PATHOLOGISTS' CLUB
OF NEW YORK

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May 13, 1999

Mount Sinai Medical Center
1 Gustave L. Levy Place
(corner of 101st St & 5th Ave)
New York, New York 10029

Host:
Alan L. Schiller, MD
Chairman & Professor
Department of Pathology

Reception & Dinner
Annenberg West Lobby
6:00 PM to 7:00 PM

Scientific Session
Annenberg 13th Floor
Room 1301 (classroom)
7:00 PM to 9:00 PM

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To reach Mt. Sinai:

by Bus - M1,2,3, or 4 stop at 99th St & 5th Ave (northbound)
98th St & Madison (southbound)

by Subway - Lexington Ave (No.6) to 96th St & Lexington

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Next Meeting
June 3, 1999
St. Vincent's Hospital & Medical Center

PATHOLGISTS' CLUB OF NEW YORK
MT. SINAI MEDICAL CENTER
MAY 13, 1999
CASE HISTORIES

CASE 1 (99-3678)

A 60 year old woman presented with a palpable mass in the upper outer quadrant of the left breast. The mass was described as somewhat superficial clinically, and, although it was present for an unknown duration,, the patient claimed to have had a normal mammogram 2 years ago. Needle biopsy of the mass was followed by lumpectomy and axillary dissection.

Speakers: Steven Goldber, MD, Staten Island University Hospital
Ira Bleiweiss, MD

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CASE 2 (S98-39761 - 2 SLIDES)

A 38 year old G7/P5015, blood type A+, white female delivered a stillborn fetus at 36 weeks gestation. Past medical history was unremarkable, although examination of a spontaneous abortion at 10 weeks gestation (when she was 36 years old) had revealed an abnormal karyotype of 48, XXX+20.

During this pregnancy the mother had received prenatal care since 9 weeks gestation. Early assess-ment, including a sonogram at 9 weeks gestation, was within normal limits. Serological evaluation revealed toxoplasmosis IgG(+) and IgM(-), rubella IgG(+), RPR(-). She was mildly anemic (hemoglobin 11.6 g/dl, hematocrit 33.4%), with platelets 167,000/ul. Screening for diabetes mellitus was negative. Maternal serous alpha-fetoprotein assay at 16-3/7 weeks gestation was low, which was interpreted as representing an increased risk (greater than 1 in 4) for Down's syndrome. The mother refused amniocentesis since abortion was not considered to be an option. Sonograms performed at 17-5/7 and 18-6/7 weeks gestation demonstrated a fetus of appropriate size for gestational age. Abnormal findings included an "echogenic intracardiac focus" that was considered suggestive of Down's syndrome, and hyperechoic lungs and bowel. The amniotic fluid volume was normal.

During the mother's routine visit at 34 weeks gestation, slightly increased amniotic fluid volume was appreciated, which was confirmed by ultrasound. This study also demonstrated a small pericardial effusion and an abnormally elevated ratio of systolic-to-diastolic blood flow in an umbilical artery, considered to be indicative of increased placental resistance and a poor prognosis for continuation of the pregnancy. Beginning at 35 weeks gestation, the mother complained of musculoskeletal back pain and fevers. The following week she reported absence of fetal movement. Her obstetrician was unable to appreciate a fetal heart by auscultation or sonography. Induction two days after loss of fetal movement, at 36-5/7 weeks gestation, led to delivery of a macerated female fetus. Autopsy permission was refused.

The placenta was oval, weighed 520 grams, and measured 18 x 15 x 2 cm. The cord arose eccentrically, 3 cm from the placental margin; it measured 20 cm in length, 2 cm in diameter, was dusky and edematous, and contained three vessels. The membranes arose from the margin and were ruptured 3 cm from the placental margin. Both the membranes and fetal surface were tan-white and cloudy. The chorionic blood vessels were engorged. The maternal surface was complete. Serial sections through the disc showed pale, spongy parenchyma with no focal lesions.

Speakers: Cynthia Kaplan, MD, University of New York at Stony Brook
Margret S. Magid, MD

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CASE 3 (WQ 98-4696)

A 26 year old man palpated a mass in his left testicle. He was seen by a urologist and scheduled for a possible left orchiectomy. A biopsy of the mass was sent for frozen section. This is the paraffin section of that tissue.

Speakers: Maria R. Dische, MD - Columbia Presbyterian Medical Center
Pamela Unger, MD

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CASE 4 (S96-40504)

A 13 year old Hispanic female presented to our pediatric dermatology clinic with a slowly enlarging mass of the right thigh. The lesion was present at birth when her mother noted a palpable 3 cm subcutaneous nodule. By the age of 18 months, flesh-colored papules began to appear on the skin above the nodule. The lesion was untreated until the age of ten when the lesion enlarged to 5 cm with darkening of the surface. The lesion was biopsied and revealed lymphangioma circumscriptum and treated partially with argon and CO2 lasers over a year. The patient was lost to follow-up, however, she presented to our pediatric dermatology clinic with a complaint of enlargement of the original lesion. At this time, the lesion was a 9 cm hemorrhagic verrucous plaque with a smaller 2 cm plaque distal to the primary lesion. Multiple biopsies were performed followed by the wide excision of the tumor.

Speakers: Hideko Kamino, MD - Dept of Dermatology, New York University Medical Center
Toru Shoji, MD

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CASE 5

A 63 year old black female underwent bipolar total hip replacement for a fracture of the left femoral neck. This was the only history received. The specimen received was a resected femoral head. The pathology resident took one representative section from the fracture line. Based upon the section through the fracture line, the specimen was retrieved and additional sections were prepared (one of these is the section you are viewing).

Speaker: Michael J. Klein, MD

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PATHOLOGIST'S CLUB
MT. SINAI MEDICAL CENTER
MAY 13, 1999
MINUTES

Case #1 (99-3678)

MERKEL CELL CARCINOMA IN THE BREAST

Dr. Goldberg (Staten Island Hospital) illustrated the histology as composed of two components, an intraductal component as well as an infiltrating one. The infiltrating component is composed of small cells with angulated hyperchromatic nuclei. The intraductal component immunostains as follows: positive for AE1/AE3,CK7, BRST2; negative for CK20, NSE, synaptophysin, chromo-granin. The infiltrating component stains with dot-like positivity for cytokeratins (including CK20, but not CK7), and is also positive for NSE and synaptophysin. Chromogranin, BRST2, LCA, vimentin, S100, NF, and O15 are all negative. In other words, this is a Merkel cell carcinoma. Of interest, the CK20 dot positivity can distinguish from oat cell carcinoma, which is negative for both CK7 and CK20.

Dr. Bleiweiss (Mt. Sinai) told us that a mastectomy and axillary node dissection were done following a positive core biopsy. The primary tumor was 4 cm, and 20 of 27 nodes were positive. EM showed neurosecretory granules. This is a Merkel cell carcinoma in the breast. Is it of the breast? The weight of evidence (associated DCIS, breast mass, positive nodes, no known skin involvement) favors a breast primary, with a poorer prognosis expected, and Dr. Bleiweiss proposed classifying Merkel cell carcinoma of the breast as a type of metaplastic carcinoma. Why not?

<u>References:</u>

-Chan et al. Cytokeratin 20 immunoreactivity distinguishes Merkel cell CAs and salivary gland small cell Cas from small cells Cas of various sites. AJSP 1997, 21(2):226-234.
-Schnabel T, Glag M. Breast metastases of Merkel cell carcinoma. Eur J Cancer 1996, 32A(9):1617-1618.
-Scopsi et al. Argyrophilia and granin expression in female breast carcinoma. AJSP 1992, 16(6), 561-576.
-Papotti et al. Neuroendocrine differentiation in carcinomas of the breast: a study of 51 cases. Sem Diag Pathol 1989, 6(2), 174-178.
-Maluf et al. Spindle-cell argyrophilic mucin-producing carcinoma of the breast. AJSP 1991, 15(7):677-686.
-Tsang W, Chan J. Endocrine ductal carcinoma in situ of the breast. AJSP 1996, 20(8), 921-43 .
-Wade et al. Small cell neuroendocrine (oat cell) carcinoma of the breast. Cancer 1983, 52(1):121-125.
-Ruffolo EF, Koerner FC, Maluf HM. Metaplastic carcinoma of the breast with melanocytic differentiation. Modern Pathol. 1997, 10-(6):592-596.

Case #2 (S98-39761)

PLACENTA WITH NON-IMMUNE HYDROPS AT 36 WEEKS, FETAL DEATH OF AT LEAST 48 HOURS, AND WITH LEUKEMOID REACTION, ASSOCIATED WITH DOWN'S SYNDROME

Dr. Kaplan (SUNY Stony Brook) began by pointing out the value of placental examination in perinatal deaths, particularly in instances like the current one, where the stillborn was macerated, and an autopsy was not granted. The time of fetal demise was placed at 2-10 days based on the appearance of karyorrhexis (present 6 hours after demise, stromal calcification (present 24 hours after demise), and stem vessel abnormalities (present 48 hours after demise). Extreme villous fibrosis such as would be seen after demise of 2 weeks was not present.

The villi were abnormally large (equivalent to a 16-week gestation) and the inner cytotrophoblast layer was inappropriately prominent for 36 weeks gestational age, consistent with non-immune hydrops. The blood vessels contained strikingly abnormal cells resembling immature myeloid cells, confirmed by myeloperoxidase positivity. Leukemoid reaction is favored over congenital leukemia, although that distinction can be very difficult. The history points to a high likelihood of Down's syndrome. Dr. Magid (Mt. Sinai) confirmed the presence of Down's syndrome by FISH studies which showed trisomy 21, and went on to discuss the FISH technique.

Case #3 (WQ 98-4696)

SPLENO-GONADAL FUSION

Dr. Dische (Columbia-Presbyterian) described the findings as spleen in the testis, with characteristic white and red pulp. Immunostudies were not contributory since the tissue had been frozen. She discussed the embryology by elegantly demonstrating the proximity of the fetal spleen to the ridge from which the urogenital organs develop.

Dr. Unger (Mt. Sinai), who saw this case at the time of frozen section, saved the patient from an unnecessary orchiectomy. Only 100 cases of spleno-gonadal fusion have been reported, and all but one are left-sided. Children present more often than adults, and the finding is usually incidental. The continuous type (60%), in which there is a thread of splenic tissue from the spleen to the testis, is slightly more common than the discontinuous type (40%), in which there is no connection between the spleen and the testis. Associated congenital abnormalities are most commonly limb defects and micrognathia.

<u>References:</u>

-Gouw A, Elema JD, et al. The spectrum of splenogonadal fusion. Case report and review of 84 cases. Eur J Pediatr 144:316-323, 1985.
-Putschar W, Manion W. Splenic-gonadal fusion. Am J Pathol 32:15-33, 1956.
-Pauli M, Greenlaw A. Limb deficiency and splenogonadal fusion. AM J Med Genet 13;81-90, 1982.

Case #4 (S96-40504)

DABSKA TUMOR (MALIGNANT ENDOVASCULAR PAPILLARY ANGIOENDOTHELIOMA)

Dr. Kamino (NYU) illustrated the histology. A skin biopsy showed papillary epidermal hyperplasia with dilated lymphatics and high endothelial cells. The soft tissue showed vascular channels with high endothelial cells, papillations, glomeruloid structures, solid cellular aggregates with cells at the periphery, and associated lymphocytes and plasma cells. Based on this histology, the diagnosis is Dabska tumor. The endothelial cells are positive for ulex, factor 8, and CD31. The central hyalinized material in the papillations is positive for collagen type 4, consistent with basement membrane material. The lymphocytes associated with the high endothelial cells are T lymphocytes, while those further away are B lymphocytes. The differential diagnosis, which includes Kaposiform hemangioendothelioma, glomeruloid hemangioma of POEMS syndrome, papillary endothelial hyperplasia (Masson tumor), and other entities was discussed and illustrated.

Dr. Shoji (Mt. Sinai)concurred, and showed the gross appearance of the tumor under discussion. Only 18 cases of this entity are reported. The age ranges from 4 months to 83 years, with a mean age of 21 years. Male and female occurrence is about equal, and size ranges from 1 to 14 cm. The presentation is of diffuse skin swelling (1/3), or of intradermal nodules (2/3). Location varies. Only 2 cases have metastasized.

Case #5

FEMORAL HEAD WITH AMYLOID (BETA-2-MICROGLOBULIN), CHANGES OF HYPERTHYROIDISM, AND ALUMINUM-ASSOCIATED OSTEOMALACIA

Dr. Klein (Mt. Sinai) used Kurasowa's brilliant film Rashomon, in which the same story is told from multiple points of view, as an illustration of the current state of medical practice, in which the various specialties involved in patient care, each narrow-mindedly focused, have their own "story" of the patient's condition. Pathology received a femoral head without any history, and initially assumed that this was the usual type of osteoarthritis with which we are all so familiar. The nephrologist knew that this was a hemodialysis patient with longterm renal failure, and therefore assumed this was an instance of beta-2-microglobulin amyloid. The radiologist saw a pathologic intracapsular fracture, and a chest X ray with multiple lucent lesions and thought of tumor and/or brown tumor. The orthopedist's pre-operative diagnosis was renal osteodystrophy with secondary hyperparathyroidism and osteomalacia, and actually wanted to know how much of the osteomalacia was secondary to aluminum deposition, (although he never communicated that to pathology!). Pathologic examination of the specimen showed the presence of amyloid, and changes of hyperpara-thyroidism with a porous cortex and thick cancellous bone. The presence of aluminum (50ug/g) was confirmed by mass spectrometric studies. Knowledge of all the clinical parameters is essential.

References:

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Gejyo F,Marumaya H, Arakawa M. Amyloidosis assciated with long-term hemodialysis. Nippon Jinzo Gakkai Shi Jan 37(1):1-6, 1995.

Hardy P, Benoit J, Donneau B et al. Pathologic fractures of the femoral neck in hemodialyzed patients. Apropos of 26 cases. Rev. Chir. Orthop. Reparatrice Appar Mot 80(8);702-710, 1994.

Heller DS, Klein MJ, Gordon RE, Good P, Perl D. Intraosseious beta-2-microglobulin amyloidosis. J Bone Joint Surg 71A(7)1083-1089, 1989. THIS IS THE PRESENTED CASE

Koda Y, Nishi Sm, et al. Switch from conventional to high-flux membrane reduces the risk of carpal tunnel syndrome and mortality of hemodialysis patients. Kidney Int. Oct; 52(4):1096-1101, 1997.

Mourad G. Argiles A. Renal transplantation relieves the symptoms but does not reverse beta-2-microglobulin amyloidosis. J Am Soc Nephrol 7(5):798-804, 1996.

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