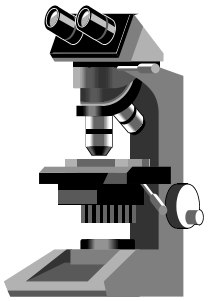
CALIFORNIA
TUMOR TISSUE REGISTRY

BONE/SOFT TISSUE PATHOLOGY

Minutes – Subscription A

MAY 2016



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FILE DIAGNOSES

CTTR Subscription A MAY 2016

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CASE #1: **Accession No. 31832**

DIAGNOSIS: OSTEOCHONDROMA, LEFT FIBULA

Diagnoses submitted in decreasing order of frequency:

Osteochondroma (articular, with focal lipomatous differentiation, exostosis)
Atypical lipoma

Discussion

Osteochondroma (OC) is the most common benign bone tumor and usually occurs in the metaphyseal region of the long bones, often at sites of tendon insertion. This tumor takes the form of a cartilage-capped bony outgrowth on the surface of the bone. Most lesions appear in children and adolescents as painless, slow-growing masses, which may be sessile or pedunculated. OC may not represent true neoplasm, it is rather a malformation resulting from displaced epiphyseal cartilage that herniates through a periosteal defect, and then continues to grow at 90 degrees to the normal growth plane. It is covered with periosteum, and grows synchronously with the epiphyseal plate during the first two decades of life.

The majority of osteochondromas present as solitary, nonhereditary lesions. Approximately 15% of cases occur in an autosomal dominant hereditary multiple osteochondromatosis / multiple hereditary exotoses disease, due to germline mutations in either of two tumor suppressor genes: EXT1 or exostosis EXT2. The EXT1 and EXT2 proteins function in the biosynthesis of heparin sulfate proteoglycans involved in growth signaling pathways of the normal epiphyseal growth plate. Reduced EXT1 or EXT2 expression in OCs is associated with defective endochondral ossification which is likely to be involved in the formation of OCs. There is as a higher risk of malignant transformation in multiple hereditary exostoses 5-10% (less than 1% in solitary cases). A thick cartilaginous cap (>20mm) should raise suspicion of malignant transformation.

CASE #2: **Accession No. 14596**

DIAGNOSIS: GIANT CELL TUMOR, TIBIA

Diagnoses submitted in decreasing order of frequency:

Giant cell tumor (aggressive, malignant)
Osteosarcoma (giant cell rich variant)

Discussion

Giant cell tumor (GCT, aka osteoclastoma) accounts for < 10% of all primary bony tumors. It is most common in young adults during the 3rd decade of life, presenting with pain or a pathologic fracture. Women are more often affected. It is more common in the far Eastern countries. It may be associated with Paget disease of bone. GCTs are usually found in the long bones, most often the distal femur, proximal tibia, and distal radius. It is unclear whether the GCT arises in the epiphysis or distal metaphysis, but GCTs only occur after the epiphyseal plates have closed. Radiologically there is a “soap bubble” appearance with a well-defined defect in the metaphysis and epiphysis, with destruction of the medullary cavity and adjacent cortex.

GCT of bone is a benign locally aggressive lesion that is a usually solitary. Rarely GCT has the potential for metastasis to the lungs where they usually behave in an indolent manner requiring no treatment. A chest CT scan is recommended for all patients newly diagnosed with GCT.

Microscopically tumor shows a regular distribution of numerous multinucleated osteoclast-like giant cells in a background of spindle shaped to epitheliod mononuclear cells. The giant cells may contain very large numbers of nuclei (10-50 or more). There are no atypical mitoses, atypia or chondroid differentiation. Necrosis and hemorrhage may be present. Giant cells are derived from blood monocytes and are acid phosphatase, lysozyme, alpha-1-antitrypsin, alpha-1-antichymotrypsin, cyclin D1, and estrogen receptor +. The spindle shaped cells are the neoplastic cells.

Differential Diagnosis: Brown tumors of hypoparathyroidism, aneurysmal bone cyst, chondroblastomas, osteoblastoma, and osteosarcoma (other giant cell tumors usually have only focal giant cells).

CASE #3: **Accession No. 31980**

DIAGNOSIS: AMELOBLASTIC FIBROSARCOMA, LEFT MANDIBLE

Diagnoses submitted in decreasing order of frequency:

Ameloblastoma (aggressive)
Ameloblastic fibroma /fibrosarcoma
Odontogenic fibroma
Adamantimoma, classical type

Discussion

This osteodestructive biphasic odontogenic neoplasm consists of a proliferation of cytologically bland ameloblastic epithelium in an abundant hypercellular (low- grade) atypical stroma, the latter showing focal peri-epithelial condensation reminiscent of a "cambium" layer.

Ameloblastic fibrosarcoma (AFS) is a rare malignant mixed odontogenic tumor, consisting of benign ameloblastic epithelium and a malignant mesenchymal stroma. AFS can arise de novo, however one-third of cases may arise from a recurrent ameloblastic fibroma (as in this patient), in which case they appear to present at an older age. Most common site is the mandible.

AFS presents as destructive expansile mass. The epithelial component consists of nests and branching cords with anastomosing strands of odontogenic epithelium exhibiting peripheral palisading. The mesenchymal cells vary from spindle to stellate and exhibit nuclear pleomorphism. The sarcomatous component of AFS is positive for p53 and shows higher Ki-67 labeling as compared to non-recurrent ameloblastic fibroma (AF). There is positive BCL-2 expression within the sarcomatous portion of the tumor, while negative in the epithelial component. This staining pattern is the opposite in AF.

Differential diagnosis: Other odontogenic sarcomas (contain dysplastic dentine or enamel and dentine), ameloblastic carcinosarcoma (both carcinomatous and sarcomatous components) and spindle cell carcinoma (biphasic tumor with squamous cell carcinoma and a malignant spindle cell components) and especially ameloblastic fibroma as a minority of AFS arise from a pre-existing AF (stroma is benign in AF).

CASE #4: **Accession No. 14595**

DIAGNOSIS: CHONDROMYXOID FIBROMA, DISTAL FEMUR

Diagnoses submitted in decreasing order of frequency:

Chondromyxoid fibroma
Fibrous cortical defect
Osteosarcoma: osteogenic pattern
Chondroblastoma
Non-ossifying fibroma
Aneurysmal bone cyst
Giant cell tumor
Osteoid osteoma
Giant cell reparative granuloma
Benign fibrous histiocytoma

Discussion

Chondromyxoid fibroma (CMF) is an extremely rare benign cartilaginous neoplasm (< 1% bone tumors). The majority of cases occur in the second and third decades. CMFs are well circumscribed, lytic lesions mostly located in the metaphyseal region of long bones. The tumor comprises a variable combination of chondroid, myxoid, and fibrous tissue components organized in a pseudolobulated architecture. Occasional osteoclast-like giant multinucleated cells are encountered particularly at the periphery. Most cells are morphologically bland, and mitotic figures are rare.

Most cases are characterized by GRM1 gene fusion or promoter swapping. It may be associated with t(1;5)(p13;p13).

Differential diagnosis: Fibromyxoma (older adults, no cartilaginous areas), chondroblastoma (not lobulated), fibrous dysplasia with myxoid change (not lobulated), chondrosarcoma (infiltrating tumor).

CASE NO #5: **Accession No. 14489**

DIAGNOSIS: EWING SARCOMA, LEFT HUMERUS

Diagnoses submitted in decreasing order of frequency:

Ewing sarcoma /PNET

Discussion

This is a distinctive small round cell sarcoma, typically found in patients 5-25 years of age. Males are more commonly affected. It is second most common malignant bone tumor in children after osteosarcoma. The pelvis, long bones of the lower extremity and humerus are most common sites. Tumors may also arise in soft tissue. It is uncommon in African Americans and Chinese populations. Genetics: t(11:22) translocation, formation of a fusion protein (EWS-FLI1). Radiologically: large destructive metaphyseal or diaphyseal bone lesions with a moth-eaten appearance, onion-skinning patterns. Microscopically tumors consist of sheets of small round uniform blue cells with scant cytoplasm and indistinct cell membranes. Stroma is scant.

Immunostains: CD 99, PAS (glycogen), NSE, FLI1 protein, vimentin +. Molecular: t(11,22)(q24;q12), t(21;22)(q22;q12) in 5-10% - ERG and EWS

Differential diagnosis: Metastatic neuroblastoma (< 5 yrs, known primary), rhabdomyosarcoma (muscle markers +), lymphoma (CD 45, CD 20+), desmoplastic small round cell tumor (t(11;22)(p13;q12), perinuclear desmin +)

CASE #6: **Accession No. 32054**

DIAGNOSIS: CALCINOSIS ("CUTIS CALCINOSIS"), KNEE

Diagnoses submitted in decreasing order of frequency:

Calcinosis (universalis, tumoral cutis, dystrophic, circumscribed)
Fat necrosis (with dystrophic calcification)
Aneurysmal bone cyst

Discussion

Calcinosis universalis is a form of secondary tumoral calcinosis with calcification in the skin and subcutis, with normal serum calcium and phosphorus levels. These multiple nodules or plaques are associated with scleroderma and dermatomyositis. Clinical and laboratory evaluation for systemic or localized connective disease can discriminate these lesions from primary tumoral calcinosis.

Tumoral calcinosis (TC) is an uncommon disorder characterized by the presence of calcified, para-articular masses. Unlike similar calcifications associated with chronic renal failure, malignancy and hypervitaminosis D, tumoral calcinosis shows no abnormalities in calcium metabolism. Non-autoimmune disease associated primary TC has been found predominantly in young male patients in Africa and some of their family members. TC usually presents as a painless solitary swelling or multiple painless swellings of large joints, particularly the extensor aspects of the hips, elbows, shoulders, and knees. There is often a history of trauma.

The white friable masses show irregular contours, and a granular, chalky cut surface. Microscopically active granulomatous lesions, acellular fibrotic areas, cystic cavities and psammoma-like bodies may be present.

CASE #7: **Accession No. 26343**

DIAGNOSIS: INTRAMUSCULAR MIXED CAPILLARY/CAVERNOUS HEMANGIOMA, BACK

Diagnoses submitted in decreasing order of frequency:

Intramascular hemangioma (venous, arteriovenous, lobular capillary)
Arteriovenous malformation (hemangiomatous), hamartoma, angiomatosis
Angiofibroma retroperitoneal
Angiomyolipoma
Hemangioendothelioma
Solitary fibrous tumor

Discussion

Intramuscular hemangiomas are benign, uncommon vascular lesions which most commonly occur in the trunk and extremities (particularly in thigh muscles). Although traditionally considered to be vascular neoplasms, most are likely arteriovenous malformations. They tend to enlarge slowly. Malignant transformation is rare. Intramuscular hemangiomas present as enlarging soft tissue masses with or without pain. 90% of the cases occur before the age of 30 years. These may be classified as capillary, cavernous, venous, and arteriovenous malformations depending on the predominant anomalous vascular channels. The vascular channels are oriented parallel to each other in a striated pattern on radiologic examination. Microscopically there is separation of muscle fibers by proliferating vessels. Angiolipomas of muscle contain a significant admixture of fat.

Differential diagnosis: cavernous hemangioma, angiosarcoma (uncommon in skeletal muscle, freely anastomosing sinusoidal pattern, atypia, high cellularity and mitoses).

CASE #8: Accession No. 32040

DIAGNOSIS: NASOPHARYNGEAL ANGIOFIBROMA

Diagnoses submitted in decreasing order of frequency:

Angiofibroma (Nasopharyngeal, Juvenile, with thrombus/embolization matter)
Solitary fibrous tumor, Hemangiopericytoma
Glial heterotopia

Discussion

Nasopharyngeal angiofibroma (NAF) is an uncommon, benign, fibrovascular tumor with a distinct predilection for adolescent males and accounts for less than 1% of all head and neck neoplasms. Tumors may be hormonally related as they show the presence of androgen, testosterone, and dihydrotestosterone receptors and lack estrogen and progesterone receptors. A diagnosis in a female patient remains controversial and should be viewed with skepticism.

Microscopically there is a mixture of stellate and staghorn blood vessels of varying caliber in a fibrous stroma. Stromal cells are stellate fibroblasts with small pyknotic to large vesicular nuclei. Mitotic figures are rare. Tumor is CD31, CD 34, beta catenin (nuclear) and androgen receptor +. CD 117 may also be +.

NAF may represent a vascular malformation. Clinically, NAF presents as a nasal mass or obstruction with repeated episodes of epistaxis. The lesion is currently presumed to arise from erectile-like fibrovascular stroma in the pterygopalatine fossa region and may proliferate into the surrounding anatomic areas. The diagnosis is usually made upon appropriate clinical history of young patient age, sex and characteristic radiographic appearance. Biopsy prior to definitive treatment is generally considered as unnecessary and potentially hazardous. Preoperative embolization of tumor is recommended to reduce the risk of intraoperative hemorrhage (as in this case). Despite an aggressive nature, and 20 - 40% recurrence rate the overall prognosis is excellent with a less than 1% mortality related to uncontrollable hemorrhage and intracranial extension. Rare cases show sarcomatous transformation after radiation therapy.

Differential diagnosis: lobular capillary hemangioma (less fibrous tissue), hemangiopericytoma /solitary fibrous tumor, and angiosarcoma.

CASE #9: **Accession No. 31916**

DIAGNOSIS: **FIBROMATOSIS, LEFT ARM**

Diagnoses submitted in decreasing order of frequency:

Fibromatosis (deep, desmoid, extra abdominal, intramuscular)
Neurofibroma
Leiomyoma, Leiomyosarcoma

Discussion

This is an example of deep musculoaponeurotic fibromatosis. These are large, aggressive, rapidly growing neoplasms with a high recurrence rate. Desmoid tumor is also used as a synonym for this type of fibromatosis. These are most common in patients 15-40 years of age. Tumors are poorly circumscribed and infiltrative. There are long interlacing bundles of bipolar fibroblasts and varying amounts of interstitial collagen with thin-walled, curvilinear or ectatic vessels. Perivascular lymphoid aggregates are present at the edges. Vimentin, CD 117, ER, nuclear B catenin +. SMA and MSA are variable.

Fibromatosis is a locally aggressive clonal fibroblastic proliferation of deep soft tissue with infiltrative growth. Fibromatosis may be associated with Gardner's syndrome/FAP syndrome, familial desmoid syndrome, endocrine factors, trauma and radiation. Prognosis depends on patient age, tumor size and site.

Differential diagnosis: Fibrosarcoma (more uniformly hypercellular, atypia, mitoses), leiomyoma (eosinophilic smooth muscle, desmin+), low grade fibromyxoid sarcoma (myxoid areas, large collagen rosettes, beta catenin -), neurofibroma (S100+, beta catenin -).

CASE #10: **Accession No. 31992**

DIAGNOSIS: PIGMENTED VILLONODULAR SYNOVITIS, LEFT KNEE

Diagnoses submitted in decreasing order of frequency:

Pigmented villonodular tenosynovitis (diffuse type tenosynovial giant cell tumor)
Lipoma arborescens with pigmented papillary synovial hyperplasia
Arterio-venous malformation
Aneurysmal bone cyst

Discussion

Pigmented villonodular synovitis (PVNS) is a rare neoplastic-like exuberant villonodular hyperplasia of synovium and tendon sheaths in young adults composed of mononuclear cells and multinuclear giant cells with hemosiderin deposition, similar to the diffuse form of tenosynovial giant cell tumor. PVNS develop in the synovial lining of joints usually of knee (80%), ankle, hip, shoulder and elbow joint. Most are

monoarticular, locally aggressive lesions which may recur. PVNS is thought to be a reactive process as half of patients report prior history of trauma to the afflicted joint. Local recurrence is common. Rare tumors are malignant (nodular invasive growth, necrosis, mitoses, cytologic atypia).

Microscopically there is papillary synovial hyperplasia, histiocytes, osteoclastic giant cell differentiation and hemosiderin-laden macrophages. Mitoses are absent/rare. Vimentin and CD 68 (giant and stromal cells) +. Molecular features: Trisomy 5 and 7, translocation and increased expression of CSF1.

Differential diagnosis: Fibrosarcoma, hemosiderotic synovitis (hemophilia, intra-articular bleeding, no mononuclear or giant cell nodular cellular proliferation), synovial sarcoma

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