CASE 1

Guest Discussant: Pamela Unger, M.D., Mt. Sinai Medical Center
Host Discussant: Susan Jormark, M.D., Lenox Hill Hospital

The patient is a 73 year old female who complained of generalized weakness and vague abdominal symptoms of a few weeks duration. She was seen at an outside hospital where she was noted to be anemic and to have a left renal mass on ultrasound and CT scan. An FNA suggested renal cell carcinoma. She was transferred to LHH for a left nephrectomy.

Aside from a splenectomy 30 years previously, status post motor vehicle accident, the patient was in good health and had no significant past medical, surgical, family, or social history. Physical exam was unremarkable. Laboratory studies showed normochromic normocytic anemia. Abdominal ultrasound showed an 8 cm solid mass extending from the upper pole of the left kidney. CT scan showed an left upper retroperitoneal mass superior and lateral to the kidney. Exploratory laparotomy revealed a highly vascular LUQ lesion unrelated to the kidney, three omental masses, and a mass close to the tail of the pancreas.

CASE 2

Guest Discussant: Gloria Gallo, M.D., NYU Medical Center
Host Discussant: Samuel Wahl, M.D., Lenox Hill Hospital

The patient is a 42 year old black Hispanic female from the Dominican Republic. She has been HIV+ since 1992, and is asymptomatic in regard to HIV-related illness. Recently she was found to have azotemia, (creatinine 3.5/BUN 21). She denies hematuria or dysuria. She is on a triple drug regimen including a protease inhibitor for HIV infection. Blood pressure and physical exam are without significant abnormalities. There is no lymphadenopathy. Renal sonogram showed slight decrease in size of the left kidney and was otherwise normal.

Laboratory Data: U/A: 1+ protein; (-) RBCs; 10 WBCs; (-) eosinophils; rare crystals; pH 6. 24-hour urine protein: 227 mg., creatinine clearance 34cc/min. Serum chemistry: BUN 32mg/dl, uric acid 7.1 mg/dl; sodium 139 mEq/l, potassium 4.1 mEq/l; chloride 105 mEq/l; glucose 116 mg/dl; phos 3.1 mg/dl. ABC: hematocrit 36%, hemoglobin 12.3 g/dl, WBC 7.6 K, platelets 277 K. (-) ANA and hepatitis serologies.

CASE 3

Guest Discussant: Artemis Nash, M.D., Lawrence Hospital
Host Discussant: Ileana Green, M.D., Lenox Hill Hospital

A 91 year old woman with a history of melanoma 25 years ago presented with a right thigh mass. The mass was found incidentally during a work-up for abdominal pain. It was grossly circumscribed and measured 6.5 x 5.5 x 3.5 cm. The cut surface was vaguely lobulated, tan, and glistening.

CASE 4

Guest Discussant: Scott McNutt, M.D., Cornell Medical College
Host Discussant: John A Terzakis, M.D., Lenox Hill Hospital

This 68 year old woman had a mass of the chest adjacent to the left breast mediially. The referring physician reported mild continuous tenderness. Mammography did not reveal a lesion that was clinically obvious skin nodule. There was no mammographic evidence for malignancy.
PATHOLOGISTS' CLUB

THURSDAY, JANUARY 7, 1999
LENNOX HILL HOSPITAL
EINHORN AUDITORIUM

RECEPTION
5:30 - 6:00 P.M.

DINNER
6:00 - 7:00 P.M.

SCIENTIFIC SESSION
7:00 - 9:00 P.M.

Entrance to the Einhorn Auditorium directly at 131 East 76 Street

Subway: Lexington Avenue line (local)
77street stop in front of the hospital

Buses: Lexington Avenue (downtown)
Madison and Third Avenue (uptown)

Parking: Garages on 77 and 76 Street
between Lexington and Third Avenue

For any additional information please contact
Ms. T. Bamberger tel: 434-2330.
Case #1

Dr. Unger reviewed the history, and described the histology, notably an encapsulated mass with a compartmentalized heterogeneous cellular population. There are lymphoid aggregates with germinal centers, with plasma cells, and bone marrow elements. There is a separate population of histiocytes with abundant feathery eosinophilic cytoplasm. These histiocytes are PAS+, PAS-D+, Fe+, and AFB-. They are KP1+, Ham56+, and CAM 5.2-. The plasma cells are polyclonal. Based on these findings, the diagnosis is splenosis with Gaucher's Disease Type I, and extamedullary hematopoiesis.

Dr. Jormark showed that the gross appearance of the nodules resembles splenic tissue. A rib showed bone marrow involved by Gaucher's Disease. Ultrastructural data showed the characteristic inclusions. Dr. Jormark went onto present an amazingly comprehensive yet concise review of Gaucher's Disease, that included the biochemistry, genetics, clinical subtypes (I = adult non-neuropathic, 99% of cases; II = acute infantile neuropathic; III = subacute juvenile neuropathic), clinical presentation, and current diagnosis and treatment. Among the highlights: The presentation and clinical outcome of Gaucher's Disease are highly variable, with marked differences in severity and site of involvement. Pulmonary involvement and an ichthyosis-like skin disorder may occur. Therefore, for any patient, the prognosis is uncertain. There is an increased risk of neoplasia, most likely related to increased cytokine production. Diagnosis has classically been by bone marrow aspiration, with identification of the Gaucher cells. However, direct enzyme assay and genotyping are coming into vogue. Treatment has traditionally been symptomatic. However, we are on the threshold of a new era of enzyme replacement therapy, which reverses visceral but not neurologic symptoms. Bone marrow transplantation is efficacious but not recommended. Gene transfer is under research. A lively discussion followed the presentation concerning the issue of prenatal diagnosis and elective termination of pregnancy in view of the highly variable clinical manifestations of the disease. Indeed, the patient under discussion made it to age 73 without difficulty!
Case #2

Dr. Gallo used this case as a takeoff to review HIV-related kidney disease. The main categories include collapsing glomerulopathy, characterized by heavy proteinuria without edema, and tubuloreticulic particles on ultrastructural study; coinfection with HIV, HCV and HB, producing membranoproliferative, mesangiproliferative or membranous glomerulonephritis; drug-related disease (eg IV heroin); and treatment related disease causing acute interstitial nephritis or granulomatous interstitial nephritis. The patient under discussion does not fit HIV nephropathy (she had a normal serum albumin and only 1+ edema).

Dr. Gallo reviewed an NYU series of 18 HIV+ patients with renal disease (4 membranoproliferative GN, 10 mesangiproliferative GN, 1 IgA nephropathy, 2 membranous GN, 1 glomerulosclerosis with immune complex deposition). 12/12 had positive serum anti-HCV antibodies.

The patient's glomeruli and vessels were unremarkable. However, she had interstitial crystalline granulomas, along with crystalline tubular casts. Diagnosis: Granulomatous interstitial nephritis related to therapy.

Dr. Wahl concurred, his diagnosis being tubulo-interstitial nephritis with crystalline cast formation. The patient was on epivir and retrovir (reverse transcriptase inhibitors), and crixivan, a protease inhibitor, which is most likely the offending agent in this case. Immunofluorescence and ultrastructural studies in the patient were non-contributory. Crystalluria syndromes in the setting of HIV disease include sulfadiazene, acyclovir, and protease inhibitors (indinavir, ritonavir). Upto 20% of patients may have asymptomatic crystalluria with these agents. (References: NEJM 1997, 336; 1138-1140; Ann Int Med 1997, 127; 119-125.)

Case #3

Dr. Nash used this case as an opportunity to discuss the differential diagnosis of myxoid soft tissue lesions. The histology of this thigh mass from a 91 year old female was of an encapsulated myxoid mass with mild to moderate cellularity, some dense fibrous tissue, large dilated vessels, some with luminal eosinophilic material, some thrombosed, and smaller delicate vascular channels as well. There was no necrosis. The cells are mildly pleomorphic, spindle or stellate shaped, somewhat epithelioid, with dense nuclei. Lipomatous elements are noted, and some multinucleated giant cells display a floret pattern. Mast cells are easily found.

Trichrome stain showed no myoid differentiation. Vimentin was the only positive immunostain. Muscle specific and smooth muscle actins, desmin (rare + cell?), S100 and CD 34 were all negative.

The dx includes malignant myxoid liposarcoma (ruled out), intramuscular myxoma, myxoid nodular fasciitis, cutaneous angiomyxoma, aggressive angiomyxoma (uncircumscribed borders and positive myoid markers rule it out), and angiomyoﬁbroblastoma. Cutaneous angiomyxoma may be solitary or multiple, is associated with Carney’s complex (neuroendocrine neoplasia, cardiac myxoma), has variable borders, usually involves skin, and is composed of bland cells. Immunohistochemically it displays no myoid differentiation and is ER/PR negative.

Angiomyoﬁbroblastoma occurs mainly in females, tends to to
involve the superficial vulva or vagina, is well circumscribed, composed of bland cells, and does not recur. Myoid differentiation is weak if present, but ER/PR is positive.

Dr. Nash showed the current case to be strongly ER+ (PR was rare+), and on that basis made a diagnosis of angiomyofibroblastoma.

Dr. Green showed the FNA material that preceded the surgical resection. The FNA diagnosis was myxoid spindle cell neoplasm. The excised mass weighed 80g. The histology was as previously described by Dr. Nash, with the exception of a single infiltrative focus. Desmin was positive in the pleomorphic cells, but EM showed no skeletal muscle differentiation.

Dr. Green’s ddx included schwannoma (ruled out by negative S100), myxoid MFH (ruled out by low mitotic index). Her diagnosis was pleomorphic hyalinizing angiectatic tumor of soft parts, an entity recently described by Weiss and colleagues (Smith ME, Fisher C, Weiss SW, Pleomorphic hyalinizing angiectatic tumor of soft parts. A low-grade neoplasm resembling neurilemoma. Am J Surg Pathol 1996, 20:21-9). This entity has an equal male to female occurrence, and a wide age distribution. It presents as a slowly enlarging mass, the treatment of which is excision. Four of 8 recurred locally. These tumors share several features with neurilemomas, such as their unusual vasculature, intranuclear cytoplasmic inclusions, lack of mitoses, and abundance of mast cells. Unlike neurilemomas they are S-100 negative, and have infiltrative margins.

After the two presentations, Dr. Iochim pointed out that the diagnosis of pleomorphic hyalinizing angiectatic tumor of soft parts was a completely descriptive term and sheds no light on the nature of the cell responsible for the proliferation.
Dr. McNutt used this case as an illustrative example of how far one can go in arriving at a diagnosis strictly by histomorphology and immunohistochemistry in the absence of relevant clinical history, unfortunately a predicament we are all too familiar with!

The lesion was described as a well-circumscribed adnexal tumor in the dermis with a lobular arrangement and a small uniform epithelial cellular population. There are mitoses, some necrosis and some cribiforming. Small glandular lumens are present in addition to the more solid areas. A focus of probable perineural invasion is noted.

The chief issue here is whether this is a sweat gland carcinoma or a breast carcinoma metastatic to skin. In deciding the issue, history is of paramount importance, i.e., is the lesion solitary or multiple? Is the growth slow or rapid?

Immunohistochemistry is useful in this differential diagnosis. Sweat glands have S100+ myoepithelial cells. Sweat glands are GCDFP-15 (BRST)+ as well with variable positivity. Strong and uniform ER positivity favors breast carcinoma, while weak immunopositivity might be expected in sweat gland carcinoma. Finally p53 immunostaining is positive in more than 60% of breast carcinomas, but negative in sweat gland carcinoma, (except for extra-mammary Paget's disease). The case under discussion showed focally positive and variable GCDFP-15 positivity, ER positivity, and S-100 negativity.

Dr. McNutt's diagnosis is primary sweat gland carcinoma arising in mammary-like sweat glands of skin.

Dr. Terzakis provided the missing clinical information which favors a diagnosis of sweat gland carcinoma: The lesion was solitary and had been present for 5 years. Moreover, there is no breast carcinoma.

The lesion has overtly malignant features, i.e., it is invasive into fat, and displays both lymphatic and perineural invasion. The cells are positive for GCDFP, PR, ER, and CK. They are negative for S100, CD34, and SMA. Apocrine carcinomas are GCDFP15 positive and S100 negative, eccrine carcinomas have the inverse pattern.

Dr. Terzakis' diagnosis is malignant eccrine spiradenoma. Dr. McNutt agreed with that diagnosis, but pointed out that there were no areas of benign spiradenoma.