of nerve sheath origin.

John Chan: Morphologically, I favor a diagnosis of palisaded myofibroblastoma. The rosettes seen here are different from the perivascular rosettes seen in typical ependymoma.

Thomas Colby: Not sure what this is. There are parts that look good for ependymoma but given the location of course my first thought was of a peculiar looking palisaded myofibroblastoma. I look forward to what others think about it.

Kum Cooper: I must confess that I would have called this an intranodal myofibroblastoma given the location and peripheral nodal tissue. My slide also has metaplastic bone. Interestingly the MSK group showed that the extra-axial ependymomas (Am J Surg Pathol, May 2008) are both morphologically and immunohistochemically distinct but they both expressed GFAP diffusely.

Ivan Damjanov: We had a lively discussion at our place about this lesion with our resident and we still do not know why is this not a palisaded myofibroblastoma? Is the GFAP so convincing?

Otto Dietze: I cannot offer another diagnosis; it reminds me of palisaded myofibroblastoma.

Hugo Dominguez-Malagon: Palisaded myofibroblastoma seems reasonable to me. The intercellular material has the appearance of dense collagen.

Göran ElMBERGER: Difficult case. I believe final interpretation is strongly dependent on outcome/interpretation of IHC and if possible EM. Given the right support, I could reluctantly accept the suggested diagnosis. Cited GFAP over expression does partially support it. The reason for hesitation is the location within inguinal lymph node. As you suggest, my main differential is intranodal palisaded myofibroblastoma. The characteristic pseudorosettes in this case are mainly with distinct amianthoid fibres-like structures and possibly also of perivascular type. I could not find true rosettes of ependymoma-type. Secondary effects such as haemorrhage, fibrosis and bone formation are probably rather non-specific. Cyclin D1 has been reported as a good marker for IPM. Other ddx to be contemplated are soft tissue myoepithelioma and extrapleural SFT. Extended IHC might be of value to penetrate.

Vincenzo Eusebi: Ependymoma is a nice guess, but on H&E I would be more happy to regard this tumour as palisaded myofibroblastoma with amianthoid bodies.

Giovanni Falconieri: Palisaded myofibroblastoma seems to fit better given size and overall lesion morphology site. However, the fibrillary quality of cytoplasm would not go along well with this as well as other options that Dr. Montgomery mentioned. So, why not ependymoma?

Cyril Fisher: I agree with your observation, although clinically bizarre. EM would be of interest.

Christopher Fletcher: Without knowing about the immunohistochemistry, I would have guessed that this was a palisaded myofibroblastoma which seems to be located in lymph node. Having said that, I have seen a couple of examples of ectopic ependymoma in the sacrococcygeal region which gave rise to inguinal lymph node metastasis.

Andrew Folpe: I'm not really sure. I'd favor myofibroblastoma. Showed it to Scheithauer, who didn't think it was an ependymoma.

Jerónimo Forteza Vila: Thank you for this so interesting case.

Masaharu Fukunaga: A very interesting case. I have a similar case in the foot of a young lady. It looks like palisading myofibroblastoma?

Allen Gown: I'm not sure why this isn't just a nerve sheath tumor, and this would be supported by the immunophenotype you found.

Thomas Krausz: Before reading your discussion, I was considering palisaded myofibroblastoma of lymph node (I understand that immuno does not support this diagnosis). Ependymoma is a great idea but

Michal Michal: It has some features of ossifying fibromyxoid tumor of the soft tissues.

Thomas Mentzel: What a surprise ! I was thinking on intranodal myofibroblastoma with amianthoid fibres.

Markku Miettinen: Palisading myofibroblastoma of lymph node, with metaplastic bone.

Santiago Ramon y Cajal: I would favor a palisaded myofibroblastic tumor of the lymph node with amianthoid fibers.

Juan Rosai: Ectopic ependymoma? No way! One is a little nervous arguing the case with a soft tissue tumor expert and with one of the foremost authorities in neuropathology, but this has to be a mesenchymal neoplasm. Specifically, its inguinal location, lymph node remnant and "amianthoid fibers" are consistent with the "intranodal hemorrhagic spindle cell tumor with amianthoid fibers" of Suster et al (Am J Surg Pathol 13: 347,1989) (sorry, I meant palisaded myofibroblastoma) despite the lack of evidence of recent or old hemorrhages and the stated negativity for smooth muscle actin.

Joshua Sichel: I assumed this was a palisaded myofibroblastoma (Suster-Rosai tumor). Once you've decided on a diagnosis of intranodal ependymoma, can an occult metastatic lesion ever be ruled out?

Dominic Spagnolo: I favor a palisaded myofibroblastoma. Any FISH done in respect of hyalinizing spindle cell tumor with giant rosettes, which was my other thought too? I don't like it much for ependymoma.

James Strauchen: I thought this was an intranodal hemorrhagic spindle cells tumor with amianthoid fibers/palisaded myofibroblastoma. There is some lymphoid tissue at the periphery which may be residual lymph node. These are misdiagnosed as schwannoma because of failure to appreciate the nodal nature of the lesion.

Saul Suster: Very difficult and unusual case! Everything about this tumor is off for either diagnosis. Although there is definitely lymphoid tissue present, there are no sinuses making it difficult to determine whether this is in an actual lymph node (at least in my slide). The morphology on H&E is absolutely perfect for palisaded myofibroblastoma (WHO-preferred terminology!), except for the rim of bone and the fibrillary quality of the cytoplasm. The absence of SMA staining doesn't bother me as much as the positive GFAP. On the other hand, GFAP positivity in ependymoma is usually diffuse rather than focal, so I wonder if this may not have been spurious staining. Another stain you might want to try is CD99, which is strongly and diffusely positive in all types of ependymoma. Things against ependymoma are the location, the metaplastic bone, and the amianthoid fibers (which to my knowledge have apparently not been described in ependymoma before – but everything is possible under the sun!). Things against palisaded myofibroblastoma include the IHC stains and the lack of intranodal definition. I think this case could definitely benefit from an ultrastructural examination. The clinical evolution of a benign tumor without recurrence and without any lesion in proximity to the spinal cord in my mind favors a palisaded myofibroblastoma. I also think an unusual form of palisaded myofibroblastoma with granular/fibrillary cytoplasm and metaplastic bone would still be more likely than an ectopic ependymoma at this location.

CASE NO. 13 – CONTRIBUTED BY GIUSEPPE PELOSI:

N. Volkan Adsay: We occasionally see this in the retroperitoneum and peripancreatic region where cystic degeneration can be quite prominent, such that it has been dignified in the literature as “multicystic schwannoma”.

Phil Allen: Large (16 cm) ancient schwannoma, posterior mediastinum. I only start to worry about these when the S100 is negative, whereupon, I usually change my diagnosis to pleomorphic hyalinizing angiectatic tumor.

Carlos Bacchi: Nice example of neurinoma of the mediastinum with extensive regressive changes.

David Ben-Dor: I agree that the large size and relatively inaccessible location would make one uncomfortable in making a benign diagnosis in the presence of such worrisome microscopic findings.

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Neurinoma with extensive regressive changes including pseudocystic spaces (ancient Schwannoma). Classical example of this lesion. Thanks, Giuseppe. Likely, this is the first case (of ancient type) I see in the mediastinum, despite the fact of having seen several classic schwannomas in the posterior mediastinum (which parenthetically is a classic site for schwannomas, even for dumbbell shaped examples). Instead, I have personally seen ancient variants in several others locations, even exotic, including the most recent one involving the adrenal (primary of the adrenal).

Ira Bleiweiss: Schwannoma.

Thomas Colby: Agree with diagnosis. I thought I had seen a few ganglion cells (i.e. ancient ganglioneuroma) but their presence was apparently not borne out immunohistochemically.

Kum Cooper: Ancient schwannoma. Some of the cells in my slide looked epithelioid but I could not find any melanin (except for the hemosiderin).

Ivan Damjanov: Ancient schwannoma.

Otto Dietze: I agree with your diagnosis, however, I find it difficult to differentiate it from ganglioneuroblastoma on pure morphological grounds if you have to deal with a small needle biopsy (I remember a recent case with too less material for IHC).

Hugo Dominguez-Malagon: I agree, nice case of ancient schwannoma.

Göran Elmberger: Agree. Neurilemmoma with degenerative – ancient –changes. Uncommon lesion. Characteristic location. Thanks.

Vincenzo Eusebi: Thank you very much for sending this case of ancient schwannoma.

Giovanni Falconieri: Totally agree with ancient schwannoma. I also believe that the irregularly thickened vessel walls are another clue to lesion benignancy.

Cyril Fisher: Schwannoma with cystic change.

Christopher Fletcher: Nice example of ancient schwannoma.

Andrew Folpe: Agree with ancient schwannoma.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Ancient schwannoma, agree. It looks like pleomorphic hyalinizing angiectatic tumor, but the present case was positive for S100 and it is against that tumor.

Thomas Krausz: Nice example.

Thomas Mentzel: An interesting example of ancient schwannoma showing quite prominent (pseudo)cystic spaces.

Markku Miettinen: Agree on schwannoma with cystic change.

Liz Montgomery: Nice schwannoma.

Santiago Ramon y Cajal: Thank you for this example of mediastinal ancient schwannoma.

Juan Rosai: Nice case of "ancient" schwannoma. The fact that Lauren Ackerman was apparently the first to use the qualifier "ancient" makes me nostalgic, just as the name "neurinoma" used by Giuseppe Pelosi, a term which I think was first used by Verocay, an Uruguayan pathologist.

Joshua Sickel: Nice example of schwannoma with ancient change.

Dominic Spagnolo: Nice example of a degenerate, ancient cystic schwannoma.

James Strauchen: Schwannoma with "ancient" change. Nice example! We had a recent hemangioma with similar changes in the stroma.

Saul Suster: Agree with diagnosis. The cystic changes can be quite prominent in this tumor. We had a case a few years ago that looked like a veritable Swiss cheese!

CASE NO. 14 – CONTRIBUTED BY SANTIAGO RAMON y CAJAL:

N. Volkan Adsay: Nice case.

Phil Allen: Primary ovarian fibrosarcoma. Some of the tumor resembles a leiomyosarcoma. I note that Irving and McCluggage (reference 10) had trouble separating ovarian leiomyosarcomas from fibrosarcomas, despite the assistance of immunohistochemistry.

Carlos Bacchi: I agree.

David Ben-Dor: Some years ago, I saw a cellular spindle tumor of the ovary which I sent off in consultation and remember being rather surprised when the consultants diagnosed it as benign. Thus, this type of case can be confusing. Here the high mitotic count and Ki-67 positivity are in favor of malignancy.

Gerald Berry: The histology and immunoprofile supports fibrosarcoma.

Michele Bisceglia: Primary ovarian fibrosarcoma. Agree, Santiago. I think that necrosis and atypia coupled with mitotic activity exclude mitotically active cellular fibroma.

Ira Bleiweiss: Agree.

Tom Colby: Agree with diagnosis of sarcoma (i.e. fibrosarcoma).

Kum Cooper: Fibrosarcoma (ovary). Dr. Young and Clement (ref 13: Am J Surg Path Aug 2006) outlined their criteria to rule out mitotically active cellular fibroma (that have an uneventful outcome even though they can have up to 19 mitoses/10HPF). Essentially, the diagnosis for fibrosarcoma, as in the present case, must be accompanied by cytological atypia. Nevertheless long term follow-up is essential in all mitotically active fibromas.

Ivan Damjanov: Agree with the diagnosis of fibrosarcoma, although without immunohistochemistry I favored the diagnosis of leiomyosarcoma.

Otto Dietze: A difficult diagnosis in absence of a specific IHC profile.

Hugo Dominguez-Malagon: Ovarian fibrosarcoma, nice case.

Göran Elmberger: Thanks for this unusual case. Agree with dx.

Giovanni Falconieri: Agree that this is malignant; once other sarcomatoid lesions are ruled out, fibrosarcoma is the best I could say as well. Nice case, Ramon.

Christopher Fletcher: To me, cellular fibromas and fibrosarcomas of ovary always seem to have more prominent eosinophilic cytoplasm than their counterparts elsewhere, likely reflecting that these are in reality specialized stromal cells.

Cyril Fisher: Ovarian fibrosarcoma seems a good diagnosis if everything else is ruled out. It would be of interest to know whether the cells are ultrastructurally fibroblastic.

Andrew Folpe: Ovarian fibrosarcoma sounds pretty good.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: Agree. How about CD21, CD35, a possibility of follicular dendritic c cell tumor?

Allen Gown: I wonder if markers such as CD10 or estrogen receptor were present in these tumor cells.

Thomas Krausz: Agree with diagnosis.

Janez Lamovec: Malignant spindle cell tumor of ovary. I am not sure if I called it fibrosarcoma.

Thomas Mentzel: Thanks for this nice example of a rare entity in this location.

Markku Miettinen: Malignant sarcomatoid neoplasm. Fibrosarcoma is possible but cannot directly connect with a malignant fibrothecoma. One possibility could be a somatic sarcoma (fibrosarcoma) arising in a teratoma. Difficult to prove, unless residual elements of teratoma are found. Cysts may raise some suspicion of such. Studies for inhibin and calretinin would be of interest for sex-cord stromal tumor connection.

Liz Montgomery: Very interesting case. The monotonous cytology suggests that this is a translocation sarcoma (?akin to infantile fibrosarcoma/mesoblastic nephroma), though I cannot claim to know anything about ovarian primary lesions that look like this.

Juan Rosai: This is a sarcoma all right, but it just does not look like a bonafide fibrosarcoma, which I would regard a diagnosis of exclusion. I know this sounds crazy and is surely wrong, but one area reminded me of a tumor of dendritic/reticulum cells. What about doing CD21 and CD23 stains?

Joshua Sichel: Thanks for this collector's item.

Dominic Spagnolo: Agree with ovarian fibrosarcoma. Without the history, was thinking GIST.

James Strauchen: Primary ovarian fibrosarcoma. Thank you, I have never seen one before!

Saul Suster: This for sure is malignant. Never seen a fibrosarcoma of the ovary before. There seems to be a subtle nesting pattern of growth seen in some areas that is somewhat reminiscent of a transitional cell proliferation. Has a cytokeratin been done in this tumor? Could this be a malignant ("proliferating") Brenner tumor (i.e., transitional cell carcinoma of the ovary) with sarcomatous overgrowth?

CASE NO. 15 – CONTRIBUTED BY JOSHUA SICKEL:

N. Volkan Adsay: Great example. None of the three cases of ECIPS (epidermoid cyst in intrapancreatic accessory spleen) in my files have goblet cells to this extent (only one had scattered goblet cells). We do see goblet cells quite often in lymphoepithelial cysts though.

Phil Allen: True mucoepidermoid cyst arising within an intra pancreatic accessory spleen. Yet another amazing case. I wonder if this is in any way related to lymphoepithelial cysts in the pancreas. I agree that the mucin production in the epithelial cells makes this case apparently unique. Thanks too for the work-up and references.

David Ben-Dor: A lesion within a lesion within a lesion- like those Russian babushka dolls. In any case, extremely interesting.

Gerald Berry: Nice example. I have seen epidermoid cysts and squamous carcinoma arising from the epidermoid cyst. This case displays the admixture of goblet cells and squamous cells.

Michele Bisceglia: True epithelial "mucoepidermoid" cyst arising within an intrapancreatic accessory spleen. Never seen one such sophisticated case before. Have not seen an intrapancreatic accessory spleen without a cyst either. Instead, I take here the opportunity to say that I have seen 2 cases in which Langerhans' cell islets heterotopically occurred in the spleen (one of these was in consultation with the Langerhans' groups of cells having being misinterpreted as metastatic carcinoid).

Ira Bleiweiss: A new one for me. Very Warthin's-like.

John Chan: A spectacular case of intrapancreatic accessory spleen with epithelial cyst! Have not seen this before. In splenic epithelial cysts, some mucinous cells can be present among the squamous or squamoid cells, but rarely are they as prominent.

Thomas Colby: Mucoepidermoid cyst sounds reasonable, but in other sites, notably the salivary glands (cousins to the pancreas) might we not call this a low-grade mucoepidermoid carcinoma?

Kum Cooper: I am intrigued by the epithelial lining which looks very much urothelial to me. Whilst the p63 is not discerning (from squamous), perhaps an uroplakin should highlight the umbrella cells?

Ivan Damjanov: Agree. It is probably just a variant of the more common pure epidermoid cyst in an ectopic spleen.

Otto Dietze: I was unaware of this association like you.

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

Göran Elmberger: Great case. Agree with the diagnosis and interpretation. Only comment- I sometimes have some problems in establishing the threshold towards low-grade mucoepidermoid carcinoma.

Vincenzo Eusebi: Very nice case of giant epidermoid cyst within an intrapancreatic accessory spleen and occasional mucous cells.

Giovanni Falconieri: Quite a case! Inclusion cyst in an intrapancreatic spleen!

Christopher Fletcher: Thanks Josh – I have never seen anything like this – it seems to me that you are almost ready to work in San Giovanni Rotondo !

Andrew Folpe: What a bizarre case! Definitely a cyst with mucoepidermoid lining within an intrapancreatic spleen. What exactly this means, I have no idea. Why isn't it a mucoepidermoid carcinoma?

Jerónimo Forteza Vila: I agree with the diagnosis. It is good to know that it can exist, this entity.

Masaharu Fukunaga: I have never seen this type of epithelial cyst in an intrapancreatic accessory spleen. Thank you very much for sharing the extremely unusual lesion with a beautiful gross picture.

Thomas Krausz: Amazing combination of components. I haven't seen this before. I am also wondering whether in addition to the goblet cells, are there rare neuroendocrine cells in the epithelium – so I would do immuno in this direction.

Janez Lamovec: Most interesting. Never heard or seen before.

Thomas Mentzel: A wonderful case!

Markku Miettinen: Agree on intrapancreatic spleen with epithelial cysts (apparently immunohistochemistry does not support mesothelial derivation).

Liz Montgomery: Very cute and presumably very heterotopic!

Santiago Ramon y Cajal: Very nice case of true epithelial mucoepidermoid cyst arising within an intrapancreatic accessory spleen.

Juan Rosai: Another green dragon. I have seen several cases of epithelial-lined cysts of the spleen, but they were all epidermoid, whereas this is clearly mucoepidermoid (or adenosquamous). I cannot even begin to figure out the pathogenesis, although the fact that the spleen was intrapancreatic probably has something to do with it.

Dominic Spagnolo: Fascinating case! I had stumbled across this in the literature only, but have never seen a case. It is spectacular. Mucinous cells have rarely been mentioned in the largely epidermoid linings (Pathol Int 1994; 44:652-654).

James Strauchen: Most epidermoid cysts of the spleen are believed to arise by squamous metaplasia of mesothelial inclusions, but ours seems truly pancreatic!

Saul Suster: Never seen this before! Thank you for the contribution.

CASE NO. 16 – CONTRIBUTED BY ELVIO SILVA:

N. Volkan Adsay: There is a similar type of pattern of carcinoma in the pancreas. Unfortunately, in the pancreas, the term microcystic has already been used for other entities. I would like to illustrate this pattern in a publication but don't know which term to use for it: vacuolated?, secretory?. Would greatly appreciate any suggestions.

Phil Allen: Primary microcystic left ovarian carcinoma with signet ring cells associated with an adenofibroma. Once again, this is the first case I have recognized. Thanks for the contribution and the reference.

Carlos Bacchi: Thanks, Elvio, for teaching me how to differentiate metastatic from primary carcinoma of the ovary. As you know, we often face this diagnostic dilemma.

David Ben-Dor: The fact that signet ring cells can be present in mullerian tumors may not be widely appreciated and can lead to confusion. Recently, we had a case of primary peritoneal carcinoma presenting as massive ascites with numerous signet ring cells in the effusion which obviously brought up the issue of metastasis from an abdominal non-gynecological primary. GI workup was negative. The patient eventually underwent bilateral B.S.O., and in one tube there was a small mucosal epithelial mass also containing signet ring cells which was assumed to be the primary. I'm glad this possibility was pointed out to me. In this contributed case, the tumor cells in my opinion have a serous "look", with the basophilic cytoplasm and the large nucleoli. I don't follow the reasoning about the presence of cystic spaces supporting the lesion being primary instead of metastatic; also I thought that bilateral ovarian involvement is more a feature of metastatic tumors to the ovary (at least insofar as mucinous tumors are concerned). Interestingly, Young and associates have recently published two papers on signet ring cells in primary ovarian tumors- one stromal.

Michele Bisceglia: Primary ovarian carcinoma, microcystic type. This is the first case I have seen. Thank you, Elvio, for teaching.

Ira Bleiweiss: Agree.

Thomas Colby: I would have probably called this high-grade carcinoma but it does indeed show the features that Elvio described.

Kum Cooper: Thank you, Elvio. Never seen this pattern before. Without IHC, I was convinced this was metastatic! Have urothelial markers been done in your previous series?

Ivan Damjanov: Thanks for this slide—I would have signed it out as a clear cell adenocarcinoma of the ovary.

Otto Dietze: Thank you for this teaching case, the microcystic spaces seem to me the important diagnostic clue.

Hugo Dominguez-Malagon: Difficult case of primary ovarian carcinoma, easily confused with metastatic.

Göran Elmberger: Difficult to classify according to present WHO classification. Very peculiar look with targetoid structures. Combination with fibroma must be very unusual – not mentioned in standard textbooks. Teratomatous? I believe it fits what you described earlier in your cited publication as microcystic pattern even if the microcystic features in this case (my section) is not as typical as those published. Why did we stop using the unclassified/unclassifiable group? The earlier was part of most WHO classifications. Collective hubris or just presupposed?

Giovanni Falconieri: Very difficult. I could recognize clues to malignancy but I have missed the key features of the case. Thanks, Elvio, for submitting this challenging and unusual example of ovarian pathology.

Cyril Fisher: Microcystic carcinoma, very interesting. Useful discussion, thanks.

Andrew Folpe: Agree. Nice example of something I haven't seen before- thanks.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: I thought it represented the metastatic lesion. Is the entity of "microcytic type carcinoma of the ovary" prevailed among OB-GY pathologist?

Thomas Krausz: This case fooled me as I was considering metastasis. Thanks for the helpful clues.

Thomas Mentzel: Which kind of ovarian carcinoma represents the shown case?

Markku Miettinen: Thank you, new entity for me. Certainly makes you wonder about metastatic signet ring cell carcinoma, unless you know this is primary.

Santiago Ramon y Cajal: Thank you very much for the very interesting discussion in morphologic differentiation of primary vs. metastatic ovarian carcinoma.

Juan Rosai: If it were not Elvio Silva to make the proposal, I would not have accepted this lesion as a primary tumor of the ovary and favored a metastatic origin, probably from the breast (It even has target or bull-eye's cells).

Joshua SICKEL: I favored a metastatic lesion.

Dominic Spagnolo: I would have called it adenocarcinoma, unclassified. Was not aware of your publication. Thanks for the case.

James Strauchen: I was previously unaware of this type of ovarian carcinoma and would have considered a metastasis. Thank you for this informative case!

Saul Suster: I agree that the term "microcystic" is probably the best descriptor for this growth pattern. In areas it looks somewhat like an adenomatoid tumor, except this is obviously malignant. This is very distinctive morphologically and definitely deserves recognition as a distinct and separate "entity".

CASE NO. 17 – CONTRIBUTED BY DOMINIC SPAGNOLO:

N. Volkan Adsay: Nice case.

Phil Allen: Gastric schwannoma. I don't think that I have seen one of these for years, probably because the population of South Australia is shrinking, while Western Australia was, until very recently, expanding to service the mining boom.

Carlos Bacchi: Thanks for this example of gastric schwannoma. It is amazing how morphologically it does show similarities with GIST.

David Ben-Dor: It's good to be reminded that not all spindle cell tumors in this location have to be GIST. I focally found some neural type wavy fibers and focal possible but vague palisading. Interesting coincidence that earlier on in this seminar we saw a sinonasal schwannoma, another unlikely location, but with more classical features

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Gastric schwannoma. Agree. Another such case was contributed by Markku Miettinen in Seminar 49. You are right, Dominic, that this lesion is rare and that we must think also of it in this era of GIST. Have 2-3 such cases: the lymphoplasmacytic peripheral cuff seems to be a consistent finding in gastric schwannomas, as Prevot S et al (your ref. 6) first noted. This reactive cuff was present even in Markku's case and in all those I have seen so far.

Ira Bleiweiss: Agree. Schwannoma- This seminar's theme?

Thomas Colby: Agree with diagnosis (peripheral nerve sheath tumors have certainly been well represented in this group!).

Kum Cooper: Thanks Dom. I find the cuff of lymphoid cells a useful feature.

Ivan Damjanov: Agree. Lymphoid follicles at the periphery are always a good warning sign, at least for me.

Otto Dietze: I agree, benign schwannoma.

Hugo Dominguez-Malagon: Gastric schwannoma, well documented, thank you.

Göran Elmberger: Thanks for this interesting case. Nowadays, one almost expects all GI spindle cell tumors to be GIST, and we probably would do c-kit and PDGFR mutational analyses before excluding the possibility due to potential therapy response.

Vincenzo Eusebi: Gastric schwannoma.

Giovanni Falconieri: Another schwannoma (is this coincidental?, 3 in the same slide seminar!).

Cyril Fisher: Gastric schwannoma, very nice example, thanks, Dom.

Christopher Fletcher: Very nice and characteristic example of gastric schwannoma.

Andrew Folpe: Agree with gastric schwannoma. The theme of the seminar?

Jerónimo Forteza Vila: Thank you for this so interesting case.

Masaharu Fukunaga: Thank you very much for the beautiful case with photos, Dominic.

Thomas Krausz: I have seen a few similar cases before. This is a beautiful example, thank you.

Thomas Mentzel: See case 8.

Janez Lamovec: Similar case was presented by Markku – AMR # 49, case 14.

Markku Miettinen: Fully agree on gastric schwannoma, a typical example.

Liz Montgomery: No diagnostic problem. Very classic gastric “schwannoma” with the nice lymphoid cuff. These are interesting since, as pointed out by Dr. Miettinen, they lack NF2 alterations [unlike somatic schwannomas] and calretinin IHC.

Santiago Ramon y Cajal: Nice example of benign gastric schwannoma.

Juan Rosai: Nice example of gastric schwannoma, showing two common features of this tumor type in this location: lack of encapsulation (like in those from the upper respiratory tract, see Case 8); and a prominent lymphoid ring with germinal centers all around it.

Joshua Sickel: Beautiful example of gastric schwannoma. Those reactive lymphoid nodules are helpful in making the diagnosis.

James Strauchen: Gastric schwannoma! Seems to lack the typical histologic features of schwannomas at other sites.

Saul Suster: Very nice example. The cuff of lymphoid follicles is a constant finding and a great tipoff on H&E.

CASE NO. 18– CONTRIBUTED BY BRUCE WENIG:

N. Volkan Adsay: The distribution of lymphocytes with emperipolesis is very interesting. Focal sinusoidal pattern is also very interesting.

Phil Allen: Oncocytoma, probably arising in an intranodal salivary gland rest, neck at the level of the hyoid bone. At first glance, I thought it was Rosai-Dorfman disease but it is clearly epithelial and oncocytic. I, too, am unable to find any similar cases in a quick review of the last 10 years' pathology literature.

Carlos Bacchi: Intranodal oncocytic epithelial neoplasm with no morphological features of malignancy.

David Ben-Dor: Too bad there is no immunohistochemical stain specific for salivary parenchyma. Another thought could be ectopic thyroid tissue with Hashimoto changes- I saw this once in a thyroglossal duct cyst specimen and the hyoid location could be supportive but the immuno results would rule this out. There is a brisk plasma cell proliferation immediately adjacent to the proliferation which may be specific for it and not part of a pre-existing lymph node- I wonder if the lymphoid parenchyma is also reactive to the lesion (rather than being a pre-existing lymph node)?

Gerald Berry: I am reluctant to label this lesion as unequivocally benign. I admit the cytology is bland but the proliferation is clearly present within a lymph node. As possible local sites of origin of a neoplasm have been excluded, I think this is a lesion that will have to await the “test of time.”

Michele Bisceglia: Oncocytoma likely arising from intranodal salivary gland parenchyma. Difficult case. I am not sure of what this lesion is, and for sure would have not been able to make the same diagnosis you made, especially if I had been aware in advance of a midline neck location. It is an oncocytic tumor. Likely you are right, Bruce.

Ira Bleiweiss: Agree.

John Chan: I am worried that this might be an oncocytic carcinoma rather than oncocytoma. The cells have a higher N/C ratio, bigger nuclei and more prominent nucleoli than usual salivary gland oncocytoma. Also there is also somewhat more variation in nuclear size.

Thomas Colby: I am not sure what this is but I agree that it may very well have arisen in the node, and I am not sure it has anything to do with the thyroid gland.

Kum Cooper: Bruce, to add my two cents worth to your already complex problem: metastatic hepatoid gastric carcinoma (hepar-1) and dendritic cell tumor (follicular or interdigitating)? The p63/CK 7 immunoreactivity does raise the possibility of a thymic tumor??

Ivan Damjanov: Reasonable interpretation. I would agree especially since you have excluded neuroendocrine neoplasia.

Otto Dietze: I believe that this is the correct diagnosis.

Hugo Dominguez-Malagon: The best possibility is oncocytoma, however the histology worries me, I would advise a careful follow-up.

Göran Elmberger: Given results of IHC and morphological observations, I have no better suggestion. However, I am a little worried by the sinusoidal growth pattern and the intimate relationship between epithelium and plasma cell dominated lymphoid proliferation. Not what I would expect from intraglandular oncocytoma. Hurtheloid thyroid lesions and metastatic renal carcinoma would be in my differential from a pure morphological point of view, but your IHC results are against those alternatives. Was kidneys radiologically examined?

Vincenzo Eusebi: I do not know how to interpret this lesion. Oncocytic tumours can arise within lymph nodes, but their cells show a cohesive pattern. The fact that in this case the cells are keratin positive is probative on their epithelial nature. On H&E they remind me "oncocytic histiocytes". This is pure theory. In this case I would not dismiss a primary from kidney, lung and thyroid. Some neoplastic cells show emperipolesis.

Giovanni Falconieri: Very difficult Bruce. I must admit that the cells have worrisome features including irregular chromatin pattern and nucleolar prominency. I do not know how I would sign this, but I would not call it benign.

Cyril Fisher: Oncocytic proliferation in lymph node, good explanation!

Christopher Fletcher: I think that your suggested diagnosis is entirely convincing, Bruce ! Given the information provided, it seems difficult to come up with a meaningful alternative.

Andrew Folpe: Unusual oncocytic neoplasm.

Jerónimo Forteza Vila: I agree with the diagnosis.

Masaharu Fukunaga: A very challenging case. Thank you very much for the detailed discussion. I have recently encountered oncocytoma in the submandibular gland.

Allen Gown: Interesting case and diagnosis, but wouldn't p63 expression argue against the diagnosis of oncocytoma?

Thomas Krausz: I find this case diagnostically difficult. Before reading your excellent discussion, I was considering in my differential metastatic epithelioid mesothelioma (of course the negative WT1 excludes this possibility).

Janez Lamovec: Although this case is an oddity, I must agree with your interpretation.

Thomas Mentzel: To be honest, for me the tumour cells were not so bland looking having enlarged vesicular nuclei containing enlarged and prominent nucleoli. Can we really exclude a metastasis?

Markku Miettinen: Agree on oncocytoma with lymphoplasmacytic reaction. I don't have real experience on these but wondered if prominent nucleoli had any significance (? Atypical variant).

Elizabeth Montgomery: What a cool case. I certainly would have been fooled and thought it was a met but your discussion makes sense!

Santiago Ramon y Cajal: Agree with you. Favor oncocytoma, even if the location is not the most common.

Juan Rosai: Bruce Wening's arguments are very persuasive, but I still cannot rule out a lymph node metastasis from a carcinoma with oncocytic features of the head and neck region.

Joshua Sickel: Very weird case. At first glance, I thought those cells were histiocytic in origin. I don't think I would have been brave enough to call this completely benign. Thanks for the great discussion.

Dominic Spagnolo: What an extraordinary case. I agree with your reasoning, and in the absence of anything elsewhere, it would seem to be a primary intranodal process. Maybe analogous to intranodal Warthin tumor showing extreme oncocyctic change.

James Strauchen: Oncocytoma versus metastasis of oncocytic carcinoma. This seems to be within a true lymph node based on the presence of lymph node sinuses. Time will tell!

Saul Suster: Sorry – don't know what this is! I think this case might benefit from the clinical follow-up. Although I agree that your interpretation makes a lot of sense given the circumstances, I still am concerned about the total absence of salivary gland remnants. Also, most oncocytomas grow in an expansile fashion forming a discrete mass, unlike the diffusely permeative growth of this lesion. The prominence of nucleoli (despite the absence of mitoses) is another worrisome feature. I would definitely keep an eye on the patient to see if some other primary site becomes manifest.

Paul Wakely, Jr.: These sure look like oncocytes to me, and it does not look malignant. Still, I would have liked to see a CD68 stain to make sure they are not histiocytes, and it would have been great to have had EM on those large cells to confirm their mitochondria-rich nature.

CASE NO. 19– CONTRIBUTED BY SAUL SUSTER:

N. Volkan Adsay: I've never seen this. In terms of etiopathogenetic theories proposed in the literature I'm not sure I buy the "inflammatory polyp" hypothesis. I think the process is too clean and neatly organized for that. To my eye the vascularity in the cores of the polyps is very peculiar which made me wonder about a malformative process. Great case.

Phil Allen: Filiform polyposis coli. As usual with these AMR club cases, I had never heard of it before. The decline in modern dancing styles, which have spiralled from the classical minuet to the latter-day tango, justifies Saul's dancing long worm metaphor.

Carlos Bacchi: Never seen that before.

David Ben-Dor: The endoscopist must have been startled by this unexpected lesion, which seems like something which would be expected in deep sea diving but not in someone's colon. The mucosal inflammatory findings are probably secondary but how about IBD limited to these polyps? To be honest, the cores look to me like routine submucosa.

Gerald Berry: Agree. Nice example.

Michele Bisceglia: Filiform polyposis of the colon. Have not seen one before. Thank you, Saul.

Ira Bleiweiss: Never seen this before.

Thomas Colby: Agree with diagnosis; new meaning to the term "filiform."

Kum Cooper: Filiform polyposis (never heard of it!). What a wonderful way to end a great seminar!

Ivan Damjanov: Agree. Rarity-never seen one before.

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

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

Vincenzo Eusebi: Very nice case of filiform polyps.

Göran Elmberger: First time for me. Thanks for bringing up this unusual pattern. Quick glance in PUBMED reveals association to various conditions such as IBD, non-IBD, Cowden, FAP, histiocytosis X, and ganglioneuromatosis coli. Interesting non-specific (?) pattern.

Giovanni Falconieri: Did not know the existence of filiform polyp- will keep our GI team informed! Thanks for this additional educational opportunity!

Cyril Fisher: Filiform polyposis of colon, I have never seen this before.

Christopher Fletcher: Yet another first for me – I had never seen such as case nor heard of this condition – many thanks, Saul.

Andrew Folpe: Very interesting. Looks like a very strange inflammatory polyp.

Jerónimo Forteza Vila: Thank you for this so interesting case.

Masaharu Fukunaga: Thank you very much for sharing this nice case, Saul. I have never seen it before.

Allen Gown: Thank you! I have never seen a case of this before.

Thomas Krausz: I was not familiar this entity before. Thanks for submitting it.

Thomas Mentzel: Many thanks for sharing this unusual case, and I believe that the macroscopic aspect represents the most important clue for the diagnosis.

Michal Michal: By chance, yesterday I read the article describing this interesting entity.

Elizabeth Montgomery: These are fun to see. We have a few patients with inflammatory bowel disease who get them in our population but your case has dull history. Also, often the ones in IBD are missing the muscularis mucosae on one side of the "worm" whereas it seems intact on both sides in your case, so maybe your theory of hamartomas in this case has something to it.

Markku Miettinen: Agree on filiform polyp, certainly gross endoscopical appearance is part of the diagnosis.

Santiago Ramon y Cajal: Thanks, Saul . First time I've seen a case so clear of filiform polyposis of the colon.

Juan Rosai: This is the second case I see of this peculiar condition, which is more spectacular grossly than microscopically. It is said to be a form of pseudopolyposis secondary to inflammatory bowel disease, but neither in this case nor in the one I saw before was there much inflammation in the bowel mucosa or – for that matter - within the filiform polyps.

Joshua Sickel: Fantastic case. Were any gross photographs taken?

Dominic Spagnolo: Agree with filiform polyposis. I remember suggesting this in a case I saw in 2001, however, that was a solitary polyp with filiform morphology, also without underlying IBD

James Strauchen: Filiform pseudopolyps! These resemble the "bridging" pseudopolyps in IBD but seem to be covered by a completely normal mucosa so maybe the hamartomatous is correct!.

Saul Suster: This is my case. Phil's comment is well-taken. I don't understand modern dance anymore, so I still stick with salsa (works for me all the time!). If I had been born in Argentina my favorite would be the tango. But all compliments go to our dear friend Ivan Damjanov who showed us his incredible talents and dancing skills during our last AMR Symposium in Mexico City!