

AMR Seminar # 47 – Short Summary of Cases

- Case 1:** 51-year-old woman with history of a lump in the left heel.
- Case 2:** This 13 month-old boy was admitted for surgical correction of an apparently inguinal hernia.
- Case 3:** This is a periadrenal cystic mass in a 49-year-old woman.
- Case 4:** Nonspecific heart problems in a 53-year-old man.
- Case 5:** 33-year old lady, who underwent curetting for bleeding abnormalities and a polypoid mass in the uterus.
- Case 6:** This is a breast tumor (right breast) of 2.5 cm (radiology) present for 10 years that in the last month had increased in size. FNA resulted in a C4 diagnosis.
- Case 7:** A 58 year old man presented with a 6 cm diameter tumor in the popliteal fossa.
- Case 8:** A 14-year-old boy presented with nasal obstruction and was found to have a 4.0 cm lobulated intranasal mass which was excised piecemeal.
- Case 9:** A 37-year-old woman was admitted in Emergency Department with cephalgia and fever
- Case 10:** A 57-year-old male with asymptomatic expansive tumor in the head of pancreas.
- Case 11:** A 47-year-old woman underwent a abdominal hysterectomy and unilateral, left ovariectomy for multiple uterine leiomyomas.
- Case 12:** 36-year-old woman with a popliteal mass 6 x 4 x 4 cm. Yellowish, firm, with focally softer, mucoid areas.
- Case 13:** 57-year-old man with a jejunal tumor.
- Case 14:** 45-year-old female with vaginal bleeding.
- Case 15:** This 52-year-old woman presented in 1999 with cholestatic jaundice.
- Case 16:** A 65-year-old man was admitted to the hospital with presumed acute prostatitis.
- Case 17:** This is a 54 year old man who presented with abdominal fullness and bloating.

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CASE 1

Contributed by: P W Allen.

Case (FMC 04/S08804) referred by Dr. Cindy Forest, Fremantle Hospital & Health Service, PO Box 480, Fremantle, Western Australia, 6959

History as supplied by Dr. Forest: "This 51 year old woman gave a two year history of a lump on the left heel. The histological appearances resemble hobnail/retiform hemangioendothelioma with unusual myxoid stroma. I would very much appreciate your opinion on this case".

Diagnosis: Retiform hemangioendothelioma (Dabska), skin of left heel.

My opinion (PWA): "I agree with your diagnosis of retiform hemangioendothelioma as described in Am J Surg Pathol 18: 115-125, 1994. The only point of concern is the myxoid interstitial change, which is not mentioned in Calonje's article, but there is some slight myxoid change in some of the pictures in Enzinger.

I think the Calonje article gives the most reliable prognostic information available which indicates a high recurrence rate, a low metastasis rate and zero fatality rate. It is important to note that five of the fifteen cases reported by Calonje did not recur, so while there is a high probability of local recurrence, they don't always recur and if they do, they can be managed by re-excision.

I suppose the final decision should be left to the patient after an explanation of the likely morbidity and complications if the tumour is more widely excised now, but one could make a case for merely following the patient carefully.

I think retiform hemangioendothelioma is the same as Dabska's tumour but it is quite different from targetoid haemosiderotic haemangioma. I doubt that finding hobnail cells indicates a family of tumors. As far as I know, I have not seen any of the sections of the 62 cases of "hobnail haemangioma" reported by Mentzel, but the large number of cases makes me fairly confident that most or all of them were probably targetoid haemosiderotic hemangiomas, which are much more common than retiform. I must have at least half a dozen cases of targetoid hemangiomas but I have no more than two cases of Dabska's tumour and I have been searching for them for 40 years. I only started to recognize targetoid haemosiderotic hemangiomas about 5 years ago.

Your offer to send 40 unstained spares for circulation to the AMR club is greatly appreciated. It is my turn to circulate a case. This one will incite considerable interest and no doubt some controversial comments. **DIAGNOSIS: Retiform hemangioendothelioma (Dabska), skin of left heel."**

Comments: I incorrectly diagnosed one of the last cases I contributed to the club as retiform hemangio-endothelioma, only to have to correct the diagnosis to spindle cell hemangioendothelioma after the slides have been circulated. Will the club members accept this as a Dabska tumor and what are the views on the myxoid interstitial change and the hobnail tumor family? I suspect that the parents were never married, and have been trying for some years to seduce pathologists into believing their children are legitimate.

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CASE 2

Contributed by: Carlos E. Bacchi, MD

Clinical History: This 13 month-old boy was admitted for surgical correction of an apparently inguinal hernia. The surgeon found an enlarged right testis and performed an orchiectomy. When the diagnosis of a LCT was entertained the patient was referred to the Oncology Clinic where clinical examination disclosed increased weight for age, hoarse voice, penis of increased size, presence of genital hairs, and right testis increased in size and consistency. Serum levels (one and two months after surgery) of cortisol, alfa-hydroxiprogsterone, androstenedione, and estradiol were normal. Dehydroepiandrosterone (DHEA) levels were 15.0ug/ml, and <15.0ug/ml, respectively (normal for age: <0.5ug/ml). The values for total testosterone were <10.0ng/dl and 43.4ng/dl (normal for age and sex: 5-50ng/dl). Free testosterone was non detectable in the first exam while the level was 0.1pg/ml in the second. Aldosterone changed from 830.0pg/ml in the first determination to 174.0pg/ml in the second. Although an initial ultrasound exam seemed to depict enlarged lymph nodes in the right iliac fosse, 60 days afterwards a new exam revealed absence of pelvic and retroperitoneal lymph nodes as well as normal adrenal glands. Moreover, the clinical features of isosexual pseudoprecocity regressed but the enlargement of the penis. Ultra-sound examination performed 4 months after surgery revealed neither residual tumor nor metastatic disease. Adrenal glands were unremarkable.

Pathology findings: The surgical specimen included a 4.5 x 2.5 x 2.0 cm testis which on sectioning contained a tan nodular mass. The histological sections showed an infiltrating epithelioid proliferation constituted by medium to large polygonal cells with finely granular eosinophilic cytoplasm, some containing vacuoles. The cells displayed nuclei accordingly to the size of the cytoplasm, the larger ones frequently showing cytoplasmic invaginations, the overall picture indicating remarkable size variation (pleomorphism). Mitosis figures were frequent, some of them with atypical features. The cells arranged in irregular clusters which were somewhat delimited by thin fibrous septa. At the periphery of the tumor, the neoplastic cells were infiltrating among remaining seminiferous tubules. Also present were small foci of necrosis with calcific deposits. Neither lipochrome nor crystals of Reinke were recognized. The cells of the tumor proved to be strongly and uniformly positive for inhibin and Melan A and focally positive for cytokeratin (monoclonal antibodies AE1/AE3 and CAM 5.2) and synaptophysin. Immunostaining for calretinin showed about 20% of the cells exhibiting cytoplasmic and nuclear positivity. S-100 protein and chromogranin A were negative. MIB-1 activity was found in 40% of the cells while P53 protein was positive in approximately 50% and bcl-2 in 15% of the cells.

Diagnosis: Malignant Leydig cell tumor of the testis in a 1 year-old boy with isosexual pseudoprecocity.

Discussion: Criteria for defining malignant LCT have resulted from retrospective analysis of cases developing metastasis and leading to death. These include clinical and pathologic ones. Clinical observations related to malignancy encompass older patients, symptoms of shorter duration, and absence of endocrine manifestations. Pathology findings favoring malignancy include size (larger being more frequently malignant), infiltrative margin, extension beyond the testis, blood vessels or lymphatic invasion, greater degree of cellular atypia and necrosis, and a high mitotic rate (3-5). Recently these criteria have been refined (4). Cheville et al. (4) found that a mitotic index of more than 10/hpf, atypical mitotic figures, necrosis, and infiltrative margin were statistically significant for metastasizing LCT. Present case showed all these criteria. Although several varieties of LCT cells departing from

classical ones are now well described in the literature (6, 7), the histology of the tumor in the actual case exhibited the most classical one albeit with calcified foci. Although frequent and useful for diagnosis lipochrome and crystalloids of Reinke are not consistent findings in LCT. None of the two were found in the tumor we studied. LCT may be functional and secrete androgens, estrogens or corticosteroids (3) resulting in accordingly clinical manifestations (1-3). Unfortunately in the present patient the laboratory studies issued for detecting serum hormonal levels were done later, after the tumor was resected. However, a still evident increase of DHEA was evident. This hormone has been referred as one which may be produced by LCT (2) and its effects may explain the clinical findings. Moreover, most of those effects had regressed 60 days afterwards. Notably the levels of testosterone raised from the first study to the second a month later. We hypothesized that this resulted from a rebound effect on the secretion of LH from the adenohypophysis, initially strongly suppressed by the effect of the LCT. The literature registers a case of precocious puberty after treatment of LCT of the testis (8). Immunohistochemistry studies resulted in positive staining for the well-known markers of LCT (1-3) as well as for Melan A (A103). This marker, originally thought to be specific for melanoma, it was later demonstrated that immunoreactivity may happen in other types of cells including adrenocortical cells and Leydig cells. This resulted in Busam et al's paper (9) referring its use for the diagnosis of adrenocortical and other steroid producing tumors. These authors include 4 LCTs in their study all of which proved to be positive for A103 (Melan A). This appears to be the only reference in the literature mentioning such results, leading the AA to state "Therefore, adrenocortical tumors need to be distinguished from extra-adrenal steroid tumors on histologic and clinical grounds. Primary adrenocortical tumors and LCTs, for example, can be distinguished from each other based on clinical setting of a testicular versus adrenal mass and histologically on the basis of pathognomonic crystalloids of Reinke, which are present in approximately 25-40% of LCTs. Conversely, extratesticular or metastatic LCTs may be exceedingly difficult to distinguish from adrenocortical carcinomas. Fortunately, however, such LCTs are exceedingly rare and the clinical setting is usually distinctly different from adrenocortical carcinoma" (9).

Calretinin has recently been referred as a possible marker of testicular normal and neoplastic Leydig cells (10). The marker proved to be positive in the present patient. As to the other immunohistochemical data indicating bcl-2 positivity (11), high P53 index (11, 12), and high proliferation index (MIB-1) (4), are all favoring the diagnosis of malignant LCT. Differential diagnosis off LCT includes nodular Leydig cell hyperplasia (usually 1 cm or less and multifocal), large calcifying Sertoli cell tumor (usually multifocal, bilateral and showing intratubular growth), testicular tumor of adrenogenital syndrome (bilateral multifocal and usually benign) and metastatic adrenocortical carcinoma (evidence of primary adrenal tumor) (1-3).

In summary, this is a case of malignant Leydig cell tumor classified as such using histopathological and immunohistochemical accepted criteria for malignancy in retrospective studies of the literature, in apparently the youngest child ever diagnosed, who presented with isosexual pseudoprecocity at the age of 1 year.

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Figure 1: LCT cells infiltrating among seminiferous tubules (a) depicting frequent typical and atypical mitotic figures (b). H-Ex100 (a); x400 (b).

Figure 2: LCT cells showing frequent Melan-A (a) and calretinin (b) positive cells. Notice nuclear and cytoplasmic calretinin positive immunostaining. x100 (a); x400 (b).

Figure 3: Mib-1 (a) and P53 (b) nuclear staining of the LCT cells. x100.

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CASE 3

Contributed by: Kum Cooper, MD

Clinical History: This is a periadrenal cystic mass in a 49-year-old woman.

Gross: The specimen weighed 220 grams and measured 17 x 10.5 x 3.5 cm. The external surface was smooth and the compressed adrenal gland identified. The cut surface appeared microcystic and contained necrotic debris and blood clot.

Microscopic: The tumor comprises a multinodular proliferation of uniform cells with pale eosinophilic cytoplasm and vesicular nuclei. There is minimal atypia and pleomorphism. These tumor cells are associated with a dense fibrous pseudocapsule with prominent chronic inflammation including germinal centre formation. Immunostains: showed strong diffuse EMA positivity. S-100, HMB-45, inhibin, Mart-1, synaptophysin, chromogranin, calretinin, actins, and GFAP were all negative. Focal keratin positivity was noted.

Diagnosis: Angiomatoid fibrous histiocytoma (previously AKA angiomatoid "MFH").

Comment: Clearly from the battery of stains it is evident that I was unable to arrive at a diagnosis and sent this off to Chris Fletcher, who correctly identified this as a so-called angiomatoid "MFH" arising in an exceptional location. In Chris' collection of about 150 examples, this is the first he has seen in the abdomen. I thought that members may want to share in this unusual location.

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CASE 4

Contributed by: Ivan Damjanov, MD

Clinical history: Nonspecific heart problems in 53 year old man. A mass identified in the right atrium by ultrasound.

Gross findings: A gelatinous tumor measuring 3.5 cm in diameter removed from the left atrium.

Pathologic diagnosis : Atrial myxoma with glandular inclusions.

Comment: I am sending you this atrial myxoma for two reasons: because it was so cellular and because it contained glandular inclusions. These epithelial components are found in approximately 5% of all atrial myxomas. The cells lining these epithelial structures contain mucus. They stained with antibodies to keratin and calretinin.

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CASE 5

Contributed by: Otto Dietze, MD

History: The material is from a 33-year old lady, who underwent curetting for bleeding abnormalities and a polypoid mass in the uterus.

Pathology: The tumor consists of epithelial and mesenchymal structures partly infiltrating myometrium with a low degree of cytological abnormalities and mature appearing tissue despite the cell rich hyaline chondroid areas. Immunostaining did not contribute for further differentiation, (CK-7 positive epithelial structure, negativ staining for alpha-inhibin and p53, low Ki-67 activity)

The case was seen in consultation by local gynecopathologists who supported the diagnosis of a low grade Mullerian mixed tumor.

Comment: I cannot offer another diagnosis and despite several cases of malignant mixed Mullerian tumors in our files we have never seen a similar one. Although some features resemble tumors described in the series of Murray S.K. et al (Am J Surg Pathol, 29, 2, 157-66:2005) this seems to be a different entity. In the first sections of the block no infiltrative growth was to be seen, but in most of the slides for the seminar infiltration of muscle is present.

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CASE 6

Contributed by: Vincenzo Eusebi, MD

Clinical History: This is a breast tumour (right breast) of 2.5 cm (radiology) present for 10 years that in the last month had increased in size. FNA resulted in a C4 diagnosis.

Histologic Findings: This cystic papillary lesion consisted of proliferating cells with large eosinophilic granular cytoplasm. Some cells were arranged in solid nests. Nuclei are irregular with several grooves. The neoplastic cells are ER and PR negative. Actin does not outline myoepithelial cells around solid nests. As the histologic features were reminiscent of a papillary carcinoma of thyroid, TTF 1 and thyroglobulin were obtained that were negative. Antimitochondrium antibody was strongly and consistently positive.

Diagnosis: The tumour therefore was classified as (2) invasive "breast tumor resembling the tall cell variant of papillary carcinoma of thyroid".

Comment: Simple mastectomy was performed and an intramammary lymph node contained a metastasis. Most of the cells were loaded with mitochondria. I leave to you the question whether to regard this case as "mitochondrion rich" or oncocytic(1). RET/PTC activation was not observed in 3 of such breast carcinomas(3)

References

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CASE 7

Contributor: Cyril Fisher, Royal Marsden NHS Trust, London, UK

Case History: A 58-year-old man presented with a 6 cm diameter tumor in the popliteal fossa.

Pathology: This is a biphasic tumor with islands of focally keratinizing, sometimes cystic squamous epithelium separated by sheets of uniform spindle cells.

Diagnosis: Synovial sarcoma with squamous differentiation.

Comment: This is a diagnostically straightforward case of synovial sarcoma with extensive and keratinizing squamous differentiation in a prominent epithelial component. This is an unusual feature which has been noted in occasional reports,^{1, 2} and sometimes focally in older patients.³ My experience is that extensive squamous change with keratinization is rare, in around 1% of synovial sarcomas.

A further point of interest is that this case is found genetically to have SYT-SSX2 fusion gene transcripts; this is rare in biphasic SS which usually has SYT-SSX1.

This case can be compared with previously submitted cases of synovial sarcoma with a predominantly glandular component (seminar case 33/09) and with myxoid change (seminar case 37/07).

References

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CASE 8

Contributor: Christopher D.M. Fletcher
Case No: S03-35377

Clinical history: A 14-year-old boy presented with nasal obstruction and was found to have a 4.0 cm lobulated intranasal mass which was excised piecemeal.

Diagnosis: Nasal chondromesenchymal hamartoma (??)

Comment: This polypoid intranasal lesion (kindly shared with me by Dr. Jeff Goldsmith in Boston) has, in my opinion, very unusual appearances but seems to fit best with the entity described by Dehner some years ago – *Am J Surg Pathol* 1998; 22:425-433. The stroma of the papillae is composed mainly of primitive-looking but uniform spindle shaped cells organized around numerous small nodules of variably primitive cartilaginous tissue. This case seems rather less polymorphic than those described by Dehner and lacks the aneurysmal bone cyst-like component – in addition, Dehner's cases occurred in much younger children. However, there is a report of a similar lesion in an older child – *Int J Pediatr Otorhinolaryngol* 2003; 67:669-672 – which seems very similar to this one and which apparently was also reviewed by Dehner. I would be most interested to hear if anyone has experience with similar lesions, since I have not personally seen anything else quite like this.

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CASE 9

Contributed by: Jeronimo Forteza-Vila, MD

Clinical History: A 37-year-old woman was admitted in Emergency Department with cephalgia and fever. The cephalgia was located in the frontal area. Neurologic examination revealed a slight nuchal rigidity. CSF analysis: 413 cells/ml with 92% mononuclear cells. CT scan and cranial MRI showed only brain edema. The clinical diagnosis was acute lymphocytic meningitis. The patient was discharged, but the headache did not respond to analgesic treatment, so she was admitted in the Department of Internal Medicine. On admission the patient presented with partial motor seizures. After one crisis her left eye was deviated to the right on physical examination. She was transferred to the Intensive Care Unit, but suffered a progressive neurologic deterioration and died 15 days later. Hemorrhagic areas were found in MRI performed 24 h before died. CSF cultures were all negative.

Pathologic finding: Sections of areas of cortex with meninges show a variable degree of cortical necrosis associated with thrombosis of superficial and engorged vessels. Multiple fresh hemorrhages area present within the cortex and necrotic brain tissue. A number of mononuclear cells are noted focally in the subarachnoid space. No significant inflammation is noted in the parenchyma and no inclusions are identified in neurones or glial cells.

Staining for GFAP shows focal gliosis particularly within the cortex. CD68 immunostaining reveals microglial activation and collection of perivascular macrophages focally within the white matter. Staining with Luxol Fast Blue for myelin shows the presence of areas of focal myelin pallor.

The immunohistochemical study for HSV, EBV, CMV, HHV-8, Varicella-Zoster, Adenovirus and PrP was negative. Fresh brain tissue was sent to the Department of Microbiology. The PCR assay for the presence of viral DNA was negative. Assay for Anti-cardiolipin antibodies were also negative

Comment: The history of this acute illness suggests a postinfectious process, particularly in the absence of positive viral culture. The features seen are not entirely typical in that thrombosis is present and the myelin pallor does not have a predominantly perivascular distribution. We are not able to achieve a firm diagnosis but we think the most likely diagnosis is venous infarction although the possibility of a postinfectious hemorrhagic leukoencephalopathy has been considered. Anyone had any suggestion about the etiopathogenesis of vascular lesion of this case?

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CASE 10

Contributed by: Janez Lamovec, M.D.
Case 3443-05

History: A 57-year-old male patient was found to have an asymptomatic expansive formation in the head of pancreas on routine ultrasound examination of abdomen. On follow-up US the formation increased in size. Fine needle biopsy of the lesion was unsuccessful. Exploratory laparotomy was followed by Whipple's surgical procedure.

Pathological findings: Grossly, a 30 x 25 mm tumor was found in the head of the pancreas, that was adherent to duodenum. On cut surface, it was described as a firm mass, white-gray in color that was not so clearly circumscribed. The deep surgical margin was involved by tumor. No cystic areas were seen grossly.

Microscopically, the tumor shows complex papillary growths pattern with most of the papillary structures being intraductal/intracystic but some of them definitely invasive. In several foci, intraepithelial lumina inside epithelial fronds are present giving a cribriform aspect to those foci. Invasive foci appear ductal/papillary with cellular stromal reaction surrounding them. Pancreatic tissue at the invasive frontline shows features of chronic pancreatitis.

Neoplastic cells forming papillary structures of varied complexity are columnar in shape, one-cell in thickness or stratified, with abundant eosinophilic cytoplasm generally showing fine granularity; in many cells abundant apical mucin was present, and goblet type cells were also seen, scattered or lining some papillary structures. Nuclei were oval, mildly to moderately pleomorphic, with finely dispersed chromatin and small nucleoli. Mitoses were moderate in number. No metastases were present in peripancreatic lymph nodes.

Tumor cells were positive for CK 7, CK 19, CAM 5.2, chymotrypsin, focally for CEA, and very strongly, diffusely, for mitochondrial antibody. They were negative for CK 20, chromogranin, synaptophysin, p63, and amylase. MIB 1 decorated 20 to 30% of tumor nuclei while p53 was positive in < 5% of the latter. Lumina of the cysts/ducts and cribriform spaces showed abundant alcian blue positive mucin; the latter also filled goblet cells.

Diagnosis: Intraductal and invasive oncocytic papillary-mucinous carcinoma of the pancreas.

Comment: While intraductal papillary-mucinous carcinoma of pancreas has been known for quite some time, the description of an oncocytic variant of such a tumor is of relatively recent date (1). In the original series of 11 patients, the mean age of patients at presentation was 62 years, they were of both sexes, and patients presented with different complaints, such as epigastric discomfort, abdominal pain, bloating, etc. Grossly the tumors were cystic, often multilocular, and mucinous. Microscopically, they were intraductal/intracystic neoplasms with papillary fronds lined by predominantly oncocytic, but also gastric foveolar type mucinous cells and goblet cells. Cribriform foci were characteristic. Invasive foci were detected in two cases, appearing as solid nests of oncocytic cells. Ultrastructurally, many tumor cells were packed with mitochondria, and mucin was also identified. The prognosis was good; in none of the patients distant metastases developed, although in two patients there was a local recurrence.

Recently, similar tumors were also described in the liver (2, 3).

Our case differs from cases in the original series in at least two respects. Gross presentation of the submitted tumor was not cystic and mucinous but solid, and not different from more usual types of

pancreatic carcinoma. In addition, invasive foci were quite similar to intraductal ones, and in a number of foci it was difficult to determine which is which. We did not perform EM on this tumor but the reaction to mitochondrial antibody was very strong. Since this is a recent case, we don't have any meaningful follow-up information.

Literature:

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CASE 11

Contributed by: Michal Michal, Pilsen, the Czech Republic.

Case History: A 47-year-old woman underwent an abdominal hysterectomy and unilateral, left ovariectomy for multiple uterine leiomyomas. Four months after the hysterectomy the patient presented with a right-sided vaginal vault tumor, which was 3 cm in diameter. No signs of pregnancy were observed in the patient. Two years after the excision of the tumor, the patient is well and without signs of recurrence. Grossly, botryoid-looking excised tumor had a red color and myxoid to gelatinous consistency. The main bulk of the tumor was composed of large areas consisting of richly vascularized stroma arranged in retiform pattern. The stroma in these areas was composed of thin bipolar cells with tapered nuclei to stellate-shaped cells with minimal amount of cytoplasm. The tumor contained also some glandular tubal inclusions. The stroma around the glandular inclusions displayed a different appearance from that of the predominantly stromal areas, being composed of small epithelioid-looking cells with eosinophilic cytoplasm. The stroma in these areas contained a small amount of fibrous tissue and lacked the myxoid quality of the purely stromal regions. A scant amount of round inflammatory cells was seen throughout in both lesions. Immunohistochemically the tumor stroma was actin, cytokeratin and S-100 protein negative, whilst it resulted and CD 34 and desmin strongly positive.

Diagnosis: Prolapse of the fallopian tube after hysterectomy associated with exuberant angiomyofibroblastic stromal response.

DISCUSSION

Prolapse of the fallopian tube is a long known and histologically misleading phenomenon. Prolapse of the fallopian tube can easily be confused with adenocarcinoma. The exuberant stromal formation in tubal prolapse is an additional feature, making it difficult to diagnose this lesion. Morphological as well as immunohistochemical profile of the stroma is similar, if not identical, to that of cervical and vaginal angiomyofibroblastoma. This case was recently published **(1)**. There is on record a similar case in the literatures **(2)**.

References

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CASE 12

Contributed by: Markku Miettinen, MD

Case History: 36-year-old woman with a popliteal mass 6 x 4 x 4 cm. Yellowish, firm, with focally softer, mucoid areas.

Diagnosis: Round cell liposarcoma with cord-like growth pattern.

Comment: This is a typical example of round cell liposarcoma (high-grade variant of myxoid liposarcoma). The tumor shows compact, cellular areas that can look like a small round cell tumor or even a lymphoma. In this case, an unusual corded pattern is present. Some slides contain small areas of typical myxoid liposarcoma.

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CASE 13

Contributed by: Markku Miettinen, MD
Case 8630

History: The jejunum was aneurysmally dilated in an area of 5 x 5 cm, and this area contained a plaque-like infiltration. No other tumors were clinically known.

Diagnosis: True leiomyosarcoma of jejunum, high grade.

Comment: This tumor is composed of differentiated smooth muscle cells. The necrotic zone represent luminal aspect, where no preserved mucosa is seen in most slides. The tumor cells are positive for alpha-smooth muscle actin and desmin, and are negative for KIT, CD34, and S100 protein. The tumor showed neither KIT (exon 9,11,13,17) nor PDGFRA (exon 12,14,18) mutation.

This represents a true leiomyosarcoma that differs from a GIST. These tumors are much less common than GISTs and occur throughout the GI tract. However, in our experience, they are more common in the intestines than in the stomach. Plaque-like tumor forming an aneurismal intestinal dilatation is one of the gross patterns. Metastatic leiomyosarcomas often form multiple polypoid intraluminal masses, and primary tumors can also form a polypoid intraluminal mass.

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CASE 14

Contributed by: Elvio G. Silva, MD

History: 45-year-old female with vaginal bleeding. Pelvic exam: Large mass in the uterus protruding through the cervix. A biopsy of this mass was diagnosed as possible sarcoma.

TAH-BSO: A malignant tumor involving endometrium and myometrium (25 of 27 mm), right paraaortic and left pelvic nodes.

Diagnosis: Dedifferentiated endometrioid adenocarcinoma.

Comment: I had only 1 block with both tumors (well differentiated adenocarcinoma and undifferentiated ca) together but the WD disappeared after 25 recuts, so I am including this section where both components are separated. Most sections showed only the undifferentiated carcinoma.

I am including the abstract of our study accepted for publication in the International Journal of Surgical Pathology. There is another paper that is going to be published in the AJSP soon on undifferentiated ca of the endometrium. We believe that when the ca in the endometrium is totally solid, it is not a diagnostic problem because the neoplasm is recognized as a high-grade malignancy. However, when a low-grade endometrial ca has foci of undifferentiated carcinoma it is not unusual to diagnose the tumor as a grade 3 or worse, a grade 2 endometrial ca. It is very important to recognize the undifferentiated features of the solid component and to diagnose the case as an endometrial ca associated with undifferentiated ca or dedifferentiated endometrioid carcinoma.

The Association of Low Grade Endometrioid Carcinoma of the Uterus and Ovary with Undifferentiated Carcinoma. A New type of Dedifferentiated Carcinoma?

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ABSTRACT

Low-grade endometrioid carcinomas, either of the endometrium or the ovaries, usually have an excellent prognosis. The association of this type of tumor with undifferentiated carcinoma is rare. In this study we present the clinicopathologic features of 25 such cases.

The age of the patients ranged from 30-82 years (median 51). At presentation, the patients had either vaginal bleeding or pelvic pain. The endometrioid carcinoma involved the endometrium in 14 cases, the endometrium and one or both ovaries in 9 cases, and the ovaries in 2 cases. Undifferentiated carcinoma associated with low-grade endometrioid carcinoma was found at presentation in 19 grade 1 or 2 endometrioid carcinomas, 15 in the endometrium and 5 in the ovary. In one of these cases undifferentiated carcinoma was found in the endometrium and the ovary. Undifferentiated carcinoma was found in the endometrium and the ovary. Undifferentiated carcinomas were found following resection of low-grade endometrioid carcinoma in 6 cases, involving the retroperitoneum, pelvis, vagina or liver. The undifferentiated carcinoma was composed exclusively of diffuse sheets and solid nests of epithelial cells in 10 cases. Epithelial cells with isolated foci of keratinization were seen in nine cases, and rhabdoid cells in a myxoid background in six cases. Twenty-four patients were treated with total

abdominal hysterectomy and with bilateral salpingoophorectomy. Twenty-two patients received additional therapy as follows: chemotherapy (19), radiotherapy (4), and Tamoxifen (1). Follow-up showed that 15 patients died of disease in 1 to 60 months (median 6 months) and five patients are alive with progressive disease with a follow-up between 6 to 8 months, one patient is alive with no evidence of disease at 104 months. In four cases the diagnosis has been made recently, they have a short follow-up of 3 and 4 months.

Foci of undifferentiated carcinoma may be confused with solid endometrioid adenocarcinoma erroneously leading to the diagnosis of a grade 3 or a significantly less aggressive grade 2 endometrioid carcinoma. The recognition of undifferentiated carcinoma in an otherwise low-grade endometrioid adenocarcinoma is extremely important since it indicates an aggressive behavior. In asynchronous cases, being aware of this association can explain the absence of a second primary.

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CASE 15

Contributed by: James A. Strauchen, MD

History: This 52-year-old woman presented in 1999 with cholestatic jaundice. Liver biopsy showed periductal fibrosis with bile duct loss, portal fibrosis with formation of fibrous septae, and proliferation of bile ductules. The changes were considered consistent with primary sclerosing cholangitis. Colonoscopy showed no evidence of inflammatory bowel disease. In June of this year, she was noted to have a mass in the right lobe of the liver on CT scan and resection of the mass and cholecystectomy was performed.

Pathology: The specimen consisted of a wedge resection measuring 5.6 x 5.4 x 2.8 cm and weighing 35 gm. This contained a tan, fleshy nodule measuring 3.5 x 2.1 x 2.5 cm. Microscopic sections showed cirrhotic liver containing a lymphoid infiltrate composed of centrocyte-like cells with islands of residual hepatic parenchyma showing infiltration by lymphocytes with lymphoepithelial-like lesions. Immunohistochemical studies showed a B cell phenotype (CD5 negative, CD10 negative, CD20 positive, CD 79a positive, BCL2 positive, BCL6 negative) with a low Ki-67 proliferation index, consistent with extranodal marginal-zone B cell lymphoma of mucosa-associated lymphoid tissue type.

Diagnosis: Hepatic "MALT" lymphoma (extranodal marginal-zone B cell lymphoma of mucosa-associated lymphoid tissue type) associated with primary sclerosing cholangitis.

Comment: MALT lymphomas have now been reported in virtually all mucosal and mucosa-related sites including the gastrointestinal tract, upper and lower respiratory tract, salivary glands, ocular adnexa, thyroid, breast, kidney, prostate, thymus, skin, dura, etc. Predisposing conditions include chronic infection (e.g. *Helicobacter pylori* in gastric lymphoma, *Campylobacter jejuni* in immunoproliferative small intestinal disease, *Chlamydia psittaci* in ocular lymphoma, *Borrelia burgdorferi* in cutaneous lymphoma, Hepatitis C) and autoimmune diseases (Sjogren's syndrome, Hashimoto's thyroiditis). The unifying factor appears to be prolonged antigenic stimulation leading to acquired MALT. Antibiotics induce remission by eliminating the source of antigenic stimulation. MALT lymphoma of the liver is rare. Previous cases have been reported in association with primary biliary cirrhosis, supporting a relation to autoimmune disease (1). The present case was associated with primary sclerosing cholangitis, another autoimmune disease, supporting a relation to prolonged antigenic stimulation. Cases have also been reported in association with Hepatitis C. A striking feature in the present case was the occurrence of numerous lymphoepithelial-like lesions involving hepatocytes.

References:

1. Ye MQ, Suriawinata A, Black, Min AD, Strauchen J, Thung SN. Primary hepatic marginal-zone B-cell lymphomas of mucosa-associated lymphoid tissue type in a patient with primary biliary cirrhosis. Arch. Pathol Lab Med 2000; 124:604-608.

AMR SEMINAR #47

Case 16

Contributed by: Paul E. Wakely, MD

History: A 65-year-old man was admitted to the hospital with presumed acute prostatitis. Pelvic ultrasound showed an incidental 3.5- x 3-cm, solid, enhancing mass arising from the lower pole of the left kidney. There was no evidence of retroperitoneal adenopathy, renal vein invasion, local extension, or visceral metastases. A partial nephrectomy was performed.

Pathology: A 3.2 cm. red-brown mass with a central stellate scar was found during gross examination. There were no other visible lesions. The mass consisted of a pure population of oncocytes typical of Renal Oncocytoma. In addition to this mass, however, multiple small oncocytic nodules that ranged from < 0.1 cm. to as much as 0.5 cm. were observed randomly scattered in the renal cortex. These blended almost imperceptibly with the normal renal tubules without the benefit of a fibrous capsule. Those that were 1 mm. or less could be overlooked easily.

Diagnosis: Renal Oncocytosis.

Comment: I have not submitted a slide of the oncocytoma since the club is very familiar with this neoplasm. The reason for submitting the case was to briefly discuss renal oncocytosis and the Birt-Hogg-Dubé (BHD) syndrome. Since I used this case at the recent AMR gathering in the Czech Republic, I apologize to all for the small size of the remaining nodules in these glass slides, but the remaining blocks have been nearly depleted of the oncocytic nodules. I have dotted each slide to alert you to what I believe is a focus of oncocytosis, and have included a POWERPoint slide of a larger nodule for your viewing enjoyment.

Renal oncocytosis (oncocytomatosis) is rare. The largest series was presented by Tickoo et al. All patients (x= 64 years) had their kidneys removed for a dominant mass that in 68% of cases was a renal oncocytoma. The other tumors were either a chromophobe cell carcinoma or a hybrid tumor showing features of both chromophobe cell carcinoma and oncocytoma. Oncocytic nodules varied from a microscopic collection of a few cells to visible nodules with no maximum size mentioned in that paper. All but 2 of these had the histopathology of oncocytoma, and only rarely was an infiltrative pattern present. Other features included diffuse oncocytic change in normal renal tubules (50% of cases), and oncocytic-lined cortical cysts (29%).

Birt-Hogg-Dubé (BHD) syndrome is a rare genodermatosis that predisposes individuals to a variety of renal and cutaneous tumors, and less often pulmonary cysts, pneumothorax, and multiple lipomas. It is an autosomal dominant condition with incomplete penetrance. About 15-25% of individuals develops a renal neoplasm, and if so, these arise in the 6th decade of life. The BHD gene maps to chromosome 17p11.2 and codes for a novel protein called folliculin. A large review encompassing 130 renal tumors from 30 BHD patients showed the following breakdown: (Pavlovich et al)

of renal tumors

65 (50%)
44 (34%)
12 (9%)
7 (5%)
2 (2%)

histologic type

hybrid tumors [oncocytoma + chromophobe CA]
chromophobe renal cell CA
clear cell renal cell CA
oncocytoma
papillary renal cell CA

Over half (58.5%) of the patients had evidence of renal oncocytosis. All but 1 patient with oncocytosis had more than one macroscopic renal tumor. The conclusion by these authors was that these foci of oncocytosis represented incipient renal neoplasia & may be commonplace in the apparently normal kidneys of BHD patients. This patient had genetic testing and had no evidence of BHD syndrome.

References

1. Tickoo SK, Reuter VE, Amin MB, et al. Renal oncocytosis: a morphologic study of fourteen cases. *Am J Surg Pathol* 1999; 23: 1094-101.
2. Khoo SK, Giraud S, Kahnoski K, et al. Clinical and genetic studies of Birt-Hogg-Dube syndrome. *J Med Genet* 2002; 39: 906-12.
3. Pavlovich CP, Walther MM, Eyler RA, et al. Renal tumors in the Birt-Hogg-Dube syndrome. *Am J Surg Pathol* 2002; 26: 1542-52.
4. Linehan WM, Vasselli J, Srinivasan R, et al. Genetic basis of cancer of the kidney: disease-specific approaches to therapy. *Clin Cancer Res* 2004;10 (18 Pt 2): 6282S-9S.
5. Nagashima Y, Mitsuya T, Shioi KI, et al. Renal oncocytosis. *Pathol Int.* 2005;55:210-5.

AMR SEMINAR #47

Case 17

Contributed by: Lawrence Weiss, MD

History: This is a 54 year old man who presented with abdominal fullness and bloating. Physical examination revealed increased abdominal girth with a large intra-abdominal mass. CT scan was performed (see attached). Pseudomyxoma peritonei was suspected clinically.

Gross: The main specimen was received as one piece of tissue, which included a 7 kg, 40 x 29 x 11 multiloculated mass, with grape-like projections (see attached), with attached right hemicolectomy. An appendiceal stump was identified, and found to be normal. A separately received specimen consisted of peritoneum with focal areas of induration (which microscopically showed the same process).

Special stains:	PAS	positive
	PAS+D	negative
	Mucin	negative
	Keratin 5/6	positive
	Keratin 7	positive
	WT1	positive
	Calretinin	negative
	CD34	negative
	CD31	negative
	CEA	negative
	MOC31	negative
	BG8	negative

Diagnosis: Benign multicystic mesothelioma.

Comment: Pseudomyxoma peritonei was thought to be unlikely on the gross examination, as it virtually never comes out a single discrete mass. In addition, it lacked the characteristic slimy mucus, and had grape-like clusters of cysts. Benign multicystic mesothelioma usually occurs in young women, although it has been described in all ages, and about 1/6 of cases occur in men. These neoplasms are usually much smaller than seen in our case (and sometimes even called multilocular inclusion cyst), but can on occasion be enormous. There is no association with asbestos.

AMR SEMINAR #47

QUIZ CASE 1

Contributed by: (Janez Lamovec, M.D.): 1363-00

A 79-year-old woman with a breast carcinoma that increased in size during tamoxifen treatment.