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MINNESOTA SOCIETY OF CLINICAL PATHOLOGISTS

Case 63

The patient is a 50-year-old white male with a history of malignancy. The patient was admitted to the hospital for a second opinion regarding the nature of a mass palpable in the lower part of the abdomen. The mass was first noted by the patient in June 1985. The patient had a history of prostate cancer treated with radiotherapy in 1981. The mass was noted by the patient in June 1985 and became symptomatic in July 1985. The mass was removed surgically in July 1985. The mass was diagnosed as a malignant tumor. The patient was treated with chemotherapy and has remained asymptomatic.

Case 64

The patient is a 60-year-old white female with a history of malignancy. The patient was admitted to the hospital for a second opinion regarding the nature of a mass palpable in the lower part of the abdomen. The mass was first noted by the patient in June 1985. The mass was noted by the patient in June 1985 and became symptomatic in July 1985. The mass was removed surgically in July 1985. The mass was diagnosed as a malignant tumor. The patient was treated with chemotherapy and has remained asymptomatic.

Topic: Tumor Seminar

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CASE #1

This 28-year-old female was in good health until August of 1982 following the delivery of her second child, at which time she began to experience increasing back pain. X-rays were reported to be normal and she was treated symptomatically. The patient returned six months later with continued back pain and was treated with local cortisone injection. When her back pain continued, she was subsequently treated with diathermy and ultrasound for a total of 46 treatments. Prompted by intractable pain, the patient sought aid from a chiropractor, who treated her with massage and manipulation. In July of 1983 she sought the aid of an acupuncturist--no improvement followed. On the way to her third acupuncture treatment, she was involved in an auto accident and was transported to a local emergency room where x-rays were taken. The x-rays showed an abnormality in the region of the costovertebral junction of the 5th rib posteriorly. Biopsy of the mass was performed. (Contributed by Dr. L. E. Wold, Mayo Clinic)

CASE #2

The patient is a 9-year-old male with a large lytic lesion in the body of the right mandible. The process was initially biopsied, then curetted, and was eventually removed by way of a resection of the right mandibular body. (Contributed by Dr. R. Vickers, Minneapolis, MN)

CASE #3

The patient is a 70-year-old asymptomatic female with a lump on the scalp, clinically thought to be a lipoma. At the time of excision, it was found that the tumor had eroded the outer table of the skull. X-rays showed a large lytic lesion involving the outer portion of the bone. (Contributed by Dr. J Popowich, Minneapolis, MN)

CASE #4

Three years ago, this 63-year-old white male had a spontaneous small bowel perforation for which no cause was found. Six months later he had a four-week episode of fever and weight loss. An extensive work-up failed to reveal the cause. In December 1984, he developed recurrent fever and weight loss, as well as post-prandial lower sternal pain. Gastroscopy disclosed a 2.0 cm ulcer just below the esophago-gastric junction. Gastroscopic biopsy provided diagnostic material. Your slide is taken from a subsequently performed gastrectomy. (Contributed by Dr. L. B. Kahn, New Hyde Park, NY)
CASE #5

The patient is a 66-year-old male with a solitary nodule in the skin of the scalp. The lesion had been noted several months previously. Grossly, it was a pancake-like nodule, measuring 4.5x5x1 cm and showed an area of central ulceration. Local excision was carried out. The cut surface of the nodule had a greyish-white color and a fish flesh consistency. (Contributed by Dr. T. R. Arlander, Minneapolis, MN)

CASE #6

Chronic lymphocytic leukemia was diagnosed 2½ years earlier in this 71-year-old man. One year ago, with the WBC rising slowly to 100,000 and with a detectable serum IgM-lambda monoclonal protein, a course of cyclophosphamide and prednisone was begun and the patient's WBC fell to 7,000. Over the past three months there was rapid enlargement of left axillary lymph nodes. At surgery a fixed axillary mass 12x8x5 cm was resected. (Contributed by Dr. P. M. Banks, Mayo Clinic)

CASE #7

The patient is a 52-year-old male with a 10-year history of low back and leg pain. The symptoms recently increased in severity and the pain radiated to the right leg. A neurogenic bladder was noted. The routine spinal x-rays were unremarkable, but a myelogram showed total block by an intradural mass at the L1-L3 level. The CSF protein level was 2,500 mg%. At surgery a 4.1x2x1.3 cm ovoid-elongate, red, rubbery tumor was attached to the filum terminale and had a prominent feeder vessel. The caudal nerve roots were displaced and compressed. (Contributed by Dr. P. R. L. Sonneland, Milwaukee, WI)

CASE #8

The patient is a 16-year-old Italian male who, over a period of two months, noted a lump in the soft tissues medial to the left scapula. Physical examination disclosed a somewhat tender 2 cm nodule in the soft tissues unassociated with cutaneous changes. A biopsy was performed in Italy, and a diagnosis of "metastatic epithelioma" was made. The patient was referred in May 1982 for further evaluation. Physical examination, chest, x-ray, KUB, CT of chest and abdomen, radioisotopic bone scan, metastatic bone survey, bone marrow aspirate and biopsy, as well as hepatic and renal function tests were negative. A slight nodularity was noted in the biopsy site and prompted a wide resection; only reactive changes were noted. The patient was discharged but returned nine months thereafter with a 6x2.5x2 centimeter recurrence in the soft tissues beneath the incision. The mass was removed with generous margins. Radiotherapy was given (3000 rads over a 20x20 cm field). He remains disease free at followup on 9-84. (Contributed by Dr. M. R. Wick, Minneapolis, MN)
CASE #9

The patient, a 23-month-old female, was found to have a large hepatic tumor. A medial lobectomy was performed. The gross specimen consisted of a large ovoid mass measuring 13x12x9 cm and weighing 625 grams. The tumor was surrounded by a thin rim of liver tissue. The cut surface was lobulated and yellow with extensive hemorrhage and necrosis. Approximately 25% of the tumor was represented by a central ossified mass, measuring 5.5 cm. (Contributed by Dr. C. Manivel, Minneapolis, MN)

CASE #10

The patient is a 26-year-old male with a rapidly enlarging subcutaneous tumor involving the left thigh. The clinical diagnosis was "sebaceous cyst". The overlying skin was unremarkable. The patient underwent an excisional biopsy at which time a 2 cm nodular, pink-tan mass was removed. A diagnosis of malignancy was made, and the site was subsequently re-excised; some residual tumor was found. At present, the followup is 20 months and the patient is free of tumor. He has no other cutaneous lesions or central or peripheral nervous system abnormalities. (Contributed by Dr. B. W. Scheithauer, Mayo Clinic).

CASE #11

This 83-year-old female gave a three-month history of increasing abdominal girth, a 30-pound weight loss and malaise. She had had her menopause at age 40 years. A Pap smear one week prior to admission was reported as abnormal. On examination, she was found to have 2+ pitting pre-tibial edema, a left adnexal mass and a small atrophic uterus. A total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. A 10.0 cm partially cystic mass replaced the left ovary. Three-thousand milliliters of milky ascitic fluid were also noted. (Contributed by Dr. L. B. Kahn, New Hyde Park, NY)

CASE #12

The patient is a 69-year-old male with obstructive urinary symptoms of long duration. No stones, infections or hematuria had been noted. Urologic examination disclosed trilobar enlargement of the prostate, decompression of the urinary bladder with diverticulum formation and dilation of the distal ureters bilaterally. 150 cc urine residual was noted. At TURP, 75 grams of prostatic tissue were resected. Grossly, one-half of the fragments appeared grey and semi-translucent. (Contributed by Dr. A. R. Cohen, San Diego, CA)
CASE #13

The patient is a 48-year-old female with a 2 cm para-areolar mass found incidentally on examination of the left breast. No discharge was evident. Attempts at aspiration were unsuccessful. An excisional biopsy was performed. (Contributed by Dr. D. J. Nollet, Hibbing, MN)

CASE #14

The patient is an 87-year-old female with a history of radiation therapy to the right upper lid for a tumor diagnosed as basal cell carcinoma. Four years following treatment, a recurrent tumor of the right upper lid was surgically excised. The patient eventually underwent exenteration of the right orbit. (Contributed by Dr. J. D. Cameron, Minneapolis, MN)

CASE #15

A 73-year-old white female was admitted with complaints of heartburn and epigastric pain. Work-up revealed a retrogastric mass which was resected in June 1981. The mass was dark-colored and had a multicystic, hemorrhagic cut surface. The patient was readmitted with similar complaints in January of 1985 and on this occasion, a 3.0 cm firm, brownish, circumscribed mass was resected from the wall of the stomach. Your slide is from the initially resected lesion. (Contributed by Dr. L. B. Kahn, New Hyde Park, NY)

CASE #16

An 82-year-old male was found to have two retroperitoneal tumors. One lesion measured 19x17x13.2 cm, and weighed 2600 gm; the other appeared grossly to be lipomatous, measured 5.5x5.2x3.5 cm, and weighed 49 gm. (Contributed by Dr. T. R. Hallin, Waconia, MN)

CASE #17

Five weeks prior to admission, this 55-year-old mailman first noticed a painless hard mass in his right shoulder. He had sustained "trauma" to the region about a year previously as a consequence of being caught in the elevator doors while engaging in delivering mail. A 6.0 cm mass was found to be fixed to the deltoid muscle and was locally excised. (Contributed by Dr. L. B. Kahn, New Hyde Park, NY)

CASE #18

This 8-year-old male was admitted for excision of cutaneous tumors involving the left ear and finger. At the age of one year, he was noted to have swollen gums and over the years has had excisions of tumors from the forehead, right toe, right and left ear and the right occipit. A brother has similar lesions. (Contributed by Dr. L. B. Kahn, New Hyde Park, NY)
CASE #19

The patient, a 5-year-old male, was first seen at the Mayo Clinic in July 1980. He had not been eating well for five months and had had a low-grade fever in the afternoons for three weeks. He presented with a temperature of 102 and appeared ill and dehydrated. Chest x-ray showed a mass replacing the right upper lobe of the lung. Additional findings included: clubbing of the fingers, increased immunoglobulins, increased sedimentation rate, anemia and thrombocytopenia.

On 7-29-80 the patient underwent right upper lobe lobectomy. A 11x7x7 cm mass completely replaced the right upper lobe. The right lower lobe and right middle lobe were normal. The surgeon noted that the lesion did not involve the anterior or posterior mediastinum but did extend to intimately involve the hilus of the lung and that some of the lesion was left behind. The patient recovered without complications and did well until 2-26-82 when he was noted to have a recurrence of the lesion. A 4x3x2 cm mass was found in the superior segment of the right lower lobe. The mass extended across the fissure onto the lateral segment of the middle lobe. The mass was resected. The patient again recovered without complication and did well until 8-7-84 when another recurrence was detected by chest x-ray. A 3.5x3x3 cm mass around the previous staple line was found in the apex of the right lower lobe. The lesion extended to the chest wall and infiltrated the intercostal muscle. The chest wall margin was re-excised and examined microscopically. It was found to be negative.

Because of the multiple recurrences and the fact that the intercostal muscle was infiltrated by the lesion, the patient received a course of ancillary radiation therapy in November, 1984. He was last seen on December 19, 1984. He was well with a persistent Horner's syndrome. Chest x-ray showed a cavity in the right upper thorax with a fluid level but there was no suggestion of recurrent lesion. (Contributed by Dr. H. A. Carpenter, Mayo Clinic)

CASE #20

This 13-year-old female was in apparent good health until the day before admission when she noted chest pains during a game of soccer. The pain was aggravated by deep inspiration. A chest roentgenogram revealed an anterior mediastinal mass. At thoracotomy, a right upper lobectomy was performed. The lobe contained a large mass with a necrotic and mucoid cut surface. (Contributed by L. B. Kahn, New Hyde Park, NY)
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<td>Myxoid variant of malignant fibrous histiocytoma of the lung</td>
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Case 1

AGGRESSIVE OSTEOBLASTOMA

The biopsy shows an osteoblastic neoplasm composed of a network of woven bone trabeculae of fairly uniform thickness separated by a cellular, fibrovascular stroma containing plump mesenchymal cells and numerous osteoclasts. The bony trabeculae are all rimmed by a layer of large, polygonal (epithelioid type) osteoblasts. A liberal sprinkling of mitotic figures is noted amongst the osteoblastic and stromal cells. These features, taken in conjunction with the radiologic appearance, are quite typical of an osteoblastoma. About 40% of osteoblastomas involve the posterior elements of the spine. The histologic features of an ostoid osteoma are quite similar but can be readily distinguished by its smaller size and densely sclerotic periphery.

The distinction of osteoblastoma from a low-grade osteosarcoma may on occasion be difficult but is of the utmost importance. Radiologically, the majority of osteoblastomas are well-circumscribed, radiolucent lesions and may show surrounding sclerosis and patchy central sclerosis whereas osteosarcomas show poor circumscription with evidence of irregular sclerosis and lysis. However, in about one-quarter of cases, the osteoblastoma may have a disturbing radiologic appearance while osteosarcoma may on occasion appear deceptively benign. The table enumerates the histologic features which distinguish the two lesions.

Several variants of osteoblastomas with atypical features have been described. Dorfman and Weiss have coined the term aggressive osteoblastoma to describe a lesion in which the osteoblasts are large and polygonal with prominent nucleoli (epithelioid osteoblasts) and in which brisker mitotic activity is noted within these cells and within the stromal cells. Such features were noted in the present case. In about one-half of the aggressive osteoblastomas documented by Dorfman and Weiss focal areas of ostoid deposition with a disturbing lace-like or sheet-like pattern were also observed. Osteoblastomas with these features have a considerable potential for recurrence but do not have metastatic potential. The term malignant osteoblastoma, suggested for such lesions by Schajowicz is therefore, inappropriate. Fifteen of 58 (26%) osteoblastomas in the series of Dorfman and Weiss were categorized as aggressive; seven of these developed recurrences (cf. a recurrence rate of only 1 15% in the usual type of osteoblastoma). The concept of aggressive osteoblastoma is complicated by a recent publication of Bertoni et al. in which they claim that all such aggressive osteoblastomas are in fact osteosarcomas mimicking osteoblastomas and document seven mortalities amongst 17 such lesions. However, all lesions were culled from the Mayo clinic and consultation files with an already established diagnosis of osteosarcoma. Rare examples of evolution of an osteoblastoma into osteosarcoma have been described and are more appropriately termed malignant transformation of osteoblastoma. Mirra has described a benign-behaving osteoblastoma in which the tumor cells showed extreme nuclear pleomorphism in the absence of any mitoses and suggested the term pseudomalignant osteoblastoma.
### Case 1

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<th><strong>HISTOLOGIC FEATURES</strong></th>
<th><strong>OSTEOMA</strong></th>
<th><strong>OSTEOSARCOMA</strong></th>
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<td><strong>Osteoid &amp; Bone Matrix</strong></td>
<td>Regular, thick, of uniform width.</td>
<td>Irregular &amp; much variation in size; delicate linear or lace-like formations and expansive sheets.</td>
</tr>
<tr>
<td><strong>Stroma</strong></td>
<td>Of similar width to the bone trabeculae; vascular with numerous osteoclasts.</td>
<td>Irregular in width; more cellular and less vascular; osteoclasts irregular in distribution.</td>
</tr>
<tr>
<td><strong>Cartilage</strong></td>
<td>Absent (except in presence of pathologic fracture with callus formation).</td>
<td>Frequently present with/without cytologic atypia.</td>
</tr>
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<td><strong>Margin of Lesion</strong></td>
<td>Sharp circumscription from adjacent uninvolved bone and narrow spaces; shell of reactive bone frequently present.</td>
<td>Tendency to infiltrate into marrow spaces between bone lamellae.</td>
</tr>
<tr>
<td><strong>Osteoblasts</strong></td>
<td>Plump &amp; active but lack true anaplasia; uniform rimming of bone trabeculae; mitoses sparse and normal.</td>
<td>Cellular anaplasia; less uniform rimming of bone matrix; mitoses numerous and may include abnormal forms.</td>
</tr>
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REFERENCES:


Case 2

FIBRO-OSSEOUS LESION OF MANDIBLE/DESMOPLASTIC FIBROMA

Histologically, this lesion shows areas of moderately cellular fibroblastic and collagenous tissue, within which are irregular spicules of woven bone resembling Chinese script characters. Rimming by plump osteoblastic cells is an inconstant feature of the lesion. In some areas, there is an absence of bone formation, and the lesional tissue is less cellular and more collagenous, resembling a fibromatosis.

The differential diagnosis would include the fibro-osseous lesions, (fibrous dysplasia and ossifying fibroma) and desmoplastic fibroma.

Fibrous dysplasia (cranio-facial dysplasia) is believed to be a developmental malformation and is usually diagnosed during the first two decades. In the jawbones, its radiologic appearance is that of a somewhat ill-defined lytic lesion with a ground-glass appearance. It may insinuate between and wrap around the roots of the teeth without causing root erosion or tooth displacement. Histologically, the woven bone trabeculae appear to arise directly from the stromal cells and are not rimmed by plump osteoblasts. The lesions grow slowly and tend to stabilize early in adult life. Surgery may be required for cosmetic or functional purposes and should be deferred until active growth phase has slowed. A shave down procedure is usually performed. By contrast, ossifying (and cementifying) fibromas are considered to be true neoplasms occurring over a wide age range with a peak in the third and fourth decade and involving the mandible with greater frequency than the maxilla. The mandibular premolar-molar area is the most common location. Radiologically, the lesions are lytic, with or without a calcified component, well-delineated and may expand the involved bone. Displacement of teeth and even root resorption may be seen. Histologically, ossifying fibroma is distinguished from fibrous dysplasia by the presence of a layer of plump osteoblasts adjacent to the bony trabeculae. The overlapping histologic features of fibrous dysplasia and ossifying fibroma are such that an attempt to distinguish these lesions on a purely histologic basis is usually not possible. Ossifying fibroma is usually readily enucleated because of its sharp circumscription. The terms 'aggressive' or 'active' or
'juvenile' ossifying fibroma have been variously applied to lesions which clinically exhibit rapid growth and reach large size as well as to histologically more cellular lesions with plump osteoblasts and thin 'streams' of osteoid. Some authorities consider juvenile active ossifying fibroma and osteoblastomas to be the same entity. Lesions of this type may recur following local removal.

The desmoplastic fibroma is considered to be the osseous analogue of the soft tissue desmoid. Most of the cases occur during the first three decades and in the jawbones, the mandible is more frequently involved than the maxilla. The lesion is much less common than the fibro-osseous lesions, to date only a handful of cases having been documented in the jawbones. Radiologically, the lesion is lytic and expansile with well-defined trabeculated margins. Grossly, it has the firm, white, rubbery texture of a fibromatosis and histologically resembles its soft-tissue counterpart. Its distinction from a low-grade fibrosarcoma may be difficult but the absence of mitotic activity, cellularity and cellular anaplasia should aid in distinguishing these lesions. Despite its radiologic circumscription, the lesion tends to infiltrate between lamellar bone at the margins so that recurrence may follow incomplete curettage or resection. The recurrence rate from all sites in reported cases is about 10%.

REFERENCES:


Case 3

SIGNET-RING CELL LYMPHOMA

The scalp lesion is a lympho-reticular neoplasm composed of sheets of atypical lymphoid cells with somewhat irregular nuclei and containing scanty mitoses. A notable feature is the presence of numerous Russel-like bodies within the lesion; the nuclei within the Russel-body containing cells are compressed to the periphery to produce a 'signet-ring' cell appearance. Scanty mature plasma cells are also noted. Our histochemical studies showed intense granular PAS-positive staining of the Russel-bodies and their precursors while immunoperoxidase stains demonstrated monoclonal IgM-\lambda staining of these same structures.

This lesion would fall into the category of an immunoglobulin secreting B cell lymphoma (lymphoplasmacytoid immunocytoima of Lennert). The present case
is distinguished by the fact that the secreted immunoglobulin (Ig) is retained within the cytoplasm to produce the Russel-body phenomenon with no evidence of a monoclonal hyperglobulinemia. Three specific lesions may be responsible for such a pattern - myeloma, diffuse well-differentiated lymphocytic lymphoma (DWDL) with plasmacytoid differentiation and a signet-ring cell lymphoma. The morphology of the neoplastic cells is more consistent with a follicle center cell lymphoma than with a myeloma or a small cell lymphocytic lymphoma, while the monoclonal IgM production would be unusual for a myeloma. Immunoglobulin producing DWDLs frequently have associated hyperglobulinemia.

Seven examples of a signet-ring cell lymphoma were first described by Kim et al. in 1978, and to date, 29 cases have been documented. These lymphomas are all of follicle center cell type and the majority have a nodular or a nodular and diffuse pattern. The retained intracytoplasmic Ig produces a peripheral displacement of the nucleus with either a clearing of the cytoplasm (signet-ring cell) or a dense eosinophilic inclusion (Russel-body). Kim et al. chose to categorize both cellular types as signet-ring cell lymphomas. The clear cell type shows only a paucity of cells exhibiting PAS positive staining and corresponding monoclonal Ig staining, usually of IgG type. Ultrastructurally, the inclusions take the form of compact masses of even-sized microspherules or vesicles. In the Russel-body type, numerous cells show both PAS positivity and corresponding Ig staining, usually of IgM type. Ultrastructurally, the bodies are homogeneous and electron dense bounded by a membrane derived from the endoplasmic reticulum. Three of the original seven cases of Kim et al. were of this latter type. Weiss et al. reported two signet-ring cell lymphomas of the clear cell type which proved to be of T cell origin and suggested that the microspherules found in the clear cell variant may be of lysosomal origin. While the presence of the retained Ig appears to confer no special prognostic significance to the lymphoma, its recognition is important in order to avoid misdiagnoses, in particular metastatic signet-ring cell carcinoma and liposarcoma.

REFERENCES:

Case 4

PRIMARY T CELL LYMPHOMA OF THE STOMACH

At laparotomy, this patient was found to have extensive involvement of the stomach as well as segmental involvement of his small bowel by diffuse non-Hodgkin's lymphoma of mixed small and large lymphoid cell type. Immunologically,
the tumor cells stained positively for pan-T surface markers. Small numbers of polyclonal reactive B cells and larger numbers of histiocytic cells were admixed with the tumor cells.

Only a few isolated examples of primary T cell lymphomas of the gastrointestinal tract have been documented. Foucar et al. described an epitheliotropic lymphoma of the jejunum composed of T cytotoxic-suppressor cells and they drew attention to epitheliotropic properties of normal T suppressor cells in the gastrointestinal tract. Primary T cell lymphomas have also been documented twice in the oropharynx, once in the stomach and four times at unspecified sites in the gastrointestinal tract. Peripheral T cell lymphomas and leukemias are derived from post-thymic T cells and include peripheral node-based lymphomas (T-zone lymphomas; multilobated large cell lymphomas; lympho-epithelioid cell lymphomas), cutaneous T cell lymphomas; Japanese non-Hodgkin's lymphomas/leukemia and T chronic lymphatic leukemia. Involvement of the gastrointestinal tract at the time of presentation is extremely uncommon in any of the above but has been documented in 12% of one series of Japanese T cell lymphomas.

Considerable controversy exists concerning the histogenesis of primary gastrointestinal lymphomas (PGL) occurring in Westernized, developed countries. Lymphoid cells, plasma cells or true histiocytes have been proposed by various authors as the cell of origin of the majority of such lymphomas. We have performed a retrospective, immunohistochemical study of 76 primary gastrointestinal lymphomas. The majority of our cases stained (27) negatively or could not be classified because of bitypic staining for kappa and lambda, 22 marked as B cells and 7 cases stained positively for one or more of the three histiocytic enzymes studies. An interesting observation was the demonstration of numerous admixed reactive histiocytes in 20 of the 76 cases (histiocyte-rich lymphomas).

REFERENCES:


Case 5

MALIGNANT LYMPHOMA OF SKIN

This section from a large scalp nodule in a 66-year-old male shows features of a primary epitheliotropic lymphoma of probable T cell origin. It is composed of a dense dermal infiltrate of predominantly atypical, fairly monotonous, lymphoid cells with smaller numbers of more mature-looking small lymphocytes. There is an infiltrative growth pattern splaying dermal collagen bundles and permeating subcuticular fat. Mitoses are readily identifiable. Two distinctive features indicative of a T cell derivation include the prominent migration into
Case 5

COMPARISON OF SKIN LYMPHOMAS OR B AND T CELL ORIGIN

B Cell

Clinical:
Uniform. Single or multiple, reddish nodules without ulceration.
Confined to one region.
Early & frequent neoplastic nodal involvement.
Short history (1-2 yrs).

Morphologic:
Subepidermal grenz zone.
Nodular, dense, infiltrate in mid- and deep dermis.
Monomorphic infiltrate; spectrum of B cell types.

T Cell

Polymorphic. Patches, plaques & nodules with ulceration.
Disseminated.
Late & infrequent neoplastic nodal involvement.
Long history (5-20 yrs).

Epidermotropism (exocytosis).
Band-like infiltrate in mid- and upper dermis.
Polymorphic infiltrate; neoplastic cells with mixed inflammatory cell infiltrate; may be many epithelioid histiocytes; may be so numerous as to simulate a granulomatous disease; prominent nuclear convolutions in neoplastic cells.
the overlying epidermis (epitheliotropism, exocytosis) and the extreme degree of nuclear convolution exhibited by the majority of the neoplastic cells (Lutzner cells, cerebriform nuclei).

Lymphomas are considered to be primary in the skin when this constitutes the only or the initial site of involvement. Primary lymphomas of the skin are second only to the gastrointestinal tract as the most frequent site of primary extranodal involvement and skin involvement is said to occur in about 20% of all non-Hodgkin's lymphomas. Lymphomas of the skin can be categorized in those of B and those of T cell origin. The table lists some of the chief distinguishing features. Small cleaved cell lymphomas of B cell origin (poorly differentiated lymphocytic of Rappaport) and non-epidermotropic T cell lymphomas may be difficult to distinguish without recourse to immunologic studies. It is also important, when performing immunologic studies, to remember that non-neoplastic activated T cells may constitute from 20 to 50% of the cell population in some B cell lymphomas. Iwashara and Hashimoto have studied the nuclear contour index (NCI) of the neoplastic T lymphocytes as well as of non-neoplastic lymphocytes in inflammatory dermatoses. They concluded that a NCI of > 6.5 in >25% of a pan-T monoclonal antibody positive cell population is highly suggestive of cutaneous T cell lymphoma. Recently van den Oord et al. described 5 cases of lymphomas involving both skin and nodes and composed of T helper cells. Morphologically, the infiltrate has the polymorphic characteristics and neoplastic nuclear irregularities described in other nodal peripheral T cell lymphomas.

Lymphomas need be distinguished from a variety of non-neoplastic inflammatory or pseudo-lymphomatous lesions. The latter can usually be distinguished by the presence of a mixed inflammatory cell infiltrate and reactive germinal centers, and the absence of a population of monomorphic atypical lymphoid cells. In B cell lymphomas, the demonstration of the clonality of the cells by immunoperoxidase techniques could establish their neoplastic or inflammatory nature. A light chain ratio of at least 10:1 should be observed in lymphomas whereas the ratio should not exceed 5:1 in pseudolymphoma. In conditions where the infiltrate is composed primarily of mature-looking small lymphocytes and/or plasmacytoid cells, the distinction of lymphomas of small cell type from conditions such as lymphocytic infiltration of Jessner or lymphocytoma cutis may be extremely difficult. The demonstration of monoclonal surface antigen using frozen sections and monoclonal antibody could be very helpful in suggesting a diagnosis of lymphoma in such cases. In conditions such as lymphomatoid papulosis and actinic reticuloid, the dermal infiltrate may be quite atypical and simulate a lymphoma, especially of T cell type so that careful clinico-pathologic correlation is imperative.

REFERENCES:
Case 6

CHRONIC LYMPHATIC LEUKEMIA COMPLICATED BY

Richter's Syndrome or Hodgkin's Disease

This case presents an interesting diagnostic challenge. A patient with documented chronic lymphocytic leukemia (CLL) associated with IgM gammopathy develops rapidly enlarging axillary adenopathy. Histologically, the nodal architecture is effaced by sheets of fairly mature-looking lymphocytes but containing moderate numbers of large atypical cells, some of which are binucleate and have prominent eosinophilic nucleoli. Irregular fibrous bands also transverse parts of the node. Does this represent Hodgkin's disease (HD) developing in a patient with CLL or does this represent transformation of neoplastic lymphoid cells into immunoblastic forms [Richter's syndrome (RS)]?

Richter's syndrome was first documented in 1928 and should be suspected when a patient with CLL develops weight loss, lymphocytopenia and a persistent febrile illness associated with localized adenopathy and monoclonal gammopathy (IgM). Histologically, the transformed lymphoid cells (immunoblasts) may bear a close resemblance to Hodgkin's and Reed-Sternberg type cells. Lennert noted the development of this syndrome in 3.8% of his autopsied cases of CLL. Several examples of HD complicating CLL have been described; the presence of irregular fibrosis within these nodes and the polymorphic cell population including epithelioid histiocytes, eosinophils and plasma cells are said to help in distinguishing this lesion from RS. It is possible that some of these cases may, in fact, be examples of RS. Modern immunologic techniques should facilitate this distinction by demonstrating monoclonal B cell markers showing an identity with the CLL cells in cases of RS in contrast to the demonstration of a set of markers which have been demonstrated in Reed-Sternberg cells. The latter include the presence of intracytoplasmic albumin, both light chain types, IgG and IgA, histiocytic enzyme markers (alpha-a-antitrypsin, muramidase) and the presence of Leu M1 antigen. In this case, we were able to demonstrate the presence of Leu M1 antigen in many of the multinucleated tumor cells. A few large lymphoid cells demonstrated monoclonal lambda light chain. Negative results were obtained for kappa light chain, IgM, IgG, IgA, albumin, muramidase and alpha-1-antitrypsin. These findings indicate the presence of Hodgkin's disease complicating chronic lymphocytic leukemia.


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**Case 7**

**PARAGANGLIOMA OF THE CAUDA EQUINA**

Histologically, this intradural tumor attached to the filum terminale presents an interesting diagnostic challenge. In areas the tumor has an adenoid and papillary configuration. The lining of these structures is composed of one to several layers of uniform cuboidal type cells and the central connective tissue core contains endothelial-lined vascular structures and acellular connective tissue showing hyaline and mucinous change. These features are suggestive of a myxo-papillary ependymoma. The bulk of the tumor, however, is composed of more solid nests of these cells separated by dilated sinusoidal type vascular channels, a pattern very suggestive of paraganglionic tumor. Mature neurons and intermediate forms may be seen in about one-half of the cases.

The cells of a cauda equina paraganglioma may exhibit argyrophilia and are strongly positive for neurone specific enolase and neurofilament protein by immunoperoxidase techniques. Many also showed somatostatin or serotonin reactivity. Ultrastructurally, the cells contain dense-core neurosecretory type granules ranging from 100 to 400 nm in diameter. A feature unique to cauda equina paragangliomas is the presence of whorled intracytoplasmic filament bundles. The ependymal cells may exhibit positive staining for glial-fibrillary acidic protein. Ultrastructurally, numerous microvilli are present on the luminal surface with only rare cilia. There may be complex cellular interdigitations with cellular attachments of zonula adherens type. The cells are delimited on their outer surface by a continuous, well-formed undulating basement membrane with additional electron-dense basement-material applied to the surface, a feature linked to the normal structure of filum terminale and conus medullaris. The immunohistochemical and ultrastructural findings in this case confirm a diagnosis of paraganglioma.

Paragangliomas are uncommon neoplasms of the extraadrenal paraganglionic system and most commonly arise from the carotid body or glomus jugulare. The paraganglionic tissue is composed of collections of neural-crest-derived,
neurosecretory, chemoreceptor cells of the autonomic nervous system associated with blood vessels, cranial nerves, sympathetic ganglia and visceral organs. Cerebrospinal axis paragangliomas are extremely rare and have been described in the pituitary and pineal glands and in the cauda equina and filum terminale. Lerman et al. recognized the first case involving the cauda equina in 1972 and by 1985, a total of 24 such cases had been documented. Sonneland et al. have since documented the largest series of 30 such cases. The tumor is intradural and extramedullary in location and is attached to the conus medullaris, filum terminale, nerve roots or vascular pedicle. Its slow growth is associated with insidious onset of symptomatology resulting from cord or root compression. Symptomatology includes low back pain and sensory and/or motor deficit affecting lower limbs, bladder and rectum. These tumors are non-functional although biogenic amines have been demonstrated in a single case. The rarity of and unfamiliarity with this lesion has resulted in misdiagnoses such as 'secretory ependymoma' and metastatic carcinoma. The tumor must also be distinguished from a capillary hemangioblastoma. Complete resection has been possible in most cases; incomplete resection necessitates postoperative radiotherapy and long term follow-up because of danger of late recurrence (10% of all cases) and extradural extension (9% of all cases). Sonneland et al. reported cures following resection in all of 24 patients whose tumors were encapsulated and showed no more than secondary attachment to caudal nerve roots.

REFERENCES:


Case 8

NEUROEPITHELICOMA OF SOFT TISSUES
(Primitive neuroectodermal tumor)
(Malignant neuroepithelioma)
(Peripheral neuroblastoma)

Classical neuroblastoma is a neoplasm of infancy and childhood originating from the adrenal medulla or from the autonomic nervous system in the posterior thorax or posterior abdomen. An identical tumor has been described within the brain and, rarely, within the peripheral soft tissue and skeleton. The first documentation of such a peripherally located neuroblastoma was that of Stout
in 1918. The peripheral neuroblastoma may occur in children or adults and is located most commonly in the soft tissues of the lower extremity or trunk. Histologically, it is a small round cell tumor whose infrequency, unusual location, and age distribution may cause difficulties in distinguishing it from other small round cell tumors. The most distinctive light microscopic features include formation of Homer-Wright rosettes and a fibrillary matrix. Occasionally, tumor cells may show ganglionic differentiation. Areas of tumor necrosis are common. Neurone specific enolase has been demonstrated by immunoperoxidase techniques in most of these tumors while electron microscopy has revealed neuritic cell processes with neurofilaments and neurotubules as well as dense core neurosecretory type granules. Jaffe et al. demonstrated the development of elongated neuritic processes in long term cell cultures from peripheral skeletal neuroblastomas.

The differential diagnosis includes embryonal rhabdomyosarcoma, skeletal and extraskeletal Ewing's sarcoma, lymphoma, and metastatic small cell carcinoma. While the light microscopic features of peripheral neuroblastoma should be sufficiently distinctive to indicate the appropriate diagnosis, immunohistochemical and ultrastructural studies will demonstrate many differences between these lesions (table).

The histogenesis of Ewing's tumor remains enigmatic and the possibility of its representing an extremely undifferentiated or primitive form of a neuroectodermal tumor has been raised. Evidence for such a hypothesis includes the presence of rosettes in some cases, the demonstration of neuroectodermal antigens on Ewing cell lines and a genetic translocation, t(11:22), demonstrated in both Ewing's and peripheral neuroblastoma. The small cell tumor described by Askin et al. involving the thoraco-pulmonary region may be closely related or identical to the peripheral neuroblastoma. In 50% of the cases, structures suggestive of Homer-Wright rosettes were seen and ultrastructural study of a few cases showed neuroepitheliomatous differentiation.

REFERENCES:


## Case 8

### Differential Features of Small Round Cell Tumors

<table>
<thead>
<tr>
<th></th>
<th>Glycogen</th>
<th>Immunohistochemistry</th>
<th>Electron Microscopy</th>
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<tbody>
<tr>
<td>Peripheral neuroblastoma</td>
<td>Scant/absent</td>
<td>Neurone specific enolase.</td>
<td>Neurotubules &amp; filaments, Dense core granules.</td>
</tr>
<tr>
<td>Ewing's sarcoma</td>
<td>Abundant</td>
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<td>Glycogen, Scanty desmosomes.</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Absent</td>
<td>Immunoglobulins, B or T cell markers.</td>
<td>Polar mitochondria, Ribosomes.</td>
</tr>
<tr>
<td>Metastatic small cell carcinoma</td>
<td>Absent</td>
<td>---</td>
<td>Scanty dense core granules, May show squamous or glandular differentiation.</td>
</tr>
<tr>
<td>Embryonal rhabdomyosarcoma</td>
<td>Present</td>
<td>Myoglobin.</td>
<td>Actin-myosin filaments, Sarcomeric differentiation</td>
</tr>
<tr>
<td>Merkel cell tumor</td>
<td>Absent</td>
<td>Neurone specific enolase.</td>
<td>Peripheral dense core granules, Paranuclear filament bundles.</td>
</tr>
</tbody>
</table>
HEPATOBlastOMA

Hepatoblastomas occur before the age of five years, the majority before the age of two years, and they are far less frequent than neuroblastoma and Wilms' tumor. They are usually detected as an abdominal mass and take the form of a solitary mass lesion. Histologically, several types have been described. The embryonal type is composed of sheets or trabeculae of immature epithelial type cells which bear little resemblance of mature hepatocytes. Tubular rosette and pseudorosette-like structures may be observed. The fetal type is composed of cords of liver cells two or more plates in thickness clothed by endothelial cells and resembling fetal liver cells. A distinctive feature of this type is the presence of extramedullary hematopoiesis. An anaplastic type is composed of uniform sheets of primitive cells resembling neuroblastoma cells. The mixed type contains features of either embryonal or fetal types together with a malignant mesenchymal component. The mesenchyme frequently contains osteoid but hardly ever produces cartilage or skeletal muscle elements. Neuroectodermal elements in the form of tubules and even ganglion-like cells have been demonstrated in the present case. The latter were identified utilizing an immunoperoxidase stain for neuron specific enolase. It would be of interest to assess the frequency of this phenomenon in view of the presence of rosette-like structures in embryonal hepatoblastomas and the neuroblastomatous appearance of the anaplastic type.

Hepatoblastomas need to be distinguished from hepatocellular carcinoma occurring in children. The latter usually occur after the age of five years, tend to form multiple tumor masses, microscopically resemble adult hepatocellular carcinomas and have a dismal prognosis. A variant of hepatocellular carcinoma characterized by nests and cords of large polygonal eosinophilic cells with prominent eosinophilic nucleoli and separated by lamellated bands of fibrous tissue has been referred to as polygonal cell type with fibrous stroma or fibrolamellar carcinoma. It occurs in adolescents and young adults with equal sex distribution and has a much higher operability rate and longer average survival time (± 3 years) than hepatocellular carcinoma of the usual type. Teratomas, usually benign, may also occur in the liver but can be distinguished from mixed hepatoblastomas but the presence of derivatives of all three germ layers and the absence of hepatocytic elements.

Hepatoblastomas may be associated with a number of features, notably osteoporosis, isosexual precocity and hemihypertrophy. Early diagnosis may be facilitated by the finding of raised serum levels of alpha-fetoprotein and alpha-1 antitrypsin and the presence of cystathioninuria.

The overall mortality rate from hepatoblastomas has ranged from 60-80%. The prognosis has been uniformly poor in the anaplastic and embryonal forms, but has been relatively favorable in the fetal type. Kasai and Watanabe demonstrated metastases at autopsy in 80% of the embryonal type but in only 29% of the fetal type. Following resection of the fetal type, prolonged survival has been documented in 45% or more of such cases. The presence of mesenchymal elements with osteoid appears to have no adverse effect on prognosis. Radiotherapy has not proved to be of value and too few cases are yet available to assess the value of combination type chemotherapy.
REFERENCES:


Case 10

NEUROTHEKEOMA

This tumor located in the dermis and subcutis is composed of highly distinctive round or ovoid nests of cells. Individual cells vary from spindle to epithelioid forms and are loosely set in an acid-mucopolysaccharide-rich stroma. The cell nests are delineated by delicate fibrous stroma. There is usually little cellular atypism and a paucity of mitoses. Nerve twigs may be found at the periphery of the tumor with tumor cells in close apposition but axons have not been demonstrated within the body of the tumor. The tumor is separated from the overlying epidermis. These features are diagnostic of neurothekeoma of the skin, a term derived from the Greek word 'sheath' and coined by Gallagher and Helwig to draw attention to the apparent relationship of this tumor to Schwann cells of peripheral nerves. Atypical features in some cases may create more difficulty in recognizing this lesion. These include a more diffuse rather than nested growth pattern and the presence of cellular atypism and even mitotic activity. The present case shows considerable pleomorphism and some mitotic activity. Ultrastructural examination has shown prominent folding of the plasma membrane and the presence of basement membrane, features consistent with Schwann cell derivation. However, the absence of S100 protein in this case and the demonstration of perineural fibroblasts ultrastructurally in other neurofibromas with tactile-like structures suggest that the perineural fibroblast may be the dominant cell comprising the tumor.
In a large series of 53 cases from the AFIP, over 70% of the cases occurred under the age of 30 years with a 4:1 F:M ratio and over 70% involving the face, arm and shoulder regions. Recurrences were noted in only two incompletely resected lesions; all other cases pursued a benign course.

This tumor needs to be distinguished from several other lesions, in particular, neurofibromas with a loosely myxoid or plexiform pattern and Pacinian neurofibromas. The Pacinian neurofibroma is also characterized by discrete nests of concentrically arranged spindle cells but the nests are said not to be mucin-rich and they are set in a background of typical neurofibromatous tissue. The nests may be cellular or may be composed of thin fibrous lamellae perhaps corresponding to be embryologic development of the Vater-Pacinian corpuscle between the fourth and seventh month of fetal life. Several of the cases in the literature described as Pacinian neurofibromas appear to be identical to the neurothekeoma. However, neurofibromas of all types have cells with delicate fibrillar processes producing a neurofibrillary background, a feature not present in neurothekeomas. The nerve sheath myxoma is the lesion that most closely resembles a neurothekeoma; indeed Gallagher and Helwig believe these two entities may overlap. Typically, the myxoma is more deeply located, and its component cells small and stellate rather than spindle-shaped and epithelioid. Angervall et al. studied two such cases and suggested a perineurial cell origin on the basis of the ultrastructural findings. Both tumor were positive for S100 protein. A neuronevus usually shows junctional activity and contains melanin pigment. Fibrohistiocytic lesions in the skin usually have ill-defined stellate margins rather than the nodular and circumscribed margins of a neurothekeoma.

REFERENCES:


Case 11

PRIMARY INSULAR CARCINOID OVARY

This solid unilateral ovarian tumor has a tan-yellow cut surface and is composed of islands of uniform polygonal cells with regular, round nuclei and coarsely clumped chromatin and well-defined cell borders. Well-formed glandular
lumina are present within the cell masses. Many of the cells, especially towards the periphery of the island, contain reddish-brown granules in the infra-nuclear portion of their cytoplasm. These proved to be argyrophilic and argentaffilic. Serotonin as well as a wide range of peptides associated with the APUDoma series have been demonstrated within the cells by immunoperoxidase techniques. These features are characteristic of an insular type carcinoid.

It is important to distinguish between primary and secondary ovarian carcinoids. The former are usually unilateral and are seldom associated with evidence of metastasis. A majority of primary ovarian carcinoid tumors constitute portion of a teratoma and, in a small percentage, a dermoid cyst or mucinous tumor is present in the contralateral ovary. The carcinoid may also be associated with thyroid tissue (ovarian strumal carcinoid). Secondary ovarian carcinoids are usually bilateral and unassociated with other neoplastic elements. There are frequently metastases elsewhere in the abdomen. The presence of bilateral ovarian carcinoids should always prompt careful search for an intestinal primary. The majority of primary ovarian carcinoids behave in a benign fashion with a 95% five-year survival rate. In the present case, the lesion was unilateral but was associated with a small peritoneal nodal metastasis. Manifestations of the carcinoid syndrome have been observed in about one-third of patients with primary insular ovarian carcinoids. This occurs in the absence of metastatic disease as the ovarian venous drainage bypasses the portal circulation.

Ovarian carcinoids are of three different histologic types. The insular type corresponds to a mid-gut type carcinoid in that it contains pleomorphic dense-core granules. The trabecular type has a ribbon-like pattern and contains uniform round dense core granules as is seen in fore-gut carcinoids. The goblet cell carcinoid (adenocarcinoid) is composed of a mixture of enterochromaffin and the usual enteric type of carcinoma cell. Goblet cell carcinoids behave in a much more aggressive fashion.

The insular pattern of the insular carcinoid is closely mimicked by the granulosa cell tumor. However, attention to cytologic detail will reveal somewhat grooved nuclei and ill-defined or absent cell borders in granulosa cell tumors. The Call-Exner bodies differ from the glandular lumina of the carcinoid in that they are formed by cell degeneration and so lack the well-defined limiting membrane of a gland lumen. Cytoplasmic granularity is absent in granulosa cell tumors. Ultrastructurally, granulosa cell tumors have nuclear invaginations, zonula adherens type cells junctions, scanty rough endoplasmic reticulum, mitochondria with lamellar cristae, whorled cytoplasmic filaments and a limiting basement membrane. The Call-Exner bodies are composed of cellular organelles resulting from disintegrating cells.

REFERENCES:

Case 12

BASAL CELL HYPERPLASIA OF PROSTATE

In this slide, crowded prostatic acini are filled with basaloid-looking cells with a well-defined palisaded peripheral layer. Individual acini are surrounded by fibromuscular prostatic stromal elements in an essentially undisturbed epithelial-stromal relationship. Cytologically, the basal cells are uniform, well polarized and lack mitotic activity. These features are quite typical of basal cell hyperplasia (BCH) of the prostate.

Basal cell hyperplasia of the prostate has only recently been brought to attention in the literature in a publication of 13 cases by Cleary et al. All patients were over the age of 60 years and the lesions were found incidentally in association with typical benign glandular hyperplasia and frequently showed transitional features with that lesion. Basal cell hyperplasia is frequently multinodular. In addition to the histologic features described above, basal cell nests may show central lumen formation and even differentiation into secretory glandular cells lining such lumina. These basal cells derive from the basal layer of the double-layered prostatic acini, and these cells have been referred to as myoepithelial or reserve cells. However, ultrastructurally they show none of the characteristics of myoepithelial cells but resemble primitive basal or reserve cells of stratified epithelia. Indeed contractile function in the prostate is effected by stromal myogenic cells rather than ductal or acinar myoepithelial cells. Dermer has shown that these basal cells stain well with toluidine blue in 1% epon embedded sections in contradistinction to secretory cells which remain unstained. Tritiated thymidine uptake studies demonstrated that proliferative activity was confined to these cells. Immunoperoxidase stains for prostatic specific antigen and prostatic acid phosphatase have been negative.

The importance of recognition of this lesion is in avoiding a misdiagnosis of prostatic carcinoma, a diagnosis initially rendered in a number of these cases. Transitional and squamous cell metaplasias may bear some resemblance to this lesion but the maturation into cells with more abundant cytoplasm and the frequent association with prostatic infarction should make for easy recognition. Transitional cell carcinomas arising within prostatic ducts show cytologic atypism and mitotic activity. There are isolated reports of circumscribed prostatic neoplasms with basaloid features. They differ from basal cell hyperplasia in that they produce a distinct tumor nodule and the induced fibromyxoid stromal component is devoid of myogenic cells. The presence of a cribriform pattern in some cases has led to a diagnosis of adenoid cystic carcinoma although the typical hyaline cylinders, hyaline basement membranes and perineural space invasion have not been present. In addition, evidence of clinically aggressive behavior has not been demonstrated in these cases. Reed has described similar cases and has preferred the non-committal term, adenoid basal cell tumor. A single case of a malignant tumor of the prostate with histologic features of a malignant mixed tumor of salivary gland type has been described and an origin from ectopic serous-mucinous prostatic glands postulated. In that case, areas resembling adenoid cystic carcinoma were described.
REFERENCES:


Case 13

PAPILLOMA OF THE BREAST

This solitary papillary lesion of the breast shows typical histologic features of a benign papilloma. The following features need to be carefully examined in order to distinguish papilloma from papillary carcinoma. The most important is the preservation in the papilloma of a biphasic cell population of epithelial and myoepithelial cells throughout most of the lesion although, in areas, oblique sectioning as well as a predominant growth of one of the cell types may produce a more uniform cell population. In papillary carcinoma, a monotonous proliferation of only one cell type is seen although a flattened preserved myoepithelial layer may persist at the periphery. In the papilloma, individual papillae are well supported by fibrovascular connective tissue stalks, a feature frequently but not always absent in papillary carcinoma. The absence of connective tissue support results in the formation of more solid or cribriform areas of growth as well as formation of intraluminal bridging, so-called Roman bridge effect. It also results in a tendency for loss of cellular cohesion with isolated or groups of cells floating free in the lumen as well as the development of ischemic necrosis of groups of cells. In papilloma, there is a tendency to hyaline sclerosis at the periphery of the lesion with entrapment of epithelial structures mimicking carcinomatous invasion but the entrapped epithelium shows progressively atrophic change. In invasive papillary carcinoma, the invasive elements are not atrophic and induce a more cellular fibroblastic desmoplasia. Foci of apocrine metaplasia are common in duct papillomas and absent in papillary carcinoma. At the cytologic level, the papillomas are composed of bland myoepithelial and secretory cells with a paucity of mitoses; papillary carcinoma are composed of cells with enlarged nuclei with coarse, hyperchromatic features and readily identifiable mitoses. Abnormal mitoses are found only in carcinoma.

There are three major papillary lesions confronting the surgical pathologist. The solitary duct papilloma is usually a solitary lesion arising from the extra-lobular duct system and in about 90% of cases is located close to the nipple and areola. Clinically, about 90% present with a blood nipple discharge and about 50% as a palpable mass. The lesion is usually only a few millimeters in
diameter but bleeding may produce a larger cystic structure. Localization by
the surgeon using point pressure to induce a discharge from the affected duct
and careful probing and dissection of that duct system should be followed by
careful opening and exposure of the duct by the surgeon and/or pathologist.
It is probably unwise to freeze entire small lesions, thereby excluding any
possibility for examination of unfrozen tissue. There is controversy in the
literature concerning the significance of such lesions. However, a majority
of publications indicate an incidence of associated or subsequent cancer risk
no greater than matched controls. Underdiagnosis of papillary carcinomas as
duct papillomas as well as overdiagnosis of papilloma as carcinoma on the
basis of pseudo-invasion account for some of the reports of high incidence of
carcinoma in association with duct papilloma.

The second lesion is duct papillomatosis (multiple papillomas), in which
multiple grossly visible duct papillomas arise from the extralobular duct
system. Such lesions are extremely rare as attested to by the paucity of
publications dealing with series of such cases. The majority of these lesions
are more peripherally located in the breast. Histologically, the lesions are
identical to the solitary lesion described above and they are usually unassociated
with florid forms of fibrocystic disease. Histologically, foci of papillary
carcinoma have been described in association with a significant number of these
lesions (15 of 39 cases (38%) in Haagensen's series, 6 of 21 (29%) in the series
of Murad et al., and in 5 of 15 (33%) in the series of Ohuchi et al.) The last
named authors used a loborous serial sectioning technique to study the lesions
in their entirety. These patients are prone to develop local recurrence
following conservative surgery although careful post-operative follow up may
obviate the need for more radical procedures such as simple mastectomy.

The third lesion is the association of microscopic papillomatosis associated
with the fibrocystic disease complex and which is not considered to have any
premalignant biologic potential. The term papillomatosis is also frequently
loosely used to refer to the solid and cribriform epitheliotic lesions in the
fibrocystic disease complex.

REFERENCES:

1. Ohuchi N, Abe R, Kasai M. Possible cancerous change of intraduct papillomas
   of the breast. A 3-D reconstruction study of 25 cases. Cancer 54:

2. Murad TM, Contesso G, Mouriesse H. Papillary tumors of large lactiferous

3. Azzopardi JG. Papilloma and papillary carcinoma. In: Problems in Breast
   Pathology, Vol. 2, Major Problems in Pathology, (Bennington JL, ed.)

Case 14

SEBACEOUS CARCINOMA OF THE EYELID

This slide shows a subepidermal tumor composed of nests of malignant epithelial cells, in which some of the more centrally placed cells show a coarse vacuolization of the cytoplasm, presumably lipidic in nature. These features are characteristic of a sebaceous gland carcinoma of the eyelids. Such tumors may arise from Meibomian glands located within the tarsus, glands of Zeis at the lid margin and those associated with the caruncle, eyebrow and fine hair follicles throughout the cutaneous surface of the lids. They constitute about 1% of eyelid neoplasms.

Clinically, they present as a nodule in the eyelid and are frequently misdiagnosed initially as a chalazion. The tumor may also be mistaken clinically for blepharitis of conjunctivitis, especially in the presence of pagetoid spread to the conjunctival epithelium. Histologically, the tumor may be mistaken for other neoplasms whose cells have clear cytoplasm. Eccrine sweat gland tumors, squamous carcinomas and metastatic renal cell carcinoma may have clear cytoplasm due to abundant glycogen storage but the cytoplasm is uniformly clear and lacks the coarse vacuolated appearance of sebaceous gland carcinoma. Metastatic histiocytoid breast carcinoma may also mimic a sebaceous neoplasm. Balloon cell nevi and melanomas have finely vacuolated cytoplasm and other melanocytic features. The pagetoid spread of sebaceous carcinoma may result in a confluent epidermal growth mimicking Bowen's disease so that such an appearance in the presence of an underlying nodular lesion should always raise the suspicion of a sebaceous carcinoma. Pagetoid spread in sebaceous carcinoma is a frequent occurrence and was observed in 16% of 104 cases reported by Rao et al.

Sebaceous carcinoma is an aggressive lesion with a propensity to local recurrence, regional node metastases in the pre-auricular and upper cervical region and even, rarely, distant metastases. The local recurrence rate is between 20 to 30%, rate of lymph node metastasis about 20% and the mortality rate has varied from 6 to 40%. In a detailed analysis of 104 cases by Rao et al., a number of parameters were found to be of prognostic significance. Of these, pagetoid invasion was associated with a 59% mortality rate (cf 11%). Other adverse prognostic features included larger size (> 1 cm), multicentricity, highly invasive growth pattern and poor differentiation. These tumors require a wide local excision and the presence of orbital extension or extensive pagetoid spread probably necessitates orbital exenteration. It is of interest that sebaceous carcinoma arising in an extra-ocular location is exceedingly rare and behaves in a relatively benign fashion. The incidence of local recurrence is low and metastases are exceedingly rare.

REFERENCES:


Case 15

MELANOTIC SCHWANNOMA

This pre-vertebral mass was unassociated with any visceral organ and is composed of an admixture of rather uniform, polygonal cells as well as ovoid or spindle-shaped cells with prominent dendritic processes. Mitoses are infrequent. Many of the cells are heavily melanin pigmented. The diagnosis that perhaps first comes to mind is metastatic malignant melanoma but the presence of dendritic cells, the lack of significant anaplasia and the paucity of mitoses argue against such a diagnosis. A malignant melanoma may also originate from the adrenal medulla but this tumor was not associated with adrenal tissue. In fact the features are quite typical of a rare tumor sharing histogenetic features of both melanocytes and Schwann cells. Ultrastructurally, in this and all other cases so studied, the tumor cells have been shown to contain melanosomes in all stages of maturation (melanocytic features), as well as formation of complex interdigitating cell processes intimately invested by basal lamina and occasionally associated with 1050 Å periodicity collagen (Luse body) in the stroma (Schwannian feature). Immunohistochemically, positivity for both neurone-specific enolase and S-100 protein has been demonstrated.

As of 1984, 22 cases of melanotic Schwannoma had been reported, the majority (12) arising from spinal nerve roots and causing a variety of sensorimotor deficits. Six were of peripheral soft tissue origin and single cases were reported in the acoustic nerve, heart, esophagus and mandible. The patients ranged in age from 10 to 59 years. Follow-up was available in 13 cases, all of whom were alive and well; three had had local recurrences.

Eight examples of a tumor with identical histologic features but arising from the sympathetic chain have been reviewed by Krausz et al. in 1984. The prognosis was found to be very poor in the tumors arising in this location, 6 of the 8 having died with widespread metastases. These lesions have been termed malignant melanotic Schwannoma by Krausz et al.

The histogenesis of this group of tumors has stimulated much speculation. The common derivation of melanocytes and Schwann cells from the neural crest suggests that an uncommitted stem cell may differentiate simultaneously along a melanocytic and neurogenous pathway. A more plausible theory favors a progressive transformation of a neurogenic tumor into a melanocytic tumor. Experimentally, Spence et al. have induced such aberrant differentiation of
Schwann cells into melanocytic cells with the application of ethylnitrosourea in rats. A third but unlikely histogenesis suggest simultaneous proliferation of two cell populations, melanocytic and Schwannian.

REFERENCES:


Case 16

DEDIFFERENTIATED LIPOSARCOMA

The two slides submitted from this large retroperitoneal tumor show two distinctly different patterns, namely, a lipomatous tumor containing a predominance of mature lipocytes with a few admixed atypical lipoblastic cells and a highly cellular undifferentiated sarcomatous tumor. This juxtaposition of well-differentiated liposarcoma with undifferentiated sarcoma has been referred to by Evans as dedifferentiated liposarcoma (DL), analogous to the dedifferentiated chondrosarcoma.

These DLs constituted 8 of 55 cases (14.5%) of liposarcomas reviewed by Evans from the MD Anderson Hospital over a 27 year period. The dedifferentiated component may be present in the initial lesion and/or in the recurrences. Recurrences tend to show a predominance of the undifferentiated element and metastases are composed exclusively of this element. Histologically, in addition to the undifferentiated sarcomatous pattern of the undifferentiated element as seen in this case, the pattern may also be that of a typical malignant fibrous histiocytoma. The dedifferentiated component may be recognizable grossly as a more solid, fleshy area. All DLs occurred in the retroperitoneum. The other type occurring in this location is the well-differentiated form. All liposarcomas in this location tend to have a high local recurrence rate with the tendency towards lack of control of these recurrences. Metastases are uncommon and were noted in only 2 of the 8 DLs in Evans' series.
The most frequent type of liposarcoma is the myxoid liposarcoma, which constituted 29 of Evans' 55 cases (53%) and they are all located in the limb or limb girdle. These myxoid tumors are composed of stellate mesenchymal cells set in a mucin-rich stroma. Of particular importance in establishing a diagnosis of myxoid liposarcoma is the rich capillary network (chicken-wire effect) and the presence of cells with multiple cytoplasmic (lipid) vacuoles, some of which produce nuclear indentations (pseudonuclear vacuoles). This type exhibits two histologic features which may lead to a misdiagnosis. Pooling of mucin results in formation of pseudoacinar patterns and a mimicry of a lymphangitis or lymphangiosarcoma, while interstitial hemorrhage creates a resemblance to a vascular neoplasm. The mucinous ground substance is hyaluronidase-sensitive. Myxoid liposarcomas have a significant potential for both local recurrence and blood-born metastases. Metastases are prevalent in the soft tissues and these have been interpreted as multicentric lesions. Excision followed by radiation has resulted in a significantly reduced rate of local recurrence as compared with excision alone. The round cell type of the Enzinger-Winslow classification is uncommon and Evans believes these cases merely represent more cellular variants of myxoid and pleomorphic liposarcomas. The well-differentiation liposarcoma has been described as occurring predominantly in two locations, the extremities and the retroperitoneum. Histologically, they resemble their benign counterparts except for mild nuclear irregularities and occasional lipoblasts. The extremity lesions never metastasize but may, on occasion, recur locally usually following the passage of several years. For this reason, Evans prefers to regard the tumor in that location as an atypical lipoma. The retroperitoneal lesions, by contrast, are aggressively recurring lesions as described above. Histologic variants of the well-differentiated lesion in the retroperitoneum include an inflammatory variant with an admixture of inflammatory cells including foamy histiocytes, a sclerosing variant with densely collagenized relatively sparsely cellular areas and a mixed well-differentiated/pleomorphic variant. The pleomorphic liposarcoma is a rare type (4 of 55 in Evans' series) with a highly cellular, pleomorphic histologic appearance, including many bizarre vacuolated tumor giant cells. Such lesions may involve the extremities or retroperitoneum and have a high metastatic rate.

Liposarcoma needs to be differentiated from other sarcomas, notably malignant fibrous histiocytoma, as well as from a variety of benign lesions with prominent myxoid and/or atypical lipogenic features (pleomorphic, spindle cell and myxoid lipomas, lipoblastomatosis and mucoid-rich variant of nodular fasciitis. The most useful special techniques for identifying lipoblastic cells include stains for neutral lipid and electron microscopy. Ultrastructurally lipoblasts have non-membrane bound cytoplasmic lipid vacuoles and basal-lamina material.

The chief prognostic parameters are the histologic type and the location. Location in the retroperitoneum as mentioned previously is associated with a less favorable outcome (39% 5-year survival rate in the AFIP series as compared with a 71% 5-year survival rate for other locations).

REFERENCES:


Case 17

NODULAR FASCIITIS

(Pseudosarcomatous fasciitis)
(Infiltrative fasciitis)
(Pseudosarcomatous fibromatosis)

This is a characteristic example of a mucin-rich variant of nodular fasciitis, one of a group of reactive or reparative soft tissue lesions that, histologically, may be readily confused with a sarcoma. This group of lesions share in common a history of trauma in a minority of cases and the rapid development of a soft tissue nodule or mass within days to weeks. The lesions are usually less than 6 cm in greatest dimension and tend to have ill-defined stellate margins. Histologically, the lesions resemble actively proliferating granulation tissue, the most distinctive cell being a plump fibroblastic cell frequently showing myofibroblastic ultrastructural features. The cellularity, poor circumscription and frequent brisk mitotic activity of the lesion constitute the reasons for the pathologist's misdiagnosis of sarcoma in some instances. However, careful attention to the clinical features, the small size of the lesions, the histologic resemblance to actively proliferating granulation tissue, and an absence of anaplasia should obviate incorrect histologic diagnoses. The following is a brief resume of the distinguishing features of each of the types within this group.

Nodular fasciitis. This is by far the most frequently occurring lesion in the group. It involves mainly the upper half of the body and is associated with a preceding history to trauma in only 10-15% of cases. The lesion is attached to fascial sheaths of muscle and usually extends into the subcutis or less commonly into muscle. Histologically, it has a loose textured ('feathery') appearance due to an abundance of ground substance between the proliferating fibroblasts and capillaries. A sprinkling of chronic inflammatory cells is also present. Malignant, fibrous and cellular variants have been described but it is common to see a range of such patterns in individual lesions.

Proliferative myositis. The fibroblastic proliferation involves the endo-, peri- and epi-mysial connective tissues causing wide separation of groups of muscle fibers as well as separation of individual fibers from one another within fascicles, producing a checkerboard pattern. Muscle fibers are spared but may show some atrophic changes. A characteristic feature is the presence of large ganglion-like cells amongst the proliferating fibroblasts. Despite their resemblance to regenerating rhabdomyoblasts, they have been shown ultrastructurally to be fibroblasts or myofibroblasts. In a minority of cases, small
foci of ossification may be seen within the lesion creating a resemblance to myositis ossificans.

Proliferative fasciitis. This lesion shares features in common with both nodular fasciitis and proliferative myositis. Its location and overall histologic appearances are those of nodular fasciitis but, like proliferative myositis, it contains numerous large ganglion-like fibroblastic cells.

Parosteal fasciitis. This is histologically identical to nodular fasciitis but arises from periosteum and is associated with either cortical sclerosis or erosion of underlying bone.

Cranial fasciitis of childhood. This occurs in infants and young children, histologically resembles nodular fasciitis and is associated with a scalloping or defect in the outer table of the cranial bone.

Intravascular fasciitis. In this variant, part or all of the lesional tissue is present within vascular channels.

REFERENCES:


Case 18

JUVENILE HYALIN FIBROMATOSIS
(Fibromatosis hyalinica multiplex juvenalis)
(Drescher-Murray syndrome)

The clinical and histopathologic features in this case are characteristic of juvenile hyalin fibromatosis. It is an extremely rare familial probably autosomal recessive disorder first described by Murray in 1873. Clinically, it is characterized by the presence of widely disseminated multiple dermal and subcutaneous, and osteolytic tumors occurring during the first few years of life. The head is disproportionately involved. It may be associated with thickening of the gums, joint contractures, and mental retardation. The lesions are indolent, non-recurrent and non-regressive. Histologically, spindle shaped fibroblastic cells
<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>Location</th>
<th>Solitary</th>
<th>Multiple</th>
<th>Recurrence</th>
<th>Regression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrous hamartoma</td>
<td>B-2</td>
<td>Axillary &amp; inguinal regions</td>
<td>+</td>
<td>-</td>
<td>Rare</td>
<td>-</td>
</tr>
<tr>
<td>Infantile myofibromatosis</td>
<td>B-2</td>
<td>Soft tissue, bone &amp; viscera</td>
<td>+</td>
<td>+</td>
<td>Rare</td>
<td>+</td>
</tr>
<tr>
<td>Fibromatosis coli</td>
<td>B-2</td>
<td>Sternocleidomastoid muscle</td>
<td>+</td>
<td>Bil.</td>
<td>Rare</td>
<td>+</td>
</tr>
<tr>
<td>Digital fibromatosis</td>
<td>B-2</td>
<td>Fingers &amp; toes</td>
<td>+</td>
<td>+</td>
<td>Common</td>
<td>+</td>
</tr>
<tr>
<td>Infantile desmoid-type fibromatosis</td>
<td>B-5</td>
<td>Musculature</td>
<td>+</td>
<td>-</td>
<td>Common</td>
<td>-</td>
</tr>
<tr>
<td>Calcifying aponeurotic</td>
<td>2-A</td>
<td>Hands &amp; feet</td>
<td>+</td>
<td>-</td>
<td>Common</td>
<td>+</td>
</tr>
<tr>
<td>Hyalin fibromatosis</td>
<td>2-A</td>
<td>Dermis &amp; subcutis</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
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</table>

(B - birth; A - adult life; Bil - bilateral)
singly or in small groups are separated by an abundant 'hyalinized' matrix. Ultrastructurally, the spindle-shaped cells have been shown to contain membrane-bound globules filled with delicate 70Å fibrils in a whorled configuration. Some of these balls have racket-like handles which appear to be continuous with prominent Golgi tubules and suggest an origin therefrom. The cells also contain prominent profiles of rough endoplasmic reticulum containing finely granular material. The abundant intercellular matrix is comprised of three elements - copious fine 70Å fibrils similar to those seen in the fibril-filled balls, scanty regular 640Å collagen fibrils, and scattered profiles of long-spaced collagen. These ultrastructural features suggest a disordered maturation in the development of the collagen fibers. However, biochemical analysis in a single case has demonstrated a normal pattern of type I and III dermal collagen.

Several other fibromatosus proliferative disorders occurring in infancy and childhood are listed in the table. Infantile myofibromatosis is the only other fibromatosis which manifest with multiple dermal and subcuticular nodules. It has also been described under the terms congenital generalized and solitary fibromatosis, diffuse congenital fibromatosis, congenital fibrosarcoma, multiple congenital neoplasms of soft tissues, benign mesenchymoma, multiple mesenchymal hamartoma, generalized hamartomatosis, and multiple vascular leiomyomas of soft tissue. The lesion usually manifests in infants or neonates as solitary or multiple nodules within the skin or muscle which tend to regress in time. In the multicentric form, lytic bony lesions with a sharply-defined sclerotic margin may occur. The multicentric form may also involve the viscera and such involvement may presage a fatal outcome. The disease is thought to be inherited as a Mendelian dominant trait with low penetrance or as a polygenic form of inheritance. Histologically, the ill-defined nodule is composed of a uniform population of plump, fibrocytic-type cells infiltrating skeletal muscle. The cells are arranged in interlacing fascicles of moderate cellularity. There are occasional mitotic figures but none are abnormal. An important diagnostic feature is the presence of hemangioendothelioma-like areas towards the center of the lesion. The entity has recently been renamed infantile myofibromatosis because of the ultrastructural demonstration of the myofibroblastic nature of the tumor cells. It is of utmost importance not to mistake these and other similar lesions in infancy and childhood for fibrosarcomas. Despite their cellularity, mitotic activity and even foci of necrosis and intravascular extension, they have no metastatic potential.

REFERENCES:


Case 19

PLASMA CELL GRANULOMA OF LUNG

Plasma cell granuloma of the lung is an inflammatory tumor mass of variable size arising within the lung and it may occur at any age. If located
near the pleural surface it may become adherent to the chest wall as in the present case and if located near a main bronchus, it may present as an endobronchial lesion. In some of the cases, a preceding history of a pulmonary infective process is obtained and suggests a post-inflammatory etiology for the disease.

The mass is composed of a variable admixture of reparative and inflammatory cells and the predominance of one or other cell type accounts for the many terms used to designate the lesion. All contain prominent fibroblastic and vascular endothelial elements with a variable admixture of inflammatory cells. The fibromatous element may proliferate in a storiform configuration. A heavy preponderance of plasma cells, mast cells or histiocytes have resulted in usage of the terms, plasma cell granuloma, mast cell granuloma and xanthogranuloma (fibrous histiocytoma) respectively. Other terms used include pulmonary endothelioma and inflammatory pseudotumor. Resection of the lesion is usually curative.

In the differential diagnosis, an organizing pneumonia, especially an aspiration or obstructive type lipid-pneumonia may show histologic similarities to plasma cell granuloma. However, that lesion does not usually form a tumor-like mass. True fibrohistiocytic tumors of the lung have been described but are extremely rare (see case 20 of this seminar). In a series of 27 pulmonary plasma cell granulomas described by Spencer, two showed areas of the tumor in which a sarcomatous element was present and the author postulated an evolution from an inflammatory proliferative process to a malignant neoplastic process. Unfortunately, no follow-up was provided in these two cases. Another pulmonary lesion with which pulmonary plasma cell granuloma has been confused is the sclerosing hemangioma of the lung. These two lesions are probably quite unrelated to one another. Sclerosing hemangioma of the lung also forms a tumorous mass in the lung, often with a hemorrhagic spongy consistency. Histologically it has three main elements: Multiple spaces, often blood-filled are lined by plump alveolar pneumocytes; there are also papillary projections lined by the pneumocytes into these spaces; the vascularized septa separating the spaces are of variable thickness and in places infiltrated by sheets of uniform, polygonal cells with abundant pale cytoplasm and well-defined borders. The histogenesis of these cells is in dispute with electron microscopic studies claiming a type II pneumocytic, endothelial or histiocytic origin. Fibrosis within the septa may be prominent and entrap nests of the polygonal cells and even single cells. In some cases, an intense infiltration of mast cells is also seen. The pathogenesis of this lesion is also obscure and removal of the lesion results in cure. Sclerosing mediastinitis may produce a histologic picture very similar to pulmonary plasma cell granuloma but the lesion is primarily mediastinal in location and may be associated with sclerosing lesions in other locations such as retroperitoneum and biliary tree.

REFERENCES:

Case 20

MYXOID VARIANT OF MALIGNANT FIBROUS HISTIOCYTOMA OF THE LUNG

This large, circumscribed tumor had a frankly gelatinous and necrotic cut surface. Histologically, it contains elements which clearly identify it as being of fibrohistiocytic derivation. The predominant cell is a spindle-shaped cell arranged in a fasciculated and vaguely storiform pattern. In addition, numerous foamy histiocytes of both uni- and multi-nucleate type are present. An admixture of moderate numbers of inflammatory cells (lymphocytes, plasma cells and eosinophils) completes the cellular elements of the lesion. In many areas, an abundant acid-mucopolysaccharide-rich stroma is being produced by fibrohistiocytic cells with copious foamy cytoplasm. Large areas of tumor necrosis are seen.

There are only two possible diagnoses for this lesion. The first is the inflammatory pseudotumor of the lung (xanthogranuloma, plasma cell granuloma), the commonest tumor in the lung in children. It is thought to represent a localized inflammatory reaction rather than a true neoplasm. Histologically, it may show all the features enumerated above except for the presence of extensive necrosis. A single example with a richly mucoid matrix producing a gelatinous cut surface as in the present case has been described. In addition, fibrosis may be prominent and variants rich in plasma cells or in mast cells are well recognized. The correct diagnosis in this case is myxoid variant of malignant fibrous histiocytoma (MFH). This shares all of the features described in the inflammatory pseudotumor but can be distinguished from that entity by the presence of frank tumor necrosis, numerous mitoses and cellular atypism in areas with a more monomorphic sarcomatous appearance. Less than 10 cases of primary pulmonary MFH have been reported, all in adults; only one of these was of the myxoid type. Several of these cases had died of their disease with widespread metastases.

A number of histologic variants of MFH have been described:

Inflammatory variant. This variant described by Kyriakos and Kempson is characterized by an intense infiltration of the tumor by acute and chronic inflammatory cells. Its behavior is no different from that of the usual MFH.

Myxoid variant (myxofibrosarcoma). Enzinger and Weiss described a myxoid variant in which 25% or more of the lesion was composed of loose mesenchymal cells in a myxomatous stroma. The significance of this variant resided in its improved prognosis (23% metastatic rate) as compared to the usual MFH (42% metastatic rate) and even within this subtype, an inverse relationship between quantity of myxoid element and metastasis was noted. In order to ensure prognostic relevance of this variant, Enzinger and Weiss recommended that the lesion be so diagnosed only when 50% or more of the lesion had myxoid features. It is also important to distinguish the lesion from other highly myxoid lesions such as nodular fasciitis, intramuscular myxoma, myxoma of the jaw, and myxoid variants of liposarcoma. This is usually easily achieved by examining an adequate number of sections and demonstrating areas of typical MFH. Lipoblast-like cells with coarse cytoplasmic vacuolization may be seen in this lesion but these vacuoles contain acid-mucin rather than neutral fat. In this regard it should be mentioned that hybrid tumors with features of both MFH and liposarcoma can occur.
Angiomatoid variant. This most recently described variant of MFH occurs as a nodular, subcutaneous tumor during the first to third decades. Histologically, there are hemorrhagic spaces within the tumor associated with accumulation of hemosiderin and lipid, and infiltration of many inflammatory cells, predominantly lymphocytes and plasma cells. The cellular component of the lesion in composed of fibroblastic and histiocytic type cells, the latter often phagocytic for hemosiderin and lipid. There is a variable degree of pleomorphism and mitotic activity. The characteristic storiform pattern of MFH is rarely seen. The lesion, in Enzinger series of 24 cases, had a high recurrence rate (50%) but metastases occurred in only five patients.

Retroperitoneal variant. This lesion, first described by Oberling as a xanthogranuloma of the retroperitoneum, is also associated with a prominent inflammatory cell infiltrate. Lesions with obvious histologic malignant features behave like other deep seated MFHs but even lesions with a histologically bland appearance resembling a retroperitoneal inflammatory mass may behave aggressively.

Giant cell type (malignant giant cell tumor of soft parts). This variant contains numerous benign appearing osteoclast type giant cells and resembles an osteoclastoma of bone.

With regard to prognosis of MFH, the review of 200 cases from the AFIP demonstrated a 44% local recurrence rate and a 42% rate of metastasis. The lungs (82%), lymph nodes (32%), liver (15%) and bone (15%) were the most frequent sites of metastasis.

REFERENCES: