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PATHOLOGISTS' CLUB
OF NEW YORK

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MEETING

DATE: Thursday, February 1, 1996

PLACE: Lenox Hill Hospital
100 East 77th Street
New York, New York 10021

HOST: Dr. Harry Ioachim

INFORMATION: Mrs. Tova Bamberger
(212) 434-2330

RECEPTION AND DINNER: 5:15 - 7:00 P.M. Cronin Cafeteria, First Floor

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

DIRECTIONS:

The Pathologists' Club session will be held in the Einhorn Auditorium of Lenox Hill Hospital.

It can be reached directly from the street at 131 East 76th Street or through the main entrance of the hospital at 100 East 77th Street. The subway station of the Lexington Uptown #6 line is located at the corner of East 77th Street and Lexington Avenue adjacent to Lenox Hill Hospital.

MTA buses run in an uptown direction on Third Avenue and Park Avenue and downtown on Lexington Avenue.

Dinner will be available from 5:15 to 7:00 PM. The Scientific meeting will be held from 7:00 to 9:00 PM.

CASE HISTORIES 2/1/96 Lenox Hill Hospital PATHOLOGIST'S CLUB

CASE #1: DISCUSSANTS:

Thomas Wright, M.D. Columbia Presbyterian Medical Ctr.
Maria Shevchuk, M.D. Lenox Hill Hospital

A 48 year old patient presented with a 20 x 12 x 2.5 cm. pelvic mass. She had undergone a TAH-BSO 3.5 years earlier, for benign disease.

CASE #2: DISCUSSANTS:

Thomas Godwin, M.D. New York Hospital Medical Ctr. of Queens
Susan Jormark, M.D. Lenox Hill Hospital

This 64 year old female, a former heavy smoker with a history of COPD, was admitted for rapidly progressive respiratory failure with severe dyspnea and hypoxemia starting approximately 8 months prior to admission. Chest x-ray showed pulmonary vascular congestion with small bilateral pleural effusions, shown to be transudates on pleural tap. Ventilation perfusion scan showed normal perfusion with no evidence of pulmonary emboli. Pulmonary angiography also showed no evidence of emboli, but was significant for peripheral pruning. Cardiac catheterization revealed marked pulmonary hypertension with right atrial pressure =15, right ventricular pressure =90/15, pulmonary artery pressure =90/34 and pulmonary capillary wedge pressure =8. Echocardiogram showed normal left ventricular function with good ejection fraction and dilated right atrium and right ventricle consistent with pulmonary hypertension. Infectious disease work-up was negative. The patient failed to respond to antibiotics, steroids, diuretics, broncho-dilators, or anti-coagulants. She died nine days after admission. An autopsy, limited to biopsy of the lungs, was performed.

CASE #3: DISCUSSANTS:

Ira S. Schwartz, M.D. Elmhurst Hospital Center
Samuel Wahl, M.D. Lenox Hill Hospital

A 66 year old white female without prior medical history was found to have a non-palpable density in the posterior aspect of the right breast on routine mammogram. Excisional biopsy of the lesion following stereotactic localization was performed. Grossly, the lesion consisted of an irregular pink-white fibrotic area which measured 3 x 2 x 2 cm.

CASE #4: DISCUSSANTS:

Lillian Deligdisch, M.D. Mt. Sinai Hospital
Elana Opher, M.D. Lenox Hill Hospital

A 54 year old white female, G3 P3 presented with a 1 week history of lower abdominal pain. Sonogram was inconclusive. CT scan revealed a left adnexal mass for which patient underwent abdominal hysterectomy, bilateral salpingo-oophorectomy, omentectomy and appendectomy. The left ovary was replaced by a smooth surfaced 17 cm., 1.9 kg. mass which on section appeared multiloculated, filled with yellow gelatinous fluid. No solid nodule was noted except for an eccentric area of tan-white fibrotic appearing tissue. The uterus, contralateral adnexa, omentum and appendix were grossly unremarkable.

CASE #5: DISCUSSANTS:

Andrew G. Huvos, M.D. Sloan Kettering Medical Center
John A. Terzakis, M.D. Lenox Hill Hospital

The patient first appeared at Lenox Hill Hospital in 1993 at age 37 for excision of a lesion of the lip which was diagnosed as a malignant neoplasm of salivary gland type. Two years later he returned to LHH for a lesion of the left scalp which slide is distributed. A month later he underwent "wide excision" of the scalp lesion. A more detailed history revealed that the patient underwent nephrectomy for Wilm's tumor as a newborn. Mitral valve prolapse was also reported at the time. At age 32, skin lesions began to appear and included a benign nevus as well as two malignant soft tissue tumors of the buttocks (Cabrini Medical Center). At age 37, two skin adnexal neoplasms respectively of right lower back and right upper abdomen were removed (NYU Medical Center) just two months prior to his appearance at LHH. These latter appeared quite similar to the lesion of the left scalp removed at LHH.

Minutes of The Pathologists' Club
Lenox Hill Hospital February 1, 1996

First, my apologies for the error in the Minutes from the last meeting which mistakenly indicated Lenox Hill rather than St. Vincent's as the host institution.

There was snow on the ground and the temperature a bit nippy, but the atmosphere inside Einhorn Auditorium was warm and collegial for this meeting of the Pathologist's Club. Dr. Ioachim, our gracious host, with the assistance of Ms. Tova Bamberger, arranged for both a delicious meal and a lively scientific session. After introductory and welcoming remarks by Dr. Ioachim and the Club's President, Dr. Valsalmis, the following applications for membership were approved; Drs. Antonio Cajigas, Mohamed Aziz, and Christina Vallejo.

CASE #1: A forty eight year old patient presented with a 20 x 12 x 2.5 cm. pelvic mass. She had undergone a TAH/BSO 3.5 years earlier for benign disease. Dr. Wright described the histology -that of a glandular and stromal neoplasm- and concluded that both elements were malignant. He classified the glandular component as endometrioid, and showed areas interpreted as merging between the glandular and stromal elements. His diagnosis, then, was carcinosarcoma (MMMT) in which one sees an intimate admixture of carcinomatous and sarcomatous elements. In these tumors, the epithelial component is most frequently endometrioid and the stromal component is usually undifferentiated. Heterologous stromal differentiation may be seen in 50% of cases but has no prognostic significance. Immunologic studies of such tumors have shown simultaneous expression of cytokeratin, EMA, and vimentin in both the epithelial and stromal components, lending credence to the hypothesis that these may represent metaplastic carcinomas. The most common site of origin for these tumors is the uterus, followed by ovary, and case reports of tumors arising in the cervix, fallopian tube and extragenital sites. Of the extragenital tumors that have been reported, these occurred in older patients and in locations including the parametria and bowel serosa. All were associated with a poor outcome. Among the theories for the pathogenesis of carcinosarcomas are that they represent collision tumors, metaplastic carcinomas, or that both components arise from a common stem cell precursor. The carcinomatous elements of these tumors seem to drive their behavior in that those having a more poorly differentiated carcinomatous component do worse and metastases are frequently restricted to the carcinomatous component alone. Dr. Shevchuk provided additional history on this patient. In 4/87 a right oophorectomy was performed at the age of 40 for "endometriosis". At the time of hysterectomy in 1/92, a 4.5 cm. adnexal mass showed, in addition to endometriosis, glandular hyperplasia with atypia and decidualization of the stroma. Of note was the fact that the endometrium in the utuerus was a normal day 16 endometrium. The material currently submitted for review was also interpreted as showing complex atypical hyperplasia, insufficient to diagnose carcinoma, and a neoplastic stromal proliferation. The diagnosis rendered was adenosarcoma. Subsequently the patient was treated with high doses of progesterone and in 12/95 a recurrent pelvic mass was removed. Microscopic examination of this mass showed the glands to be inactive lined by flattened epithelial cells, the stroma focally decidualized, but with some areas of stromal overgrowth. Dr. Shevchuks' diagnosis then was extra uterine adenosarcoma. In these mixed glandular and stromal neoplasms the epithelium is benign but may be complex and atypical. Recurrences are frequent within two years, and the tumors metastasize as sarcoma.

DIAGNOSIS: EXTRA UTERINE ADENOSARCOMA

REFERENCES:

Clement PB, Scully RE: Mullerian Adenosarcoma of the Uterus. Human Pathology

21:363-81,1990.
Clement PB, Scully RE: Extrauterine mesodermal (Mullerian) adenocarcinoma. AmJ. Clin Pathol 69: 276-283, 1978.
Kao, GF, Norris HJ: Benign and low grade variants of mixed mesodermal tumor (adenosarcoma) of
the ovary and adnexal region. Cancer 42:1314-1324.

CASE #2: This sixty four year old female, a former heavy smoker with a history of COPD was admitted for rapidly progressive respiratory failure beginning 8 months prior to admission. Chest x-ray showed pulmonary vascular congestion, and pulmonary angiography was significant for peripheral pruning. Cardiac catheterization revealed marked pulmonary hypertension and a normal pulmonary capillary wedge pressure. Infectious disease workup was negative. The patient failed to respond to supportive care and died nine days after admission. An autopsy limited to biopsy of the lungs was performed. Dr. Godwin reviewed the microscopic findings which included marked congestion, subpleural fibrosis, and marked vascular thickening involving arteries to the level of the arterioles and capillaries as well as veins. There was no evidence of embolic lesions. Among the causes of severe pulmonary hypertension are increased pulmonary blood flow (ASD,VSD), prolonged left atrial hypertension (mitral stenosis), organizing vascular obstruction (pulmonary embolism, pulmonary veno-occlusive disease), pulmonary vaso-constriction (COPD), and primary pulmonary hypertension (unexplained). In this instance the clinical and pathologic findings are compatible with pulmonary veto-occlusive disease. Of note was the intense capillary congestion which some have diagnosed as pulmonary capillary hemangiomatosis, but it is not clear whether this is a separate entity or merely a form of veno-occlusive disease. Dr. Jormark agreed with Dr. Godwin's assessment of the case. The clinical findings of peripheral pruning, vascular congestion, pulmonary edema, and a normal wedge pressure are all compatible with veno-occlusive disease. This disease effects both small and large vessels. Elastin stains may be helpful in defining the degree of luminal obstruction. Both Drs. Goodwin and Jormark commented on the helpfulness of anatomic location in distinguishing arteries (located by airways) from veins (located along the septa). Dr. Jormark also noted that the entity capillary hemangiomatosis may simply be part of the disease spectrum in pulmonary veno-occlusive disease. It is still controversial whether or not the arterial changes are secondary to the venous changes or are primary. The etiology of pulmonary veno-occlusive disease is unknown. It has been described in a variety of clinical settings and may represent a final common pathway to endothelial injury. To date there is no effective treatment, and transplantation may be the only therapeutic choice.

DIAGNOSIS: PULMONARY VENO-OCCLUSIVE DISEASE

REFERENCES:

Pietra GG: Histopathology of primary pulmonary hypertension. Chest 105 (2) supplement:25-65, 1994.
Burke AP, Farb A, Virmani R: The pathology of primary pulmonary hypertension. Modern Pathology 4 (2) 269-282, 1991.
NEJM Weekly CPC, 314 (22):1435-45, May 1986.

CASE #3: A sixty six year old white female was found to have a non-palpable density of the breast on routine mammogram, and an excisional biopsy was performed. Grossly the lesion consisted of an irregular pink-white fibrotic area measuring 3 x 2 x 2 cm. Dr. Schwartz described the microscopic findings - fibrocystic changes including mild to moderate epitheliaal hyperplasia anddense stromal areas with slit-like spaces lined by flattened cells. Arguably these could be interpreted as vascular spaces but no red cells were found in the lumens and stains for CD31 and Factor VIII were

negative. In addition, the histologic appearance of a low grade angiosarcoma, the differential diagnosis in this case, is that of irregular gaping lumina lined by plump cells which may form intraluminal papillae. Given the absence of these features, Dr. Schwartz' diagnosis was pseudoangiomatous stromal hyperplasia of the breast. This is a benign condition first described in 1986 which may produce a lump and may be confused with angiosarcoma. These changes have also been described in hamartomas of the breast. Dr. Wahl agreed with Dr. Schwartz' assessment of the case. In addition to CD31 and Factor VIII, an immunostain for PECAM-1 (platelet endothelial cell adhesion molecule) was performed and was also negative. Stains for vimentin, actin and CD34 were positive. CD34 may be positive in endothelial cells, but is also positive in myeloid progenitor cells and in a variety of mesenchymal cells. Electron microscopy in this case showed that the lining cells had a well developed rough endoplasmic reticulum but no pinocytotic vesicles or Weibel-Palade bodies.

DIAGNOSIS: PSEUDOANGIOMATOUS STROMAL HYPERPLASIA OF THE BREAST

REFERENCES:

Vuitch MF, Rosen PP, Erlandson RA: Pseudoangiomatous hyperplasia of mammary stroma. Hum Pathol 17:185-191, 1986.

Ibrahim RE, Sciotto GS, Weidner N: Pseudoangiomatous hyperplasia of mammary stroma: Some observations regarding its clinicopathologic specturm. Cancer 63:1154-1160, 1989.

Anderson C, Ricci A Jr., Pedersen CA, et al: Immunocytochemical analysis of estrogen and progesterone receptors in benign stromal lesions of the breast: Evidence for hormonal etiology in pseudoangiomatous hyperplasia of mammary stroma. Am J Surg Pathol 15:145-149, 1991.

CASE #4: A fifty four year old white female underwent TAH/BSO, omentectomy and appendectomy for a 17 cm. left adnexal mass. On section this mass was multiloculated, filled with yellow gelatinous fluid and with no solid areas except for an eccentric tan white fibrous area. The uterus, contralateral adnexa, omentum and appendix were unremarkable. Dr. Deligdisch described two components in the histology. One was a borderline mucinous tumor of intestinal type in which goblet cells were apparent. The other component was a solid mass of heterogeneous appearing cells associated with necrosis. This second component included small round cells and large polyognal cells including multinucleate and bizarre forms which blended with spindle cells. Mitoses including atypical forms were present. Also seen was spillage of mucinous material associated with an osteoclast giant cell reaction and inflammatory changes: pseudomyxoma ovarii. PAS stains were negative in the solid areas except in muciphages adjacent to the mucinous component. Cytokeratin was positive not only in the mucinous areas but also in the spindled and polygonal cells, as was EMA and CEA. Dr. Deligdischs' diagnosis was ovarian mucinous tumor with mural nodule. This is an entity that was first described by Pratt and Scully in 1979. The solid nodule is composed of a mixture of inflammatory cells, multinucleate giant cells and bizarre spindle cells. Cytokeratin and EMA may be positive in these areas and the nodules are seen in association with borderline and malignant mucinous tumors of the ovary. The differential diagosis for such a lesion includes anaplastic carcinoma, sarcoma, MMMT, and the sarcoma-like nodule. The nature of this lesion - reactive or neoplastic, benign or malignant, epithelial or stromal- is as yet unclear. This may represent a dedifferentiation of the mucinous tumor. The prognosis is related to the malignant potential of the mural nodule. If the nodule is small, the prognosis is good. The prognosis declines if metastases are present. Dr. Opher agreed with Dr. Deligdisch's overall assessment of the case. She noted that the gross appearance of this tumor was not unusual except for focal thickening of the capsule. Sections of this thickened area however revealed spillage of mucin

into the stroma, reactive inflammatory changes, and a stalk in which solid sheets of epithelioid cells could be identified. Additional microscopic evaluation showed necrosis of the tumor and infiltrating margins. While Pratt and Scully initially interpreted this as a reactive process to the mucin in the tumor, additional cases with a malignant course were subsequently reported and the suggestion made that these may represent anaplastic carcinomas. Dr. Opher noted that these may in fact all be malignant but do well when they are small and encapsulated. In this case, the patient subsequently developed hip pain and in 11/95 was diagnosed as having metastatic poorly differentiated carcinoma in bone.

DIAGNOSIS: ANAPLASTIC CARCINOMA IN A MURAL NODULE ARISING IN A MUCINOUS OVARIAN TUMOR

REFERENCES:

Prat J, Scully RE: Ovarian mucinous tumors with sarcoma-like mural nodules. Cancer 44:1332-1344, 1979.
Prat J, Young RH, Scully RE: Ovarian mucinous tumors with foci of anaplastic carcinoma Cancer 50: 300-304, 1982.
Nichols GE, Mills SE et al. Spindle cell mural nodules in cystic ovarian mucinous tumors. clinocopathologic and immunohistochemical study. AM J Surg Pathol 15:1055-62, 1991.

CASE #5: This thirty nine year old male, S/P nephrectomy for Wilm's tumor as a new born, has a history of multiple soft tissue and adnexal neoplasms. At the age of 32, skin lesions began to appear, and two skin adnexal neoplasms were resected two months prior to his presentation at Lenox Hill Hospital. At 37, a lesion of the lip was diagnosed as a malignant neoplasm of salivary gland type. Two years later he returned to Lenox Hill Hospital for a lesion of the left scalp which was the slide distributed to members of the Club. Dr. Huvos showed the histology: an infiltrating glandular pattern of variably sized and shaped tubules lined by a double layer of cells. Mitoses were present. Dr. Huvos' diagnosis was eccrine duct adenocarcinoma, tubular type. PAS and stains for laminin both highlighted basment membrane material. In his discussion, Dr. Huvos considered whether this represented a primary vs. secondary lesion. The blood supply and lymphatic system of the scalp is widely anastamotic and the scalp is a common site for metastases. The lesion of the lip, which was classified as a salivary gland type tumor, could have been a basal cell adenoma or adenocarcinoma. Dermal cylindromas and basal cell adenomas bear a strong histologic resemblance to each other, and 20% of basal cell adenomas occur in the upper lip. There is an association between salivary basal cell adenomas and dermal cylindromas, trichoepitheliomas, or eccrine spiradenomas, known collectively as "dermal anlage tumors". With this patient's history of multiple neoplasms, it seem clear that he must have some kind of syndrome or inherited tumor diathesis. In this instance a P53 mutation was identified, and Dr. Huvos suspects that the patient has Li-Fraumeni syndrome. This is a syndrome linked to germ line mutations of the P53 tumor suppressor gene, and these patients are candidates for developing multiple neoplasms at a young age. In his discussion, Dr. Terzakis showed additional histology of the scalp lesion as well as reviewing the prior lip lesion. Both basal cell features and a cylindromatous pattern were present and there was perineural involvement. These cases had been consulted to a number of institutions, and opinions varied, but Dr. Terzakis favored the diagnosis of malignant cylindroma-adenoid cystic carcinoma. He agreed with Dr. Huvos that the patient suffers from an inherited tumor diathesis.

DIAGNOSIS: ECCRINE DUCT ADENOCARCINOMA, SUSPECT LI-FRAUMENI SYNDROME

VS. MALIGNANT CYLINDROMA-ADENOCYSTIC CARCINOMA

REFERENCES:

Batsakis JG, Luna AM: Basaloid salivary carcinoma. Ann Otol Rhinol Laryngol 100:785-787, 1991.

Bernacki EG, Batsakis JG, Johns ME: Basal cell adenoma. Arch Otolaryngol 99:84-87, 1974.

Ellis GL, Wiscovitch JG: Basal cell adenocaricnomas of the major salivary glands. Oral Srug Oral Med Oral Pathol 69: 461-9, 1990.

Respectfully submitted,

Joan G. Jones, M.D.

FUTURE MEETINGS:

May 2 Einstein/Montefiore
June 6 NYU