AMR Seminar #57 – Short Summary of Cases:

Case 1: 35-year-old female with a tumour on the left shoulder/back.

Case 2: 55-year-old female with an ovarian tumor.

Case 3: 38-year-old woman with palpable subareolar breast mass.

Case 4: 63-year-old Caucasian woman presented with a vulvar mass.

Case 5: 18-year-old woman with a renal tumor.

Case 6: 1-month-old girl with buccal tumor in the gingiva.

Case 7: 14-year-old boy with history of otitis with erosion of bone, now invading the posterior fossa.

Case 8: 45-year-old man with sickle cell trait presented with a large mass in the left upper quadrant, and pulmonary metastases on imaging.

Case 9: 38-year-old man presented with a slowly growing subcutaneous mass in the nuchal region.

Case 10: 45-year-old man with a large retroperitoneal mass.

Case 11: 67-year-old man with recurrent episodes of abdominal pain and weight loss and small bowel obstruction.

Case 12: 55-year-old man with 6 cm mass in neck, involving thyroid gland.

Case 13: 17-year-old girl with a cystic lesion in the head of her left fibula.

Case 14: 60-year-old woman with a tumor of the ovary 7,5 x 6,5 x 4,5 cm.

Case 15: 50-year-old man with a 2 cm nodule in the left thumb.

Case 16: 58-year-old woman with an ovarian tumor and multiple metastases in the peritoneum and omentum.

Case 17: 49-year-old man with a mass in the right ventricle.

Case 18: A middle-aged man with a left shoulder mass of unknown duration.

Case 19: 48-year-old woman with a maxillary mass and headache.

Case 20: 64-year-old woman with a history of NF type 1 and an adrenal mass.

Case 21: 32-year-old woman with an enlarging right neck mass.

Case 22: 74-year-old woman was seen for diplopia caused by an extraconal, orbital soft tissue mass.

Case 23: 14-year-old woman was seen for a slow growing subcutaneous nodule in her right forearm.

Case 24: 39-year-old woman with a diagnosis of neurofibromatosis and a mass in the left interscapular region.

Case 25: 26 year old woman with 2 cm. nodule in the distal third of ureter.

AMR SEMINAR #57
CASE 1

Contributed by: Philip Allen, M.D., Flinders Medical Centre, South Australia
(Case received from Dr. Daniel James, Royal Brisbane Hospital, Queensland, Australia)

History: 35-year-old female with a tumour on the left shoulder/back.

Diagnosis: Inflammatory myxo-hyaline tumor, dermis and subcutis, left shoulder and back.

Question: Will club members accept a diagnosis of ectopic inflammatory myxo-hyaline tumor?

AMR SEMINAR #57
CASE 2

Contributed by: Carlos E. Bacchi, M.D.

Clinical History: This is a case of a 55-year-old female with an ovarian tumor. Unfortunately, this case is very recent and I was unable to get more specific and detailed clinical and gross information.

Pathological findings: This ovarian tumor shows at low-power microcysts with variably amount of solid cellular areas and fibrous stroma. In some slides, one can appreciate the presence of lobular demarcation as well as sharp separation from the ovarian stroma. The microcysts are characterized by small to rounded oval cystic spaces, sometimes coalescing into larger irregular channels. Intracytoplasmic lumens or vacuoles are also present. The cells reveal moderate abundant finely granular, eosinophilic cytoplasm with bland, round to oval or spindle-shaped nuclei with fine chromatin and indistinct nucleoli. There areas of hemorrhage. Mitotic figures are very hard to find.

Immunohistochemistry Studies: The tumor cells were strongly positive for CD10 and vimentin with no expression of S-100 protein, calretinin, inhibin, EMA, cytokeratin, Melan A, Estrogen receptor, desmin, chromogranin A, synaptophysin, WT1 and CD34.

Diagnosis: Microcystic stromal tumor of the ovary.

Comment: This tumor has recently been described by Irving and Young (2009) as a previously uncharacterized ovarian neoplasm, most likely of stromal origin. There are several different diagnoses to be included, such as thecoma, steroid cell tumor with oxyphil cells, sclerosing stromal tumors, signet ring stromal tumor, Sertoli-Leydig cell tumor, among others. According to these authors all these tumors have different morphological and immunohistochemical characteristics compared to microcystic stromal tumor of the ovary. I would recommend reading this article by Irving and Young, especially about the differential diagnosis part.

Reference

Irving JA, Young RH. Microcystic stromal tumor of the ovary. Report of 16 cases of a hitherto uncharacterized distinctive ovarian neoplasm. Am J Surg Pathol 33(3): 367-375, 2009.

AMR SEMINAR #57
CASE 3

Contributed by: Ira Bleiweiss, M.D.

Case History: 38-year-old woman with palpable subareolar breast mass of unknown duration. The surgeon did an incisional biopsy.

Diagnosis: Syringomatous adenoma of nipple.

Comment: This came to me in consultation with a differential diagnosis of florid papillomatosis of nipple. I don't think this is diagnostically challenging once one realizes that the tumor glands really don't look like breast ducts. Just a nice example of a benign rare entity, the largest one that I can remember seeing.

AMR SEMINAR #57
CASE 4

Contributed by: Kum Cooper, M.D.

Clinical History: This 63-year-old Caucasian woman presented with a vulvar mass.

Gross Examination: The tumor is vaguely lobular with large areas of central necrosis (>50% overall) and centered in the dermis with sparing of the overlying mucosa. The tumor comprised sheets of large pleomorphic cells with prominent vesicular nuclei and prominent nucleoli and numerous mitotic figures (42/10 HPF). Focal areas of rhabdoid features were best appreciated in the lymph node metastases (21/22 positive) from the right inguinal excision.

Diagnosis: Epithelioid sarcoma, proximal type.

Immunohistochemistry: Keratin AE1-AE3 positive; EMA positive; CD34 patchy positive; CD31 negative; LCA negative; S-100 negative; p63 patchy positive; CK5/6 patchy positive. INI-1 (thanks to Thomas Krausz) showed loss of nuclear expression in the tumor cells (see photomicrograph on website).

Discussion: I thought to share this case with the members to remind us of two features:
1. The heterogeneity of the morphology (between cases) in the handful of cases I have seen.
2. The recent confirmation of INI-1 deletion (joining classic epithelioid sarcoma, rhabdoid tumors and atypical teratoid tumors).

Selected References:
1. Am J Surg Pathol 2009; 33(4): 542-550 (loss of INI expression).
2. Am J Surg Pathol 1997; 21(2):130-146 (the seminal series).

AMR SEMINAR #57
CASE 5

Contributed by: Ivan Damjanov, M.D.

Clinical History: 18-year-old woman with a renal tumor. The tumor was solid, tan-white, measuring 12x 6x 6 cm.

Diagnosis: Wilms' tumor with heterologous elements and diffuse anaplasia.

Comment: This is the first Wilms tumor in an adolescent we saw in Kansas in the last 15 years. In that age group Wilms tumors account for 30% of renal tumors, and are less common than classical renal cell carcinomas, which account for 50% of all renal tumors in the age group from 11 to 20 years (1). Histologically it has obviously the same features as the more common Wilms tumors of infancy and early childhood.

Our tumor had areas composed of eosinophilic globules. A picture of that material was included in the last AFIP Atlas, Series 4, Fascicle 1 (Murphy, WM et al), fig 1-45, without comments. Does anybody know what is that material?

Reference:

Grabowski J, Silberstein J, Saltzstein SL, Saenz N. Renal tumors in the second decade of life: results from the California Cancer Registry. J Ped Surg 2009; 44: 1148-51.

In the period from 1988 to 2004 the registry has records of 77 tumors in patients 11-20 years of age. Of these tumors 51% were RCC, 30% Wilms tumors. The 5 year survival rate of patients with Wilms tumor was 77%, which is somewhat less than the average survival rate for Wilms tumors overall (85%). Patients with RCC had a 54% survival rate in this age group.

AMR SEMINAR #57
CASE 6

Case contributed by: Otto Dietze, M.D.

History: Congenital gingival “fibroma” in a 1-month-old girl in the region 32 (buccal).

Diagnosis: Congenital granular cell tumor.

Comment: With H&E morphology this lesion is indistinguishable from adult granular cell tumor. However, its main difference is the lack of S100 expression and the expression of vimentin, A1AT and CD68. Our case was only positive for vimentin, staining with myogenic markers also was negative. This possibly reflects a very primitive mesenchymal stem cell origin. In contrast to adult granular cell tumor, the congenital variant is much more rare and I can’ remember another case within the last decades in our institute.

Reference:

Filie AC et al, Mod Pathol 1996 9: 882-92.

AMR SEMINAR #57
CASE 7

Contributed by: Vincenzo Eusebi, M.D. (Case # 08-20941)

History: This is a 14-year-old male with history (six months) of otitis with erosion of bone that for one reason or another was labelled as cholesteatoma. The proliferation (fibrous as you will see in the slide) has gained access into the leptomeningeal spaces and the foramen magnum and occupies the posterior fossa. The neuroimaging is typical of pachymeningitis. We received some fragments that we have labeled as fibromatosis, possibly of idiopathic hypertrophic cranial pachymeningitis type[1]. IgG4 was negative. No infectious conditions present of any type.

Diagnosis: Idiopathic hypertrophic cranial pachymeningitis.

Comment: I sent the slides to Mark Rosenblum (Memorial Sloan-Kettering Cancer Center, New York) as he is one of the authors of the quoted paper. He did not feel he could confirm the diagnosis of hypertrophic pachymeningitis and he does not know what this lesion is. He has repeated IgG4 immunostain with negative results. The patient has been put on steroids and it seems that not only the progression of fibrous proliferation has stopped but the lesion is regressing. I wonder if someone else has seen a similar case.

References:

1. Mamelak AN, Kelly WM, Davis RL, et al. Idiopathic hypertrophiC cranial pachymeningitis. Report of three cases . *J Neurosurg*. 1993;79:270-6.

AMR SEMINAR #57
CASE 8

Contributed by: Cyril Fisher, M.D., Royal Marsden Hospital, London, UK. (2 slides A&B)

Clinical History: A 45-year-old male with sickle cell trait presented with abdominal swelling for one year. He was found to have a large mass in the left upper quadrant, and pulmonary metastases on imaging. At surgery following core biopsy, the mass lay between spleen and kidney, was lightly adherent to pancreas and left colon, and was related to a huge adrenal vein 3 cm in diameter. Lymph nodes were found in splenic hilum and around superior mesenteric vessels. Tumor, kidney and spleen were excised.

Pathology: The excised tumor was circumscribed and large - 24 cm diameter. It was received intact after a delay so that unfortunately there is slight autolysis. The cut surface was firm and tan, with several paler nodules scattered throughout as well as foci of necrosis. The kidney was uninvolved and the adrenal was stretched over the rim of the tumor. Most of the tumor (slide A) was uniform and composed of sheets of oval and polygonal cells with oval vesicular nuclei with moderate to focally marked nuclear pleomorphism and largely abundant eosinophilic cytoplasm. There are clusters of vacuolated cells and others with pleomorphism or prominent nucleoli. Immunohistochemistry is positive in these areas for melan-A, CD56, and very focally MNF116, and negative for S100 protein, HMB45, chromogranin, synaptophysin, AE1/AE3, CD10, inhibin, calretinin, mdm2, CDK4, desmin, SMA, h-caldesmon, and myogenin. The nodules comprise round or spindle cell sarcoma, without lipoblasts but with focal positivity for desmin and nuclear myogenin and none for the other markers. The adrenal gland appeared intact but islands of adrenal cortical tissue were found within the tumor capsule.

The lymph nodes (represented in slide B) contain metastatic pleomorphic rhabdomyosarcoma, with numerous large round rhabdomyoblasts and strap cells with striations, diffusely desmin and myogenin positive.

Diagnosis: ?Sarcomatoid adrenal cortical carcinoma with metastatic rhabdomyosarcoma in lymph nodes (and lung).

Comment: This does not appear to be of renal origin and resembles an adrenal cortical neoplasm, but the immunophenotype is incomplete. An alternative consideration might be epithelioid pleomorphic liposarcoma but I found no convincing lipoblastic differentiation in multiple sections. I would be interested if members have alternative suggestions especially as the adrenal gland is largely intact. The second component has skeletal muscle differentiation, more obvious in the metastasis. Sarcomatoid change is an unusual manifestation of adrenal cortical carcinoma with about half a dozen cases in the literature, of which two manifested prominent rhabdomyosarcomatous differentiation.[1,2] The term sarcomatoid carcinoma seems preferred to carcinosarcoma. A similar case was submitted in AMR 49 (case 10) by Dr Jerónimo Forteza Vila, and it is of interest that the adrenal gland appeared largely intact in that case also. Additionally, in one of the published cases (without rhabdomyosarcoma) normal gland remained at the periphery of a 12 cm tumor mass.[3] Conceivably, some examples might arise in accessory/ectopic adrenal tissue.

References:

1.Decorato JW, Gruber H, Petti M, Levowitz BS. Adrenal carcinosarcoma. J Surg Oncol. 1990;45:134-136.

2.Fischler DF, Nunez C, Levin HS, McMahon JT, Sheeler LR, Adelstein DJ. Adrenal carcinosarcoma presenting in a woman with clinical signs of virilization. A case report with immunohistochemical and ultrastructural findings. Am J Surg Pathol. 1992;16:626-631.

3.Sturm N, Moulai N, Laverrière MH, Chabre O, Descotes JL, Brambilla E. Primary adrenocortical sarcomatoid carcinoma: case report and review of literature. Virchows Arch. 2008; 452:215-219.

AMR SEMINAR #57
CASE 9

Contributed by: Christopher Fletcher, M.D. (Case No: CFST 2253)

Clinical History: A 38-year-old man presented with a slowly growing subcutaneous mass in the nuchal region.

Diagnosis: Hibernoma, spindle cell variant.

Comment: As noted in Markku Miettienen's large series some years ago (*Am J Surg Pathol* 2001; 25:809-814), this variant of hibernoma seems to be exceedingly rare and my own personal experience mirrors that of Markku. Given that conventional examples of spindle cell lipoma and hibernoma have quite different but consistent genetic aberrations, it would be very interesting to know what the karyotype might show in a lesion such as this, which really shows convincing overlapping morphologic features of the two entities – in fact, in one area of the block from which the sections were cut, there are even quite striking floret-type cells, further supporting the overlap with spindle cell/pleomorphic lipoma. Since spindle cell variants of hibernoma, at least to date, have only been identified in the posterior neck, then perhaps, instead, these actually represent spindle cell lipomas with brown fat differentiation, rather than the other way around. In any event, these curious lesions are entirely benign and semantics such as this are probably only of interest to soft tissue pathologists!

AMR SEMINAR #57
CASE 10

Contributed by: Andrew Folpe, M.D.

Clinical History: A 45-year-old male was found to have a large retroperitoneal mass, which was subsequently resected.

Pathological Findings: The resected specimen was partially fatty-appearing and partially solid. The great majority of submitted sections showed classical features of dedifferentiated liposarcoma, with large areas of typical well-differentiated liposarcoma and areas of pleomorphic non-lipogenic sarcoma. I have not submitted sections from these areas for your review.

The section that I have submitted to the AMR club members is from one area that caught my eye, inasmuch as it bears a striking resemblance to a spindle cell lipoma, with aggregates of relatively bland spindled cells, sometime arranged in a "school of fish" pattern, abundant wiry collagen, and variable myxoid change. Just for interest, I performed FISH for CPM amplification (carboxypeptidase M, a gene located telomeric to mdm2 on 12q15, is co-amplified with mdm2 in essentially 100% of cases [1]), which showed amplification in 66% of cells.

Diagnosis: Dedifferentiated liposarcoma (with one small focus closely resembling spindle cell lipoma).

Comment: I just found this to be an interesting case from a "theoretical perspective", as I typically think of spindle cell/pleomorphic lipoma as a rather straightforward diagnosis, and feel pretty confident about my ability to tell it from atypical lipomatous tumor/ well-differentiated liposarcoma by histology alone. When I saw this one area, I wondered whether I would have even considered WDL, if this was all I had to go with (on a smaller biopsy, for example). Obviously, in the retroperitoneum my suspicion would have been for WDL, but what about in the accessible soft tissues? I'm really not so sure I would have made the correct diagnosis.

Reference:

1. Erickson-Johnson, M.R., et al., *Carboxypeptidase M: a biomarker for the discrimination of well-differentiated liposarcoma from lipoma.* Mod Pathol, 2009. **22**(12): p. 1541-7.

AMR SEMINAR #57
CASE 11

Contributed by: Jerónimo Forteza Vila, M.D.

Clinical History: 67-year-old male with recurrent episodes of abdominal pain and weight loss. Coprocultures, tumoral markers and serologies were all negative. Abdominal CT showed small bowel loops confined to a single area and encased in a thick membrane. An exploring laparotomy was performed and peritoneal miliary dissemination affecting small bowel and parietal peritoneum was detected. A biopsy was done that ruled out neoplastic and infectious disease, just a focus of intralymphatic histiocytosis was found. Microbiologic cultures for BAAR-LOWENSTEIN were negative as well. Finally and due to symptomatology persistence, the small bowel affected segment was resected.
Histological examination showed multiple collagen nodules in the subserosal layer as the unique relevant finding. Neoplastic disease was not present after an exhaustive sampling.

Diagnosis: Idiopathic sclerosing encapsulating peritonitis (abdominal cocoon).

Discussion: Small bowel obstruction is a frequent surgical complication, being adhesions, hernias or neoplasms the most common causes. Less common etiologies accounts for a 6% and the sclerosing encapsulating peritonitis is one of them. It exists an idiopathic form called Abdominal Cocoon (AC) and secondaries to peritoneal dialysis, tuberculosis or drugs.

AC was described firstly by Dr. Foo et al in 1978, thought that affected exclusively tropical and subtropical countries young women considering the hypotheses that peritoneal damage was caused by a retrograde gynaecological infection. However, this theory is not valid as soon as men, premenopausal women and children may be affected as well.

Clinically, it presents with small bowel obstruction, nausea, weight loss or sensation of abdominal mass. There are even asymptomatic patients.

Diagnose is usually made based on an incidentally laparotomy. It is necessary that a clinical suspicious exists based on radiological findings and symptomatology so a pre-operative diagnose can be done. Abdominal CT usually shows small bowel loops covered by a fibrocollagenous sac that looks like a cocoon. It is important to have always this entity in mind in cases with intestinal obstruction, compatible radiological study and lack of other possible entities.

Histological examination is very unspecific being connective tissue proliferation and chronic inflammatory infiltrates mainly findings.

AC treatment is still on debate, however most authors agreed that surgical treatment is required. Incision of the thick membrane and extensive adhesiolysis of small bowel loops is recommended. Resection of the bowel is indicated only if it is non-viable. No surgical treatment is required in non-symptomatic patients.

In peritoneum first biopsy, only mild chronic inflammatory infiltrate and fibrous collagen proliferation was seen. We have not found neoplastic morphology and some groups of intralymphatic histiocytes were detected. We considered the possibility of “Intralymphatic Histiocytosis”, entity described in skin so far. The patient did not have Rheumatoid Arthritis that is characteristic in this disease.

Evolution of the patient was poor and due to first unspecific biopsy findings, another exploring laparotomy was performed in our Hospital with an introperatory study where our pathologist went to the operating room and analyzed “in situ” lesion. Finally, jejunal affected segment was removed. Macroscopic examination revealed a fibrous capsule covering a small bowel loop where multiple little white nodules could be seen, which gave us at the beginning the impression of peritoneal miliary dissemination. An exhaustive sampling was performed and again

neoplastic morphology was not seen but multiple collagen-like nodules in subserosal layer which made us think in two possibilities, amyloid deposits or just fibrous tissue proliferation. Congo-Red staining was negative while Masson Trichromic positive. Intralymphatic histiocytosis was not seen as in first biopsy.

References:

1- Abdominal Cocoon: Clinical Presentation, Diagnosis and Management.Debajyoti Mohanty, Bhupendra Kumar Jain, Juhi Agrawal, Arun Gupta, Vivek Agrawal. J Gastrointest Surg (2009) 13:1160–1162

2- Idiopathic sclerosing encapsulating peritonitis (or abdominal cocoon). Costas Serafimidis, Ioannis Katsarolis, Spyros Vernadakis, George Rallis, George Giannopoulos, Nikolaos Legakis, George Peros. BMC Surgery2006, 6, 2482-2486

3- Idiopathic Sclerosing Peritonitis in a Man. Chiyohiko Masuda, Yoshiaki Fujii, Tomoyoshi Kamiya, Matakichi Miyamoto, Katsuhiko Nakahara, Shigehiko Hattori, Hisataka Ohshita, Takeshi Yokoyama, Hiroyuki Yoshida, Yutaka Tsutsumi. Internal Medicine (1993) 32: 552-555

4- Sclerosing Encapsulating Peritonitis (AbdominalCocoon) after Abdominal Hysterectomy.Won Na Suh, Sang Kil Lee, Hyun Chang, Hye Jin Hwang, Woo Jin Hyung, Young Nyun Park, Tae Il Kim. The Korean Journal of Internal Medicine (2007), 22:125-129

5- Idiopathic sclerosing encapsulating peritonitis (or abdominal cocoon): A report of 5 cases. Ping Xu, Li-Hua Chen,You-Ming Li. World J Gastroenterol (2007) 14; 3649-3651

6- Idiopathic sclerosing peritonitis. T.C.B. Dehn, M.G. Lucas, R.F.M. Wood. Postgraduate Medical Journal (1985) 61, 841-842

AMR SEMINAR #57
CASE 12

Contributed by: Allen Gown, M.D.

Clinical Summary: 6 cm mass in neck, involving thyroid gland, in a 55-year-old male.

Diagnosis: Pleomorphic rhabdomyosarcoma.

Discussion: This is a rare variant of rhabdomyosarcoma that actually occurs almost exclusively in adults, more commonly in men; these tumors typically occur in the skeletal muscle of the extremities, particularly the lower extremity, presenting as large, well circumscribed lesions (1, 2).

Histologically, these are highly pleomorphic sarcomatous tumors, as in the case at hand. While many of these tumors have 'classic' rhabdomyosarcomatous features, including the presence of 'tadpole' cells, others have more round cell or spindle cell features. It is said that the most reliable histologic feature is the presence of large bizarre tumor cells with deeply eosinophilic cytoplasms, presumably containing abundant actin and intermediate filaments. In the pre-immunohistochemical era, it is likely that most pleomorphic rhabdomyosarcomas were classified as variants of malignant fibrous histiocytoma.

The immunophenotype of these tumors is highly characteristic, with uniform expression of desmin, although antibodies to muscle actins (e.g., HHF-35) are also strongly positive. While both myogenin and myoD1 can be employed as markers of this variant of rhabdomyosarcoma, as they are in embryonal and alveolar subtypes, there is often only very focal expression of myogenin and/or myoD1 in pleomorphic rhabdomyosarcoma. This focal expression may account for some reports claiming a low sensitivity for myogenin and myD1 in this rhabdomyosarcoma variant (3). Photomicrographs of some of the desmin and myogenin immunostains on this tumor have been submitted with the slide, highlighting the contrast between the strong and uniform desmin expression and the very focal expression of myogenin.

There does not appear to be a chromosomal translocation that is characteristic of this rhabdomyosarcoma variant. While in this case, given the location of the tumor adjacent to the thyroid, the differential diagnosis did include anaplastic thyroid carcinoma (ruled out by the absence of cytokeratin expression and positive muscle markers), typically the differential diagnosis of this tumor will include other variants of rhabdomyosarcoma, all of which can show foci of pleomorphism; the age of the patient is often helpful in pointing to the correct diagnosis, as the pleomorphic variant is exceedingly rare in children and young adults. The diagnosis of other pleomorphic sarcomas should also be entertained, e.g., pleomorphic liposarcoma and pleomorphic leiomyosarcoma. And while the latter tumor is also desmin positive, it does not express the skeletal muscle transcription factors, myoD1 and myogenin. And I would not want to risk offending certain members of the group by suggesting MFH as one of the other pleomorphic sarcomas in the differential.

References:

1. Gaffney EF, Dervan PA, Fletcher CD. Pleomorphic rhabdomyosarcoma in adulthood. Analysis of 11 cases with definition of diagnostic criteria. Am J Surg Pathol. 1993;17:601-609.
2. Hollowood K, Fletcher CD. Rhabdomyosarcoma in adults. Semin Diagn Pathol. 1994;11:47-57.
3. Furlong MA, Fanburg-Smith JC. Pleomorphic rhabdomyosarcoma in children: four cases in the pediatric age group. Ann Diagn Pathol. 2001;5:199-206.

AMR SEMINAR #57
CASE 13

Contributed by: Janez Lamovec, M.D. (Case #1180-09, Institute of Oncology, Ljubljana)

Clinical History: The patient is a 17-year-old girl who has had a swollen upper left lower leg of 2 months duration. An X- ray showed a cystic lesion in the head of left fibula. The biopsy was performed and a giant cell tumor of bone diagnosed that was followed by segmental resection of fibula. Histology showed a giant cell tumor destructing cortical bone and its expansive growth into the surrounding soft tissue.
One year following surgery, numerous diffuse bilateral small nodular lesions appeared in the lungs, one of them was excised.

Pathology: Grossly, in the excised fragment of the lung, there were three clearly circumscribed white-grey nodules measuring from 3 to 10 mm in diameter. Histologically, this is a classical giant cell tumor with mononuclear cell population diffusely admixed with numerous osteoclast-type giant cells. There are many mitotic figures of mononuclear cells seen.

Diagnosis: Multiple pulmonary metastases of giant cell tumor of bone.

Follow up: This is a recent case. Since the surgical excision of metastases was not feasible, the patient received four courses of chemotherapy. At the moment, 8 months following lung biopsy, the patient is asymptomatic and there is no progression in size or number of lung metastases on X-ray.

Comment: Although the phenomenon of lung metastases of a benign giant cell tumor of bone that occurs in approximately 2% of the cases is well known, I thought it might be interesting to submit this case, if nothing else to add it to your personal files for educational purposes.

AMR SEMINAR #57
CASE 14

Contributed by: Michal Michal, M.D., Czech Republic

Clinical Data: 60-year-old woman with a tumor of the ovary 7,5 x 6,5 x 4,5 cm. The tumor was inhibin, SM actin positive and CK negative

Diagnosis: Ovarian fibroma with hyaline globules.

Reference:

Michal M et al - *Ovarian Fibromas With Heavy Depositions of Hyaline Globules: a Diagnostic Pitvalo. Int J Gynecol Pathol 2009:28:356-361*

AMR SEMINAR #57
CASE 15

Contributed by: Markku Miettinen, M.D.

Clinical History: 50-year-old man with a 2 cm nodule in left thumb.

Diagnosis: Sclerosing perineurioma.

Discussion: In our experience, this is the most common form of perineurioma, and one of the least controversial ones displaying phenotypic features of meningothelial cells and the corresponding markers: EMA and Glut-1, as also seen in this case. Basement membrane proteins (collagen IV, laminin) are also present. These tumors are sometimes focally positive for SMA and keratins, but they are negative for CD34 and S100 protein. Histologically characteristic are small epithelioid cells, often seen in a corded pattern and sometimes in a concentric onion-bulb manner perivascularly or perineurally in an overall dense collagenous matrix. We have seen the corded/other patterns being mistaken as epithelioid hemangioendothelioma, sclerosing glomus tumor, mixed tumor, and fibrous histiocytoma or fibroma variants. This rare tumor typically occurs in fingers and hands of young adults and rarely in other locations. It is benign, but local recurrences are possible. NF2 gene mutations, as seen in meningiomas and schwannomas, have also been found in these perineuriomas.

References:

Am J Surg Pathol 1997;21:1433-1442,
Am J Pathol 2001;158:1223-1229,
Virchows Arch. 2003;443:159-163.

AMR SEMINAR #57
CASE 16

Contributed by: Elvio G. Silva, M.D.

Clinical History: This is a 58-year-old female with an ovarian tumor and multiple metastases in the peritoneum and omentum. This section is from one of the metastases in the omentum. I am also including two images from cases I cannot get blocks.

This is a 58-year-old female patient who in December 1997 was diagnosed with Stage IIIc ovarian carcinoma. She had optimal tumor reductive surgery and after this she was treated with Taxol® and Cysplatin® for six cycles.
June 2000: The tumor recurred in the pelvic peritoneum and she was treated again with Cysplatin® and Taxol®. However, the tumor was progressing and the Cysplatin® was changed to Hexalen®.

July 2002: CA-125 was rising and she received nine cycles of Topotecan®.

September 2002: There was tumor progression. She received Doxcil®, but the CA-125 was increasing, therefore she was changed to Hemcetavine® and Cysplatin® for ten cycles.

December 2003: The CA-125 increased to 82, so she received to BP-16 oral.

March 2004: CA-125 was 79 and she was treated for three years with Letrozole® followed by Tamoxifen®.
2007: She had tumor progression and received Arymidex®.

December 2007: CA-125 was 1,630. Since had severe abdominal pain, Lortave® was prescribed. She continued with tumor progression and only palliative medicine was prescribed.

Diagnosis: Low-grade serous carcinoma.

This is a typical history of patients with low-grade serous carcinoma, which is a tumor that will recur many times and the patients will be alive for more than 10 years and there is always tumor progression. Since the tumor is not very aggressive, the patients are alive, but slowly there is tumor progression and this type of tumor does not respond to any of the well-known therapies. Finally, most patients die of multiple intestinal obstructions.

Low grade serous carcinoma is distinguished from borderline tumors because of the stromal invasion. However, the different patterns of stromal invasions are not well-recognized and with this slide I would like to emphasize two special and typical patterns of low grade serous carcinoma which are not well recognized: the invasion within NELS and the orphan papillae.

There are two types of invasion in low grade serous carcinomas; the most common one is when a group of cells are within spaces that are not lined by epithelial cells (NELS) (Images 1A & 1B). Regarding the groups of cells within NELS, the most common situation is when there are small groups that most probably do not represent micro papillae, but just small groups or nests of cells. This type of invasion is seen in almost all low grade serous carcinomas. The second most common type is the invasion within NELS by micro papillae. The invasion by macro papillae is unusual, seen in less than 15% of low grade serous carcinoma. NELS are most probably created by retraction of the tissue during processing.

The other type of invasion is by well formed glands that since they do not get separated from the stroma, they do not have the NELS, and because it is a low grade serous carcinoma, the cytology of the tumor shows only mild to moderate atypia with rare mitoses. This invasive pattern is recognized at low power because there is a haphazard arrangement of glands with significant desmoplasia. The cells do not have serous or tubal differentiation and frequently there are areas of cribriform pattern and multiple calcifications.

The other pattern that I wanted to show in this slide is the presence of papillary projections within cystic spaces lined by epithelial cells, but the papillary projections do not maintain any special arrangement and are not attached to a central, larger papillae and this is why we call them orphan papillae (Images 2A & 2B). This pattern is seen only in serous carcinoma and it is not seen in borderline cases where there is a hierchichal arrangement of the papillae where primary papillae give origin to secondary papillae and from here there is a tertiary papillae. Frequently from this spaces lined by epithelial cells containing orphan papillae there is invasion of the stroma (Image 3). The orphan papillae are not diagnostic of invasion; however, they could represent an unusual form of invasion similar to the invasion by glands, but with papillae inside.

A very common finding in low grade serous carcinoma is the presence of calcifications. These are seen in all cases. Sometimes the calcifications are not very extensive or on the other extreme we have the psammocarcinoma which I believe represents a low grade serous carcinoma.

In low grade serous carcinoma, it is possible to see areas with intracystic and intracytoplasmic mucin. This could be extremely important because in a patient with history of a borderline tumor and a metastasis in a lymph node with cells containing mucin probably, we will look for a primary in the GI tract or other organs. It is important to remember that the most common type of tumor found in the recurrences of serous borderline tumors is low grade serous carcinoma and it can have mucin.

In summary, I wanted to emphasize two patterns of low grade serous carcinoma, the most common type of invasion, which is the invasion by tumor cells within NELS, and the orphan papillae. I also use the invasion in NELS to diagnosis invasive implants, which in my opinion represent low grade serous carcinoma.

References

1. Silva EG, Deavers MT, Malpica A. The Non-Epithelial Lined Spaces Pattern of Invasion and the Disorganized Individual Papillae, Non-Invasive Component, of Low-Grade Serous Carcinoma. *Mod Pathol* 21(1) (#1027), 2008
2. Malpica A, Deavers MT, Lu K, Bodurka DC, Atkinson EN, Gershenson DM, Silva EG. Grading ovarian serous carcinoma using a two-tier system. *Am J Surg Pathol* 28(4):496-504, 2004.
3. Gershenson DM, Sun CC, Lu KH, Coleman RL, Sood AK, Malpica A, Deavers MT, Silva EG, Bodurka DC. Clinical behavior of stage II-IV low-grade serous carcinoma of the ovary. *Obstet Gynecol* 108:361-8, 2006.
4. Malpica A, Silva EG, et al. Inter-observer and Intra-observer Variability of a Two-Tier System for Grading Ovarian Serous Carcinoma. *Am J Surg Pathol* 31:1168-74, 2007.
5. Hsu CY, Kurman RJ, Vang R, Wang TL, Baak J, Shih IeM. Nuclear size distinguishes low- from high-grade ovarian serous carcinoma and predicts outcome. *Hum Pathol* 36(10):1049-54, 2005.

Image Legends

Image 1A, 1B – Low grade serous carcinoma – small groups of tumor cells within NELS

Images 2A, 2B – Low grade serous carcinoma – orphan papillae

Image 3 – Low grade serous carcinoma – groups of tumor cells within NELS associated with orphan papillae

AMR SEMINAR #57
CASE 17

Contributed by: James Strauchen, M.D.

Case History: A 49-year-old male presented with a mass in the right ventricle. Past medical history was remarkable for aortic regurgitation status post a Ross procedure (replacement of the aortic valve with the pulmonic valve), retroperitoneal fibrosis, and hypopituitarism. Excision of the mass was performed.

Pathology: The specimen consisted of a 7.0 x 4.8 x 1.5 cm portion of rubbery tan yellow tissue. Routine H&E-stains showed dense collagenous fibrosis with an infiltrate of foamy histiocytes with scattered lymphocytes and plasma cells. Immunohistochemical stains demonstrated the histiocytes expressed the phenotype of monocyte-macrophages: CD68 positive, CD163 positive, Factor XIII positive, S100 negative, CD1a negative, CD34 negative.

Diagnosis: Erdheim-Chester disease with cardiac involvement.

Comment: Erdheim-Chester disease is a non-Langerhans cell histiocytosis characterized by proliferation of foamy histiocytes associated with fibrosis and chronic inflammatory cells. Skeletal involvement is characteristic. Pulmonary interstitial fibrosis, retroperitoneal fibrosis, and diabetes insipidus due to pituitary involvement are frequent extraskeletal manifestations. Cardiovascular involvement has been reported and is an underappreciated manifestation (1). Cardiovascular manifestations include valvular heart disease, pericardial involvement, myocardial involvement, right atrial "tumor", and periaortic fibrosis. The etiology of the aortic valve disease in our case is undetermined, but may have been due to Erdheim-Chester disease. The pathology of the aortic valve was unfortunately not available for review. Therapy has been unsatisfactory in the past, but responses to interferon-alpha have been reported (2).

References:

1. Haroche J, et al. Cardiovascular involvement, an overlooked feature of Erdheim-Chester disease. Report of 6 new cases and a literature review. Medicine 2004; 83:371-392.

2. Braiteh F, et al. Successful treatment of Erdheim-Chester disease, a non-Langerhans cell histiocytosis, with interferon-alpha. Blood 2005; 106:2992-2994.

AMR SEMINAR #57
CASE 18

Contributed by: Paul Wakely, Jr., M.D. (Case #8469)

History: A middle-aged man presented with a left shoulder mass of unknown duration.

Diagnosis: Adult type rhabdomyoma.

Comment: This is an outside case so I don't know any other clinical information including the size of the mass. Nonetheless, since I noticed there were no examples of this relatively uncommon neoplasm in the club's archives, I thought members would like to have an example of this easily recognizable lesion.

AMR SEMINAR #57
CASE 19

Contributed by: Paul Wakely, Jr., M.D**.** (Case #1427)

History: A 48-year-old woman presented with a maxillary mass and headache. An outside diagnosis of "esthesioneuroblastoma" was made.

Diagnosis: Alveolar rhabdomyosarcoma, maxilla, in an adult.

Comment: This case was uncovered in a review we did of our head and neck rhabdomyosarcomas. I thought it was particularly unusual and that members would enjoy it because of the high percentage of malignant multinucleated differentiating rhabdomyoblasts. Cells were myogenin, myoglobin, and desmin positive. Since the case is from 10 years ago, no FISH testing was performed for t(2;13).

AMR SEMINAR #57
CASE 20

Contributed by: Lawrence Weiss, M.D., City of Hope, Duarte, CA

Clinical History: This 64-year-old female has a past medical history of neurofibromatosis type 1 and a recent diagnosis of breast carcinoma treated with lumpectomy followed by chemotherapy and radiation therapy. She presented for routine follow-up surveillance imaging studies, in which a CT scan demonstrated the presence of a 3.4 cm. heterogeneously enhancing mass involving the right adrenal gland. Subsequent I-123 MIBG scintigraphy showed moderately intense focal uptake in the right adrenal lesion. The patient reported a history of hypertension of 15 years duration controlled with medication, but otherwise had no other clinical complaints. In particular, the patient denied any episodes of headache, palpitations, tremors, diaphoresis, or chest or abdominal pain. On physician examination, scattered neurofibromas and areas of freckling were observed involving the face, bilateral upper extremities, and truncal region. The abdomen was soft and flat, with no tenderness on palpation. Laboratory studies showed elevated urinary fractionated metanephrines and plasma metanephrines. Aldosterone, renin, testosterone, DHEAS, and 24 hour urinary free cortical values were normal. A laparoscopic right adrenalectomy was performed without complications.

Gross Findings: The resected adrenal gland weighed 16 grams and contained a 3.6 cm. nodule. The nodule was well-circumscribed, but unencapsulated, with a thin peripheral rim of compressed adrenal cortical tissue present at the periphery. The tumor had a vaguely lobulated cut surface which was predominantly pale tan, with patchy darker gray areas. No necrosis or hemorrhage was observed.

Immunohistochemistry: The cortical cells exhibited immunoreactivity for alpha-inhibin and Melan-A, as well as patchy positivity for synaptophysin. The pheochromocytes were positive for chromogranin A and synaptophysin, with supporting sustentacular cells demonstrating S-100 protein immunoreactivity. The spindled Schwann cell component showed strong and diffuse expression of S-100 protein, while the ganglion cells were positive for synaptophysin and neurofilament protein.

Diagnosis: Mixed cortical adenoma and composite pheochromocytoma-ganglioneuroma.

Follow-up: The patient is alive and well with no evidence of recurrent or metastatic disease 6 months after surgery.

Discussion: We have seen several recent similar cases with various combinations of two out of three components (cortical, pheo, and ganglioneuroma), so I wanted to show a case with all three. Hopefully, you have all three components on your slides.

AMR SEMINAR #57
CASE 21

Contributed by: Bruce M. Wenig, MD

Clinical History: 32-year-old woman presented with an enlarging right neck mass. Clinical work-up, including imaging identified the lesion at the bifurcation of the right common carotid artery. Preoperative ablative therapy was performed. Intraoperatively, the mass was firmly adherent to surrounding structures including encasement of the carotid artery creating difficulties in its resection.

Diagnosis: Invasive paraganglioma incompletely excised; nine regional lymph nodes negative for metastatic tumor.

Discussion: The diagnosis in this case of a carotid body paraganglioma is rather straightforward given the clinical history and classic histomorphology including cell nest/organoid growth, predominance of a chief cell proliferation characterized by dispersed nuclear chromatin with minimal nuclear pleomorphism and absence of increased mitotic activity. The lesional cells were immunoreactive for chromogranin, synaptophysin, neuron specific enolase and S100 protein, the latter with a typical peripheral sustentacular cell staining pattern. Cytokeratin and calcitonin staining, done for completion, were negative. There was a low proliferation rate (less than 1%) as seen by Ki67 (MIB1) staining.

A surgical classification of carotid body tumors into three groups according to Shamblin, include:
Group I – tumors relatively small with minimal attachment to the carotid vessels;
Group II - tumors are larger (than Group I) with moderate arterial attachment and can be resected with precise surgical dissection;
Group III – larger tumors encasing the carotid arteries and can be resected only with arterial sacrifice.
This patient's tumor would represent a Group III carotid body tumor.

In contrast to benign paragangliomas which are typically encapsulated and/or circumscribed without invasive growth, this patient's tumor shows extensive invasive growth into fibroconnective tissue, including perineural invasion (seen in your slide). Clearly, this neoplasm is not a "conventional" paraganglioma but raises the issue of classification. Unlike the surgical classification scheme detailed previously, there are less precise and/or accepted histopathologic classifications for paragangliomas. Proposed pathologic classification schemes include noninvasive paraganglioma, locally invasive (but not metastatic) paraganglioma and malignant paraganglioma. Most authorities hold that a diagnosis of malignancy in paragangliomas, including those of carotid body origin, can only be made in the presence of metastatic disease. On the basis of invasive growth but the absence of nodal metastasis, a diagnosis of invasive paraganglioma was made but given the absence of metastatic disease a diagnosis of malignant paraganglioma could not be suggested.

I am curious how the group would handle the classification and sign-out of this tumor. Would anyone classify this neoplasm as a straightforward carotid body paraganglioma? Do you agree with the designation of invasive paraganglioma? Anyone for outright malignant paraganglioma? Any other considerations? The patient has no known family history and/or any significant contributing history to the development of this neoplasm.

Reference:
Shamblin WR, Remine WH, Sheps SG, et al. Carotid body tumor (chemodectoma): clinicopathologic analysis of ninety cases. Am Surg 1971;122:732-39.

AMR SEMINAR #57
CASE 22

Contributed by: Eduardo Zambrano, M.D., Yale University School of Medicine.

Clinical History: A 74-year-old woman was seen for diplopia caused by an extraconal, orbital soft tissue mass. A CT scan revealed a 2.2 x 1.6 cm., partially calcified orbital soft tissue mass. The mass was excised in June 2008; however, in August 2009 a local recurrence was noted. The recurrent lesion measured 3 cm. in greatest diameter. The circulated slide is from the recurrent lesion.

Pathologic findings: Both the original and recurrent lesions showed similar morphologic features. The tumor is composed of fascicles and rows of cytologically bland spindle cells separated by abundant hyalinized stroma. No evidence of mitotic activity, tumor necrosis or cytological features of malignancy are identified. A panel of immunohistochemical stains was ordered on the original resection specimen to further define the tissue type. The tumor cells in the original resection were found to be positive for S100 protein, CD10, CD99 and SMA, with focal GFAP positivity. The cells were negative for cytokeratin AE1/AE3, NSE, CD34, desmin and CD57. The original resection specimen was signed out as being consistent with an ossifying fibromyxoid tumor. It was noted that the operative report described an eggshell of bone surrounding the tumor. The head and neck region is a common site for this tumor, and there has been at least one case reported involving the orbit. The recurrent lesion, however, showed somewhat different results for IHC. The tumor cells were strongly positive for CD99 and focally for SMA, but negative for S-100 protein, CD31, EMA, bcl-2. CAM.2, calponin, p63, HHF35, desmin and CD34.

Diagnosis: Unusual spindle cell lesion with extensively hyalinized stroma, NOS.

Comment: The histological features of this lesion are quite unique and distinctive. I am unable, however, to more specifically classify this tumor. The striking CD99 positivity is quite unusual and I am at a loss for how to explain it. I would greatly appreciate any insights that the members of the club can offer as well as any suggestions for additional work-up of the tumor.

AMR SEMINAR #57
CASE 23

Contributed by: Hugo Dominguez-Malagon, M.D. (Case # SE09-646)

History: A 14-year-old female was seen for a slow growing subcutaneous nodule in her right forearm. The tumor was poorly delimited, mobile and measured approximately 1 cm. It was removed marginally.

Gross findings: Two fragments measuring 1 cm and 0.4 cm, they had irregular shape, pink-yellow color, and firm consistency.

Microscopic findings: The neoplasia affects dermis and subcutaneous tissue and is characterized by formation of nodules with a plexiform appearance. The cells are large, polygonal and spindled with ample eosinophilic cytoplasm, some of the large cells are multinucleated and the nuclei have some variation in size, but no mitotic figures were seen. The intercellular matrix has a myxoid appearance. (Some of the slides do not show the whole picture because the biopsy was small)

Immunohistochemistry: Positive for: vimentin, CD68 and weakly for actin. Negative for: S100, EMA, CD34, and CK (wide spectrum).

Diagnosis: Plexiform fibrohistiocytic tumor/cellular neurothekeoma.

Discussion: The clinical picture fits well, these tumors occur in upper extremities of adolescent and has a predominance for females. The histological picture and immunologic profile is consistent with PFT/CNT but there is some pleomorphism and the background is more myxoid than usual.
A recent paper by Dr. Rosai and his group (AJSP Feb 2009) concludes that PFT and cellular neurothekeoma are the same tumor, and they share immunoreaction for CD68, vimentin and actin, different from myxoid and mixed neurothekeoma that commonly express S100, and I think this case illustrates this issue.

I would be delighted to hear your opinions.

AMR SEMINAR #57
CASE 24

Contributed by: Hugo Dominguez-Malagon, M.D. (Case # IC09-10079)

Clinical History: A 39-year-old female with the diagnosis of neurofibromatosis (established in another hospital since she was 13), developed a mass in the left interscapular region over the span of one year.
On physical examination, multiple café-au-lait spots and pedunculated nodules were observed in many regions of the body. CAT scan disclosed multiple pulmonary metastases.
The tumor was excised elsewhere and re-excised in our hospital.

Gross findings: The tumor measured 11.5 cm in diameter, the cut surface was heterogeneous with pale, myxoid and dark red areas.

Histological findings. The neoplastic cells are mainly spindled, arranged in several patterns: zones with with staghorn vessels (hemangiopericytoid), zones with spindle cells arranged in tight concentric structures (onion-leaf). Separated from this area there was an ample zone (not shown) of de-differentiation the appearance was of a high-grade spindle cell sarcoma with extensive geographic necrosis, and up to 5 mitosis per HPF.

Immunohistochemistry: In differentiated zones positive for CD34 and vimentin, weakly positive for C-Kit. Negative for EMA,BCL2, CK AE1-AE3 , CD56, Desmin, CD99, and S100. The undifferentiated zones were only positive for vimentin, and negative for CD34, CD56, CD99, Actin, S100, EMA, and Desmin.

Diagnosis: Dedifferentiated solitary fibrous tumor? Dedifferentiated peripheral nerve sheath tumor (perineurioma)? YOUR OPINION PLEASE.

Discussion: Taking in account that the patient has Von Recklinghausen, my first diagnosis was a PNST with dedifferentiation. The better differentiated zones resemble perineurioma with a nicely whorled pattern and have hemangiopericytoid zones. My surprise was that CD34 is intensely positive in this portion (negative in the high grade zones), but EMA (repeated twice), and S100 are completely negative in all areas.
Certainly the hemangiopericytoid zones have the patternless pattern similar to SFT but the whorls are not described in this tumor. Dedifferentiation in SFT has been recently described by Mosquera and Fletcher (AJSP 2009 Sep;33(9):1314-21).

AMR SEMINAR #57
CASE 25

Contributed by: Saul Suster, M.D.
(Case submitted by Dr. Rommel Ortega, Cancer Institute, Loja, Ecuador).

Clinical History: A 26-year-old woman was incidentally found to have a small, well-circumscribed 2 cm. nodule attached to the wall of her right distal ureters. The lesion was segmentally resected.

Pathologic findings: The lesion is composed of a well-circumscribed and encapsulated proliferation of spindle and small round cells embedded within a myxoid or mucinous stroma and accompanied by a dense plasma cell population. The tumor shows a hint of lobulation and in areas has a distinctive immature chondroid appearance. Many empty vacuoles are scattered throughout but no true signet-ring cells are noted. Some of the nuclei in the round cell population show cerebriform indentations of the nuclear membrane, and occasional multinucleated cells are also seen scattered about.

Special studies: A large battery of immunohistochemical stains was done on this case in an attempt to better define the cell population. The results were more confusing than illuminating. The only stain that was positive in the tumor cells was CD34, which showed a weak but distinct membrane pattern of staining in the round cells within the myxoid nodules. The positivity, however, was only patchy and inconsistent. Stains for cytokeratin AE1/AE3, SMA, desmin, Myo-D1, S-100 protein, MDM2, p63, CD31, SMMS, H-caldesmon, calponin, CD99 and CD117 were negative. Stains for kappa strongly highlighted the dense plasma cell population within the tumor; stains for Kappa were largely negative. A MIB-1 stain was negative in the nuclei of the tumor cells. Built-in controls in the periphery of the tumor stained appropriately for the various markers, indicating preserved antigenicity of the tissues.

Diagnosis: I don't know – HELP!!!

Discussion: I don't know what this tumor is. Possibilities that we considered included an epithelioid vascular neoplasm (but…CD31 is negative); a primitive cartilaginous tumor (?which type); and an extraskeletal myxoid chondrosarcoma (odd location, small size, well-circumscribed and encapsulated, no mitotic activity, nuclear features not quite right….). I still have a few blank slides in case anyone has any suggestions for further workup. I would greatly appreciate any help or suggestions from the club members.