AMR Seminar #49 – Short Summary of Cases

Case 1: F.67 with HX. of hysterectomy and unilateral oophorectomy 40 years ago for unknown Reasons, now presents with a huge mesenteric/retroperitoneal cystic mass.

Case 2: A 25-year-old white male presents with intussusception and a 5cm., polypoid mass in the ileoceal valve.

Case 3: An 80-year-old man presented with necrotizing fasciitis of the scrotum and perineum and sepsis, and multiple bone lesions in pelvis and femur. A core bx of the cystic lesions in bone was taken.

Case 4: A 5 day old boy is seen for a left renal mass.

Case 5: A 53 y.o. man is seen for a recurrent tumor in his left lower leg**.**

Case 6: A 65-year-old man is operated for a 5 cm tumor of the maxilla with infiltration into the subcutis.

Case 7: A 30 y.o. woman abruptly developed episodes of epilepsy; a 2cm. nodule attached to the meninges is removed.

Case 8: A 32 y.o. man with history of NF1 presented with a 19 cm. mass next to the small bowel.

Case 9: A 61 y.o. woman was seen for a small soft tissue nodule next to the patella.

Case 10: A 65-year-old woman with Hx. of nephrectomy , TAH-BSO, and an adenoma of the left adrenal gland was found on follow-up tomograms to show an increase in the size of the adrenal tumor. An adrenalectomy was performed.

Case 11: A 31 y.o. woman undergoes excision of a 2 cm. nodule in the breast.

Case 12: A 41-year-old woman with multiple hemangiomas of the skin complained that one of these lesions on the foot has been bothering her. The lesion was treated by sclerotherapy, and because of progressive enlargement was resected.

Case 13: A 65-year-old woman presented with a swelling on the right side of the chest wall that she first noticed 5 months previously. The tumor measured 4.3 cm and was located in the subcutaneous fat just beneath the right breast.

Case 14: A 64-year-old woman had a large, 10 x 8 x 6 cm mass in the gastric wall beneath apparently normal mucosa.

Case 15: A 59-year-old male was seen for a well-circumscribed subcutaneous soft tissue tumor of the trunk measuring 3 cm in greatest diameter.

Case 16: A 45-year-old woman was seen for abdominal swelling. A right adnexal mass measuring 12x8x7 was found.

Case 17: A 51-year-old man presented with a contrast-enhancing left frontal brain lesion.

Case 18: A 54 year old woman was seen for a slow-growing soft tissue mass in her right thigh.

Case 19: A 53-year-old woman presented a right ovarian mass and had debridement of multiple

implants throughout the abdomen and retroperitoneum

Case 20: A 74-year-old man presents with what is described by the surgeon as a "nasal polyp".

Case 21: A 65-year-old man with a history of neurofibromatosis is found to have a retroperitoneal gland attached to his adrenal gland.

Quiz Case 1: A 58-year-old woman was found to have anemia during a yearly health evaluation. A 10 cm. mass was removed from her colon.

AMR SEMINAR #49
CASE 1

Contributed by: Phil Allen (FMC 06/S01121)

History: Female aged 67 in 2006. A hysterectomy and unilateral oophorectomy were performed approximately 40 years ago for unknown reasons. A multilobulated "mesenteric cyst" was diagnosed in 1995. Biopsies from the cyst in 1995 and 1997 were considered to be consistent with a serous epithelial tumour with no evidence of malignancy (Clinpath 2028084 & 1329189). Repeated aspiration showed either serous or hemo-serous fluid. A cyst-to-vein Denver shunt was inserted in 2003 because the cyst fluid rapidly re-accumulated after aspirations. The shunt became infected and non-functional in mid 2005. An attempt to insert another venous shunt in December 2005 was unsuccessful. Around this time, repeat imaging showed the cyst to be more solid than previously. At operation in Feb 2006, a huge mesenteric/retroperitoneal cystic mass was present. The cyst was firmly adherent to the bladder, requiring cystotomy. In addition, both ureters were draped over the cyst and displaced anteriorly. The cyst was stuck to the descending colon and rectum. The colon distal to the mid-sigmoid and the rectum were excised en-bloc with the cyst. The ovary, said to have been left behind after the hysterectomy 40 years ago, was not identified.

Pathologic findings: The specimen, designated colon with mesenteric cyst, comprised a length of colon measuring 180 mm long, 50 mm in diameter and with a wall thickness of 5 mm. The attached mesentery measured 28x26x11 cm and was associated with numerous (>100) cysts ranging in size from 8x5x5 mm to 12x8x8 cm. The cysts were variably filled with thin, serous, haemo-serous or mucinous material. Some appeared multiloculated. The largest was filled with cream to pink mucin while some of the others were filled with yellow serous material or pale yellow mucinous fluid. There was a cream polypoid mass measuring 20x20x20 mm protruded into one of the cysts, and another solid pale grey nodule measuring 8x8x8 mm as well as a pale grey, cystic, calcified nodule measuring 10x10x6 mm. No colonic mucosal involvement was identified and the colon itself appeared normal.

Question. Will Club members accept this as a FATWO?

Proposed Diagnosis: Female adnexal tumor of probable Wolffian origin (FATWO), mesentery and retroperitoneum.

AMR SEMINAR #49
CASE 2

Contributed by: Carlos E. Bacchi, MD

Clinical History: This is a 25-year-old white male previously healthy with a 2-week history of abdominal pain, mainly located in the periumbilical area associated with nausea. There was no fever but the pain progressively increased and the patient started having episodes of vomiting. Ultrasound examination revealed findings consistent with intussusception. A laparotomy was performed and an ileal intussesception was found 60 cm from the ileal-cecal valve due to a 5 cm tumor present in the intestinal wall (ileum). The tumor was removed and the patient had an uneventfully recovery after the surgery. Grossly (see figure), the tumor measured 5 cm, was ulcerated, had a polypoid appearance and bosselated surface. The cut surface showed a bright whitish tumor mass apparently with a pedicle and areas of hemorrhage.

Pathological findings
This is a neoplasm involving the submucosa and muscle layer. There is one area of ulceration. The tumor cells are mainly bland spindle cells with ovoid to elongated nuclei and indistinct cytoplasm. The neoplasm is highly vascularized showing mostly small rounded vessels. There is a tendency of the tumor cells to be located around these vessels in striking whorls. There is no clear-cut atypia or pleomorphism. In some areas, the tumor seems to infiltrate the muscle coat. The stroma is hyalinized in some areas and myxoid in another ones. The tumor cells were strongly positive for EMA, while S-100 protein, CD117, CD34, cytokeratin, smooth muscle actin and desmin were all negative.

Diagnosis: Intestinal perineurioma with infiltrative features.

Comment: I found this case very challenging to diagnose. Luckily, I recently had read the manuscript by Chris Fletcher (see reference) describing intestinal perineurioma. Naturally, I sent the case to Chris and he diagnosed intestinal perineurioma. Until this study by Chris, this tumor had not been described in the gastrointestinal tract. Interesting that in the 10 cases described in his study, 9 were present in the colon and 1 was in the jejunum with no ileal case like this one.
Perineurioma by itself is an uncommon benign peripheral nerve sheath tumor occurring mainly in the subcutis but it may also arise in soft tissues or intraneural. In the GI tract it usually presents as asymptomatic intramucosal lesion, which is detected by screening. Our case developed symptoms related to intussesception. Many of the morphological features present in this case were described in those 10 cases of GI tract perineuriomas including uniform bland spindle cells with ovoid to elongated nuclei and pale indistinct eosinophilic cytoplasm with myxoid or collagenous stroma with very rare mitotic figures. EMA, like in this case, was a useful marker in order to confirm the diagnosis of perineurioma. It seems that this tumor in the GI tract probably has a benign clinical course. The most important differential diagnoses in this situation are GIST and schwannomas. GISTs are usually composed of spindle cells, epithelioid cells or mixed; they are in more than 90% of the cases positive for CD117, they don't show this type of vessels proliferation (tumor cells located around these vessels in striking whorls) and EMA is negative. GI tract schwannomas are rare neoplasms arising more commonly in the stomach. They are usually cellular being often surrounded by a prominent cuff of lymphoplasmacytic inflammation, including germinal center formation. Immunohistochemistry can easily separate GI schwannomas from perineuriomas, since the former are positive for S-100 protein and glial fibrillary acidic protein and the latter are positive for EMA.

In summary, this is description of a rare tumor in an unusual location. If anyone is interested in learning more about this tumor I recommend reading the original manuscript by Chris describing intestinal perineurioma (see reference below).

References

Hornick JL, Fletcher CDM: Intestinal perineuriomas. Clinicopathologic definition of a new anatomic subset in a series of 10 cases. Am J Surg Pathol 29(70: 859-865, 2005.

AMR SEMINAR #49
CASE 3

Contributed by: Ofer Ben-Itzhak, MD

History:
A 80-year-old man presented with necrotizing fasciitis of the scrotum and perineum and sepsis. CT scan disclosed multiple lytic lesions of the pelvic bones and proximal femur. Needle biopsies of the bone lesions was performed. The enclosed CT figure shows lytic destruction of the left ilium, sacral wing and posterior vertebral body with extension to pelvic soft tissue.

Histologic findings:
The slide shows fibrofatty and bony tissue with short fragments of eosinophilic laminated membrane and pale-degenerated membranes, surrounded by giant cells and macrophages. The membranes were strongly positive with PAS stain. In addition, necrotic tissue with scattered calcifications is present. In very rare calcifications refractile degenerated hooklets were seen (not seen in most of the slides).

Diagnosis: Hydatid cyst (echinococcosis) of bone.

Follow-up:
Following diagnosis, the patient's family informed the clinicians that he was treated by Albendazole years ago for echinococcosis. He was a farmer from a village in northern Israel. The patient underwent several surgical procedures due to perineal abscess and necrotizing fasciitis, later developed deep vein thrombosis and died. Autopsy was not performed.

Discussion:
Hydatid cyst is caused by ingestion of food contaminated with echinococcal eggs which are shed by dogs (E. Granulosus) or foxes (E. Multilocularis). Once ingested, in the human intestines the eggs hatch, release oncospheres which penetrate the mucosa, enter the circulation, implant in various tissues and develop into hydatid cysts.
Since sheep are the intermediate host of E. Granulosus (the more prevalent type of echinococcus), the disease is seen in rural areas of sheep raising people.
The incidence of surgical excision of hydatid cysts has sharply decreased in our hospital (a major tertiary hospital in Northern Israel) in the last 10 to 20 years.
Most hydatid cysts develop in the liver (50-70%), followed by the lung (about 20%). It is much less frequent in other organs, including soft tissue and muscle, kidney, brain, spleen and bone.[1] Bony involvement is seen in 1-4% of the cases.
Skeletal hydatid cyst is usually limited to one bone[2], and is most prevalent in the spine[3,4,5]. However, it may affect also the pelvis[6], long-bones[6], and skull[7]. Although vertebral involvement may result in neurologic symptoms and paraplegia[5], the osseous involvement, like most hepatic cases, maybe asymptomatic. In spite of surgical resections followed by antihelminthic drugs, the recurrence rate of osseous hydatid cysts is high[3,6].
This case represents an unexpected needle biopsy finding of a rare disease.

References:
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4. Awasthy N, Chand K: Primary hydatid disease of the spine. Br. J. Neurosurg. 19:425-7, 2005.
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6. Loudige H et al: Hydatid disease of bone. Review of 11 cases. Joint Bone Spine 70:352-5, 2003.
7. Jlidi K et al: Bone hydatidosis. 12 cases. Ann. Pathol. 12:98-101, 1992.

AMR SEMINAR #49
CASE 4

Contributed by: Ira Bleiweiss, MD

History: 5 day old boy with left renal mass. Grossly the tumor was round, measured 5.4 cm, and was yellow/tan with a fibrous consistency. Histologically there is a combination of a fibromatosis-like spindle cell proliferation and cellular undifferentiated stroma. Rare foci of cartilage were found within the tumor (perhaps not present on all your slides).

Diagnosis: Cellular type of congenital mesoblastic nephroma.

Comment: I must confess, even though we get a fair amount of pediatric pathology here, I've never seen a case of this rare tumor, even in its more common form, the non-cellular type. Then again, I probably spend too much time looking at breast. From what I've been able to learn, the prognosis for these tumors is excellent, even for the cellular ones, despite their nasty histologic appearance. Local recurrences may occur, but are less likely with complete excision. Just thought the members would like a nice example of a rare, but known entity, for a change.

AMR SEMINAR #49
CASE 5

Contributed by: Kum Cooper, MD

History: This is a lesion on the left lower leg (on the shin) of a 53-year-old man. The lesion was first seen in 1995 and excised, but recurred in 1998 and 2006. The slide is from the latest recurrence.

Diagnosis: Phosphaturic mesenchymal tumor.

Comment: The interesting aspect about this patient is that both the serum and urinary calcium/phosphate levels were normal. According to Chris Fletcher, who diagnosed the 1998 lesion (the 1995 lesion was only described!) a small but significant subset of these lesions may show no associated phosphaturia. Otherwise, to learn more about this enigmatic tumor, I refer you to Andrew Folpe's magnificent comprehensive review paper on the subject – all 30 pages of it! (Am J Surg Path 2004; 28:1-30).

AMR SEMINAR #49
CASE 6

Contributed by: Otto Dietze, MD

History and clinical presentation: 65-year-old patient with a 5 cm tumor of the maxilla with perforation of the left side and a soft tissue component into the subcutis of the left cheek. The tumor infiltrates and destructs the alveolar process on the left side (see fig.).
After initial biopsy, an en bloc resection was performed. Two months after surgery the patient is well. There is no evidence of lymph node or distant metastases.

Histology: The biopsy and the subsequent resection material display features of a keratinizing tumor component. Within the resection specimen clear cells dominate with palisading at the periphery suggestive of ameloblastic epithelium. Immunohistochemistry reveals positive staining for pankeratin, CK 8/18, vimentin and S 100 protein.

Diagnosis: Ameloblastic carcinoma.

Comment: In the initial biopsy the keratinizing component of the tumor was dominating and we considered intraosseous squamous carcinoma as a differential diagnosis. When the resection specimen was available, clear cell odontogenic carcinoma (CCOC) came up as a possible differential diagnosis. However, because of the immunoprofile published in the literature (vimentin+, S 100+), and the low degree of stroma reaction, we prefer the original diagnosis. I am very interested in the comments of the group.

References:
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Brinck U et al, Virchows Archive, 2001, 438: 412-17

AMR SEMINAR #49
CASE 7

Contributed by: Vincenzo Eusebi, MD

History: A 30-year–old lady abruptly developed episodes of epilepsy. MR with and without contrast evidenced a 2 cm nodule attached to the meninges . The nodule had pushing borders, was located in the left temporal lobe and the pre-operatory diagnosis was that of a possible meningioma.
The lady after 10 years is well with no signs of disease. She gave birth to 3 children and presently is the owner of a fancy restaurant in Sant'Arcangelo di Romagna, a small town by the Adriatic Sea.
This case was entered to welcome Dr. Rosai to the seminar.

Comment: Histology shows e cellular proliferation partly involving the dura but also extending into the cortex. Proliferating cells are multinucleated, have large eosinophilic cytoplasm and are admixed with lymphocytes, occasional plasma cells and granulocytes. Emperipolesis is evident (both lymphocytes and granulocytes). The cells are positive for CD 68 & S-100 protein.
Our diagnosis was that of intracranial Rosai- Dorfman disease.

The case was submitted to Dr. Rosai via telepathology (this was 10 years ago) who confirmed the diagnosis. I hope he is confirming also the diagnosis on the real slide.

I would like to have comments on the intratumoural fibrosis that is unusual in CNS tissue. Intracranial localization is not frequent (we have found intracranial involvement mentioned in no more than 30 cases) and follow up in the reported cases does not exceeds 6 years. A minority of published cases involved meninges and nervous tissue at the same time.

I wonder what is the outlook for this patient.

AMR SEMINAR #49
CASE 8

Contributed by: Cyril Fisher, MD, Royal Marsden Hospital, London, UK

History A man aged 32 known to have neurofibromatosis type 1 presented with abdominal pain and loss of appetite. He was found to have a tumor 19 cm diameter in the right paracolic gutter and in addition a length of the terminal ileum had irregular thickening of the wall. A hemicolectomy was performed including 42 cm of terminal ileum.

Pathology: The large retroperitoneal tumor proved to be an extensively necrotic high grade malignant peripheral nerve sheath tumor with peripheral foci of residual neurofibroma (sections not provided). The terminal ileum displayed irregular coarse mucosal swelling with focal ulceration, and focal transmural thickening. The section provided is from the abnormal area and shows neurofibromatous (predominantly schwannian) infiltration involving the mucosa and submucosa, with neural hyperplasia and disruption in submucosa and myenteric plexuses. Clusters of ganglion cells are seen both in mucosa (mostly just above the muscularis mucosae, but focally more superficially) and in submucosal neurofibromatous tissue. S100 protein is diffusely positive in the lesional tissue, which extends along the mucosa (Fig 1) and is present at the macroscopically normal ileal resection margin. Ganglion cells are outlined by S100 protein Fig 2) and highlighted by NSE (Fig 3), neurofilament proteins and synaptophysin. Desmin is negative. The mesentery contained a large plexiform neurofibroma.

Diagnosis Neurofibromatous involvement of ileum with 'diffuse ganglioneuromatosis' in a patient with NF-1 and retroperitoneal malignant peripheral nerve sheath tumor.

Comment Intestinal 'ganglioneuromatosis' is a recognized complication of NF-1 (when it is usually predominantly mucosal) and has also been associated with MENIIb and with adenoma or adenocarcinoma of colon. The term has been used both for hypertrophy of myenteric plexuses (focally evident here) and for neurofibromatous involvement of mucosa with ganglion cells. A similar case has also been described in a patient apparently without other features of NF-1 or any other associated condition.[1] The various intestinal manifestations of NF-1 include neurofibromas, GIST (small, multiple) and duodenal somatostatinoma.

1. Hirata K, Kitahara K, Momosaka Y, et al. Diffuse ganglioneuromatosis with plexiform neurofibromas limited to the gastrointestinal tract involving a large segment of small intestine. J Gastroenterol 1996; 31:263-267.

AMR SEMINAR #49
CASE 9

Contributed by: Christopher D.M. Fletcher (Case No: CFST 1955)

History: A 61-year-old female had a small, long-standing prepatellar nodule excised.

Diagnosis: Oncocytic glomus tumour.

Comment: Glomus tumors showing oncocytic change seem to be very unusual and, at least personally, I have only seen two or three examples. Remarkably, this seems to be one of the few mesenchymal lesions to ever show this morphologic alteration – as panel members well know, oncocytic change is more usually a feature of epithelial or myoepithelial neoplasms. As far as I am aware, this morphologic pattern in glomus tumours has no biologic significance.

AMR SEMINAR #49
CASE 10

Contributed by: Jerónimo Forteza Vila

History: A 65-year-old woman had a history of nephrectomy secondary to pyelonephritis 37 years ago. A hysterectomy with BSO caused for benign pathology was done 20 years ago. Three years ago she had an adenoma identified in her left adrenal gland. In October 2005, tomography confirmed an increase in the size of the mass and a laparoscopic excision of tumour was done.

Pathologic findings: The tumour weighed 118 grams and measured 7x6x5 cm, had a whitish color and nodular configuration. Microscopically, different areas were seen in the well-circumscribed nodules, which were made up of fusiform cells and some multinucleated giant cells and showed frequent tumoral mitoses and necrosis.

Immunohistochemistry: the neoplastic cells were positive for HHF35, Actin-SM and Vimentin. A minority of the neoplastic cells were also immunoreactive for EMA, ENE and some fusiform areas were positive focally for Desmin.

Diagnosis: Sarcomatoid carcinoma of the adrenal gland.

Comment: Sarcomatoid carcinoma is a well-defined biphasic tumor with anatomic sites most commonly in the head, neck, respiratory tract and genitourinary tract (1). Sarcomatoid carcinoma is a rare adrenal malignancy that shows both epithelial and mesenchymal-like differentiations including areas of rhabdomyosarcoma. Though embryologically the adrenal cortex is of mesenchymal origin, growth of the adrenocortical neoplasm as a sarcoma is exceptional (2,3). In this case the focal immunoreactivity for EMA and ENE helped to recognize the carcinomatous nature of tumor (4).

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2) Decorato JW,Cruber H,Petti M, Levowitz BS.adrenal carcinosarcoma.J Surg Oncol 1990;45:134-6
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4) Allolio B, Fassancht M. Adrenocortical carcinoma: Clinical Update. J Clin Endocrin Metab.2006; 10.1210/jc.2005-2639.

AMR SEMINAR #49
CASE 11

Contributed by: Allen Gown, MD

History: A 2 cm nodule in the breast of a 31 year old female with no significant medical history.

Pathology: The tumor is a very well circumscribed tumor with epithelioid features and a modest amount of cytoplasm. The tumor is somewhat lobulated, and the nuclei show some atypia and nucleoli, but there are only rare mitotic figures. The tumor cells are cytokeratin negative but strikingly and uniformly S100-positive. In addition, the tumor cells show abundant type IV collagen expression around individual cells (see accompanying image). Other markers (e.g., EMA, gp100 [HMB-45], are negative.

Diagnosis: Epithelioid schwannoma.

Comment: This lesion shows histologic and immunophenotypic features characteristic of epithelioid schwannoma, a type of benign epithelioid peripheral nerve sheath tumor of soft tissue. There was a recent update and review of these tumors published by Laskin et al (Am J Surg Pathol 29:39-51, 2005). They are typically dermal or subcutaneous, and, like this example, present as well circumscribed uninodular or multinodular masses. Many can show a bland spindle cell component, not well seen in this tumor. Mitotic figures can range from 0 to 6 per 50 high power fields. A subset, as the case at hand, show some nuclear and nucleolar enlargement. While our tumor did not display this, antibodies to EMA can decorate perineural cells present in the tumor, and antibodies to CD34 are often positive on a subset of fibroblastlike cells within the lesion. Based on histology and immunophenotype, some can be classified as epithelioid schwannomas, some as neurofibromas, and some as tumors of indeterminate histogenesis. These tumors, including those with cytologic atypia, have an excellent prognosis if completely resected.

AMR SEMINAR #49
CASE 12

Contributed by: Ivan Damjanov, MD

Clinical findings: A 41-year-old woman with multiple hemangiomas of the skin complained that one of these lesions on the foot has been bothering her. This dermal-subcutaneous lesion was treated by sclerotherapy and since it did not involute but actually enlarged it was surgically removed. In addition to a large hemangioma the specimen contained at its edge a myxoid lesion which is submitted here. A wider re-excision was performed three weeks later and it also contained parts of the same myxoid tumor. At that time the resection margins were free of neoplasia.

Microscopic findings: The lesion consists of dense collagenous connective tissue extending into the fat and alternating with myxoid areas. There are numerous chronic inflammatory cells, mostly lymphocytes and macrophages. Parts of the tumor are cellular and composed of plump fibroblast-like cells. The myxoid part contains cells with large hyperchromatic nuclei and prominent nucleoli and an often vacuolated cytoplasm. Immunohistochemically these large cells stained with antibodies to CD34 and CD68, and were unreactive with antibodies to S100 and smooth muscle actin. MIB-1 staining showed groups of strongly immunoreactive cells is some of the myxoid and dense collagenous areas.

Diagnosis: Acral myxoinflammatory fibroblastic sarcoma (inflammatory myxohyaline tumor).

Comment: We did not recognize this lesion in the frozen sections, most likely because there was a bona fide hemangioma that got most of our attention. Also the history of "sclerotherapy" sent us flipping through the books for the tissue effects of whatever that fancy treatment modality does to tissues. In any case the slide that was sent to you has the typical components of the myxoinflammatory fibroblastic sarcoma. I hope that everybody will see the hyalinized collagenous and myxoid parts of the tumor and the large atypical cells with prominent nucleoli ("virocytes"), and the prominent chronic inflammation. The re-excision proved that the tumor was not fully removed, but by that time we learned how to recognize such tumors in frozen sections and the final margins were free of tumor.

It was only after I had the slides cut and reviewed the literature that I realized how many AMR Seminar members have written about this tumor. My apologies to all of you who find this case too mundane. On the other hand, I could be brief and skip a lengthy review of the literature.

The question that intrigued me the most was: how common are acral myxoinflammatory tumors? We have never seen one before here in Kansas. In the residents' section of Archives of Pathology and Laboratory Medicine, Naqui et al (Arch Pathol Lab Med 2005; 129:1343) wrote that there were 121 published cases till the end of 2004, 95 of which came out of the first two major series (Montgomery et al, Mod Pathol 1998; 11:384; Meis-Kindblom and Kindblom, Am J Surg Pathol 1998; 22: 911). On the other hand, the latest PubMed reference (Lang et al, Clin Orthop Relat Res. 2006;445:254) reporting 5 cases seen over the period of two years at Duke University suggests that acral myxoinflammatory sarcomas are probably much more common than previously thought. Many of you would probably agree. Hence my question for the panel: From your experience, how common are these tumors?

AMR SEMINAR #49
CASE 13

Contributed by: Janez Lamovec, MD

History: A 65-year-old woman presented with a swelling on the right side of the chest wall that she first noticed 5 months previously. FNAB was performed elsewhere and showed spindle cell sarcoma. On physical examination, a non-tender tumor on the right lateral chest wall was palpated; it measured 4.5 cm. It was located just beneath the right breast in mid-axillary line, it was not fixed to skin or rib cage. Ultrasound examination showed a transsonic well circumscribed tumor in subcutaneous adipose tissue. A wide resection was performed.

Pathological findings: Grossly, the tumor was clearly delineated, lying in a subcutaneous adipose tissue and measured 4.3 x 2 x 2 cm. The underlying skeletal muscle tissue was not involved by it. On cut surface, it was deeply yellow, homogenous, of relatively firm consistency (unfortunately, I don't have a gross photograph).

Histologically, this is a clear cell tumor with a mixture of small and medium sized epithelioid and spindle cells and numerous bizarre giant cells with large clear, often multiple nuclei, prominent nucleoli, with cytoplasmic nuclear inclusions, and with pale mostly vacuolated cytoplasm (lipoblast-like cells). Admixed are numerous foam cell, lymphocytes and plasma cells. Mitoses are not numerous but most of them are atypical. There is a vague storiform arrangement of cells focally, and in some slides cells nests of spindle cells with sort of onion-like layering are present (see attached microphotograph). Vascularization of the tumor is quite prominent (mostly thin-walled, capillary type vessels), collagen deposition is uneven, relatively abundant. No myxoid areas are found. At the periphery, there are some lymphoid follicles. Resection margins (not present in the submitted slide) were far away from the tumor.

We did all kinds of immunos and the only positive reactions were those for vimentin, KP1 and PGM1 (for the most part not in bizarre cells) and CD10 (also in bizarre cells). All the rest, including muscle markers, ALK, CD34, S-100 protein, HMB-45, CD21, CD30, keratins , EMA etc, was negative.
EM showed clusters and fascicles of epithelioid cells with long thin cytoplasmic processes, incompletely invested by an external lamina-like material. Nuclei were atypical, cytoplasm abundant with some organelles (RER, lysosomes, lipid droplets) without filaments and glycogen. There was no evidence of myoid or neural differentiation. The tissue for EM was suboptimal for examination; it was fixed in formalin.

Diagnosis: Unclassified malignant epithelioid and spindle cell tumor with clear cell features and bizarre giant cells and prominent inflammatory and foam cell component.

Comment: I don't know if there are any specific characteristics to better classify this tumor except for giving it a descriptive diagnosis. I don't think this is any kind of liposarcoma. I was playing with the idea of this tumor being a kind of myxoinflammatory fibroblastic tumor (without myxoid component!). I sent this case to Chris who called it as an unclassified epithelioid malignant tumor with clear cell features. He reminded me that a similar case had

been sent to him by a colleague of mine several years ago. I checked that tumor and indeed it was similar though not identical, it had more pronounced epithelioid features and minor inflammatory component, mostly associated with necrotic foci, but contained almost identical bizarre giant cells. The latter tumor was found in the subcutis of the arm. After wide resection, the patient, an elderly woman, is still alive with no evidence of disease, 10 years after surgery, with no additional treatment. In our case, the follow up is short, 6 months, and the patient is O.K.

I am really curious to hear the opinion of a great number of distinguished pathologists on this tumor and to find out if any of you had encountered similar cases.

AMR SEMINAR #49
CASE 14

Contributed by: Markku Miettinen, MD

History: This 64-year-old woman had a large, 10 x 8 x 6 cm mass in the gastric wall beneath apparently normal mucosa.

Diagnosis: Gastric schwannoma.

Comments: This tumor, first reported by Dr. Y Daimaru et al. in 1988 represents relatively typical, although an unusually large example of GI- schwannoma – most of these tumors are < 5cm. This slide has a solid growth pattern – these tumors often have a microtrabecular appearance, as was in this tumor in other areas. Typical features in this case include peritumoral lymphoid cuff with small germinal centers, and focal nuclear atypia. The submitted section represents the external portion of the tumor facing the peritoneum.

Approximately 2/3 of GI schwannomas occur in the stomach; the rest are seen in the colon and only very few in small intestine and esophagus. Occurrence in older adults is typical. These tumors probably represent schwannomas arising in the autonomic nerve system of the GI tract, and this fact may give them some peculiarity, as compared with ordinary soft tissue schwannomas. Mitotic activity is low in this tumor, and in GI schwannomas it almost never exceeds 5 mitoses per 50 HPFs. In our as well as published experience, there does not seem to be a malignant counterpart. This tumor is not associated with neurofibromatoses 1 or 2. Pathogenetically, it may differ from typical schwannoma, because allelic losses in chromosome 22 in NF2 loci and NF2 mutations seem to be rare if they occur.

Immunohistochemically, this tumor was positive for S100 protein and it also had a substantial GFAP-positive component, whereas it was negative for c-KIT, CD34, SMA, and desmin. This profile is typical of GI schwannoma.

The differential diagnosis includes S100-positive primary GI tumors, such as the rare clear cell sarcoma. The latter tumor in GI tract sometimes has osteoclastic giant cells. Plexiform neurofibromas and small mucosal neurofibromas are the most common neurofibromas in the GI tract and they both differ obviously from the GI schwannoma. GI schwannoma is easy to separate from GIST, if not otherwise, then by immunohistochemical profile. The frequency of gastric schwannoma vs. gastric GIST in AFIP files is approximately 1:50; in the colon this relative frequency is highest, 1:2.

References:

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AMR SEMINAR #49
CASE 15

Contributed by: Michal Michal, MD (M48845/06)

History: A 59-year-old male with a well-circumscribed subcutaneous soft tissue tumor of the trunk measuring 3 x 1.5 x 2 cm. The lesion is composed of ovoid, round to spindled cells that have interdigitating processes creating focally a spider-like appearance. The cells show minimal pleomorphism and there are some atypical mitotic figures, but on the whole the tumor appeared as a well-differentiated sarcoma. Immunohistochemically, the neoplastic cells are strongly positive for CD34 a EMA and are negative for CD117, GFAP, synaptophysin, NSE, p63, actins, desmin, HMB45, AE1-AE3, chromogranin. Glut1 reacted weakly positively. EM studies showed that lesion indeed may have perineurial differentiation, as we identified attachment sites and, possibly, pinocytic vesicles (the study was performed form paraffin the quality was suboptimal).

Please, what is your opinion? Round-cell variant of low-grade perineurial sarcoma?

AMR SEMINAR #49
Case 16

Contributed by: Elvio Silva, MD

History: A 45-year-old woman consulted because of abdominal swelling. A right adnexal mass measuring 12x8x7 was found.

The case belongs to a series of cases that I am publishing with Robert Young. We have been collecting these cases for several years. I am including the abstract of the paper we are sending for publication. We believe it is important to separate this tumor from secretory endometrioid carcinoma (a very low grade and homogenous neoplasm) and from clear cell carcinoma (a neoplasm with different patterns).

The Spectrum of Clear Cells in Endometrioid Neoplasms of the Female Genital System. A Report of 21 Cases in which the Alteration is not of Typical Secretory Type:

Clear cells apparently unrelated to typical secretory changes or the clearing commonly seen in foci of squamous differentiation are uncommon in endometrioid tumors and they often create diagnostic problems and their spectrum has not been well documented.

We reviewed 21 endometrioid tumors that occurred in patients from 27 to 88 (median 64) years. Most had an adnexal mass (13) or abdominal swelling (4), but 4 presented with vaginal bleeding. One tumor involved the right fallopian tube, one the endometrium, and 18 the ovary. One tumor was a cystadenofibroma, one a borderline tumor and 19 were adenocarcinomas. Twelve patients had stage I, 4 stage III, 1 stage IV and 4 were unstaged. All were treated with abdominal hysterectomy and salpingoophorectomy. All the neoplasms had the typical architecture of endometrioid tumors but differed markedly in their cytoplasmic features. In 18 of the tumors at least one-third of the cells had clear cytoplasm and three had only clear cells. The clear cytoplasm varied from foamy to empty and the nuclei had a variable location, basilar, central, and apical. The clear cells were associated with squamous differentiation in only one case in which the change appeared hydropic. By immunohistocytochemistry, the clear cells were focally positive in most cases but in some cases one or more of these immunostains were negative. Tubulocystic, solid, and papillary patterns of clear cell carcinoma were absent. PAS was focally positive for glycogen in the cytoplasm in 5 cases.

Follow-up was obtained for 11 patients. Five are free of disease at 12 to 84 months, median 27 months, 1 patient died of other causes at 84 months, 1 is alive with progressive disease at 24 months, and 4 died of disease at 17 to 52 months median 27 months.
Endometrioid neoplasms can have extensive areas with an unusual spectrum of clear cells changes ranging from foamy to empty and the cells have a variable location of their nuclei. Although a few cases had a focal slight resemblance to secretory endometrioid carcinoma most did not and the orderly morphology of classic secretory carcinoma was noteworthy for its absence. The nature of the cytoplasmic clarity is usually uncertain but is likely variably due to lipid, mucin or glycogen accumulation, or is a hydropic change. The distinction from clear cell carcinoma depends on awareness of this unusual variant of endometrioid neoplasia and a lack of the distinctive patterns of clear cell carcinoma; at this time, special studies, including immunohistochemistry, do not aid significantly although certainly negative reactions, such as for the thyroglobulin (arguing against clear cell struma ovarii) may play a role in some differential diagnostic considerations. There are prognostic and therapeutic implications in the distinction with clear cell carcinoma.

AMR SEMINAR #49
CASE 17

Contributed by: James A. Strauchen, MD

History: This 51-year-old man presented with a contrast-enhancing left frontal brain lesion. There was no relevant prior history of other neoplasm. Subtotal resection was performed.

Pathology: The specimen consisted of multiple fragments of soft, tan, hemorrhagic tissue, measuring 10 x 6 cm in aggregative. Sections showed a malignant neoplasm composed of small cells in sheets and lobules with foci composed of small whorled nests with gland-like formations in a myxoid stroma. The tumor cells were positive for vimentin; negative for CAM5.2, AE-1/AE-3, EMA, CEA, HMB-45, CD31, CD34, CD45, CD68, CD99, CD117, FVIII, desmin, SMA, GFAP, NF, synaptophysin, S100, and NSE. The tumor cells demonstrated a high proliferation index (MIB-1 >90%).

Diagnosis: "Adenoid" glioblastoma (malignant astrocytoma, WHO grade 4, with divergent epithelial-mesenchymal differentiation).

Comment: This phenomenon may be familiar to neuropathologists, but I found it rather unusual and instructive. The "adenoid" formations resemble those of an epithelial neoplasm, reminiscent of adenoid cystic carcinoma. These were, however, negative for epithelial markers and there was no history of a primary carcinoma. Primitive neuroectodermal tumor (central or peripheral) was also considered, based on the more solid areas, however, the immunohistochemical studies did not support this diagnosis either. Our neuropathologist was equally perplexed and sent it for consultation to Marc Rosenblum at Memorial Sloan-Kettering, who observed that he had seen several demonstrably atroglial neoplasms which exhibited similar lobulated, sclerosing, and adenoid features, and considered this phenomenon to represent de-differentiation in an astrocytoma. There are also examples in the literature (References 1-5, the last two in Japanese!).

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AMR SEMINAR #49
CASE 18

Contributed by: Saul Suster, MD

History: A 54 year old woman was seen for a slow-growing soft tissue mass in her right thigh. She had no previous significant history. A resection of the mass was undertaken. The tumor measured 10 x 5 x 2.5 cm, was well-circumscribed and encapsulated, and did not show any attachment to any of the surrounding structures.

Diagnosis: Lipoblastic nerve sheath tumor with signet-ring lipoblastic cells.

Comment: This corresponds to case No. 3 in our recently reported short series of cases published in Am J Surg Pathol (Vol.30:337-344, 2006). We initially saw two cases in our routine cases, and subsequent review of our files disclosed three additional cases. Although there is nothing really dramatic regarding biologic behavior about these lesions (so far all of our cases have behaved as benign neoplasms), we felt the lipoblastic signet-ring cells scattered throughout the lesion were quite striking and unusual. I thought the members of the club might want to have a slide of this rare and unusual lesion. I also wonder how many other club members have seen this before? I was recently contacted by e-mail by two separate groups from Europe indicating that they have also observed similar cases. I would appreciate any thoughts regarding these tumors.

AMR SEMINAR #49
CASE 19

Contributed by: Paul E. Wakely, Jr., MD

History: A 53-year-old woman presented with a right ovarian mass and had debridement of multiple implants throughout the abdomen and retroperitoneum.

Pathology: Grossly, the ovary was both solid and cystic with cysts lacking papillary excrescences. Cell nodules of variable size are seen in the submitted H&E slide from the ovary. These are composed of back-to-back primitive tubules (many resembling neuroepithelial rosettes) and short papillae lined by a remarkably monotonous columnar cell population. The latter shows stratification or pseudostratification around tubular lumens. Most lumina are empty, but some contain degenerating cells. No mucin is present.

Diagnosis: Adult Wilms' tumor, monophasic epithelial type, metastatic.

Comment: I am embarrassed to admit that I initially signed this case out as a well-differentiated endometrioid adenocarcinoma of the ovary. Unknown to me at the time of microscopic diagnosis, however, was that this patient had a primary renal mass removed 27 years earlier when she was 26 years old. After I was informed of this, and realized an egregious *faux pas* on my part, the old slides were searched for and eventually found. The slides from that 1975 case showed a histologically absolutely identical tumor – in fact, that kidney tumor was erroneously diagnosed as papillary renal cell carcinoma in 1975. Further examination and subsequent immunostaining with WT-1 (diffusely positive) revealed the true nature of this malignancy, a Wilms tumor (WT) that is entirely epithelial with no blastemal or stromal component, and no evidence of anaplasia (as defined by the National Wilms Tumor Study Group).

Adult WT is extremely uncommon. A study of 11 cases from M.D. Anderson Hospital showed a triphasic histologic pattern in 7 cases, and a biphasic (epithelial & blastemal) in 4 cases. None showed a nearly pure epithelial dominant pattern as in this case. Their patients ranged from 21 yr. to 67 yrs. of age and developed metastases to abdominal lymph nodes, lungs, and peritoneum, but none produced an ovarian mass. Huser J, Grignon D, Ro JY, Ayala A, et al. Adult Wlims' Tumor: A clinicopathologic study of 11 cases. Mod Pathol 1990;3:321-26.

The survival is improved in adult WT, but not better than in the pediatric population. A recent report of 45 patients from the NWTS showed an overall survival rate of 82%. Kalapurakal J, Nan B, Norkool P, et al. Treatment outcomes in adults with favorable histologic type Wilms tumor – an update from the National Wilms Tumor Study Group. Int J Radiation Oncology Biol. Phys. 2004;60:1379-84. A review of the literature by Terenziani et al. from Milan showed even lower survival rates in Europe. Terenziani M, Spreafico F, Collini P, et al. Adult Wilms' Tumor: A monoinstitutional experience and a review of the literature. Cancer 2004; 101: 289-93.

Were this mass a primary renal neoplasm instead of an ovarian one, one could also consider a metanephric adenoma (MA) in the differential diagnosis. However, since MA is supposedly devoid of nearly any mitotic activity, and our tumor harbors numerous mitotic figures, metanephric adenoma is excluded from consideration. I have included a photo of the WT-1 stain.

AMR SEMINAR #49
CASE 20

Contributed by: Paul E. Wakely, Jr., MD

History: A 74-year-old man presented with what was described by the surgeon as a "nasal polyp". Since this biopsy was performed at a private doctor's office, I have no other history than the patient was diagnosed in the past with lymphoma and prostatic carcinoma. The surgeon's question was whether this "polyp" represented metastatic prostate cancer.

Pathology: We received a 0.5cm. tissue fragment. In some slides the squamous mucosa is intact, while in others it is ulcerated. A monotonous population of spindle cells in a vague storiform arrangement is seen mixed with a heavy infiltrate of neutrophils. Occasional mitoses can be seen, but none are atypical.

Diagnosis: Mycobacterial spindle cell pseudotumor.

Comment: Since there was concern for metastatic carcinoma I performed pan-cytokeratin, and PSA stain, and a CD34 stain for possible Kaposi's sarcoma – all were negative. In examining the spindle cells at high power, I thought that some of them displayed the features of epithelioid histiocyte nuclei as seen in FNA smears. These have smooth elongated contours, and a slight indentation on one side of the nucleus, producing the "banana", or "boomerang" shape one sees mentioned all the time in cytology texts. Many of the nuclei however are rounded and oval. Nonetheless, because of this elongated shape I also ordered an AFB stain up front, which gave me my diagnosis (photo of Ziehl-Neelsen AFB stain is provided).

Mycobacterial spindle cell pseudotumor is familiar to this audience having been presented by Dr. Damjanov at the AMR meeting in Srni, and perhaps in one of the early AMR seminars. I wanted to share this example with club members because it is the first example that I have seen that *did not occur in a lymph node*. The differential diagnosis that I considered was a spindle cell carcinoma, inflammatory pseudotumor, KS, granulation tissue, and much less likely, an inflamed follicular dendritic cell sarcoma. After I received the AFB stain and negative cytokeratin/CD34 stains, I did not bother to perform any other markers. I am aware of a report of this lesion occurring in the nasal septum, but have had trouble getting the paper Gunia S, et al. Mycobacterial spindle cell pseudotumor of the nasal septum clinically mimicking Kaposi's sarcoma: case report. Rhinology 2005; 43: 70-71. Since a metastatic carcinoma was the major consideration in this case none of the tissue was submitted to the microbiology laboratory so I don't know precisely that these bacilli are of Mycobacterium avium-intracellulare, but they probably are. The patient's HIV status is unknown, nor is it known what kind of lymphoma he was diagnosed with in the past, or how long ago that took place.

AMR SEMINAR #49
CASE 21

Contributed by: Lawrence Weiss, MD

History: This is a 65-year-old man with a history of neurofibromatosis (only revealed to us retrospectively) with a retroperitoneal mass attached to the adrenal gland.

Gross: The specimen was 8.0 cm and showed central necrosis. While adherent to the mass, the adrenal itself was uninvolved.

Special Stains:	S-100	positive (strong and diffuse in all spindled cells)
	Desmin	negative
	HMB-45	negative
	Actin	negative
	KI-67	occasional cells positive, <1%

Comment: There are clearcut areas of ganglioneuroma; these areas formed a good proportion of the entire neoplasm. There are other focal areas of neurofibroma, (only really present on this one slide). Finally there are areas with high cellularity and atypical cells, the latter particularly associated with areas of necrosis. I did not see mitotic figures.

Diagnosis: Ganglioneuroma, with focal neurofibroma and atypical areas.

Discussion: The presence of nuclear atypica, necrosis, and increased cellularly is usually associated with malignancy in neurofibroma. However, the presence of nuclear atypia and cellularity in neurofibroma is not synonymous with malignancy (see Lina BT, Weiss LM, Medeiros LJ Neurofibroma and cellular neurofibroma with atypia: a report of 14 tumors. Am J Surg Pathol 199:21:1443-9). Ganglioneuromas are almost invariably benign, although case reports of secondary neurofibrosarcomatous change exist (Fletcher CD, Fernancy IN, Braimbridge MV, McKee PH, Lyall JR. Malignant nerve sheath tumor arising in a ganglioneuromas. Histopathology 1988:12:445-8).

My gut feeling is that this tumor is benign. I base my opinion on the absence of mitoses, the low Ki-67 index, the inflammatory cell background, and the type of necrosis, which is not really tumor cell necrosis, but seems more degenerative in nature. Does everyone agree, or would anyone call this tumor malignant or, at least, of uncertain malignant potential?

AMR SEMINAR #49
QUIZ CASE 1

Contributed by: Mark Wick, MD

A 58-year-old woman was found to have anemia during a yearly health evaluation, with a hematocrit of 28%. Testing of the stool yielded a positive guaiac result. Colonoscopy was performed, showing a 10 cm mass in the cecum. After a biopsy, a right hemicolectomy was performed, from which this section was taken.

FOLLOW UP
SEMINAR #10 CASE 6

Contributed by: Hugo Dominguez-Malagon, MD

This case was originally contributed by me to AMR seminar #10, case 6 (November 1992). It concerned a 62-year-old female with a soft tissue mass in the right thigh. The tumor was made up of polygonal cells in solid and alveolar patterns, it was positive for vimentin and CEA. All other IHC markers including HMB45 and S100 were negative. By EM intracysternal microtubules were seen. At that time several entities were considered including metastatic melanoma, epithelioid angiosarcoma and metastatic carcinoma.

16 years later the tumor has recurred locally. The morphology is identical but the cells this time are strongly positive for HMB45, S100 protein and vimentin, weakly positive for BCl-2, and negative for keratin, EMA and CD34. Due to the localized nature of the tumor, without there being evidence of any other primary tumor and absence of metastasis after 16 years, my final diagnosis is primary melanoma of soft tissue.

(Editorial Note: review of the comments from this slide seminar shows that Dr. John Chan, Chris Fletcher, Janez Lamovec, Cesar Moran, and Saul Suster favored a diagnosis of melanoma based on H&E).