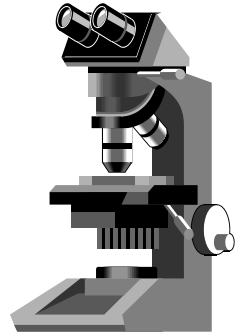


CALIFORNIA
TUMOR TISSUE REGISTRY

SOFT TISSUE PATHOLOGY

Minutes – Subscription A

October 2015



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FILE DIAGNOSES

CTTR Subscription A

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CASE #1:

Accession No. 31733

DIAGNOSIS: INTRAMUSCULAR MYXOMA, Thigh

Diagnoses submitted in decreasing order of frequency:

- Intramuscular Myxoma
- Myxoma
- Myxofibrosarcoma, low grade
- Spindle cell lipoma
- Liposarcoma, myxoid type

Discussion

The tumor is generally hypocellular consisting of single predominantly evenly spaced spindled and stellate cells separated by a mucoid matrix. The tumor vascularity is minimal and delicate. No mitoses or necrosis are identified. The tumor is well circumscribed, but shows peripheral skeletal muscle invasion in a “reverse honeycomb” pattern.

Intramuscular myxoma is a benign mesenchymal tumor occurring in patients 40 to 70 years of age. About two-third of patients are women. Clinically, most patients present with a painless, palpable and solitary mass that is slightly movable and fluctuant. Most frequent sites involved are large muscles of the thigh, shoulder, buttocks and upper arm. Multiple intramuscular myxomas are thought to be associated with fibrous dysplasia of the bone at same anatomic location. Activating missense mutations in the Arg201 codon of the gene encoding alpha subunit of Gs (GNAS1) have been recognized in intramuscular myxomas with or without fibrous dysplasia of bone. Microscopically, the tumor is composed of inconspicuous cells in a background of abundant mucoid material and a loose meshwork of reticulin fibers. The cellularity can be variable, but the tumor cells lack nuclear atypia and mitotic figures. The edges of the tumor usually merge with surrounding muscle fibers. Immunohistochemically, the cells may be positive for actins suggesting myofibroblastic differentiation. The mucoid background stains positive for Alcian blue and colloidal iron stains.

Differential diagnosis: Low grade myxofibrosarcoma, although this too is a hypocellular neoplasm composed of spindle cells suspended in myxoid stroma, there is cytologic atypia and prominent curvilinear blood vessels. Myxoid liposarcoma has adipocytic differentiation (with lipoblasts) admixed with a plexiform vasculature. Cellular muscular myxoma can mimic Evans tumor (low grade fibromyxoid sarcoma, LGFMS). The clue for identifying LGFMS is the swirling arrangement of tumor cells around thin-walled capillaries, presence of large collagen rosettes and the abrupt transition between fibrous and myxoid components.

CASE #2:

Accession No. 31768

DIAGNOSIS: FIBROMA, Knee

Diagnoses submitted in decreasing order of frequency:

- Fibroma of tendon sheath
- Collagenous fibroma, Desmoplastic fibroblastoma
- Fibroma
- Nodular fibroma with myxoid change
- Myxofibroma
- Fibromatosis, desmoid tumor
- Desmoplastic fibrosarcoma
- Chondroma
- Solitary fibrous tumor
- Keloid
- Leiomyoma
- Synovial chondromatosis
- Osteochondroma

Discussion

Sections demonstrate a lobulated proliferation of bland fibromyxoid tissue with low cellularity and a stellate appearance that appears to be associated with the underlying tendon tissue. No giant cell proliferation or abnormal pigmentation is seen.

Fibroma is a slowly growing, benign fibrous mass. Occasionally myxoid and cystic areas might be found. Microscopically, the tumor is composed of spindle shaped fibroblastic cells with elongated nuclei, fine chromatin and small nucleoli, but there is no cytological atypia. Some areas appear hypocellular in a myxoid or collagenous stroma. The stellate-shaped cells may be present in the myxoid zones. A characteristic feature is the presence of elongated cleft-like vascular channels lined by flattened cells.

CASE #3:

Accession No. 31976

DIAGNOSIS: JUVENILE NASOPHARYNGEAL ANGIOFIBROMA, Right Paraclival

Diagnoses submitted in decreasing order of frequency:

- Juvenile Nasopharyngeal Angiofibroma
- Nasopharyngeal Angiofibroma
- Angiofibroma
- Pyogenic granuloma
- Osteoma

Discussion

Tumor shows a fibrocollagenous stroma with thin walled open angulated vascular channels.

Nasopharyngeal angiofibroma is a benign fibrovascular tumor almost exclusively occurring in adolescent males. It usually arises from the nasopharynx and extranasopharyngeal sites such as maxillary and ethmoid sinuses. Some FAP patients also present with nasopharyngeal angiofibroma. Clinically, most patients present with nasal obstruction, repeated epistaxis and headaches. Microscopically, the tumor contains numerous staghorn vascular channels surrounded by a dense paucicellular fibrous hyalinized stroma. The stromal tumor cells are cytologically bland, occasionally spindle or stellate in shape. The open/gaping vascular channels in the central portion of tumor typically lack an elastic lamina. Immunohistochemically, the vascular endothelial cells are positive for CD31 and CD34. Tumor is positive for androgen receptors, CD117 and β -catenin. Differential diagnosis: Capillary hemangioma.

CASE #4:

Accession No. 31981

DIAGNOSIS: CAVERNOUS HEMANGIOMA, Back

Diagnoses submitted in decreasing order of frequency:

- Hemangioma
- Cavernous hemangioma
- Capillary hemangioma
- Intramuscular hemangioma
- Arteriovenous malformation

Discussion

The excised mass consisted of large thin walled vessels filled with red blood cells, consistent with cavernous hemangioma.

Cavernous hemangioma also called venous malformation is a developmental abnormality of embryonic vasculature. Clinically, the lesion is superficial, blue and puffy with an irregular surface. It is formed by large thin walled venous vessels with irregularly attenuated or disorganized walls. The vessels are sometimes grouped or haphazardly arranged in stroma. Since the blood flow is slow, thrombi and calcification usually develop. These malformations have been associated with mutations in the VMCM1 locus on chromosome 9, which results in ligand-independent autophosphorylation of the TIE-2 receptor. The gene is responsible for endothelial growth and vascular wall remodeling. Cavernous hemangiomas may be present in the eye, cerebellum and brain stem in von Hippel Lindau disease.

CASE NO #5:

Accession No. 31978

DIAGNOSIS: NEUROFIBROMA, Right Thigh

Diagnoses submitted in decreasing order of frequency:

- Neurofibroma
- Collagenous neurofibroma
- Peripheral nerve sheath tumor
- Ancient schwannoma (with myxoid change)
- Atypical neurofibroma
- Neurilemmoma
- Inflammatory (myo)hyaline tumor
- Mammary type myofibroblastoma
- Intramuscular myxoma
- Well differentiated liposarcoma
- Leiomyoma
- Cutaneous myxoma

Discussion

This patient has a clinical history of Neurofibromatosis type 1. Sections show a spindle cell proliferation comprised of medium sized cells with mild pleomorphism and hyperchromasia consistent with degenerative changes. There is background myxoid change. Mitoses are rare. No areas of malignant transformation are identified.

Neurofibroma arises within nerves and infiltrates them causing fusiform enlargement. There are three main growth patterns: localized, diffuse, or plexiform. The localized form is seen commonly as a superficial, solitary tumor. Multiple, diffuse and plexiform forms are associated with neurofibromatosis 1. Neurofibroma grows slowly as a painless nodule and is found superficially in the dermis or subcutis. Microscopically, the most characteristic features are interlacing bundles of elongated cells with wavy, darkly stained nuclei in a collagenous matrix. The vascularity is comparatively more prominent than in myxoma. A small amount of mucoid material separates the tumor cells and collagen. No Antoni A or B areas are identified. Neurofibromatosis type I is caused by a mutation of the NF1 gene in the pericentromeric region of chromosome 17, that is responsible for cell division. The mutant gene is inherited in an autosomal dominant fashion; 50% of NF1 cases arise due to spontaneous mutation. Neurofibroma is the hallmark finding in young patients with NF1.

CASE #6:

Accession No. 24556

DIAGNOSIS: SCHWANNOMA, Brachial Plexus

Diagnoses submitted in decreasing order of frequency:

- Schwannoma, neurilemmoma
- Plexiform neurofibroma
- Traumatic neuroma
- Neurofibroma
- Neuroma
- Malignant peripheral nerve sheath tumor
- Ganglioneuroma
- Lymphangioma

Discussion

Tumor shows spindle elongate, wavy tumor cells with interspersed collagen and foam cells. Unlike the previous case of neuroma this tumor shows interspersed large gaping blood vessels with hyalinized walls. Degenerative changes may be seen in long standing cases (ancient schwannomas).

Schwannoma is an encapsulated nerve sheath tumor and usually sporadic and solitary. Grossly, small nerve tumors have a fusiform shape, whereas large nerve tumors present as eccentric masses over the nerve fiber. Microscopically, the characteristic feature of classic schwannoma is a pattern of alternating Antoni A and B areas. Antoni A is composed of compact spindle cells with twisted nuclei and indistinct cytoplasmic borders arranged in short bundles or fascicles. Verocay bodies sometimes can be seen clearly. Antoni B areas are less cellular and less orderly. Large irregularly spaced vessels, sometimes with surrounding hyalinization are common features of schwannoma. Immunohistochemically, S100, SOX10 and GFAP are positive (helpful in atypical cases such as epithelial schwannoma). About 60% sporadic and NF2-associated schwannomas are associated with frame shift mutation of NF2 gene. All the schwannomas lack protein product of NF-2 gene, Merlin.

CASE #7:

Accession No. 31983

DIAGNOSIS: EXTRA-ABDOMINAL DESMOID-TYPE FIBROMATOSIS, Left Paraspinal

Diagnoses submitted in decreasing order of frequency:

- Fibromatosis, desmoid type, extra abdominal
- Gardner fibroma
- Myofibromatosis
- Proliferative myositis
- Proliferative fasciitis
- Myofibroblastic tumor
- Desmoplastic fibroblastoma
- Ganglioneuroma
- Angiomatous lesion

Discussion

Extra-abdominal fibromatosis arises primarily from muscle and overlying fascia or aponeurosis. It mainly affects the muscle of shoulder, pelvic girdles and thigh in young adults. The tumor is locally aggressive and infiltrative with firm poorly circumscribed borders and grows insidiously. Microscopically, the tumor infiltrates the surrounding muscle and is comprised of elongated slender cellular proliferation intermixed with collagen or in a myxoid matrix. The tumor cells

and collagen fibers are arranged in long sweeping bundles. At tumor periphery, multinucleated giant cells due to striated muscle fiber atrophy can be seen. Tumor cells are positive for smooth muscle actins, vimentin and nuclear beta catenin. Intraabdominal fibromatosis is associated with Gardners syndrome (FAP and multiple osteomas).

CASE #8:

Accession No. 31939

DIAGNOSIS: MONOPHASIC SYNOVIAL SARCOMA, Thigh

Diagnoses submitted in decreasing order of frequency:

- Synovial sarcoma, monophasic
- Malignant peripheral nerve sheath tumor
- Sarcoma, NOS
- Fibrosarcoma
- Malignant perineuroma
- Liposarcoma, high grade
- Low grade fibromyxoid sarcoma

Discussion

Tumor shows a spindle cell proliferation with characterisitc “marbled” appearance (alternating light and dark areas). There are loose myxoid reticulated areas as well as densely sclerotic foci. The morphology, immunoprofile as well as the 18q11 genetic test is compatible with synovial sarcoma, predominantly monophasic fibrous type.

Synovial sarcoma occurs primarily in the para-articular regions of the extremities such as tendon sheaths, bursae and joint capsules. It occurs usually in young adults with a male-to-female ratio of about 1.2. Clinically, patients present with a palpable, deep seated swelling or mass lesion. Synovial sarcoma histologically has two major categories. Biphasic synovial sarcoma has epithelial and spindle cell components. Monomorphic synovial sarcoma has either majority of monophasic fibrous type or monophasic epithelial type, but the latter one is often unrecognized in practice. Poorly differentiated synovial sarcoma presents as round cell tumor arranged in a peritheliomatous pattern. There may be hemorrhage, necrosis or calcification. Microscopically, monophasic synovial spindle sarcoma demonstrates pure fibroblast like spindle cell proliferation, which might have perivascular hyalinization, myxoid changes, mast cell infiltrate, hemangiopericytomatous vasculature, fibrosarcoma-like areas and focal calcification. The spindle tumor cells have small amount of indistinct cytoplasm and oval dark nuclei. Immunohistochemically, most synovial sarcomas are immunoreactive for cytokeratin and EMA. Monophasic type is only focal positive for CK7, CH19 AND CK8/18. Up to 30% of tumor cells are positive for S-100. CD99 positivity is detected in 60%-70%of synovial sarcomas. BCL-2 protein is diffusely expressed in all synovial sarcoma, especially in spindle cells. Ber-Ep4 is frequently positive. TLE1 can be a helpful marker to identify the cytokeratin-negative monophasic fibrous synovial sarcoma. t (X;18)(p11;q11) is found in all synovial sarcomas, which involves fusion of SS18-SSX2 or SS18-SSX1 and confirms the diagnosis.

CASE # 9:

Accession No. 31979

DIAGNOSIS: LEIOMYOSARCOMA, Vagina

Diagnoses submitted in decreasing order of frequency:

- Leiomyosarcoma, high grade
- Rhabdomyosarcoma, Pleomorphic, Sarcoma botryoides
- Leiomyoma
- High grade sarcoma
- Schwannoma, cellular
- Dedifferentiated liposarcoma
- Aggressive angiomyxoma

Discussion

Tumor consists of a cellular spindle cell proliferation , with eosinophilic cytoplasm, abundant mitoses, and nuclear pleomorphism.

Leiomyosarcoma is a rare tumor in the vagina, occurring in the third to ninth decades and usually the patient presents in advanced clinical stage. Clinically, the patient has abnormal vaginal bleeding and bulging vagina. It accounts for 8% vaginal smooth muscle tumors. Microscopically, the tumor has hypercellular appearance with mitotic rates of >5mf/HPF with cytological nuclear atypia and high Ki67. The tumor may show epithelioid cells, occasionally with signet ring appearance and myxoid stroma. Tumor necrosis may be seen, but not as often as in uterine leiomyosarcomas. Immunohistochemically, ER, PR and desmin positivity is helpful for differentiation from extra-gastrointestinal stromal tumors.

CASE #10:

Accession No. 31984

DIAGNOSIS: MYXOID/ROUND CELL LIPOSARCOMA, Left thigh

Diagnoses submitted in decreasing order of frequency:

- Myxoid liposarcoma, round cell liposarcoma, grade 2
- Liposarcoma
- Myxoid tumor
- Fibromyxosarcoma
- Myxofibrosarcoma
- Leiomyosarcoma
- Chondrosarcoma
- Chondroid lipoma

Discussion

Myxoid/round cell liposarcoma is a more aggressive variant of myxoid liposarcoma due to the admixed round cell component. The lipoblastic differentiation is rather inconspicuous. Clinically, this form of liposarcoma occurs 50s years of age and develops preferentially in the lower extremity, particularly in medial thigh and popliteal area. Microscopically, the round cell liposarcoma component tends to have comparative hypercellularity especially in the periphery of the tumor. Discrete nodules composed of sheets of primitive round cells are present arranged tightly in a background of myxoid matrix. Tumor cells are small, with enlarged and hyperchromatic nuclei. A delicate plexiform capillary vascular network (chicken wire pattern) is the clue for distinguishing these tumors from myxomas. Nearly all myxoid/round cell liposarcomas have t (12; 16) (q13; p11), which involves the fusion of DDIT3 and FUS gene. Rarely, t (12; 22) (q13; p11) or an insertion between chromosomes 12 and 16, (12; 16) (q13; p11.2p13) occurs.

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