MINNESOTA SOCIETY OF CLINICAL PATHOLOGISTS

ANNUAL TUMOR SEMINAR

November 10, 1973

Minnesota Club, St. Paul

Dr. Gerald Fine, Moderator
Case 1. A 10 year old girl experienced the sudden onset of severe headache and lapsed into deep coma during a period of several hours. Clinical signs suggested a brain stem lesion. A ventriculogram revealed areas in the posterior 3rd ventricle and a craniotomy revealed a massive intraventricular hemorrhage. Necropsy demonstrated a 2.5 cm. hemorrhagic mass in the roof of the posterior 3rd ventricle. All ventricles were filled with blood. (Contributed by Dr. Obert).

Case 2. A woman, age 73, had an obstruction in her left colon. A 10 em. hemorrhagic and fleshy tumor was found in the "colic mesentery" and a 2 cm. mass within the lumen of the left colon. (Contributed by Dr. Riggles).

Case 3. A man, 23, suffered the rapid onset of pain in the leg and signs of spinal cord compression. At operation, within 36 hours of onset, a paraspinal tumor mass was found extending from high thoracic to lumbar areas. It was extradural and did not involve nerve roots. Portions were removed. The patient had been investigated for peripheral eosinophilia ranging up to 50% while in the Army in Japan in 1971, without a cause being discovered. (Contributed by Dr. Rydell).

Case 4. A man, age 45, noted a mass in the left groin. The surgeon's preoperative diagnosis was hernia. A mass 7 cm. in diameter was excised. (Contributed by Dr. Obert).

Case 5. A 53 year old white male noted pain and development of a mass at the anterior border of the middle third of the trapezius muscle over a period of several years with more rapid increase in size during the 3 months prior to its removal. A 6 x 4 x 3.5 cm. hard gray mass was found under the inferior fascia of the trapezius muscle. The surgeon described it as being subscapular and in the 4th and 5th rib interspaces posteriorly. (Contributed by Dr. Fine).

Case 6. A 57 year old white woman noted a painful marble sized swelling in the right epitrochlear area which increased in size over a 2 month period. Examination revealed an 8 x 4.5 cm. epitrochlear mass. X-rays disclosed multiple nodules in both lung fields and a small area of irregularity in the cortex of the medial humeral epicondyle adjacent to the mass. (Contributed by Dr. Fine).

Case 7. A woman, 59, with a large tumor of the right breast. Sections from the mastectomy specimen. (Contributed by Dr. Lu).

Case 8. A woman, 31, had noted a lump in the right leg for 3 months. X-rays showed erosion of the tibia and foci of calcification in the tumor. (Contributed by Dr. Litton).
Case 9. A 21 year old man was found to have an enlarged mediastinal shadow on routine chest x-ray. A mass was removed from the right pulmonary hilus which measured 7 cm. in diameter. (Contributed by Dr. Strand).

Case 10. A 10 year old girl with shortness of breath was found to have a massive left pleural effusion. Physical examination was otherwise negative. Serosanguinous pleural fluid was found to contain abnormal cells. Exploratory thoracotomy revealed multiple tumors involving visceral and parietal pleura from apex to diaphragm. A nodule 2 cm. in diameter was removed for examination. (Contributed by Dr. Burke).

Case 11. A 13 year old boy was seen with a 15 x 10 cm. fluctuant mass in the right gluteus maximus muscle which was biopsied and subsequently removed by a hemipelvectomy. (Contributed by Dr. G. D. Stobbe).

Case 12. A woman, 22, was found to have a posterior mediastinal mass on routine chest x-ray. She was asymptomatic. At operation, a sharply circumscribed tumor measuring 5.5 x 4 x 3.5 cm. was found over the vertebral bodies and under the pleura of the right chest. It was slightly lobulated and soft. (Contributed by Dr. Lober).

Case 13. A woman, 83, was found to have a rounded lesion in the apex of the right lung on routine chest x-ray. A wedge resection of lung revealed a 3.5 cm. firm tumor mass. Peripheral blood smears and plasma protein levels were normal. (Contributed by Dr. Scott).

Case 14. A girl, 18, noted an enlarging mass for 6 months in the postsacral area. It was thought clinically to represent a pilonidal cyst and was removed. (Contributed by Dr. Lu).

Case 15. Following a period of "drowsiness", a woman, 59, was explored for a mass in the parasellar region. At the time of exploration she was blind in the left eye and exhibited 3rd and 6th nerve palsy. Much of the floor of the middle fossa was found to be destroyed by a tumor. The patient was treated with irradiation. At necropsy a 4.5 x 3.5 x 3.5 cm. mass was found in the left parasellar region. Sections are from the necropsy material. (Contributed by Dr. Soule).
Case 16. A woman, 76, had dysphagia for 6 months with 65 lbs. weight loss. Bilateral enlarged cervical nodes were found measuring up to 2 cm. in diameter. She had recently developed a dry mouth and reduced lacrimation. Bone survey showed only generalized osteoporosis. Hemoglobin was 7.4 gms. Bone marrow examination showed 5% mature plasmacytes. There were no megaloblasts. Serum protein was 6.7 gm. with 2.5 gm. albumin and 4.5 gm. globulin. Electrophoresis showed no myeloma band. There was no urinary Bence-Jones protein. One 2 cm. lymph node from the neck was biopsied. (Contributed by Dr. Lu).

Case 17. A tumor was noted to be growing rapidly in the left maxilla of an eight-month old male. The original tumor was removed. Two months later a second lesion appeared which measured 2 x 2.5 cm. It was heavily pigmented and forced some of the tooth buds out of place. This was again removed locally with surrounding curettage. (Contributed by Dr. W. Engelstad).

Case 18. A 21 year old white man was admitted to the Henry Ford Hospital on 7/29 because of dizzy spells of approximately three weeks duration. They were intermittent and most severe during periods when food had not been consumed for some time. He had had one episode when he was semi-comatose and was taken to the hospital at which time his blood sugar was 20-30 mg./100 cc. and he was revived by intravenous glucose administration. The only positive physical finding was a large, palpable, non-tender mass in the left upper quadrant. Upper GI series showed a large mass extrinsic to and displacing the stomach. IVP's showed a mass distorting the left kidney which was felt to be intra-renal. On 8/9 a left nephrectomy and splenectomy were performed for a large renal neoplasm. (Contributed by Dr. Fine).

Case 19. A 46 year old Negro woman with a long history of anemia due to sickle cell trait was hospitalized and found to have azotemia, anemia and fever. A right nephrectomy was performed because the kidney was hydronephrotic and not functioning by IVP studies. (Contributed by Dr. G. D. Stobbe).

Case 20. A 9 year old white girl presented with an enlarged abdomen. The abdomen was explored because of a right adnexal mass. A 23 x 18 x 15 cm. right ovarian tumor was found and removed. (Contributed by Dr. G. Yee).
Minnesota Society of Clinical Pathologists

1973 Annual Tumor Seminar

Contributor's Diagnoses

1. Choriocarcinoma
2. Leiomyosarcoma
3. Chloroma
4. ? Hemangiopericytoma
5. ------
6. ------
7. Osteogenic sarcoma
8. Alveolar soft part sarcoma
9. Giant hyperplasia of lymph node
10. ? Mesothelioma
11. ------
12. Differentiated neuroblastic tumor
13. Pseudolymphoma
14. Ependymoma
15. Chondroid chordoma
16. Amyloidosis with plasmacytosis
17. Melanotic progonoma
18. ------
19. ------
20. ------

Dr. Fine's Diagnoses

Choriocarcinoma of pineal
Malignant Schwannoma
Granulocytic sarcoma
Fibrous mesothelioma
Osteogenic sarcoma
Metastatic melanoma
Osteogenic sarcoma in cystosarcoma
Metastatic hypernephroma
Angiomatous lymphoid hamartoma
Embryonal rhabdomyosarcoma
Rhabdomyosarcoma
Paraganglioma
Malignant lymphoma
Hidradenoma
Chondrosarcoma
Primary amyloidosis
Melanotic progonoma
Fibrous mesothelioma of kidney
Malacoplakia
Embryonal carcinoma of ovary
DIAGNOSIS: Choriocarcinoma, Pineal Gland

MICROSCOPIC OBSERVATION: A good part of the tissue in this section is hemorrhagic tumor with the most viable appearing tumor at the periphery of the section where there is also seen in one area a small segment of pineal gland. Three types of tumor cells are present all of which show a marked degree of nuclear variation. Those with the deeply eosin stained cytoplasm are frequently elongated and bear a superficial resemblance to muscle cells and bizarre glial elements but when taken in perspective with the other cell types one can dismiss these two considerations. Cells with clear cytoplasm and multinucleated giant cells with eosinophilic cytoplasm are the other cell types present. DISCUSSION: The combination and arrangement of the tumor cells leaves me no alternative but to consider this a choriocarcinoma. Whether it is primary in this site or a metastatic focus cannot be said with certainty, but I would guess it represents one of the rare extragenital choriocarcinomas because of the patient's age. Caution must always be exercised in diagnosing a primary extragenital choriocarcinoma in view of the inconspicuousness of some genital choriocarcinomas. Primary extragenital choriocarcinomas appear to be more frequent in men than women. Among 109 such tumors in men culled from the literature up to 1962, the sites of involvement in order of frequency was mediastinum 53, retroperitoneum 27, abdominal viscera 12, pelvic viscera 6, intracranial 8 and lung 3. The number of reported intracranial primary choriocarcinomas has now increased to ten and all have been in the pineal area of boys with and without associated precocious puberty. Although metastases have been reported, most of them have been confined to the cranial cavity.

Prior to the mid-1940's, tumors of the pineal gland region were frequently classified as pineocytoma. Recognition of the similarity between these growths and germinomas and their association with teratoid growths in this region has led to the almost complete extinction of the pineocytoma. Such tumors are now classified as germinoma, choriocarcinoma, embryonal carcinoma or teratoma depending on their microscopic features. Precocious puberty which is commonly associated with pineal tumors could be secondary to hormonal production of the tumor, effect of diencephalic alteration as seen in cases of precocious puberty unassociated with tumor or a combination of the two. Among 177 tumors in the pineal area obtained from the literature by Bing, 21 (37%) of the 56 patients less than 15 years of age had precocious puberty and of these 15 (71%) also had hypothalamic disturbances.

Confirmation of the histologic diagnosis of choriocarcinoma as well as the role by germinal tumors in the development of precocious puberty may be clarified by detection of hormone in the tumor, blood or urine or by the changes in a variety of tissues. Of the various hormones elaborated by the trophoblastic tissue - chorionic gonadotropin (C.G.), F.S.H., L.H., estrogen, and progesterone - determination of the C.G. has been the most commonly employed. Its evaluation has been made more simple by a number of sensitive tests - pregnancy test, fluorescent antigen antibody methods and radio-immunoassay - having an immunologic basis. The fluorescent antigen antibody method may prove a great asset to the tissue pathologist by permitting C.G. localization at the cellular level. Histologic changes which may be found in the testis, ovary, prostate, breast and pituitary secondary to excessive hormone production by choriocarcinoma may provide support for the doubtful cases of extragenital choriocarcinoma.
References:


CASE #2

DIAGNOSIS: Epithelioid Schwannoma, Malignant

MICROSCOPIC: The cells of this tumor are large with abundant eosin stained cytoplasm having nuclei that are uniform and round with few if any mitoses. Rarely one finds cells with lobulated hyperchromatic nuclei or multiple nuclei. In some cells the cytoplasm is clear with a cavulated appearance. Lobules of tumor cells are closely packed and separated by thin septa of closely packed spindle cells or less cellular wavy fibrillar tissue. Within the lobules the cells are subdivided into irregular groups by thin reticulin fibers. The Bodian nerve fiber stain shows occasional delicate neurites in the spindle cell septa. With the Masson trichrome stain the cytoplasm of the large cell masses is generally a moderate to deep shade of red with irregular extensions from a number of cells. Only an infrequent cell contains a few PAS positive granules that are unaffected by prior diastase digestion. The Fontana silver stain is negative. Irregularly distributed groups of plasma cells and lymphocytes are present particularly at the periphery of the growth.

DISCUSSION: The appearance and grouping of the large cells suggests a number of diagnoses: malignant melanoma, histiocytoma, granular cell myoblastoma, smooth muscle tumor (leiomyoblasto and a Schwannian tumor, epithelioid type. I believe the last diagnosis is the correct one. While the granular cell myoblastomas have a cell grouping similar to this growth and may show a relationship with nerves, they also have a distinctly granular PAS positive cytoplasm which remains so after diastase digestion - a feature not seen in this growth. The other tumors mentioned are more difficult to rule out but I believe they are because of the relationship of the small nerves, spindle cells and the larger areas of wavy, more fibrous appearing tissue, reminiscent of a neurofibromatous growth with the large epithelial appearing cells. I hesitate to make this diagnosis in the absence of a history of the tumor's association with a large nerve trunk, a history of neurofibromatosis or a more obvious transition from a neurofibroma to a malignant Schwannian growth. However, I cannot on the basis of the material at hand arrive at any other diagnosis. I consider it a malignant growth but without a great deal of conviction.

REFERENCES:
CASE #3

DIAGNOSIS: Granulocytic Sarcoma (Chloroma), Paravertebral.

MICROSCOPIC: This is a cellular growth of uniform mononuclear cells having considerable granular eosin cytoplasm. Their nuclei are vesicular generally with a single prominent nucleolus. Mitoses are not difficult to find. thin fibrovascular septa often divide the cells into irregular, poorly defined groups. This is more vividly demonstrated by the reticulin and trichrome stains. At the periphery of the section the tumor cells are smaller and are admixed with delicate fibrovascular adipose tissue. Here the nuclei are less vesicular. Eosinophils, some of which appear to be myelocytes, are haphazardly distributed among the large cells and occasionally polymorphonuclear leukocytes, some with pyknotic nuclei, and rarer small mononuclear forms are also present. The cytoplasm of the large mononuclear cells and eosinophils have considerable PAS and granular polysaccharide. A section was not available for diastase digestion. The cytoplasm was also stained by alcian blue at pH 1.0. The Leder stain for chloroaacetyl esterase was negative while control unfixed frozen sections were positive in mast cells and neutrophils.

DISCUSSION: I consider two possibilities for this growth - granulocytic sarcoma (chloroma) and eosinophilic granuloma. It is difficult to decide which is the correct diagnosis. I believe the former is based on the location of the tumor, peripheral eosinophilia, presence of what I believe are myelocytic eosinophils and the positivity of the cytoplasm with the PAS and alcian blue stains. The negative Leder stain is not in keeping with the chloroma diagnosis but I do not believe this negates it since we do not know how the tissue was treated in preparation of the sections. Examination of imprints and staining of these for esterase and peroxidase would have, I believe, established this diagnosis with certainty. This case again illustrates the need for special procedures in delineating the nature of tumor cells seen in tissue sections.

Granulocytic sarcoma may be found in a variety of sites - bone, particularly the periosteum, being the most frequent and more often in patients less than 20 years of age. They may precede blood manifestations of leukemia but generally the latter manifests itself within a year of the discovery of the tumor.

Eosinophilic granuloma is most commonly a solitary lesion of bone but may involve bone and visera or less commonly manifest itself as an extraskeletal lesion. Unlike skeletal involvement which is more prevalent in children, extraskeletal or combined skeletal and extraskeletal involvement appears to be more common in adults. Sites of involvement have been the lungs, skin, stomach and anal mucous membrane. Diabetes insipidus has been reported in a number of these cases with and without evidence of bone involvement. Among 18 cases with involvement of the vulva, 13 had diabetes insipidus and of these, 9 had bone involvement and 4 had pulmonary involvement. The ultrastructural studies of this condition has proven interesting and may provide support for such a light microscopic diagnosis. The histiocytoses had been found to have organelles known as Langerhans' granules.

REFERENCES:

EOSINOPHILIC GRANULOMA
Eosinophilic Granuloma (continued)


CASE #4

DIAGNOSIS: Fibrous Mesothelioma, benign

MICROSCOPIC: This is a fibrous growth which features areas that are loosely arranged and poorly cellular or myxomatous and areas that are more fibrous with a cellular component that has little cytoplasm and generally large, vesicular, bland looking nuclei. Perhaps the most striking feature is the irregular and haphazard arrangement of the large collagen bundles which appear to be associated with a prominent vascular component. Reticulin and collagen fibers seen in the reticulin and trichrome stains are plentiful and distributed throughout the tumor in intimate association with the cellular elements. Sprinkled here and there are face of lymphocytes and occasional plasma cells.

DISCUSSION: After considering a number of possibilities for this tumor -- neurofibromas, fibrous histiocytoma, a reactive process secondary to injection in the treatment of a hernia and fibrous mesothelioma -- I ended up with the fibrous mesothelioma as my choice. This is based on the haphazard arrangement of the collagen bundles, the appearance and relationship of the cells to these bundles and the absence of any patterns of growth suggestive of the other tumors I considered in the differential diagnosis. If one does not subscribe to the belief of Stout and Murray regarding the potential of the mesothelial cell to have the capacity to form collagen and grow in the manner of epithelium, then I suppose the terminology fibroma would be the alternative diagnosis.

Since the concept of the multipotential of mesothelial cells was introduced, the round cell and spindle cell tumors of the serous cavities have almost been eliminated from the medical literature and many of the previous tumors in these cavities considered to be metastases from undiscovered primary tumors have found a place in the classification scheme. Problems still exist in the histologic diagnosis of this group of tumors because of their resemblance to carcinomas from a variety of sites and to some mesenchymal and occasionally ectodermal tumors. This is particularly true when dealing with a small biopsy and little or no clinical data. The mesothelioma may be solitary and nodular or diffuse growths and either fibrous as in this case, epithelial appearing (tubular, papillary or mixed) or a combination of the fibrous and epithelial variety. Involvement of the inguinal region (hernial sac) by a mesothelioma is less frequent than the pleura or peritoneal involvement. Both varieties -- fibrous and epithelial-like tumors -- may be found but the latter appear to be more frequently encountered in the hernial sac and has in some instances been a part of a generalized peritoneal involvement unrecognized as such at the time of herniorrhaphy. The fibrous variety of mesothelioma is more apt to be solitary, pedunculated and benign than the epithelial variety of the tumor. I believe the growth represented in this slide is benign (non-metastasizing), but he may be plagued by recurrences which could prove to be lethal.

REFERENCES:

CASE #5

DIAGNOSIS: Osteogenic Sarcoma, Soft Tissue Scapular Region.

MICROSCOPIC: A mass of fibrofatty muscular tissue and overlying skin measuring 15 x 5 x 6 cm containing a 6 x 4 x 3.5 cm firm grey infiltrating tumor was resected.
The section you have to study is very cellular being made of of spindle cells arranged in compact fascicles some of which have been cut across so as to produce a mosaic of longitudinal and cross section of cells. In some areas the cells are different having a more pronounced wavy configuration and in some portions of the tumor foci rich in fibrous tissue there is myxomatous tissue. A rich complex of small vascular channels, some inconspicuous, are interspersed among the tumor cells in an irregular fashion. In some of the many blocks that were studied dense poorly fibrillar fibrous tissue with and without calcification were a prominent part of the tumor. These areas are reminiscent of the ossification seen in fibrous dysplasia. Mitotic activity is moderately frequent. Reticulin fibers are abundant being present between practically every cell as kinked curled fibrils frequently encompassing individual cells. Diastase labile polysaccharide is plentiful in many of the tumor cells. The Masson trichrome stain confirms the presence of the collagen and reveals an almost complete lack of affinity of the cell cytoplasm for the fuchsin in the trichrome stain. Intracellular acid polysaccharide is not demonstrated by the alcian blue stain. Histochemically, alkaline phosphatase is demonstrable in many of the tumor cells even in the areas unassociated with calcification.

DISCUSSION: I had the advantage of studying sections from a good number of blocks and the findings in some of these sections I am sure will account for difference in our diagnoses. Diagnostic considerations in a tumor of this type include fibrosarcoma, synovial sarcoma, leiomyosarcoma, malignant Schwannoma and osteogenic sarcoma. My choice is the last diagnosis. The numerous kinked reticulin fibers intertwined with the tumor cells and the paucity of cell cytoplasm and its poor staining with the trichrome stain, in my mind, rules out the myosarcoma. The same reticulin pattern and the absence of a relationship of the tumor to a nerve or an association with neurofibroma negate the malignant Schwannian growth. Synovial sarcomas have been known to contain osteogenic foci but I would not consider this a synovial sarcoma in the absence of a biphasic growth pattern. If fibrosarcoma is to be used for this growth, and it would certainly be justified from the section in the seminar set, I believe one must at least make a notation of its ossifying properties. In view of this feature, I prefer the diagnosis of osteogenic sarcoma.

The ossification present in this case is unlike that usually found in extraskeletal osteogenic sarcomas but then, so is the cell type and fibrosarcoma-like arrangement seen in this tumor. There has now been 93 cases of extraskeletal osteogenic sarcoma reported in the literature. The prognosis in this variety of soft tissue tumor has been worse than in any other soft tissue sarcoma. Eighty-two percent of the patients have died of their tumor within 5 years, 9% have survived 5 years free of tumor and the remainder have survived longer than 5 years, but succumbed to the tumor after the patient from whom this tumor was removed is alive and well without evidence of recurrence one year following resection of the tumor.

REFERENCES:

CASE #6
DIAGNOSIS: Amelanotic Malignant Melanoma in Epitrochlear Soft Tissue.
MICROSCOPIC: A 5 x 5 x 4 cm grey irregular firm non-encapsulated mass was removed. Many areas of necrosis were obvious.
The tumor cells are large with a rather abundant cytoplasm that is generally well stained with eosin but in some foci this cytoplasm is partially or completely clear. Cytoplasmic boundaries in many cells are well defined. Nuclear variation is rather prominent, mitotic activity rather frequent and occasionally multinucleated cells are observed. The cells are arranged in large, irregular aggregates separated by delicate fibrovascular septa. Reticulin fibers separate groups of tumor cells from one another in the manner generally, but not exclusively, seen in epithelial tumors. Tumor cell cytoplasm is not stained with alcian blue and only an occasional cell shows polysaccharide stainable with the PAS stain with and without prior diastase digestion. The Fontana stain is negative for intracellular argentaffin positive material.

DISCUSSION: The cellular appearance and growth pattern in this tumor are those seen in an epithelial growth. Diagnostic possibilities considered were metastatic epithelial tumor and malignant histiocytoma. We did not believe the morphology or the multiplicity of lung nodules were in keeping with a primary lung carcinoma, so, we focused our attention on a melanotic melanoma and malignant histiocytoma. A positive dopa oxidase confirmed the diagnosis of malignant melanoma. Careful inspection of the patient failed to reveal the primary site of tumor. Death occurred three months after the excision of the epithelial tumor. The liver had become enlarged. Necropsy was not permitted.

Malignant melanoma in the absence of primary tumor was described in 37 instances of 992 malignant melanomas by Das Gupta, et. al. The 37 cases included only those in which a careful examination had been made to rule out the possibility of a primary tumor and excluded those cases in which a previous mole had been cauterized or removed and those cases in which an orbital melanoma had been removed. Twenty four of the cases had only lymph node metastases, while 13 had visceral metastases and were treated by x-ray, chemotherapy or surgery. Ten of the 24 lived five or more years free of disease indicating that the presence of melanoma in lymph nodes without a known primary is not a hopeless situation. Those cases with visceral metastases did not survive five years.

This is another instance of disseminated melanoma without a primary tumor site having been discovered. The epithelial tumor could not be confirmed as a lymph node metastasis from the study of some 15 blocks. The value of a special histologic technique in tissue diagnosis is illustrated in this case. Finely distributed melanin not observed in H & E sections may be present in melanoma considered to be amelanotic and can be better demonstrated by the argentaffin reaction using an alkaline silver procedure (Fontana), Lillie's iron uptake or ferriferricyanide technique. One must, however, be ever mindful of some of the similar reactions produced by melanin, iron and lipofuchsin pigments. (Table 1) making necessary the application of more than one reaction in some instances.

**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Dopa</th>
<th>Argentaffin Reaction</th>
<th>Schmorl's Ferri-ferricyanide</th>
<th>Lillie's Fe Uptake</th>
<th>Prussian Blue</th>
<th>Turnbull Blue</th>
<th>Peroxide Bleaching</th>
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<tr>
<td>Amelanotic</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<td>+</td>
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<tr>
<td>Melanoma</td>
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<td>+</td>
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<tr>
<td>Melanin</td>
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<td>-</td>
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<td>Lipofuchsin</td>
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<td>+</td>
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REFERENCES:

CASE #7
DIAGNOSIS: Cystosarcoma Phyllodes (Osteogenic Sarcoma), Malignant, of Female Mammary Gland
MICROSCOPIC: This tumor is forming atypical osteoid, bone and cartilage having all the
cytologic attributes of malignancy. Classic type giant cells are easy to find. Compact cellular
foci in areas suggest an epithelial component but I don’t think they are. Here again I had the
advantage of studying other sections and in these fibroadenomatous areas with varying stromal
cellularity were found in addition to the osteogenic and cartilaginous foci. The epithelial
portion of the growth did not possess the attributes of a malignant tumor.
DISCUSSION: Without the study of the additional sections I would have considered this an
osteogenic sarcoma, either representing a part of a carcinosarcoma, cystosarcoma phyllodes or a
stromal sarcoma. I would not have entertained a sarcomatoid carcinoma since I see no acceptable
areas of carcinoma.

The concept of cystosarcoma phyllodes has changed since Muller's description of the tumor in the
early nineteenth century. Over the years the term has come to be applied to breast tumors even
of small size. Tumors previously classified as a particular type of sarcoma arising in a
fibroadenoma are now classified as cystosarcoma phyllodes. Stromal malignancy among the tumors
is most frequently a fibrosarcoma but liposarcoma, histiocytoma and least frequently osteogenic
sarcoma have been noted. Only rarely is a carcinoma found in the cystosarcoma. Our
surgical colleagues have been and probably will continue to be confused by the terminology of
cystosarcoma especially with the prefix benign. Suggested terminology—hypercellular adenofibroma
for the benign growths and periductal fibrosarcoma, liposarcoma, etc. for the malignant growths
probably would be more appropriate and better understood, but the term cystosarcoma has become
so entrenched in the medical literature that it would be difficult to change.

There have been approximately 116 osteogenic sarcomas of the female mammary gland reported in
the literature and it would appear that most of them have been associated with fibroadenomatous
lesions and therefore would, by today's standards, be classified as malignant cystosarcoma phyllodes.

Like other varieties of malignant cystosarcoma, those with osteogenic sarcoma require wide
local excision, simple mastectomy in some instances, to eradicate them. They appear to be
more malignant than the usual variety of cystosarcoma phyllodes (fibrosarcoma) with metastases
being blood borne. Some authors have indicated a better behavior of sarcomas associated with
epithelial ductal structures (cystosarcoma phyllodes) than those without (stromal sarcoma) a
ductal component.

REFERENCES:
2. Jernstrom, P., Lindberg, A.L. and Meland, O.N. Osteogenic sarcoma of the mammary
4. Oberman, H.A. Cystosarcoma phyllodes. A clinicopathologic study of hypercellular
5. Rottino, A. and Howley, C.P. Osteoid sarcoma of the breast: A complication of
CASE #8
DIAGNOSIS: Renal Cell Carcinoma, Clear and Granular Cell, Metastatic to Skeletal Muscle.

MICROSCOPIC: The tumor cells are arranged in large, irregular, solid clusters often well defined and delineated by thin connective tissue membranes and vascular slits. This is accentuated by the reticulin and trichrome stains. The cytoplasm of the tumor cells is either clear or granular with a varying affinity for eosin. It has infiltrated skeletal muscle and is present in blood vessels. In some areas hemorrhage is prominent in the midst of tumor cells and superficially reminds one of blood vessels. The alcian blue stain is negative in the cytoplasm of the tumor cells. The PAS stain reveals varying amounts of positive granular polysaccharides, a good deal of which is labile to diastase digestion.

DISCUSSION: The differential diagnosis in this case must include those tumors which may present an organoid growth pattern - alveolar rhabdomyosarcoma, amelanotic melanoma, paraganglioma, alveolar soft part sarcoma and renal cell carcinoma. In this tumor, I believe the clear and granular eosinophilic cells arranged as they are would be sufficient for me to make a diagnosis of renal cell carcinoma and recommend IVP studies. The abundant glycogen in many of the tumor cells further supports this diagnosis. In some instances, the distinction between the various tumors may not be as clear as I believe it is here and help in distinguishing the members of the group may be obtained by other studies (Table 1):

<table>
<thead>
<tr>
<th>Protargol Silver</th>
<th>PAS</th>
<th>Oil Red O</th>
<th>Dopa</th>
<th>Chromaffin Reaction</th>
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</thead>
<tbody>
<tr>
<td>Amelanotic Melanoma</td>
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<td>±</td>
<td>±</td>
<td>-</td>
</tr>
<tr>
<td>Alveolar Rhabdomyosarcoma</td>
<td>-</td>
<td>+**</td>
<td>±</td>
<td>-</td>
</tr>
<tr>
<td>Alveolar Soft Part Sarcoma</td>
<td>-</td>
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<tr>
<td>Renal Cell Ca.</td>
<td>-</td>
<td>+</td>
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</table>

- ± without diastase; ± with diastase; * + if melanin is present; ** Crystalline

This is one of a few tumors noted for its unusual sites of metastases which on occasion may be the first indication of a malignant process. Lungs, lymph nodes, liver and bones are frequent metastatic sites and muscle and skin are among the infrequent tissues involved. The tubular arrangement with hemorrhage may lead one to interpret a metastases as a malignant vascular growth.

REFERENCES:

CASE #9
DIAGNOSIS: Angiomatous Lymphoid Hamartoma of Mediastinum

MICROSCOPIC: This is a mass of lymphoreticular tissue with a good number of varying sized vascular channels that are particularly prominent at the periphery of the mass where they are larger and dilated. They are frequently thick-walled and when surrounded by lymphocytes are reminiscent of splenic Malpighian corpuscles. Varying sized aggregates of small lymphocytes are separated by varying numbers of small vascular channels with prominent endothelial lining cells. Only rarely are germinal centers present in the center of the lymphoid masses. Occasionally a
solid aggregate of endothelial cells in the midst of a lymphoid aggregate is suggestive of a Hassall's corpuscle.

DISCUSSION: A growth of this histologic makeup in this location forces one to consider such things as thymoma, malignant lymphoma and angiomatous lymphoid hamartoma in the differential diagnosis. The microscopic features present in this slide are classical for the last condition. In the past such a histologic appearance has been interpreted as representing hemolymph nodes, hemangiolymphoma, lymph node hyperplasia and rarely thymoma. A number of studies have established the benign character of this growth and has made known the features necessary for its recognition and distinction from the other mentioned conditions. Although predominantly found in the mediastinum, other sites - nec, retroperitoneum, muscle, axilla, pelvis, lung and soft tissue of the shoulder - have harbored this type of growth. They have varied up to 15 cm in diameter and have been present for up to 20 years before being recognized. Patients in the third to fifth decade are most frequently afflicted with an equal distribution among the sexes. Only one of 68 reported cases was less than 10 years of age.

REFERENCES:

CASE #10
DIAGNOSIS: Embryonal Rhabdomyosarcoma Involving Pleura and Diaphragm.

MICROSCOPIC: The tumor cells are large, generally round, and grow in large clusters separated by well vascularized fibrous tissue having plump fibroblasts with vesicular nuclei. In some areas, the tumor cells vary in shape and instead of being arranged in compact masses are loosely arranged, sometimes being at the periphery of irregular spaces suggesting an alveolar pattern. The cytoplasm of the large cells is abundant and is poorly stained or clear with a vacuolated appearance seen in "spider cells". One small cluster of cells and scattered individual tumor cells have a deeply eosin stained cytoplasm. Reticulin fibers surround varying sized groups of tumor cells as one expects to see in an epithelial growth. The thionine stain confirms the collagen nature of the broader septa between the groups of tumor cells. Abundant granular cytoplasmic PAS positive polysaccharide is present in many tumor cells and this reaction is abolished by prior diastase digestion. Alcian blue stain reveals considerable stromal positivity but the tumor cells are negative. The Bodian stain does not reveal any neurites.

DISCUSSION: I considered a number of possibilities for this case - neuroblastoma, Ewing tumor, Wilm's tumor, mesothelioma and rhabdomyosarcoma. I believe the appearance of the tumor cells ("spider cells") and their arrangement, their glycogen content and the strong affinity of some cells for eosin and fuchsin are more in keeping with an embryonal rhabdomyosarcoma which could be primary or secondary in this site.

REFERENCES:
See case #11

CASE #11
DIAGNOSIS: Embryonal Rhabdomyosarcoma of Soft Tissue of Thigh and Buttock
The tumor has been altered by necrosis but a grouping of the tumor cells can still be seen and is best brought out with reticulin and trichrome stains. The cells are large with abundant cytoplasm having a great affinity for eosin and fuchsin. A finely granular or fibrillar appearance can be made out in some tumor cell cytoplasm but cross striations are not seen. Granular cytoplasmic PAS positive diastase labile polysaccharide is present in a number of the tumor cells. Alcian blue stain is negative in the cytoplasm.

DISCUSSION: The variety of cells and their arrangement suggest the two possibilities for this tumor - rhabdomyosarcoma and histiocytoma. Before the concept of histiocytoma was established, I would have been less hesitant about labeling this growth a rhabdomyosarcoma. I've learned to be more cautious about making this diagnosis particularly in biopsies from large tumors. Features of this histiocytic tumor - storiform and vascular patterns and mixed lymphoreticular and osteoclastic giant cells - are absent, but so are the sine qua non of the rhabdomyosarcoma - cross striations. The fibrillar character of the cytoplasm of some of the tumor cells can be seen in histiocytic as well as muscle tumors and are not by themselves diagnostic. The deep fuchsin staining of the tumor cells is more in keeping with muscle than histiocytes. The histology together with the age of the patient makes me more inclined to the rhabdomyosarcoma.

Electron microscopic studies offered proof positive in the presence of thick and thin cytoplasmic filaments and a suggestion of Z bands. Two types of fibrils are in contrast to the single variety of cytoplasmic filaments which are seen in histiocytic tumors. The light microscopic diagnosis of rhabdomyosarcoma has always been difficult in the absence of cross striations and some observers have questioned the justification of the diagnosis in their absence. Growth patterns combined with cytology are important for making the diagnosis in such cases. Care must be taken not to under stain with eosin and thus fail to recognize the affinity of myoblasts for eosin.

I consider this an embryonal type of rhabdomyosarcoma although the cells are somewhat larger than one generally sees in this type of tumor. Embryonal rhabdomyosarcomas are more common in children and occur more frequently in the head and neck regions and less commonly in the body cavities or extremities. Included with the embryonal rhabdomyosarcomas are the botryoid and alveolar forms which have unusual gross and/or microscopic features. Differences in behavior of the various types of rhabdomyosarcomas have been questioned. Data indicates a difference in prognosis and incidence of lymph node spread among the pleomorphic and embryonal rhabdomyosarcomas. Five year cure rates among 187 pleomorphic rhabdomyosarcomas was 35 (33-36) percent as contrasted to 12 (0-26) percent among 341 embryonal rhabdomyosarcomas. Lymph node involvement has been more frequent in the embryonal than in the pleomorphic tumor - 59 of 174 (33.8%) in the former and 14 of 180 (7.7%) in the latter. It is questionable whether the prognostic significance can be attributed solely to the tumor's histologic appearance, since the embryonal rhabdomyosarcomas were most commonly found in areas difficult to treat - head and neck areas and body cavities.

A hemipelvectom y was performed for the tumor in this seminar and a 14 x 10 x 8 cm gray, soft, partially necrotic tumor was found involving the right gluteus maximus muscle and right iliac lymph nodes. Death occurred two months later with tumor in the right abdominal wall and flank, retroperitoneum, urinary bladder, testes and perineum.

REFERENCES:


CASE #12

DIAGNOSIS: Paraganglioma, Paravertebral, Thoracic.

MICROSCOPIC: The grouping of the tumor cells is distinct with most every cluster surrounded by thin vascular connective tissue septa which separate the cell groups from one another. The cells are frequently elongated at their periphery and are perpendicular to the connective tissue and vessels at the periphery of the cell masses. Their cytoplasm is finely granular or homogeneous and is generally weakly stained with eosin. Nuclear hyperchromasia and pleomorphism are noted among otherwise uniform, small nuclei. At the periphery of the tumor nerve fibers and a few ganglion cells are seen. The tumor cell cytoplasm is negative with the PAS stain and weakly eosinophilic with the trichrome stain. The Bodian stain shows a few neurites at the periphery of the growth but no granules are seen in the tumor cells. Silver positive granules are present in a good number of tumor cells with the protargol silver method for alpha cells.

DISCUSSION: A number of tumors have this organoid (endocrine) growth pattern and have to be considered in the differential diagnosis - paraganglioma, alveolar soft part sarcoma, renal cell carcinoma, alveolar rhabdomyosarcoma and amelanotic malignant melanoma. In most instances when large biopsies are obtained the diagnosis is not difficult and can generally be established with the H & E stained section. In some instances, particularly in small biopsies, the diagnosis may be difficult and one may have to rely on special techniques to establish a diagnosis; (Table 1).

I believe this tumor's microscopic morphology is distinct enough to distinguish it from the other tumor types.

<table>
<thead>
<tr>
<th></th>
<th>Protargol Silver</th>
<th>PAS</th>
<th>Oil Red O</th>
<th>Dopa</th>
<th>Chromaffin Reaction</th>
</tr>
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<tbody>
<tr>
<td>Amelanotic Melanoma</td>
<td>+*</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
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<td>+**</td>
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<td>-</td>
<td>-</td>
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<tr>
<td>Paraganglioma</td>
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<td>+</td>
<td>+</td>
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<tr>
<td>Renal Cell Ca.</td>
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<td>+</td>
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</table>
REFERENCES:

CASE #13
DIAGNOSIS: Malignant Lymphoma, Histiocytic Type, in Lung (?Primary)

MICROSCOPIC: The lung parenchyma has been replaced by a solid tumor consisting predominantly of what appear to be histiocytes (reticulum cells) and fewer large and small lymphocytes. No nodularity or germinal centers is seen. Lymphoid cells are found in the bronchial wall and pulmonary parenchyma immediately adjacent to the tumor mass. Occasional plasma cells, some with Russell bodies, are seen in a few areas in the midst of the lymphoid cells. Irregular bands of dense, poorly fibrillar connective tissue are irregularly distributed among the lymphoid cells. Granulomata of epithelioid cells, giant cells and occasionally cholesterol clefts are present in some areas.

DISCUSSION: The histogenesis of this lesion is clear. The question is one of classification - extranodal malignant lymphoma, primary or systemic, or pseudolymphoma. This type of problem is encountered more commonly in the intestinal tract than the lung and in the latter instance the problem appears to be more complex and difficult to solve. One must not only consider the pseudolymphoma but granulomatous lymphoid disease - Wegener's granulomatosis and lymphomatoid granulomatosis. The difference between these conditions are in the type of infiltrate - mixed, mature or immature, and the presence or absence of vasculitis and germinal centers (Table 1). Utilizing these criteria I would classify this case as a malignant lymphoma and consider the granulomata secondary to rather than the cause of the tumefaction. The differentiation of malignant lymphoma - pseudolymphoma and judgment of prognosis necessitates knowledge of the cell type of the tumor and whether there is lymph node involvement. In the absence of lymph node involvement surgical extirpation by lobectomy appears to be sufficient. Lymph node involvement requires the addition of radiotherapy. Concomitant regional lymph node involvement with the pulmonary lesion reduces the five year survival rate 65% among the lymphocytic tumors and from 84% to 20% among the sarcomas. In view of the difficulty in histologic differentiation of malignant lymphoid growths in the lung perhaps the best therapeutic and diagnostic approach is biopsy of regional lymph nodes.

TABLE 1

<table>
<thead>
<tr>
<th>Malignant Lymphoma</th>
<th>Pseudolymphoma</th>
<th>Wegener's</th>
<th>Granulomatosis</th>
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<tr>
<td></td>
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</tr>
<tr>
<td>Germinal Centers</td>
<td>L. N. Involvement</td>
<td>Infiltrate</td>
<td>Vasculitis</td>
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<td>+</td>
<td>UI</td>
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</tr>
<tr>
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<td>-</td>
<td>MiM</td>
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<tr>
<td>-</td>
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<td>MiM</td>
<td>-</td>
</tr>
<tr>
<td>-</td>
<td>-</td>
<td>M-M</td>
<td>+</td>
</tr>
</tbody>
</table>

U- Uniform, I- Immature, M-M Mixed, M-M Mature
REFERENCES:


CASE #14
DIAGNOSIS: Hidradenoma, mucinous, of skin of buttock

MICROSCOPIC: The growth pattern of the tumor is striking. Varying sized groups of tumor cells with uniform vesicular and nuclei and generally with poorly defined cytoplasm are separated by well vascularized connective tissue septa. In some areas the alignment of the cells is perpendicular to the connective tissue septa. Many irregular vacuoles of questionable position - intra or extracellular - are present which produce "spider" appearance in some of the cells. In a number of areas intercellular basophilic material is abundant and there is a suggestion of a papillary configuration to the tumor. Reticulin fibers are found surrounding irregular groups of tumor cells. The PAS stain is positive around blood vessels and around the vacuoles in the stroma but within the cells. Alcian blue stain is positive in the stroma around the blood vessels, around but not in the vacuoles and in occasional areas in the center of cells that have a circular arrangement. The alcian blue stain is positive at pH 2.5 and pH 1 but is less intense at the latter pH. Following hyaluronidase digestion (1 mg/ml saline for 4 hours at 37 degrees C) the alcian blue stain is negative. Oil red O and Sudan black B stains are negative on formalin fixed frozen section material.

DISCUSSION: When I first studied the H & E sections, I considered the possibility of chordoma on the basis of the cell arrangement and the vacuoles and the tumor's location in the lumbar area. I even considered the possibility of ependymoma because of the relationship of the cells to the blood vessels and the location in the lumbar area, but the mucoid appearance was against such a diagnosis. When I found a negative intracellular glycogen stain (PAS), I could not justify the chordoma diagnosis since I have not seen such a growth without a strongly positive intracellular reaction for diastase digestible polysaccharide. The vacuoles bothered me and I began to consider the possibility of an embryonal liposarcoma. It was then that I contacted Dr. Lu and learned that the tumor was in the buttock and he supplied me with formalin fixed tissue for fat stains. The relationship to the skin and the nodularity of the lesion was seen in this material. It then occurred to me that we were dealing with a sweat gland tumor having a mucinous stroma. The staining reaction of the stroma and lability of the polysaccharide to hyaluronidase indicates it is a non or poorly sulfated polysaccharide - a reaction unlike the polysaccharide of cartilage of epithelium. I would prefer the term hidradenoma with mucinous stroma. It would not surprise me to find on more extensive examination some stromal areas with cartilage and if this were the case I would then classify the lesion with the chondroid syringomas. I believe this is a benign growth because of the lack of cellular atypia and its arrangement in large cell aggregates rather than a tubular or acinar pattern. One realized that these criteria are not absolut for benignancy when examining the report of metastasizing clear cell hidradenoma by Keesby.

REFERENCES:


CASE #15
DIAGNOSIS: Chondrosarcoma With Chordoid Features, Base of Skull

MICROSCOPIC: In this tumor, the cells are set in a stroma that is for the most part homogeneous and basophilic staining. In some areas at the periphery of the tumor, the stroma is of a loose, more fibrillar character but remains basophilic. For the most part, the cells are well separated from one another, often lying in spaces but in some areas, particularly at the periphery, they are arranged in ribbon-like fashion or in groups and there is a vacuolated appearance with many of the vacuoles appearing to be extracellular. The amount of cytoplasm is variable, finely granular or finely vacuolated. A focus of ossification is seen in one area. Granular PAS positive diastase digestible polysaccharide is plentiful in the cytoplasm of the cells which lie in lacuna but the stain is generally negative in the groups of cells at the periphery of the tumor. The PAS reaction of the stroma is variable but generally weakly positive or negative. The alcian blue stain (pH 2.5 and 1.0) is strongly positive in most of the stroma including the loose fibrillar areas at the periphery (areas weakly or negatively stained with PAS) and weakly positive or negative in the cell cytoplasm, both in lacunae and in the cell groups at the periphery.

DISCUSSION: With the exception of a few foci at the periphery of the tumor, its appearance is unequivocally cartilaginous with all of the features of a malignant tumor. The question is whether the entire process is cartilaginous or whether it is a mixture of chondrosarcoma and chordoma. I consider this a cartilaginous tumor with a few small foci resembling chordoma rather than a chordoma that has a chondrosarcomatous appearance. The similarity of chondrosarcoma and chordoma is seen most frequently among the tumors arising in the area of the notocord and in particular at the base of the skull. I believe the resemblance to chordoma can also be seen, but rarely, in peripheral skeletal chondrosarcomas and it has been mentioned in at least one soft tissue tumor of the axilla. The similarity between cartilage and notochordal tissue can also be appreciated by examining sections of the normal nucleus pulposis and the surrounding fibro and articular cartilage.

The use of special and histochemical procedures - PAS, alcian blue, reticulin, PTAH and lipid stains - in distinguishing cartilaginous and chordomatous tumors are of questionable value. Crawford in 1958 believed the reticulin and PTAH staining positivity in cartilaginous tumors and negative staining in chordomatous tumors was a differential feature. EM studies of a few chordomas and chondrosarcomas indicate that their ultrastructure may be helpful in distinguishing them. The designation of tumors having this appearance as chondroid chordoma or chordoid chondrosarcoma appears to be one of individual preference and which name is employed is probably of no significance. However, their recognition and separation from the classical chordoma at the base of the skull appears to be worthwhile judging from the study of Heffelfinger et. al., in which it was found that these tumors with a dual cell appearance have a significantly longer survival than the classical chordomas arising at the base of the skull. It would be interesting to know the comparative prognosis between these tumors and the chondrosarcoma at the base of the skull.

Such data would be difficult to arrive at because of the infrequency of chondrosarcomas in this region. In Heffelfinger’s study there were only 4 chondrosarcomas - the remainder of the tumors were classified as chondroid chordomas or chordomas.
REFERENCES:

CASE # 16
DIAGNOSIS: Amyloid, cervical lymph node ? primary

MICROSCOPIC: The architecture of the lymph node has been altered. Lymphoid follicles are not seen and the medullary tissue has many mature plasma cells in addition to lymphoreticular elements. Small vessels with prominent endothelial cells and thick eosin stained walls are numerous in the medullary cords. In a few small foci, discrete homogeneous eosin stained tissue is present in which there are isolated mononuclear cells. A van Gieson stain reveals very little connective tissue. Most of the areas are khaki colored instead of the red color that one sees with fibrous tissue. Thioflavin T stain observed with ultraviolet light using a BG 12 exciter and a 53 barrier filter reveals a green fluorescence in much of the medullary areas. Congo red and crystal violet stains are respectively orange brown and metachromatic in the medullary areas. Polarization of the congo red stain is positive (green) as described in amyloid.

DISCUSSION: The special stains clearly establish the presence of amyloid in the medullary area of this lymph node. What has to be decided is the type of amyloidosis this represents - familial, primary, secondary or that associated with plasma cell myeloma. The location of the amyloid suggests the primary variety or that associated with plasma cell myeloma. Although a number of extraskeletal sites may be involved with myeloma cells in anywhere from 8 to 80 percent of the cases of plasma cell myeloma - most common in the RE system organs (lymph nodes, spleen and liver) - I don't believe this case is an example of such, because the plasma cells do not show the immaturity I would want to see to make such a diagnosis and the plasma protein studies do not support such a diagnosis realizing, of course, they need not be elevated. The positivity of all the stains employed for the detection of amyloid is somewhat unusual in cases of primary amyloidosis. We have found the thioflavin T stain a simple reliable screening stain for amyloidosis and employ it routinely in suspected cases. I would suspect the lacrimal glands and major salivary glands might be involved by amyloid deposits and accounts for the dry mouth and reduced lacrimation seen in this patient.

REFERENCES:
CASE #17

DIAGNOSIS: Melanotic neuroectodermal tumor of infancy (melanotic progonoma) of left maxilla

MICROSCOPIC: Tumor cells of two types are present in a dense fibrous stroma - large cells with vesicular nuclei and brown granular pigment in their cytoplasm and small cells with small, hyperchromatic nuclei, having infrequent brown granular pigment in their cytoplasm. The latter are grouped in irregular clusters sometime arranged in a loose acinar configuration. There is active mesenchymal bone formation and in one section I studied, there was a portion of a tooth bud. In areas, the stromal cells and the large vesicular cells are not easily separable. The pigment shows the characteristics of melanin - positive staining with Lillie's iron uptake stain, negative Turnbull blue stain and bleaching of the pigment with ammoniacal hydrogen peroxide. Bodian nerve fiber stain did not reveal any neurites.

DISCUSSION: This growth has all the microscopic features of the tumor which has been reported under a variety of names - retinal anlage tumor, melanoblastoma, melanotic adamantinoma, odontogenic hamartoma, melanotic epithelial odontoma, pigmented epulis, congenital melanotic tumor, pigmented neuroectodermal tumor of infancy and melanotic progonoma - indicating the differences of opinion regarding its histogenesis. A number of findings would support the neuroectodermal origin - melanin containing cells, presence of neurites and the ability of the tumor to produce 3-methoxy-4-hydroxy-mandelic acid (VMA) similar to what has been demonstrated in some neuroblastomas. It would seem that the neuroectoderm would be the likely source of such a growth, since it is capable of giving rise separately to neoplasms, of each of these elements - melanoma and neuroblastoma. There have been approximately 59 such tumors reported in the literature with a predilection for the jaw bones - 38 maxilla, 6 mandible, 4 anterior fontanelle, 2 skull and one each in the palate, scapula, deltoid, epididymis, mediastinum, uterus, and fourth ventricle. Tumor site was unstated in two cases. Female have been afflicted more frequently than males and except for two cases, one in the maxilla and one in the uterus, they have been in children less than one year of age. They have been nonmetastasizing growths usually cured by excision. Recurrences have been reported, 6 instances among the 33 cases of Kerr and Pullan.

REFERENCES:

CASE #18

DIAGNOSIS: Fibrous mesothelioma, benign of kidney - Insulin producing with hypoglycemia

MICROSCOPIC: This tumor was a firm well circumscribed 13 x 8.8 x 10 cm grey firm mass occupying a good part of the kidney. It distorted the pelvis and calyces but did not communicate with these structures.

The section shows striking microscopic features. Spindle and stellate shaped cells are distributed in a loosely arranged connective tissue which has frequent, irregularly shaped, deeply eosin stained fibrous tissue with a radiating fibrillar appearance. Mitotic activity is not seen and cellular pleomorphism is minimal. Trichrome and reticulin stains support the fibrous nature of the stroma including the focal discrete eosin stained areas. Alcian blue stain reveals stromal...
but not cellular positivity. In view of the clinical history, immunofluorescent studies were done using unfixed frozen sections of the tumor, guinea pig antibovine insulin and fluorescent labeled rabbit (globulin) antiguinea pig globulin. Fluorescence was detected in the cytoplasm of some, not all, of the tumor cells using ultraviolet light.

DISCUSSION: I believe this is a histologically benign mesenchymal tumor but I am uncertain as to whether it arises from the lower or upper part of the renal anlage. I think there is some similarity between this tumor and the tumor of the inguinal region, case #4, and I regard it as a fibrous mesothelioma. I have not found any other reported mesotheliomas of the kidney proper but I have seen one example which had metastasized to the psoas muscle. There was no endocrine abnormality associated with this tumor and it was a classical fibrous mesothelioma with the so-called patternless pattern described by Stout.

In addition to an unusual histology this tumor was unique because of the associated clinical hypoglycemia. A relationship between the two was demonstrated in this instance utilizing an immunofluorescent technique. Tumor cells were found to contain a protein similar to if not identical to insulin. Further support for the tumor being responsible for the hypoglycemia is found in the reversion of the patient's blood glucose to normal following removal of the tumor.

A variety of endocrine syndrome have been associated with epithelial and mesenchymal neoplasia - Cushing's syndrome, hypoglycemia, hypercalcemia, erythremia, hyperthyroidism, water retention, hyperserotonemia and precocious puberty. A variety of benign and malignant mesodermal tumors; muscle, fibroblastic, mesothelia, and lymphoid tumors and hemangiopericytomas have been believed responsible for hypoglycemia. In this instance, there was reversion of the blood sugar to normal following removal of the tumor and the patient has remained well for five years without evidence of recurrence, metastases or abnormality in blood sugar.

REFERENCES:

CASE #19
DIAGNOSIS: Malacoplakia of right kidney

MICROSCOPIC: The kidney was distorted due to dilatation of the renal pelvis and calyces the mucosal surfaces of which were irregular and shaggy. A portion of the accompanying ureter showed similar changes.

The microscopic changes are principally in the medulla and pelvis where there is a heavy cellular infiltrate of histiocytes, neutrophils, lymphocytes and plasma cells. The histiocytic cytoplasms is granular with and without round, homogenous bodies that are basophilic or lightly eosin stained. Some have a bull's eye configuration with darker central area surrounded by a clear zone and then another dark zone. These features are more clearly and vividly demonstrated by the PAS stain which is not affected by prior diastase digestion. The Von Kossa stain is positive in some of the cytoplasmic PAS positive bodies. The Prussian blue stain is negative.

DISCUSSION: The differential diagnosis includes xanthogranulomatous pyelonephritis, malacoplakia and histiocytoma. Carcinoma of the kidney is not a consideration in this section. The appearance and arrangement of the histiocytes and the degree of inflammatory infiltration and necrosis are not in keeping with histiocytoma nor is the lack of foam cells compatible with xanthogranulomatous pyelonephritis. The proof positive feature for the diagnosis in this case are the homogeneous, round, lightly eosin stained or slightly basophilic bodies (Michaelis-Gutman, M-G body), occasionally having a concentric ring configuration, that is present in
the cytoplasm of many of the histiocytes. These are more easily appreciated with special stains particularly the PAS stain. Associated with these bodies are histiocytes with granular PAS positive cytoplasm (Hansman cells) but without the M-G bodies.

Approximately 120 of these cases of malacoplakia have been reported involving principally the urinary tract - urinary bladder, kidneys and ureter in that order - but it has also been observed in the testis, colon, prostate, stomach, and recently in a disseminated form. Rarely has it been the cause of death. The extent of the disease in the present case was not determined since necropsy was not performed. The radiographically altered left kidney and ureter may have been the site of similar involvement. The etiology of malacoplakia is unknown. The basic lesion appears to be an accumulation of granular material within cells generally considered to be histiocytes but believed by some to be epithelial, endothelial, fibrocytes, etc. The composition of the cellular material has been reported histochemically to be glycoprotein by some and glycolipid by others with M-G bodies representing similar material but with encrusted salts of calcium and/or iron.

REFERENCES:

CASE #20
DIAGNOSIS: Embryonal Carcinoma (mesoblastoma, endodermal sinus tumor) of ovary

MICROSCOPIC: The ovary has been replaced by a 24 x 15 x 10 cm soft, grey, partially cystic tumor.

The tumor features cells with clear and granular cytoplasm which grow in solid, irregular groups or as glandular elements lined by cuboidal or columnar epithelium. Nuclear variation is prominent in a number of areas and lobulated forms are not infrequent. Varying sized eosin stained cytoplasmic globular material and irregular areas of eosin stained fibrillar material within the stroma or tubular lumen are present in scattered areas. Structures with a central vessel and peripherally arranged tumor cells (glomerular-like) or simulating embryoid bodies are present. Special stains help to bring out a number of features seen poorly or not at all with the H & E stain. In addition to abundant granular diastase labile PAS positive polysaccharide that is chiefly in the clear cell cytoplasm there is a moderate amount of diastase resistant polysaccharide in the clear cells and lumen of the glands. The latter is often in the form of varying sized intra- and extracellular globules. Thin, haphazardly arranged strands having the appearance of fibrin are not well seen in the H & E stain but are clearly outlined by the PAS and Masson trichrome stains. Alcin blue positive material is found in the loose areas of the stroma and rarely in the lumen of an occasional tubular structure. The oil red O stain indicated considerable lipid in the cytoplasm of many of the tumor cells.
I believe this is an example of the tumor which Teilum has called mesoblastoma and endodermal sinus tumor and which other authors have designated as embryonal carcinoma. Because of its clear cells and the original article of Schiller in which he reported this variety of tumor under the designation of mesonephroma, it has sometimes been classified as mesonephroma. Unlike the latter, the cells of these tumors are generally more loosely arranged with a vacuolated myxomatous stroma. The varying sized cytoplasmic and extracellular PAS positive diastase resistant globules and the hemorrhage and fibrin are not seen in the mesonephroma as they are in this growth. Glomerular-like and embryoid bodies are a feature of this tumor but may have to be carefully searched for since they may be sparsely distributed. This variety of ovarian tumor which should be classified with the germinal group of tumors occurs in a younger age group and are much more aggressive than the so-called mesonephric carcinoma of the ovary. The patients succumb to the disease generally within a year after the diagnosis has been made.

Because of the histology of the tumor, an immunologic pregnancy test was done on the urine postoperatively and was found to be negative. Mithramycin, Cosmegen and Proctox were given, but recurrent tumor in the periumbilical area and metastasis to the right cervical region were noted in three months following the oophorectomy. She died eleven months after the initial diagnosis was made. Liver and pulmonary metastases were present at necropsy.

REFERENCES: