AMR Seminar # 45 – Short Summary of Cases

Case 1: 40-year-old pregnant female with cyst in lower pole of left kidney

Case 2: 40-year-old female with skin tumor in right knee area

Case 3: 65-year-old woman with trigeminal nerve tumor

Case 4: 79-year-old man with testicular tumor

Case 5: 56-year-old female with 4 cm myometrial lesion

Case 6: 4-year-old male with a tumor in the right frontoparietal region

Case 7: Male patient underwent left condylectomy for a cystic lesion that recurred in 4 years

Case 8: 56-year-old female with symptoms of intestinal obstruction

Case 9: 52-year-old female with a painless subcutaneous mass in left knee region

Case 10: 79-year-old male with a mass in the anterior mediastinum

Case 11: 81-year-old female with a tumor in the nape of the neck for three years

Case 12: 80-year-old male presented with ulcerated exophytic tumor in sacral area

Case 13: 38-year-old female admitted with massive gastrointestinal bleeding

Case 14: 45-year-old male presented with 3-4 month cough, chest pain, weight loss and dysphagia

Case 15: 32-year-old woman with a large adrenal mass

AMR SEMINAR #45
CASE 1

Contributed by: Phil Allen, MD (FMC 02/S12986)

History: Female born 23 May, 1964. In 2002, an ultrasound taken during pregnancy was interpreted as showing a cyst arising from the lower pole of the left kidney. The cyst was drained under ultrasound guidance but it persisted. The drainage was repeated but the cyst remained and was then treated by open surgical "de-roofing." At operation, there was a retroperitoneal cyst with no obvious attachment to the kidney or pancreas which was not related to the ovaries. Nodular areas were noted within the cyst wall. The seminar section is the biopsy taken at the time of the de-roofing procedure. The patient did not return for follow-up and review after this surgery. She eventually represented to another doctor in September 2004 with a 30 centimetre retroperitoneal recurrence. I don't know what has happened to the patient since September.

Diagnosis: Primary borderline mucinous tumor, right infrarenal retroperitoneum.

Comment: I was not aware of this entity until I was asked to review the sections in 2002, when I discovered most of the references listed below, the abstracts of which summarize the knowledge of this rare entity much better than I can. It seems to be an unequivocal example of a primary retroperitoneal mucinous tumor which, so far, is not behaving in a high-grade fashion. I was not greatly impressed by the suggestion in one of the references below that hysterectomy and bilateral salpino-oophorectomy improves the prognosis. It seems that primary retroperitoneal mucinous tumors without anaplastic intramural nodules have a fairly good prognosis.
Do any club members have personal experience with this entity, and does anyone know what the prognosis is likely to be now, with a large local recurrence but no apparent distant metastases two years after the first biopsy?

References: Primary retroperitoneal mucinous cystoadenocarcinomas: an immunohistochemical and molecular study. Virchows Arch 1994;424(1): p53-7. Tenti P; Romagnoli S; Pellegata NS; Zappatore R; Giunta P; Ranzani GN; Carnevali L.
AB - Special immunohistochemical stains for the identification of gastroenteropancreatic antigens in two cases of primary retroperitoneal mucinous cystoadenocarcinomas (PRMC) show that these tumors have patterns similar to ovarian mucinous tumors. Markers of pyloric type gastric mucosa differentiation (M1, cathepsin E, concavavalin A, pepsinogen II) are mostly positive in benign and borderline areas with endocervical type differentiation, while immunoreactivity for intestinal cell markers (M3SI and CAR-5) and for DU-PAN-2 is present mainly in frankly malignant areas, regardless of differentiation type. DNA analysis shows a point mutation of K-ras oncogene at codon 12 (GGT to CGT) in one case. The immunohistochemical and genotypic similarity of PRMC and ovarian mucinous tumors may indicate similar mechanisms in their histogenesis.

Primary retroperitoneal mucinous cystadenoma. A case report and brief review of the literature. Zentralbl Chir 2003 Aug;128(8): p691-3. Gutsu E; Mishin I; Gagauz I.
AB - Retroperitoneal mucinous cystadenomas are extremely rare tumors found exclusively in women. An additional case of retroperitoneal mucinous cystadenoma histologically confirmed in a 41-year- old woman is reported herein. Computed tomographic (CT) scanning showed a cystic mass, 21 x 16 cm in size, in the right retroperitoneal space. Removal of the cystic tumor was performed without any other additional procedures, and further histological diagnosis was

confirmed as primary mucinous cystadenoma of borderline type. Histologic findings suggested that the tumor developed from mucinous metaplasia of the coelomic mesothelium. Clinicopathological features, diagnostic findings, therapeutic options and the outcome are analyzed in this paper having reviewed the cases reported in world literature.

Retroperitoneal primary mucinous adenocarcinoma with a mural nodule of anaplastic tumor: a case report and literature review. Int J Gynecol Pathol 2003 Apr;22(2): p205-8. Mikami M; Tei C; Takehara K; Komiyama S; Suzuki A; Hirose T.
AB - A 38-year-old female presented with a lower abdominal mass. During the operation the mass was found to be retroperitoneal and was excised. Gross examination revealed a mucin-containing cystic lesion with a mural nodule. On microscopic examination, the cystic areas were lined by an invasive mucinous adenocarcinoma and the nodule was composed of an anaplastic sarcomatoid tumor that was immunoreactive for cytokeratin. This present case is the 21st example of a retroperitoneal primary mucinous cystadenocarcinoma and the fourth with a mural nodule. Three of four cases with a mural nodule, including our case, had a rapidly fatal outcome.

Treatment of a case of primary retroperitoneal mucinous cystadenocarcinoma: is adjuvant hysterectomy and bilateral salpingo-oophorectomy justified? Am J Obstet Gynecol 2002 Jul;187(1): p227-32. Kessler TM; Kessler W; Neuweiler J; Nachbur BH.
AB - OBJECTIVE: We present a case of primary retroperitoneal mucinous cystadenocarcinoma in a 38-year-old woman. STUDY DESIGN: The tumor was resected with a segment of adjacent descending colon. Five years after the operation, the patient is well, without evidence of recurring disease, based on clinical investigation and modern imaging techniques. RESULTS: In the light of the literature, it appears most likely that this rare tumor is caused by coelomic metaplasia. On the basis of the histopathologic findings in our case and the reports from the literature, we recommend radical tumor excision en bloc with all infiltrated adjacent structures. CONCLUSION: Added removal of unaffected uterus and adnexes makes young women infertile and climacteric and is not yet validated by long-term results.

Ruptured retroperitoneal mucinous cystadenocarcinoma with synchronous gastric carcinoma and a long postoperative survival: case report. J Surg Oncol 2000 Jan;73(1): p26-30. Uematsu T; Kitamura H; Iwase M; Tomono H; Nakamura M; Yamashita K; Ogura H.
AB - We describe an 86-year-old woman with a long survival following surgery for a massive retroperitoneal mucinous cystadenocarcinoma and a synchronous gastric carcinoma. Computed tomography showed a huge tumor with septation and calcification. Upper gastrointestinal radiography showed the additional gastric lesion. At operation, the 23 x 20 x 12-cm retroperitoneal tumor had ruptured. Tumor resection and distal gastrectomy including regional lymph nodes were performed. Mucinous peritoneal implants were removed as completely as possible. Histologically, the mucinous tumor showed limited invasion, whereas the poorly differentiated gastric adenocarcinoma showed no serosal invasion. Among 18 retroperitoneal mucinous cystadenocarcinomas reported in the English literature since 1965, only ours was associated with gastric carcinoma. Despite peritoneal implants, our patient has survived for 6 years without clinical recurrence. As at other sites, retroperitoneal mucinous cystadenocarcinoma often grows slowly. Total removal, even after peritoneal dissemination, can result in long survival. [Copyright 2000 Wiley-Liss, Inc.].

Retroperitoneal mucinous cystadenoma. Arch Pathol Lab Med 2001 May;125(5): p691-4. Subramony C; Habibpour S; Hashimoto LA.
AB - Primary retroperitoneal mucinous cystadenoma is an uncommon tumor found exclusively in women. Herein, we describe a patient who had resection of a large retroperitoneal cystic mass. Histologic, immunohistochemical, and electron microscopic examination of the lining epithelial cells showed features of mesothelial cells in addition to ovarian mucinous cystadenoma. These

findings suggest that these tumors arise from inclusions of mesothelial cells and subsequent mucinous metaplasia of the lining cells to form a cystadenoma. Estrogen receptors may be implicated in tumor promotion, explaining the occurrence exclusively in women.

Primary retroperitoneal mucinous tumor of low malignant potential: histogenetic aspects and review of the literature. APMIS 1997 Jun;105(6): p483-6. Papadogiannakis N; Gad A; Ehliar B.
AB - We report an unusual mucinous tumor of low malignant potential, of ovarian-like type, arising in the retroperitoneum of an otherwise healthy 33-year-old woman. This is the fifth described case of such a tumor in the world literature, and the first reported in Scandinavia or Europe. We also discuss aspects of the histogenesis of this type of tumor and review the available literature. The histological heterogeneity and metastatic potential of the tumor warrant careful histopathologic analysis and follow-up of patients presenting with such lesions.

Two cases of primary retroperitoneal mucinous cystadenocarcinoma. Gynecol Oncol 1996 Oct;63(1): p145-50. Lee IW; Ching KC; Pang M; Ho TH.
AB - Two cases of primary retroperitoneal mucinous cystadenocarcinoma of the ovarian type in the presence of bilateral normal ovaries are reported. Benign, borderline, and malignant mucinous epithelium was present in both tumors; no separate ovarian tissue was identified. In addition to removal of the tumor, the uterus and both ovaries were removed and the patients are well with no evidence of disease at 30 and 15 months. Only 10 cases of primary retroperitoneal mucinous cystadenocarcinoma have been reported in the English literature and these are reviewed. The outcome of these limited number of cases suggests that removal of both ovaries and the uterus in addition to extirpation of the retroperitoneal tumor, even though the uterus and ovaries are normal, may improve the prognosis.

Primary mucinous cystadenocarcinoma of the retroperitoneum. Report of a case and literature review. Virchows Arch 1995;426(6): p641-5. Carabias E; Garcia Munoz H; Dihmes FP; Lopez Pino MA; Ballestin C.
AB - Primary retroperitoneal mucinous cystadenocarcinoma (PRMC) is a rare tumor, similar to its ovarian counterpart but without any evidence of ovarian, pancreatic or another extra-retroperitoneal origin. Histogenesis of this neoplasm remains uncertain. Mucinous or coelomic metaplasia of retroperitoneal mesothelium has been recently proposed as its origin. In a 43-year-old woman with a 15-cm cystic lesion in the right retroperitoneum mucinous cystadenocarcinoma was diagnosed, and no primary tumor was identified. Two peritoneal endometriotic foci were found on further surgery. We suggest a common histogenesis for PRMC and these endometriotic foci.

Primary mucinous cystoadenocarcinoma of the retroperitoneum: two cases. Gynecol Oncol 1994 Nov;55(2): p308-12. Tenti P; Carnevali L; Tateo S; Durola R.
AB - Two cases of primary retroperitoneal mucinous cystoadenocarcinoma of the ovarian type are reported. Both tumors occurred in females with bilateral normal ovaries and contained benign, borderline, and malignant mucinous epithelium. Full-thickness infiltration of the cyst wall was not found. In addition to surgery, one patient was given chemotherapy because of spillage from the tumor during intervention. There were no recurrences and no evidence of metastatic disease 19 and 33 months after diagnosis. Histologic findings suggest that the tumors had developed through mucinous metaplasia in preexisting mesothelial cysts.

Laparoscopic resection of a primary retroperitoneal mucinous cystadenoma: report of a case. Surg Today 1998;28(3): p343-5. Chen JS; Lee WJ; Chang YJ; Wu MZ; Chiu KM.
AB - Primary retroperitoneal mucinous cystic tumors are extremely rare, and although their histogenesis is still uncertain, several theories have been proposed. Traditionally, transabdominal laparotomy and enucleation of the cyst is the treatment of choice and laparoscopic resection has not previously been reported. This paper presents the case of a 48-year-old woman in whom a

primary retroperitoneal cystic mass, 15 x 13 x 9 cm in size, was successfully resected through the laparoscope. Pathological examination revealed a mucinous cystadenoma with borderline malignancy. The patient had a prompt recovery and there was no evidence of recurrence at her 8-month follow-up. However, the prevention of cystic fluid spillage during laparoscopic manipulation is important, especially when the pathology of the retroperitoneal cyst is unclear.

Primary retroperitoneal mucinous cystadenocarcinoma of low malignant potential: a case report and literature review. Gynecol Oncol 1996 Apr;61(1): p150-2. Pearl ML; Valea F; Chumas J; Chalas E.
AB - A case of primary retroperitoneal mucinous cystadenocarcinoma of low malignant potential in the presence of normal ovaries is reported. The precise etiology of these neoplasms has not been defined; however, they may arise from heterotopic ovarian tissue, monodermal teratomas, embryonal urogenital remnants, intestinal duplication, or coelomic metaplasia. Although minimal data exist to define the appropriate management, it seems reasonable to extrapolate from the treatment of analogous ovarian neoplasms.

Primary retro peritoneal mucinous cystadenoma. Acta Obstet Gynecol Scand 2003 May;82(5): p486-7. Erdemoglu E; Aydogdu T; Tokyol C.

Primary retroperitoneal mucinous cystadenoma. Acta Obstet Gynecol Scand 1998 Mar;77(3): p357-8. Yunoki Y; Oshima Y; Murakami I; Takeuchi H; Yasui Y; Tanakaya K; Konaga E.

AMR SEMINAR #45
CASE 2

Contributed by: Carlos Bacchi, MD

History: This is a 40-year-old female with history of resection of a skin tumor in 2000 (Slide A) in her right knee area. There were 3 local recurrences (2002, 2003 and 2004). In November 2004 the patient developed right inguinal lymphadenopathy. The lymph node was removed and this is represented in Slide B. I had no access to the slides of recurrences, only the original tumor (slide A) and the lymph node with metastatic disease (slide B).

Microscopic Findings: Slide A (I am sorry but when the paraffin block was cut part of the lesion was not represented in all HE sections sent). The part missing had identical histology compared to the one seen in the slide A) shows flat lesion with hyperplastic epidermis with hyperpigmentation. Mainly in the dermis there is a non-encapsulated neoplasia with the presence of a grenz zone. The tumor has a storiform growth and it is formed by variably prominent, spindle (fibroblast-like), oval to round and/or polyhedral (histiocyte-like) cells, often in a collagenous stroma. Some of the tumor cells have hyperchromatic nuclei. There is also among the tumor cells a considerable number of large histiocytes with foamy cytoplasm, some laden with hemosiderin and few lymphocytes. Coarse deposition of hemosiderin is seen. Rare multinucleated cells are present. The stroma in the less cellular areas is collagenous-type. Mitotic figures are not a common feature in this Slide A (skin lesion). Necrosis and vascular invasion are not seen.
Slide B reveals metastatic disease from the skin lesion with growth into the adjacent nodal tissue including mature fat. Although the histology is very similar compared to slide A, there are some areas where the neoplasia is more cellular in slide B. In these areas, mitotic figures reach up to 3-5 per 10HPF with the presence of atypical mitosis.

Immunohistochemical Results: The following markers were negative in the tumor cells in this case: CD34, desmin, EMA, factor XIIIa, CD68, S-100 protein and cytokeratin 8.

Diagnosis: Metastasizing cellular dermatofibroma (atypical fibrous histiocytoma?) of the skin.

Comment: I thought that it would be interesting to present this case as I believe that looking at the skin lesion alone it would be difficult to predict that this case would recur and metastasize (four years later). We do have some areas in slide A where the tumor cells have large and hyperchromatic nuclei but the mitotic rate is very low. I had no access to the slides of the recurrent disease. In these lesions, the histology could be somewhat different, compared to the original tumor, including higher cellularity and/or presence of pleomorphism and higher mitotic rate but we cannot tell, as these slides were not available. In 1996, Dr. Harry Evans from MD Anderson described two cases of metastasizing cellular dermatofibroma including metastasis to the lung in one patient. Some years before this study by Evans, Eduardo Calonje along with Dr. Mentzel and Dr. Fletcher had described the considerable frequent rate of recurrence (26% out of 74 cases) in cellular dermatofibromas. In my opinion, the main differential diagnosis in this case would be with the so-called atypical fibrous histiocytoma (pseudosarcomatous, dermatofibroma with monster cells) of the skin. AFH is an uncommon variant of cutaneous fibrous histiocytoma. Histologically, this tumor is usually a dermal lesion with pleomorphic cells set in a background of classic fibrous histiocytoma. Chris Fletcher can help us in this differential diagnosis as he published in 2002 a series of 49 cases of AFH with three patients with local recurrence and two

with distant metastases. Not knowing the lesion B how would the AMR members classify lesion A (skin lesion)?

References:

1-Kaddu S, McMenamin ME, Fletcher CD. Atypical fibrous histiocytoma of the skin: clinicopathologic analysis of 59 cases with evidence of infrequent metastasis. Am J Surg Pathol. 2002 Jan;26(1):35-46.

2- Guillou L, Gebhard S, Salmeron M, Coindre JM. Metastasizing fibrous histiocytoma of the skin: a clinicopathologic and immunohistochemical analysis of three cases. Mod Pathol. 2000 Jun;13(6):654-60.

3- Colome-Grimmer MI, Evans HL. Metastasizing cellular dermatofibroma. A report of two cases. Am J Surg Pathol. 1996 Nov;20(11):1361-7.

4- Calonje E, Mentzel T, Fletcher CDM. Cellular benign fibrous histiocytoma. Clinicopathological analysis of 74 cases of a distinctive variant of cutaneous fibrous histiocytoma with frequent recurrence. Am J Surg Pathol 1994;1:2-15.

AMR SEMINAR #45
CASE 3

Contributed by: Kum Cooper, MD

History: This is a trigeminal nerve tumor (intracranial) from a 65-year –old woman.

Diagnosis: Myxoid schwannoma.

Comment: The reason for submitting this case is that I was struck by the similarity of the myxoid lobules of this tumor to that of dermal nerve sheath myxoma (neurothekeoma). However, the latter is extremely rare outside of the skin (CDMF, personal communication). Further, on pursuing through the AFIP Fascicle #24 on tumors of the peripheral nerve (page 241, Fig. 9-26) it illustrates a beautiful example (identical to the submitted case) of a "myxoid schwannoma mimicking nerve sheath myxoma". Similarly, careful examination of the compact areas between the myxoid component reveals islands of Antoni A tissue typical of schwannoma. This case was diffuse and strongly positive for S-100 and negative for GFAP and EMA. Given the rarity of this myxoid variant of schwannoma, I thought members may like to view this case on the glass.

AMR SEMINAR #45
CASE 4

Contributed by: Ivan Damjanov, MD

History: A 79 year old man presented with a testicular tumor. An orchidectomy was performed and a few days later multiple enlarged paraaortic lymph nodes were removed.

Pathology: The testicular tumor and the lymph node metastases had the same microscopic features. The slide that you have is from a metastasis.

The tumor is composed of relatively uniform cells that have vesicular, round or oval nuclei surrounded by a small amount of amphophilic or clear cytoplasm. The cells form tubules, cords or solid nests. These nests and tubules are focally surrounded by a basement membrane. Focally the cells appear larger and have more abundant cytoplasm. There are on average 2-3 mitoses per ten high power fields. Tumor cells are seen within the lumen of some blood vessels.

Diagnosis: Malignant Sertoli cell tumor metastatic to the abdominal lymph nodes.

Comment: Just a rare tumor for your collection.

AMR SEMINAR #45
CASE 5

Contributed by: Angelo Dei Tos, MD

History: 56-year-old female presenting with 4 cm myometrial lesion.

Diagnosis: Low-grade endometrial stroma sarcoma with sex cord differentiation. The sex cord component is positive for CD10, keratin and inhibin.

AMR SEMINAR #45
CASE 6

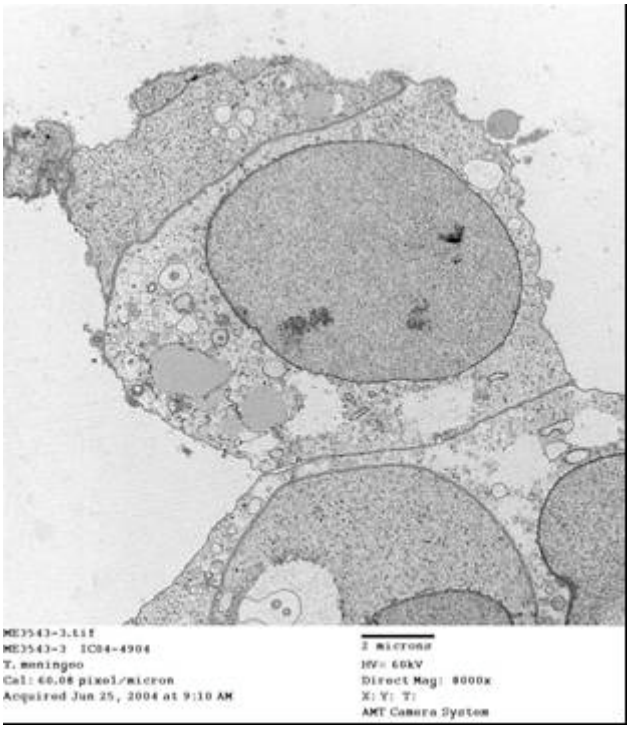
Contributed by: Hugo Dominguez-Malagon, MD

History: A four year-old male child was seen for an intracranial, apparently meningeal tumor located at the right frontoparietal region.

Histological findings.
The tumor is composed of cords and strands of cells immersed in abundant myxoid matrix that was Alcian blue positive and PAS negative. The cells are round or polygonal with moderate amount of somewhat vacuolated cytoplasm, the nuclei are slightly hyperchromatic and variable in size with few pseudo-inclusions.

Immunohistochemistry.
Cells expressed only vimentin, and were negative for cytokeratin (AE1-AE3), EMA, GFAP, chromogranin, Synaptophysin, S100, CD99, and actin.

Electron microscopy.
Polygonal cells with parallel membranes devoid of cell processes and junctions, the cytoplasm contains glycogen and inclusions of lipid material. Nuclei are ovoid, with euchromatin. The extracellular matrix is loose and granular.



Diagnosis: Chordoid Meningioma ?

Comment: Chordoid meningioma is a rare variant often associated with peritumoral lymphoplasmacellular infiltration and Castleman syndrome. In the original paper by Kepes in 1987 it was described as a meningeal tumor in young patients associated with microcytic anemia and/or dysgammaglobulinemia. The largest series is of 42 cases from Mayo clinic (senior author Dr. Sheitauer), mean age was 47 years (range 12 to 77), 88% were supratentorial, chordoid elements comprised 10 to 100% of the tumor, mild to moderate lymphoplasmacytic elements were present in 59%, and most were unassociated with systemic manifestations. It is composed of nests and cords of spindle and epithelioid cells with abundant myxoid matrix , mimicking the features of chordoma, but foci of typical meningioma can be observed.

The present case has clinical and histological features consistent with chordoid meningioma, in fact this case was seen by several pathologists in Canada and they agreed with this diagnosis; however, the immunos and the ultrastructural picture does not support this diagnosis. Any ideas?

AMR SEMINAR #45
CASE 7

Contributed by: Vincenzo Eusebi

Clinical History: Eight years ago this male patient underwent left condylectomy for a cystic lesion that was named "central reparative granuloma" (slide 96/10564). The lesion recurred 4 years later showing identical features (slide not shown) that was reported by a different pathologist and called it "giant cell tumor". Now (August 2004) (slide 04/18860) metastases are evident in 2 axillary lymph nodes.

Diagnosis: None at this time

Comment:
I have shown the case to Franco Bertoni who is inclined to call the tumor as a (bona fide) osteosarcoma. Nevertheless Franco (and also myself) cannot explain the fact that bone tissue in the tumor looks reactive and not neoplastic.

I wonder how people of the seminar would label this case:

*Is malignancy obvious in the biopsy of 1996.

* Would you call the metastasis osteosarcoma.

I am sorry but recuts have rendered the tumor very small in some sections.

AMR SEMINAR #45
CASE 8

Contributed by: Cyril Fisher, MD

History: A female aged 56 presented with symptoms of intestinal obstruction, thought to be due to adhesions following removal of a left ovarian tumor two years previously. At surgery an irregular thickening of the wall of the sigmoid colon was found and a sigmoid colectomy performed. No other lesions were seen in the abdomen.

Pathology: The gross specimen was a portion of colon with two perforations over the irregularly thickened wall. Microscopically, nodules of osteoclast-like cells in a mononuclear cell background with mild pleomorphism, mitoses, and hemosiderin pigment infiltrate the muscle coat and ulcerate the mucosa. Immunostaining is focally positive for SMA in the mononuclear cells and negative for several cytokeratins, CD117, S100 protein, CD34, HMB45 and lymphoid markers.

The left ovarian tumor removed two years previously was a borderline mucinous cystadenoma with 'thickening' of the wall which showed a histologically similar giant cell lesion (slide not submitted), with bland mononuclear cells. The colonic lesion is more mitotically active and pleomorphic than the ovarian lesion.

Diagnosis: Giant cell tumor involving sigmoid colon, following excision of borderline mucinous ovarian tumor with sarcoma-like mural nodules.

Comment: The ovarian lesion had a smooth outer surface and was apparently completely excised without tumor spillage. However, the colonic infiltration is presumably related to the lesions in the (nearby) left ovarian tumor by direct spread, metastasis, or implantation at surgery. A less likely explanation is a primary giant cell tumor involving the bowel wall. Mural nodules in ovarian mucinous tumors include benign looking "reactive" or "sarcoma"-like nodules (of which a proportion display focal cytokeratin positivity), benign mesenchymal tumors, anaplastic carcinomas, and frank sarcomas. Their behavior varies, but the sarcoma-like nodules generally do not recur or metastasize. Both the recurrence and the penetration of the bowel wall as here are unusually aggressive.

AMR SEMINAR #45
CASE 9

Contributed by: Christopher D.M. Fletcher (S04-10079)

History: A 52-year-old woman presented with a painless subcutaneous mass in the region of the left knee. There was no attachment to bone. After thorough work-up, there was no evidence of any lesion elsewhere.

Diagnosis: Extraskeletal Ewing's sarcoma / PNET

Comment: I put in this case, which was kindly sent to me by Dr. L. Gui in Jackson, MS, in order to remind all of us how the morphologic spectrum of any given tumor type is broader than we would like to think! This is an almost triphasic neoplasm, consisting of a sheet-like proliferation of monomorphic rounded cells which, indeed, would fit well with Ewing's – associated with striking nodular whorls of rather smaller rounded cells and a loose, somewhat spindled stroma with focally myxoid matrix. The round cell areas (of both types) show multifocal (not diffuse) positivity for CD99 but, in addition, the cellular whorls, and to a lesser extent the sheet-like areas, show striking positivity for keratin, S-100 protein and focally for GFAP. The spindled component set in a myxoid stroma is strongly GFAP and S-100 protein positive but CD99 negative. Additionally, the more cellular small cell nodules show strong positivity for chromogranin. When I first saw this case, with this immunophenotype, I wondered about the possibility of an unusual myoepithelial carcinoma with neuroendocrine differentiation. However, approximately 10 days later, Dr. Gui called me to let me know that their cytogenetics laboratory had found a classical t(11;22) (q24;q12) translocation characteristic of Ewing's sarcoma. I was so astonished by this result that I re-requested the block so that we could try and confirm this finding by an alternative technique. We performed FISH analysis for *EWS* gene rearrangement and, indeed, there was clear evidence of such a rearrangement, essentially putting the diagnosis beyond doubt. Only 10 days later, I saw a tumor from the femur of a 30-year-old man which had absolutely (to me!) characteristic morphology of a moderately differentiated neuroendocrine carcinoma ('atypical carcinoid') so I initially suggested that it might be a metastasis. However, immunostains were more suggestive of Ewing's sarcoma and that diagnosis was also confirmed molecularly. After these two cases, I have become much more willing to consider Ewing's/PNET with all manner of strange morphologies!

AMR SEMINAR #45
CASE 10

Contributed by: Jerónimo Forteza Vila

History: 79-year-old male patient with a mass in anterior mediastinum. The biopsy is made at another hospital and a lymphoma is diagnosed. It does not respond to chemotherapy or radiotherapy. Another biopsy is made through mediastinoscopy in our hospital.

Histology. There are neoplastic epithelial nodules due to spindle cells with oval nucleus. There is no atypia or mitosis in a lymphocytic background.

Immunohistochemistry. Neoplastic cells are AE1/AE3+, Cam5,2+ CD72+ and CD20-. The stroma is CD20+ and some isolated cells are CD5+ and CD3+.

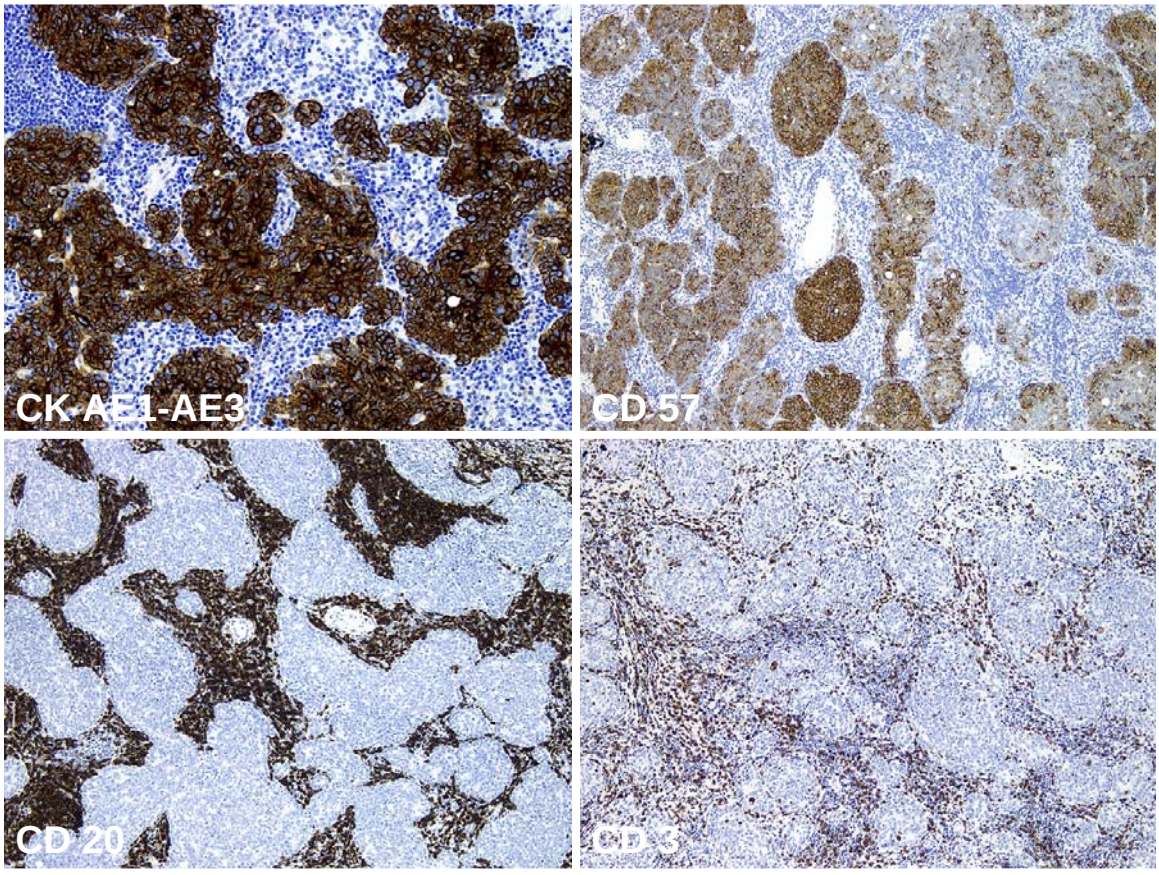
Diagnosis: Micronodular thymoma with lymphoid stroma from the WHO classification.

Comment: This entity entails 1 to 5% of all thymomas. It poses differential diagnosis with type-AB thymoma, but this has intraepithelial lymphocytes.

It is a low malignant non-metastatic tumor. Negativity for CD20 in the epithelial component is basic for the differential diagnosis with AB-type and A-type thymoma.

(See following page for pictures)

M.79 with anterior mediastinal mass.



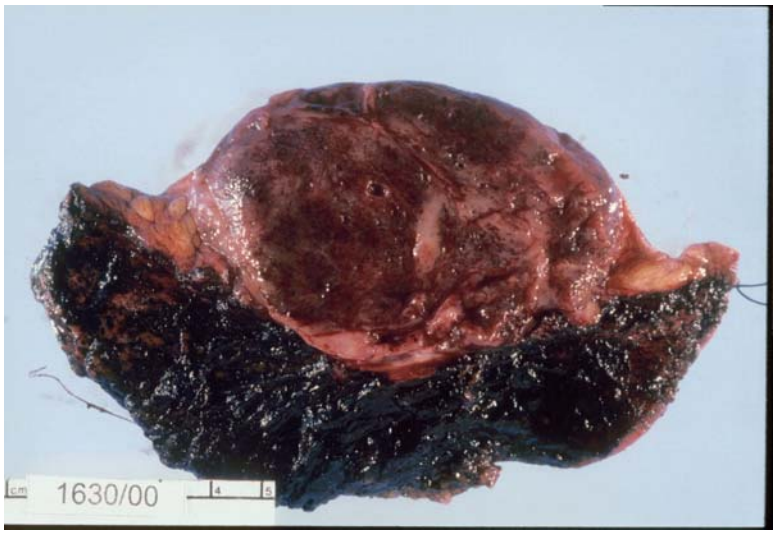
AMR SEMINAR #45
CASE 11

Contributed by: Janez Lamovec, MD (1630-00)

History: An 81-year-old woman was admitted with a tumor of the nape of the neck that she first noted three years before; it rapidly enlarged in the last couple of months. FNAB of the tumor was performed at another institution and a diagnosis of probable fibrosarcoma was suggested. The tumor was excised.

Pathological findings: Gross specimen was represented by a segment of skin and subcutaneous tissue and muscle fascia at a deep margin with a large 8.5 x 6 cm tumor that bulged the overlying skin. On cut surface, the tumor was fleshy, red-brown, soft, well circumscribed (see gross picture).
Microscopically, the tumor shows numerous cysts filled with blood or proteinaceous fluid; smaller cysts are for the most part empty. Among the cysts there is a relatively loose cellular tissue composed of spindle, oval or stellate cells with different sized relatively normochromatic nuclei and eosinophilic cytoplasm. Mitoses are difficult to find. Some cells are binucleated. The amount of collagen in the matrix varies in different fields, in the microcystic areas the stroma is more myxoid in appearance. No lipocytes or lipoblasts are present.
Tumor cells were uniformly positive for vimentin and CD34, many of them for bcl-2, and some for calponin. Many other markers were negative, including CD117, SMA and desmin. Most of the cystic spaces are lined by tumor cells and not by endothelium.

Diagnosis: I am not sure how to call this tumor. I first thought that this may be some kind of "aneurysmal" type of SFT. This case was seen by Chris Fletcher who commented that he labeled such tumors as "pericytoma-like fibroblastoma" and added that SFT and the former tumor probably form a continuum with no clear line of separation. I wonder what other members of the club think about this tumor, and also if Chris has come to some additional conclusions in this regard.



AMR SEMINAR #45
CASE 12

Contributed by: Michal Michal, MD

History: An 80-year-old man clinically presented with an ulcerated, exophytic tumor in his sacral area. Clinical differential diagnostic considerations: basal cell carcinoma, melanoma, and a malignant adnexal tumor. The neoplasm was surgically excised with a safe margin. Follow-up physical examination at 7 months after the surgery revealed no recurrence of the lesion.

Histopathological findings: There are variably sized and shaped nodules and cribriform structures composed of 'basaloid" epithelial cells that are invariably associated with mesenchymal cells resembling a specific trichogenic stroma. There is pleomorphism, nuclear crowding, individual cell necrosis and atypical mitotic figures both in the epithelial cells and mesenchymal cells. Nowhere in the tumor are there transitions between the malignant epithelial and malignant stromal component. Both the epithelial and stromal component is admixed as though being mutually dependent, with no areas revealing a high-grade tumor or dedifferentiation. There is no heterologous component. Immunohistochemically, the epithelial component was cytokeratin positive and vimentin negative, while the mesenchymal component was negative for cytokeratins and positive for vimentin.

Diagnosis: Low-grade trichoblastic carcinosarcoma of the skin (1)

Comment: The tumor is very unusual. It is a *carcinosarcoma* because it is a biphasic tumor that is composed of an epithelial and a mesenchymal component, and both are cytologically malignant. It is *"trichoblastic"* because the neoplasm is a malignant caricature of a trichoblastoma: the basaloid epithelial cells resemble follicular germinative cells and the mesenchymal cells are reminiscent of a specific trichogenic stroma. It may be the only authentic carcinosarcoma of the skin considering embryology and histogenesis of a hair follicle. The vast majority of cutaneous carcinosarcomas reported so far were probably metaplastic (sarcomatoid) carcinomas. The best comparable tumor is ameloblastic fibrosarcoma, a mixed epithelial-mesenchymal odontogenic neoplasm in which the mesenchymal component is sarcomatous, and the epithelial component can be likened to ameloblastoma.
We have recently identified a second example of this tumor. Please, if you have seen or will see such a tumor contact us.

References: 1. Kazakov DV, Kempf W, Michal M. Low-grade trichoblastic carcinosarcoma of the skin. Am J Dermatopathol 2004;26(4):304-309.

AMR SEMINAR #45
CASE 13

Contributed by: James A. Strauchen, M.D.

History: This 38-year-old woman from Colombia was admitted to our affiliated public hospital with massive gastrointestinal bleeding. At surgical exploration discrete masses were identified in the small intestine and resected.

Pathology: The specimen consisted of two segments of small bowel measuring approximately 10 cm in length and containing an ulcerated mass lesion extending from the mucosa to the serosa. Frozen section diagnosis was "granulomatous inflammation". Permanent sections show the pathology illustrated here with transmural granulomatous inflammation with marked eosinophilia and numerous degenerating larvae in the mucosa. In many of your sections at one edge the adult worms may be seen living within the mesenteric arteries.

Diagnosis: Abdominal angiostrongylosis due to Angiostrongylus costaricensis.

Comment: Abdominal angiostrongylosis is more familiar to pathologists in Central and South America, where it occurs with some frequency and mimics appendicitis or Crohn's disease. The genus Angiostrongylus are nematode worms which live in the blood vessels of mammals, including rodents and man. Slugs and snails are the intermediate host. Two species affect man: Angiostrongylus cantonensis is found from West Africa to Southeast Asia and causes an eosinophilic meningoencephalitis. Angiostrongylus costaricensis is found in Central and South America and causes abdominal angiostrongylosis. The adult worms inhabit the mesenteric arteries of the ileum, cecum, and appendix. There they lay eggs which are carried to the mucosa where they hatch into larvae which degenerate eliciting a granulomatous response with numerous eosinophils. Patients are typically children presenting with right lower quadrant abdominal pain and tenderness or mass, fever, and eosinophilia. The diagnosis is established at surgery because the eggs and larvae are not passed in the stool. Treatment is surgical resection of the affected segment. The role of antihelminths (mebendazole) is not established.

References: Loria-Cortes R, Lobo-Sanahuja JF. Clinical abdominal angiostrongylosis. A study of 116 children with intestinal eosinophilic granuloma causes by Angiostrongylus costaricensis. Am J Trop Med Hyg 1980: 29:538-544.

AMR SEMINAR #45
CASE 14

Contributed by: Paul E. Wakely, Jr.

History: A 45-year-old man presented with 3-4 months of cough, chest pain, 10-pound weight loss, and dysphagia. CT scan of the chest found an 8 cm. superior mediastinal mass that extended from the thyroid to the level of the carina encasing the R innominate and R common carotid arteries. There was compression of the airway displacing the trachea superiorly and to the left. His past surgical history is significant for his right testicle removed at age 5 yrs. Serum AFP and HCG levels are normal. Cytogenetics showed two cells with deletions of 15q. The cytogeneticist says these cells may represent the malignancy, or they may be a result of a "culturally-induced" artifact. Patient also has a 5 cm. solid renal mass that has not been biopsied after 4 months. He had a good response to initial chemotherapy and radiation treatments.

Pathology: The H&E slide shows a sheet of large cells with foci of coagulation tumor necrosis and many mitotic figures. Nuclei are large, pleomorphic, and most contain a single macronucleolus. A moderate amount of eosinophilic cytoplasm is present. In the majority of cells the nucleus is eccentrically situated with the cytoplasm forming a paranuclear globular shape. Scattered among these malignant cells are mature plasma cells. The tumor was negative for S-100, HMB-45, CD3, CD5, CD20, CD30, CD45, cytokeratin AE1/3, CD31, Alk-1, PLAP, SMA, CD34, CD68, CD35, HHF-35 actin, myogenin, low mol. weight cytokeratin, high mol. weight cytokeratin, CAM 5.2, CK7, CD138, CD15, CD7, CD4, CD2, and CD43. Diffuse positive staining occurred with vimentin. EM showed only a small number of intermediate filaments.

Comment: I was left to conclude that this is an example of a mediastinal Extrarenal Rhabdoid Tumor (undifferentiated sarcoma with rhabdoid features) in an adult. It occurred to me (as I'm sure it has to you) that this mediastinal tumor may represent a metastasis from the kidney mass. Yet, since it does not have the chromosome 22 abnormality that is reported in 80% of rhabdoid tumors of the kidney and brain, I could not be sure of that conclusion. I doubt that the kidney mass will be sampled, and to my knowledge the patient has no CNS lesions. Has anyone seen this morphology in the mediastinum of an adult after excluding a wide range of other mesenchymal and epithelial tumors from consideration? Does anyone have another suggestion for what this might be?

AMR SEMINAR #45
CASE 15

Contributed by: Lawrence Weiss, MD

History: A 32 year old woman was found to have a large adrenal mass (why and how it was found I do not know). A pancreatectomy, splenectomy and an adrenalectomy was performed.

Gross findings: The adrenal was 12 cm. in length and weighed 456 grams. On cut section, it contained a solid, firm tan mass, with a small rim of adrenal at the periphery.

Immunostains:	Keratin	-
	Neurofilament	-
	S-100 protein	-
	CD34	-
	ALK	-

Diagnosis: Inflammatory pseudotumor

Comment: To my knowledge, there are no published cases of inflammatory pseudotumor of the adrenal. We considered a few other diagnoses, but the immunostains seemed to rule out everything else we thought about. It looks more inflammatory than pseudotumor. This is not how hemorrhagic necrosis resolves-that usually turns into a pseudocyst and does not get to 12 cm. Am I missing something? Has anyone else seen something like this?
One interesting finding is that there is both compressed cortex and medulla at the edge of the lesion.

AMR SEMINAR #45
Quiz Case 1

Contributed by: Hugo Dominguez-Malagon, MD

A 32-year-old woman with gross hematuria and mild abdominal pain. A CAT scan demonstrated a 5.8 x 4.7 cm mass arising from the central portion of the right kidney. Grossly the tumor was circumscribed, without involvement of renal vessels or pelvicalyceal system.

Quiz Case 2

Contributed by: Paul E. Wakely, Jr.

I presented this case recently at our daily peer review conference, and Saul suggested I send it in to the group as a quiz case. This is a hilar lymph node from a 40 y/o woman who also had a wedge resection of a mass in the right lower lobe of her lung that turned out to be a necrotic granuloma. There is an attached photo of a GMS stained image of this node.

Follow-Up Comments
AMR # 39 - Case 19

Contributed by: Saul Suster, MD

I would like to share with the group some recent follow-up on this case which I presented about 2 years ago. The original history was that of a 59 year old woman with a large retroperitoneal mass. Her past medical history was remarkable for hysterectomy 6 years earlier for uterine leiomyomas. The tumor was very hemorrhagic and the pathologic specimen was not very well-preserved, so a definitive diagnosis could not be rendered. The diagnosis rendered was "undifferentiated malignant neoplasm, favor sarcoma". The patient was treated with chemotherapy and radiotherapy and was readmitted after 1 year with recurrence of the mass plus a metastasis to the liver. A repeat operation revealed 2 discrete lesions, one measuring 6 cm. in diameter anterior to the bifurcation of the aorta, and a smaller one in paravertebral location. An extensive immunohistochemical workup was done; the only positive stain was cytokeratin AE1/AE3, which showed focal strong, convincing positivity. In one of the sections, a strip of glandular epithelium resembling Mullerian epithelium was seen within the tumor. At that time, I felt the best I could do was to call this a "low-grade carcinoma, NOS".

The patient was recently readmitted in November 2004 with another recurrence of her pelvic and retroperitoneal mass. The new tissue shows, in my opinion, more classical features of a low-grade endometrial stromal sarcoma . We repeated the immunohistochemical stains on the new material and this time the cells strongly and convincingly labeled for CD10 antibodies. In addition, the tumor cells are strongly positive for estrogen receptors.

Although the original hysterectomy specimen was not available for review to confirm the diagnosis of uterine leiomyomas, I believe this may correspond to an extrauterine endometrial stromal sarcoma initially presenting in the retroperitoneum. The portion of normal-appearing Mullerian epithelium seen in the original sections I submitted may correspond to a residual focus of endometriosis that has been overrun by the tumor.

I would appreciate hearing the opinions of the members of the club regarding this case and whether they agree with the interpretation of endometrial stromal sarcoma.

(Slide enclosed)

Follow-Up
AMR #41 - Quiz Case 3

Contributed by: Paul E. Wakely, Jr.

As you may recall, I interpreted this case as an example of Polymorphous Hemangioendothelioma (PH). In reviewing the responses, 7 of you agreed with that diagnosis, and 10 responses were between angiosarcoma, or angiosarcoma vs. some form of hemangioendothelioma. Three months after his original surgery at an outside hospital (these were consult slides), our surgeon went back and removed all soft tissue from his left neck where the lesion arose and, that was all composed of benign fibroadipose tissue. The patient did not come back until this past December (20 months after the original diagnosis) at which time he presents with a firm large left neck mass (in the area of his prior surgery) which has occluded his left jugular vein and displaced his carotid artery. Neck CT demonstrated a lesion with irregular margins in the left posterior triangle & several enlarged lymph nodes. He has no evidence of metastatic disease.

A biopsy was taken (the mass is considered unresectable & he is receiving radiation therapy), and I have enclosed a slide for your review & for comparison with the prior quiz case slide. The tumor has lost its polymorphous architecture that existed in the original slides, but mitoses remain exceedingly uncommon (0-1 per 10 hpf), and it is still strongly CD31 positive. I am aware that 1 of the patients from John Chan's series of PH developed metastatic disease 4 yrs. after the initial operation.[as reported by Dr. Nascimiento et al. AJSP 1997;21:1083] I am currently of the opinion that this recurrent lesion should now be diagnosed as a low grade angiosarcoma. You comments would be appreciated.

Follow-Up
AMR #43 -- Case 17

Contributed by: Paul E. Wakely, Jr.

Based on the comments made by several members, I performed additional stains on this breast carcinoma for neuroendocrine, basaloid and myoepithelial differentiation. The results: negative staining for CD56, TTF-1, calponin, high molecular weight cytokeratin (34βE12), p63, smooth muscle actin, S-100, and heavy chain smooth muscle myosin (SMMS). The tumor is focally positive for cytokeratin 7. Thus, there is no good evidence for myoepithelial, neuroendocrine, or basaloid differentiation. Thank you for the suggestions.