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MEETING

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DATE: Thursday, June 6, 1996

PLACE: NYU Medical Center
560 First Avenue
New York, NY 10016

HOST: Helen Feiner, M.D.

INFORMATION: Eileen Brady
(212) 263-5475

RECEPTION AND DINNER: 5:15 - 6:45 P.M.
FACULTY DINING ROOM

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

DIRECTIONS:

The Faculty Dining Room is on the ground floor of the Schwartz Health Care Center at NYU Medical Center. Enter the Medical Center through the Main Lobby on First Ave between 31st and 32nd Streets.

The scientific program will be held in Alumni Hall, Classroom A. Enter the Medical Center through the main lobby on First Ave. between 31st and 32nd Streets.

New York University Medical Center can be reached by # M 15 buses, which run north on 1st Avenue, and south on 2nd Avenue, and by # M 16 buses which run crosstown on 34th Street. The nearest stop on a subway is at Park Avenue and 33rd Street (the IRT Lexington Avenue local train, #6). Commercial public parking is available at the Kips Bay parking lot on 1st Avenue (west side) near 32nd Street, and on the north side of 29th Street between 1st and 2nd Avenues.

Pathologists' Club of New York
N.Y.U. Medical Center
June 6, 1996

CASE #1:
S96-6196 The patient is a 63 year old woman with a history of chronic hepatitis C. She underwent orthotopic liver transplantation for endstage liver disease. The submitted slide is from the left lobe of her explanted liver.

Invited discussant: Michael Bannan, M.D.
New York Medical College
Host discussant: Neil Theise, M.D.

CASE #2:
S96-3852 The patient is a 89 year old man with a history of chronic lymphocytic leukemia diagnosed in 1994 at another institution and confirmed by peripheral blood flow cytometry studies at NYU at the same time. Labs in 1994 were WBC 12,800 (78% lymphocytes), Hb 14, Plts 114,000. Given his good performance status, he was periodically re-evaluated without chemotherapy. He did well until late 1995, when he began losing weight. In February 1996 he was seen at NYU with an enlarged left axillary node. Labs were: WBC 12.5 (82% lymphocytes), Hb 9.7, platelets 113,000. Immunoelectrophoresis and Coombs' test were negative. CT scan showed large peripancreatic/retroperitoneal nodes. A bone marrow biopsy was done.

Invited discussant: Rosalyn Stahl, M.D.
Englewood Hospital
Host discussant: Stefano Rosati, M.D.

CASE #3:
S96-1873 The patient is a 41 year old black man who is a former smoker with a history of coronary artery atherosclerosis and multiple episodes of myocardial infarction. He was symptom free since his last angioplasty in 1994. On a routine checkup, in December 1995, the patient had an abnormal stress test. At this time his chest x-ray revealed a 2 cm. "coin lesion" in a lateral segment of the right middle lobe. The patient undrewent a wedge resection.

Invited discussant: Ann Avitabile, M.D.
Roosevelt Hospital
Host discussant: Manijeh Moezzi, M.D.

CASE #4:
S94-3363 The patient is an 86 year old woman with a long history of hypertension and angina pectoris. She presented with a 3 month history of gross hematuria. A CT scan of the abdomen revealed a right renal mass with a complex cystic structure. She underwent a right nephrectomy, which revealed a well circumscribed, solid and partially cystic yellow mass at the lower pole of the kidney. The submitted slide is from the mass.

Invited discussant: Eugene Fazzini, M.D.
Somerset Medical Center
Host discussant: Jonathan Melamed, M.D.

CASE #5:

CO96-48 The patient is a 61 year old white female who presented with left lower quadrant pain, frequency of urination and increased flatulence. Physical examination was negative. An abdominal ultrasound revealed left hydronephrosis and left hydroureter with multiple paraortic hypoechoic masses medial to the left kidney and extending inferior to it. Computerized tomography of the abdomen showed enlarged paraortic and pelvic lymph nodes with a large (6 x 5 cm.) mass at the vertebral level of L2. A computerized tomography guided fine needle aspiration was performed. Kodachromes represent 100X and 400X magnification.

Invited discussant: Mark Suhrland, M.D.
Montefiore Medical Center
Host discussant: Joan Cangiarella, M.D.

Minutes of Pathologist Club
NYC Medical Center
June 6, 1996

The faculty dining room at NYU Medical Center afforded an excellent view of a sunny spring day on which to hold this year's June meeting. Dr. Helen Feiner served as Host and Dr. Jerry Waisman was on hand for quips and commentary. It was noted that each of the invited speakers had spent part of their training or professional career at NYU. After a delicious meal, the members, who seemed in particularly fine spirits, settled in for the scientific session. Dr. Valsamis welcomed the membership and observed that if no alternate nominations were made, Dr. Jones would cast her ballot for the membership as a whole for the currently proposed slate of officers. The slate approved for 1996-1998 includes: Dr. Fred B. Smith. President, Dr. Joan G. Jones, Vice President, and Dr. Sylianos Lomvardius, Secretary Treasurer. In addition the following applications for membership were approved: Dr. Dobrila Vrbanovic and Dr. Peter Fisher.

CASE #1: S-96-6196 The patient , a 63 year old woman with chronic hepatitis C, underwent orthotopic liver transplantation for end stage liver disease. Sections showed a malignant neoplasm with vascular and perineural involvement which showed a variety of patterns. Architecturally the patterns included compact, sinusoidal, trabecular, papillary, and tubular, while the cytology of the cells ranged from those resembling hepatocytes to cells which were more columnar. The differential diagnosis entertained was a combined hepatocellular cholangiocarcinoma versus a pseudoglandular hepatocellular carcinoma. To make a diagnosis of a combined tumor, unequivocal elements of both hepatocellular and chlangiocarcinoma must be identified. Hepatocellular carcinomas may contain intracellular or intracanilicullar bile, and typically show a trabecular pattern of growth. Immunomarkers include alphafeto protein and export proteins such as alpha I antitrypsin. Cholangiocarcinomas by contrast may show a definite glandular pattern, contain mucin, and stain for CA19-9, monoclonal CEA, EMA, the blood group antigen Lewis X, and amylase. Differences in keratin profiles between the two have been described but may not be terribly helpful. In this case, though, alpha feto protein and CEA were positive, with transition zones noted. Hence Dr. Bannon's diagnosis: combined hepatocellular and cholangiocarcinoma in association with cirrhosis.

Dr. Theise agreed with Dr. Bannon's diagnosis. He showed the gross appearance of the explanted liver which contained a dominant mass and satellite nodules status post chemoembolizaton. Tumor was noted in a branch of the portal vein. Regarding an approach to distinguishing hepatocellular from cholangiocarcinoma, Dr. Theise talked on the usefulness of alpha feto protein, polyclonal CEA, and HepPar 1. Alpha feta protein is a substance found in fetal hepatoblasts and is not found in the normal adult liver. It is focally positive in 40% of hepatocellular carcinomas and is more likely to be positive in more poorly differentiated tumors. It can be positive in cirrhotic nodules as well, but in cases of malignancy if it is present, it is diagnostic. The usefulness of polyclonal PCEA is that this antibody cross-reacts with a biliary glycoprotein located on the canalicular membrane. If positive it is pathognomonic for hepatocellular carcinoma. HepPar I, which stands for hepatocyte paraffin 1, is a monoclonal antibody in which positive staining forms ring-like structures in the cytoplasm which by EM may be mitochondria. This antibody stains both benign and malignant hepatocytes as well as rare stomach tumors. Dr. Theise's bottom line: don't rely too much on Alpha feto protein, don't forget pCEA, and look for HepPar 1, an antibody coming soon.

DIAGNOSIS: COMBINED HEPATOCELLULAR AND CHOLANGIOCARCINOMA

CASE #2: This 89 year old patient with a two year history of CLL developed diffuse lymphadenopathy earlier this year and underwent bone marrow biopsy. Dr. Stahl described the findings, a paratrabecular and diffuse infiltrate composed of a polymorphus population of cells including eosinophils,

R-S/ Hodgkin-like cells, and small mature lymphocytes. Her differential included Hodgkin's disease versus progression of the patient's CLL (Richter's Syndrome). Stains for LEU-M1 and Ber H2 confirmed the presence of Reed-Sternberg cells. The background mature lymphocytes were LCA and L26 positive. Hence Dr. Stahl's diagnosis was combined Hodgkin's disease and chronic lymphocytic leukemia. This has been described as a Hodgkin's disease variant of Richter's Syndorme. The survival, however, is from two months to eight years versus two to four months for classic Richter's. Some reports maintain that the Hodgkin's disease evolves from a different clone, while others think the same clone may be involved. It has also been reported that EBV may play a role in the pathogenesis of the Reed-Sternberg cells.

Dr. Rosati agreed with Dr. Stahl's assessment. The infiltrate was polymorphus, with CD20 showing a persistent CLL, and CD30 positivity confirming the presence of Reed-Sternberg cells. Approximately 3 to 10 % pf patients with CLL progress to Richter's Syndrome - ie, a large cell lymphoma superimposed on CLL,most of which are B cell neoplasms. A clonal relatedness is usually demonstrable. Other secondary malignancies complicating CLL include carcinomas of lung and brain, melanomas and Hodgkin's disease. Patient's with progression and concomitance of CLL with Hodgkin's disease have a somewhat better survival. The diseases may be found in the same or in different anatomic sites. Usually the Hodgkin's disease follows the CLL. The diagnosis is made when these atypical cells occur in the appropriate milieu and show the appropriate immunophenotype. It is possible to see isolated Reed-Sternberg or Reed-Sternberg-like cells in the setting of CLL, but usually these are EBV infected cells which only later may evolve to overt Hodgkin's disease.

DIAGNOSIS: HODGKIN'S DISEASE VARIANT OF RICHTER'S SYNDROME

REFERENCES:

Weisenberg E et al.: Hodgkin's disease associated with chronic lymphocytic leukemia. Eight additional cases , including two of nodular lymphocyte predominance type. AmJClinPathol 1995;103:479-484.

Rubin D et al.: Richter's transformation of chronic lymphocytic leukemia with Hodgkin's like cells is associated with Epstein-Barr virus infection. Modern Pathology 1994;7:91-98.

Khan G et al.: Epstein-Barr virus in Reed-Sternberg-like cells in non-Hodgkin's lymphomas. Journal of Pathology 1993;169:9-14.

Momose H et al.: Chronic lymphocytic leukemia/small lymphocytic lymphoma with Reed-Sternberg-like cells and possible transformation to Hodgkin's disease. Mediation by Epstein-Barr virus. Am J Surg Pathol 1992;16:859-867.

Brecher M and Banks P: Hodgkin's diseae variant of Richter's syndrome. Report of eight cases. Am J clin Pathol 1990; 93:333-339.

CASE #3: A 41year old black male, former smoker,was found on a routine chest x-ray to have a 2 cm. "coin lesion". Dr. Avitabile described the microscopic findings: a well demarcated non-encapsulated lesion in which one noted a proliferation of alveolar lining cells as well as interstitial cells. Dr. Avitabile's differential diagnosis included alveolar adenoma, sclerosing hemangioma, pulmonary lymphangioma, bronchioloalveolar carcinoma, and hamartoma. The cystic spaces include PAS positive material, with lining cells ranging from attenuated to cuboidal to hobnail. As stains for Factor VIII were negative

however, this was not considered a lymphangioma. Furthermore, there were no other components as one would expect in a hamartoma. The intersitium was a variable thickness and contained mononuclear cells. There were no nests of epithelial cells as would be seen in a sclerosing hemangioma. Finally, although cytokeratin was positive in the lining cells, there was no lepidic growth as one would expect in a bronchioloalveolar carcinoma. Hence Dr. Avitabile's diagnosis: Alveolar adenoma.

Dr. Moezzi agreed with Dr. Avitabile's diagnosis. Dr. Moezzi noted that the cystic spaces were larger in the central area and that the adjacent lung was compressed. Stains for mucin were negative and immunostains for keratin and Factor VIII were as described above. By electron microscopy the cells exhibited microvilli and contained lamellar bodies, both of which are characteristic of type 2 pneumocytes. This entity was first described by Dr. Yousem in 1986; the findings are as described above. There are some who consider this to be an unusual variant of a sclerosing hemangioma whereras others consider the lesion a benign adenomatous malformation of the bronchiole.

DIAGNOSIS: ALVEOLAR ADENOMA

REFERENCES:

Yousem, S. and Hochholzer,L: Alveolar Adenoma. Human Pathol 17:1066-1071, 1986.

Al-Hilli F: Lymphangioma (or alveolar adenoma ?) of the lung. Histopathology 11, 979-980, 1987.

Fantone JC, Geisinger KR, Appleman HD: Papillary adenoma of the lung with lamellar and electron dense granules. An ultrastructural study. Cancer 50: 2839, 1982.

Katzenstein ALA, Gmelich JT, Currington CB: Sclerosing hemangioma of the lung. Am J Surg Pathol 4: 343, 1980.

Ng WL, Ma L: Is sclerosing hemangioma of lung an alveolar mixed tumor? Pathology 15:205, 1983.

Bareman C L, Adair C F: Immunohistochemistry of Pneumocytes in Hyperplasia and Noeplasia: Applied Immunohistochemistry 4 (1): 61-65. 1996.

Miller, R: bronchioloalveolar Cell Adenomas: Am J Pathol 14 (10): 904-912, 1990.

CASE #4:S 94-3363 An 86 year old woman with a long history of hypertension and angina presented with gross hematuria and a CT scan revealed a right renal mass. At the time of nephrectomy an 8 cm. cystic mass was found in the inferior pole which had a variegated yellow and gelatinous appearance as well as necrosis. As Dr. Fazzini was unexpectedly unable to attend the meeting, Dr. Melamed presented the case. Light microscopy on the case showed a number of patterns. There were cysts containing mucin, and intermediate sized polygonal cells, as well as nests of cells including squamous pearls and a variable amount of myxochondroid matrex. A moderate number of mitoses were present. Of the primary renal neoplasms, including renal cell carcinomas and transitional cell carcinomas. one might consider here a diagnosis of sarcomatoid carcinoma, except that the epithelial component is usually poorly differentiated and the sarcomatoid component is most frequently spindled and shows a high degree of anaplasia. In this case the squamous epithelial component was positive for AE1, AE3, the spindled cells showed actin positivity, but there were also GFAP and S100 cells in both the chondroid and other areas. Thus the differential diagnosis was expanded to include mixed tumors and myoepithelial tumors. Ultrastructural examination revealed loosely arranged cells with rudementary cell junctions and remnants of a basal lamina

material containing abundant intermediate philaments. A literature search revealed no documentation of myoepithelial cells normally existing in the kidney nor of myoepithelial tumors. Hence the diagnosis of sarcomatoid carcinoma was favored. On consultation with Dr. Reuter at Memorial Sloan Kettering however, he favored a mixed tumor as seen in the salivary gland. There have been five cases reported of metastases to the kidney from a malignant mixed tumor of salivary gland, and on questioning this patient was found to have a history of a resected parotid tumor twenty seven years prior. Since resection of the renal mass, the patient has now developed multiple metastases including one in the scalp which was confirmed by FNA.

DIAGNOSIS: MALIGNANT MIXED TUMOR OF SALIVARY GLAND, METASTATIC TO KIDNEY

REFERENCES:

Horowitz M and Sogani P. Secondary Carcinoma of Kidney from Parotid Gland Tumor. Uroology 41 (6): 602-604, 1993

Cherian T., Sebastian P, Abraham E, et al. Unusual multiple metastases from malignant pleomorphic adenoma of the parotid gland. Journal of Laryngology and Otology 106: 652-655, 1992.

Thomas WH and Coppola ED Distant Metastases from Mixed Tumors of the Salivary glands. American Journal of Surgery 109: 724-730, 1965.

Wenig BM, Hitchcock CL, ellis GL, et al. Metastasizing Mixed Tumor of Salivary Glands. American Journal of Surgical Pathology 16 (9):845-858, 1992.

Reuter VE, Sarcomatoid Lesions of the Urogenital Tract. Seminars in Diagnostic Pathology 10 (2): 188-201, 1993.

CASE #5:CO96-48 A 61 year old woman was found to have periaortic and pelvic lymphadenopathy with a 6 cm. mass located at the L2 vertebral level. A CT guided FNA was performed. Microscopic examination showed discohesive cells with signet ring features. Dr. Suhrland reviewed the differential diagnosis for signet ring cells in a smear. These include not only carcinomas such as stomach, breast, pancreas, colon, appendix and bladder, but also lymphomas, melanomas, and sarcomas. In this particular case, lymphoglandular bodies were identified supporting a diagnosis of signet ring lymphoma. Stains for keratin and mucin were negative; stains for LCA and methyl green pyronine were positive . Hence Dr. Suhrland's diagnosis of Signet Ring Lymphoma, first described by Rappaport in 1978.

Dr. Cangiarella agreed with Dr. Suhrland's assessment of this case. Workup of the patient showed no ovarian masses, colonic masses, gastric masses , or gastric wall thickening. By light microscopy, there were dispersed as well as clumps of cells. Some, as Dr. Suhrland had also pointed out, were angulated and showed nuclear irregularity . Stains for LCA, L26 and Lambda were positive. The background cells were defined as cleaved lymphocytes. There have been approximately forty cases of signet ring lymphoma reported in the literature. Most involve lymph nodes although extranodal involvement may occur. Most are

B cell follicular center cell lymphomas, and a Bcl-2 break point has been demonstrated. Important differential diagnoses include metastatic gastric carcinoma, lobular breast carcinoma, and liposarcoma. By electron micoscopy, the cells resemble Russell bodies and contain membrane bound vacuoles thought to be the result of abnormal membrane recycling. Many of these patients follow an indolent clinical course.

DIAGNOSIS: SIGNET RING LYMPHOMA

REFERENCES:

Eyden BP et al. The ultrastructure of signet-ring cell non-Hodgkin's lymphoma. Virchows Archiv A Pathol Anat 417:395, 1990

Grogan TM et al. Signet-ring lymphoma of T-cell origin. Am J Surg Path 9:684, 1985.

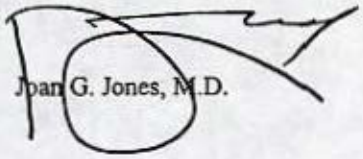
Kurotaki H et al. Fibril formation in the rough endoplasmic reticulum of lymphoma cells. A case report with histopathologic, immunocytochemical, elecron and immunoelectron microscopic studies. Path Res Pract 190:84, 1994.

Manivel-Rodriguez JC et al. Signet ring lymphoma. Report of a case. Diagn Cytopathol 2:338, 1986.

Sheibani K et al. Signet-ring cell melanoma. Am J Surg Path 12:28, 1988.

Weiss LM et al. T cell signet ring cell lymphoma. A histologic, ultrastructural and immunohistochemical study of two cases. Am J Surg Pathol 9:273, 1985.

Respectfully submitted,



Joan G. Jones, M.D.