953

PATHOLOGISTS' CLUB
OF NEW YORK

MEETING

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DATE:	**Thursday, October 5, 1995**
PLACE:	**North Shore University Hospital** **300 Community Drive** **Manhasset, New York 11030**
HOST:	**John D. Broome, M.D.**
INFORMATION:	**Lynn Bartholomew** **(516) 562-1277**
RECEPTION:	**5:30 P.M.**
DINNER:	**6:00 - 7:00 P.M.**
SCIENTIFIC SESSION:	**7:00 -9:00 P.M.**

DIRECTIONS:

Take Long Island Expressway to Exit 33. Follow Community Drive to Entrance #3 to the Hospital. Follow this to the parking garage.

Cross to the main entrance (Monti Pavilion), inside which signs will direct you to the meeting.

PATHOLOGISTS' CLUB MEETING, NORTH SHORE UNIVERSITY HOSPITAL
10/5/95 CASE HISTORIES

CASE #1 A93-18 Invited discussant: Dr. Sumi Mitsudo, Montefiore Hospital
Host discussant: Dr. Ellen Kahn

A premature male, 31 weeks gestation, with a birth weight of 975 grams, was noted to be limp, cyanotic and edematous at time of birth. He became hypotensive, developed progressive respiratory distress and died on the third day of life. Pertinent laboratory studies revealed anemia, thrombcytopenia, low albumin and increased alkaline phosphatase. The remaining hepatic enzymes were within normal limits.

CASE #2: 95-17609 Invited discussant: Dr. Marion Waxman, Our Lady of Mercy Med Ctr
Host discussant: Dr. Albert Stanek

The patient was a 43 year old woman. Approximately 15 years earlier, she had been diagnosed as having I.T.P. and a splenectomy was performed. She had no subsequent evidence of I.T.P. She presented with a pelvic mass which was found to originate in the left ovary. No other lesion was detected in the pre-operative work-up.

At surgery the left ovarian mass was removed. The mass weighed 240 grams and measured 9.5 x 7.8 x 6 cm. Multiple smooth nodules were noted on the surface. Cut sections showed a mass that was predominantly solid and composed of relatively uniform tan-yellow tissue. Occasional small cysts and areas of hemorrhage were also detected.

CASE #3 93-28895 Invited discussant: Dr. C. Guerrieri, St. Vincent's Hospital
Host discussant: Dr. Thom Smilari

A 53 year old post menopausal white female presented with hirsutism for four years. Abdominal CT scan and sonogram revealed a 9.0 cm. left adnexal mass. Physical examination was significant for dark coarse hair growth over most of the body especially on the face, breast and abdomen. The patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy.

CASE #4 95-17609 Invited discussant: Dr. Lynn Silverstein, Laboratory of Dermatopathology
(Kodachrome) Port Washington
Host discussant: Dr. Barbara McHeffey-Atkinson

The patient was an 83 year old white male with urologic malignancy, treated with local excision and 16 months of immunotherapy. He developed several 2-3 mm. papules on the glans penis.

CASE #5 S95-718 Invited discussant: Dr. Elsa Balderrama, Long Island Jewish Med Ctr
(2 slides) Host discussant: Dr. Gary Stone

The patient was a 36 year old, G4/P2/012. She had an ectopic pregnancy eight months previously, and now presented with an incomplete abortion at fourteen to fifteen weeks gestation. The patient suffererd severe hemorrhage during D&C, which necessitated an emergent hysterectomy. The submitted slides are sections of a nodular appearing region of the uterus and overlying endometrium.

Minutes of Pathologists' Club
North Shore University Hospital
October 5, 1995

95

Dr. John Broome was our gracious host for the first Pathologists' Club meeting in 1995-1996, the 35th anniversary of the Club's existence. The reception and dinner were held in a beautiful atrium with skylights, punctuated by a burst of twinkling lights set off by a fire drill! At the scientific session, Dr. Valsamis welcomed the many Club members who had braved the day's rain. Approved for membership into the Club was Dr. Diethelm Boehme. Apologies were extended to Dr. Valderrama for the misspelling of her name in the case histories. The case discussions were both thorough and stimulating.

CASE #1:

A premature male (31 weeks gestation, birth weight 975 gm.) died on the 3rd day of life. Pertinent laboratory data included anemia, thrombocytopenia, a low albumin, and increased alkaline phosphatase. Other LFTs were within normal limits. Dr. Mitsudo described the microscopic findings in the liver: collapse and destruction of the lobules, pseudoacinar proliferation, giant cell transformation of hepatocytes, and coarse brown pigment in giant cells and hepatocytes with sparing of the Kupffer cells. Trichrome stains highlighted the fibrosis, and iron stains were strongly positive in the pigmented cells. There was no significant inflammation, steatosis, or viral inclusions.

In her discussion of the differential diagnosis of advanced subacute to chronic liver disease, Dr. Mitsudo included infections, metabolic disorders, hereditary fructose intolorance, tyrosinemia, and Zellweger cerebrohepatorenal syndrome. Additional diseases which may produce neonatal liver disease are extrahepatic biliary atresia, toxins, blood group incompatibilities, ischemia, and idiopathic (neo-natal) hemochromatosis. In biliary atresia, however, bile duct proliferation is present, and in the hemoglobinopathies, iron would be present in Kupffer cells. Therefore Dr. Mitsudo's diagnosis was neonatal hemochromatosis. During pregnancy this disease may be associated with oligo or polyhydramnios, and placental edema. Intrauterine growth retardation is present, and there is a high incidence of stillbirth or premature delivery. Neonatal hemochromatosis is a clinicopathologic syndrome in which one finds abundant iron within hepatocytes. Other organ systems frequently involved include the pancreas, heart, thyroid, and less often the kidney, endocrine, and minor salivary glands. Most likely, multiple ideologies are responsible for this syndrome. One may be an abnormality in bile acid metabolism.

Dr. Kahn agreed with Dr. Mitsudo's diagnosis. In this case the pancreas, thyroid and adrenals were also involved. Dr. Kahn then shared her experience with other cases of neonatal hemochromatosis, a clinicopathologic entity that may be either sporadic or familial. Serum ferritin is characteristically elevated, and the disease is distinguished from the cerebrohepatorenal syndrome by the involvement of extra hepatic sites. LFTs may be normal. Despite the dismal prognosis, attempts at prenatal or perinatal diagnosis (ie. by labial mucosal biopsy) may become increasingly relevant since liver transplantation may be of benefit. Like

Dr. Mitsudo, Dr. Kahn emphasized that this is not a specific or distinct entity. In some cases a history of maternal infection is obtained. There are no associated genetic abnormalities.

DIAGNOSIS: IDIOPATHIC NEONATAL IRON STORAGE DISEASE

REFERENCES: Schneider BL, Setchell KD, Whitington PF et al. Delta 4-3-oxosteroid 5 beta reductase deficiency causing neonatal liver failure and hemochromatosis. J Pediatr 124:234-238, 1994.

Kershisnik MM, Knisely AS, Sun CC et al. CMV infection, fetal liver disease, and neonatal hemochromatosis. Hum Pathol 23: 1075-1080, 1992.

Wifzleben CL & Uri A. Perinatal hemochromatosis: Entity or End Result? Hum Pathol 20:335-340, 1989.

Goldfischer S, Grotsky HW, Chang CA et al. Idiopathic neonatal iron storage involving the liver, pancreas, heart and endocrine and exocrine glands. Hepatology 1:58-64, 1981

CASE #2:

An ovarian mass weighing 240 gm. and measuring 9.5 cm. in greatest dimension was removed from a 43 year old woman with a remote history of ITP and splenectomy. The cut surface was predominantly solid and yellow-tan with occasional cysts and areas of hemorrhage. Microscopic examination showed a papillary and solid pattern. Vacuolated cells resembling signet ring cells were present, but mucin stains were negative. Furthermore, although the papillations in some areas resembled Schiller-Duval bodies, stains for alphafeto protein were negative. Additional fields showed a "nevoid" pattern of growth in which the cells formed large nests and contained huge nucleoli. There was no detectable pigment in the cells, but stains for HMB-45 were positive. Given this result, Dr. Waxman's diagnosis was malignant melanoma. He attributed the signet ring pattern to the presence of vimentim. The differential diagnosis for malignant melanoma of the ovary is broad and includes small cell carcinoma, juvenile and adult granulosa cell tumor, hepatoid yolk sac tumor, steroid cell tumors, and dysgerminoma. Factors which favor an ovarian primary are a lack of history of melanoma and unilateral involvement. In this case there was no association with a mature cystic teratoma.

Dr. Stanek agreed with Dr. Waxman's assessment of the case. He also performed mucicarmine and cytokeratin stains, both of which were negative. There was no history of a prior tumor. Because in some areas the tumor cells had abundant cytoplasm and appeared nested or spindled, Dr. Stanek entertained the diagnosis of sex cord stromal tumor, and stains for vimentin were positive. On electron microscopy, however, stage II premelanosomes were identified, and subsequently stains for S100 and HMB-45 were both positive. Melanoma of the ovary may be metastatic or may arise in association with a cystic teratoma or monodermal teratoma. In this case there was no evidence of a preexisting lesion.

DIAGNOSIS: MALIGNANT MELANOMA OF OVARY

CASE #3:

A TAH/BSO was performed on a 53 year old post-menopausal woman with a history of hirsuitism for four years and a 9 cm. left adnexal mass. Dr. Guerrieri reviewed the histology: ribbons or cords of cells in a fibrous stroma. An acinar or glandular pattern was present as well, with PAS staining the luminal contents. Mucin stains were negative. Dr. Guerrieri's diffential diagnosis included Sertoli-Leydig cell tumor, sertoliform endometrioid carcinoma, and trabecular carcinoid. In side-by-side comparisons with the unknown case, Dr. Guerrieri noted that in Sertoli-Leydig cell tumors the cells have a haphazard arrangement, whereas in this case, the cells show a distinct perpendicular arrangement and low grade nuclei. The nuclei of the Sertoliform endometrioid carcinoma are more pleomorphic, and squamous differentiation, not present in this case, is an additional clue to this diagnosis. Carcinoid tumors have nuclei with a fine stippled chromatin, and frequently a retraction artifact can be seen between nests of tumor cells and the adjacent fibrous stroma. In this case, although the Grimelius stain was negative, immunostains for cytokeratin, chromogranin, and synaptophysin were positive. Dr. Guerrieri's diagnosis, then, was trabecular carcinoid of the ovary. Hirsuitism has been described in ovarian carcinoid tumors, due to the presence of luteinized stromal cells.

Dr. Smilari provided the additional clinical information of the patient's testosterone levels which were far above normal. His differential diagnosis of the tumor, which formed cribriform and solid nests as well as wavy ribbons, included poorly differentiated carcinoma, metastasis, Sertoli-Leydig cell tumor, granulosa cell tumor, and carcinoid tumor. In this case electron microscopy revealed uniform neurosecretory granules. Primary carcinoid tumors of the ovary usually occur in the postmenopausal age group and arise in association with mature cystic teratomas. They are unilateral and the prognosis is favorable. In this case, multiple sections disclosed a co-existent teratoma. The insular subtype is the most common form of ovarian carcinoid, and 1/3 of these are associated with the carcinoid syndrome. The trabecular form is rare, and shows no association with the syndrome. Strumal carcinoid, mucinous adenocarcinoids, and metastatic carcinoids, which are usually bilateral, also occur. A functional ovarian stroma is responsible for the steroid hormone production. Follow-up in this patient demonstrated a drop in testosterone levels, and the patient is alive and well 22 months after surgery.

DIAGNOSIS: TRABECULAR CARCINOID OF THE OVARY

CASE #4:

An eighty three year old white male with a history of urologic malignancy, treated by local excision and 16 months of immuno therapy, developed several 2 to 3 mm. papules on the glans penis. Dr. Silverstein showed the histology: an intact epidermis overlying a dermal granulomatous reaction with necrosis. Dr. Silverstein reviewed the histologies and clinical appearance of granulomatous diseases in the skin. There are five types of granulomatous reaction: sarcoidal, tuberculoid, necrobiotic, suppurative and foreign body. The sarcoidal granulomas seen, for example, in reactions to silica or zirconium, are "naked granulomas" and contain few associated lymphocytes. The tuberculoid granulomas of leprosy, late syphillis, and

Crohn's are not as well organized and contain more lymphocytes. In necrobiotic granulomas, there is an alteration of the collagen and no necrosis. Among the diseases which can produce this type of change are granuloma annulare, necrobiosis lipoidica, and rheumatoid arthritis. Examples of suppurative granulomatous disease are the atypical mycobacteria, deep fungal infections, and cat scratch disease. Foreign body granulomas are produced by exposure to starch, talc, and may be seen in tatoos. The findings in the current case would be best classified as a suppurative granuloma. While stains for organisms would be appropriate, Dr. Silverstein also inquired as to the possible history of instrumentation and the nature of the patient's immunotherpay.

Dr. McHeffey-Atkinson noted that the patient had a history of high-grade transitional cell carcinoma and had been treated with intravesical installation of BCG. BCG is a permanently avirulent strain of tuberculosis first isolated in 1925 by Calmette and Guerin. Since transitional cells can phagocytize BCG, intravesical BCG installation has become a treatment for both papillary transitional cell carcinomas of the bladder as well as carcinomas in-situ. The treatment provokes a granulomatous reaction in the tumor and delays recurrence. In high-grade carcinomas the response rate is less than 50% and may be complicated by cystitis, hematuria, and BCGitis. Other more infrequent complications include pneumonia, hepatitis, arthritis, and abscess formation. In this case the urologist said there was no history of trauma. Although stains for the organism may be negative, PCR may provide a more sensitive detection technique.

DIAGNOSIS: GRANULOMATOUS REACTION IN SKIN S/P BCG THERAPY FOR TRANSITIONAL CELL CARCINOMA

CASE #5:

A 36 year old female who presented with an incomplete abortion at 14-15 weeks gestation suffered severe hemorrhage during D&C and underwent emergent hysterectomy. Gross examination revealed a nodular region of the uterus and overlying endometrium. Histologically, Dr. Valderrama noted an ill-defined lesion in which a mixed population of mononuclear and multinucleate trophoblast was seen infiltrating deep into the myometrium and involving vascular channels. Stains for hPL were positive in the mononuclear cells, confirming the presence of intermediate trophoblast. The differential diagnosis for uterine lesions rich in intermediate trophoblast includes placental site trophoblastic tumor, a form of gestational trophoblastic disease, and an exxagerated placental site reaction. Placental site trophoblastic tumor is the rarest form of gestational trophoblastic disease. It may be preceded by a term pregnancy or abortion, and the pathogenesis is unknown. Usually these lesions are well demarcated but may involve the full thickness of the myometrium. On microsocpic examination, these tumors are composed predominantly of intermediate trophoblast. Although a high mitotic rate and necrosis may suggest a poorer prognosis, there are no completely reliable criteria. Only 10 to 15 % of these lesions behave in a malignant fashion. In the exaggerated placental site reaction, one sees an exuberant and infiltrative proliferation of intermediate trophoblast as well as a large number of syncytial cells. In contrast to the PSTT, there is no alteration of the normal architecture. Given the findings in this case, Dr. Valderrama's

diagnosis was exaggerated placental site reaction.

Dr. Stone agreed with this diagnosis. He noted that over 1/3 of the uterus was involved. In contrast to the confluence seen in PSTT, the trophoblast in this case infiltrated but did not destroy myometrium. The presence of some background inflammatory cells also supports the diagnosis of exaggerated placental site reaction. In the older literature, this reaction was referred to as syncytial endometritis. The course is benign.

DIAGNOSIS: EXAGGERATED PLACENTAL SITE REACTION

Respectfully submitted,

Joan G. Jones, M.D.
Secretary-Treasurer