The Armed Forces Institute of Pathology
Department of Veterinary Pathology
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Conference Moderator:
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CASE I: 2173 (AFIP 2790938).

Signalment: 3.5-month-old, male intact, Chow-Rottweiler cross, canine (*Canis familiaris*).

History: This 3.5-month-old male Chow-Rottweiler mixed breed dog was presented to a veterinary clinic with severe neck pain. No cervical vertebral lesions were seen radiographically. The dog responded to symptomatic treatment. A week later the dog again presented with neck pain and sternal recumbency. The nose was swollen, and the submandibular and popliteal lymph nodes were moderately enlarged. The body temperature was normal. A complete blood count (CBC) revealed a marked lymphocytosis (23,800 lymphocytes/uI). Over a 3-4 hour period there was a noticeable increase in the size of all peripheral lymph nodes. Treatment included systemic antibiotics and corticosteroids. The dog became ataxic and developed partial paralysis. The neurologic signs waxed and waned over a period of 7 days, and the lymphadenopathy persisted. The peripheral blood lymphocyte count 5 days after the first CBC was done revealed a lymphocyte count of 6,000 lymphocytes/uI. The clinical signs became progressively worse, and the dog was euthanized two weeks after the initial presentation.

Laboratory Results: Immunohistochemical (IHC) staining of bone marrow and lymph node sections revealed that tumor cells were negative for CD3 and CD79α.

Gross Pathology: Marked generalized lymph node enlargement was found. Cut surfaces of the nodes bulged out and had a white homogeneous appearance. The spleen was enlarged and meaty. The thymus was very small. There was marked thickening of the bones of the dorsal cranium (2 cm thick) and moderate thickening of the dorsal lamina of the cervical vertebrae.

Histopathologic Description: Bone, cranium: Histologically, there was a dense infiltrate of a uniform population of medium to large sized lymphocytes in the bone marrow of all sections of bone examined (including femur, sternebrae, and parietal bones). The slides submitted consist of sections of decalcified parietal bone. There was a dense infiltrate of neoplastic lymphocytes in all lymph nodes examined. The infiltrate almost completely obliterated the normal nodal architecture. Neoplastic lymphoid infiltrates were also found in sections of spleen. Microfocal neoplastic lymphoid infiltrates were present in the myocardium and in spinal nerve roots. The thymus was markedly atrophic, and there was lymphoid depletion in Peyer's patches of the small intestine.

Contributor's Morphologic Diagnosis: Lymphoma/Lymphocytic Leukemia, possible NC cell lymphoma

Contributor's Comment: This appears to be a case of polyostotic lymphoma with multiple tissue involvement and lymphocytic leukemia. The dog was reportedly initially presented with a pronounced lymphocytosis. There are reports of polyostotic lymphoma in dogs and the affected dogs have been young, most less than 1 year of age. In the one case of polyostotic lymphoma in which staining for T and B lymphocyte markers was performed, the neoplastic lymphocytes did not label positively for any of the marker antibodies tested. In the present case, the affected dog was very young (3.5-months-old) and the neoplastic lymphocytes did not stain with antibodies to T and B cell markers. Immunophenotypic characterization of lymphoma/lymphocytic leukemia in dogs has revealed that lymphomas are predominantly B-cell origin and lymphocytic leukemias are predominantly T-cell origin. A low percentage of both lymphomas and lymphocytic leukemias of dogs is composed of lymphocytes which do not stain

positively for either T-cell or B-cell markers. These "null cell" (NC) lymphocytic neoplasms are thought to be composed of very undifferentiated lymphocytes or natural killer (NK) lymphocytes. It is also possible that these tumors, although composed of cells resembling lymphocytes, are derived from a non-lymphoid hematopoietic cell line.

The neurologic signs in this dog were considered to have been primarily due to the marked thickening of cranial bones and dorsal laminae of cervical vertebrae. Presumably compression of brain, spinal cord, and/or spinal nerves was responsible for the neurologic sings, although no focal degenerative lesions were found in sections of brain or spinal cord. There were microfocal infiltrates of neoplastic lymphocytes in spinal nerve roots, and this infiltrate may have contributed to the neurologic signs. No lymphoid infiltrates were found in the brain or spinal cord.

AFIP Diagnosis: Bone, cranium (per contributor): Malignant lymphoma, with marked cortical osteolysis and periosteal and medullary new woven bone formation.

Conference Comment: Discussion in this case centered on the periosteal components and response to bone injury. The periosteum is composed of an outer fibrous layer and an inner cambium (or osteogenic) layer. The cells of the cambium layer immediately overlying the cortical bone are osteoprogenitor cells that possess the ability to differentiate into osteoblasts.[5,7] The osteoprogenitor cells in the non-reactive periosteum are spindled with flattened nuclei. The periosteum is well supplied with blood vessels, lymphatics and nerve endings.[5]

The typical response of the periosteum to trauma (i.e. fracture) involves differentiation of the osteoprogenitor cells into osteoblasts which rapidly produce new woven bone perpendicular to the cortex.[5,7] In conditions of low oxygen tension there can be an admixture or predominance of cartilage. Though woven bone tends to be the rule, the periosteal osteoblasts can produce lamellar bone when appositional growth is slow.[7] In addition to trauma, any process elevating the perisosteum from the subjacent cortex will result in new bone formation.[5] The new bone is not necessarily static; it can undergo osteoclastic resorption or form lamellar bone.[7] Under certain conditions, the periosteum can become osteoclastic in nature. Most commonly, there is osteoclastic remodeling during long bone growth resulting in diaphyseal narrowing.[7] Additionally, infections of the periosteum can result in osteoclastic bone resorption at the site of inflammation.[7]

In this case, there is expansion of both the fibrous and osteogenic layers. Conference participants speculated on the cause of the periosteal reaction, generating two possible scenarios. First, the tumor could be pushing through the cortex and elevating the periosteum. The second possibility is the mechanical effect of the overlying muscle use causing periosteal tension, separation and subsequent periosteal new bone growth.

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CASE II: R07-114 (AFIP 3103627).

Signalment: Adult, male, green iguana, reptile (*Iguan iguana*).

History: This iguana was kept indoors in a local zoo. Clinical findings included multiple skin wounds and osteolysis at 3rd to 7th tail vertebra. The animal died of unsuccessful treatment for the tail lesions.

Gross Pathology: The animal had poor overall appearance. The 3rd to 7th tail vertebrae were significantly enlarged where a pale/yellowish lesion measuring 10 cm x 5 cm x 5 cm in diameter with irregular margins was found. Smaller nodules (0.2 cm ~ 0.3 cm in diameter) were scattered throughout the liver, lungs, and epicardium. Both kidneys were pale, moderately to severely enlarged (10 cm x 4 cm x 3 cm) with numerous whitish, pinpoint spots on the capsular surface; the cut surface showed many whitish streaks. Serous atrophy of adipose tissue was observed in the whole body.

Laboratory Results: Microbiological culture: *Serratia marcescens* was isolated from the tail, liver, and lungs.

Histopathologic Description: Tail vertebra with associate skeletal muscle: The tail vertebra has irregular thickening of the periosteum and cortices with multiple irregular areas of necrosis and osteolysis of bone, and the inflammatory process extends outward into the skin. The disrupted bone spicules accompanied with proliferative cartilage and bone tissue of affected areas are characterized by hypereosinophilia or irregular calcification of the matrix. The necrotic foci are roughly nodular and contain variable numbers of epithelioid macrophages and lymphocytes surrounded by fibroblasts. Numerous osteoclast-like cells are present in the affected areas. The periosteum of the vertebra and surrounding skeletal muscle have multifocal to coalescing deposits of necrotic debris surrounded by fibrous connective tissue with inflammatory cells. Numerous colonies of rod bacteria are present in the center of the affected areas. Immature fibrous connective tissue, similar inflammatory cells and variable amounts of cellular debris have replaced the vertebral bone and surrounding skeletal muscle. The rod bacterial colonies were negative for the B&B stain. Other significant findings in this case were multifocal necrogranulomas randomly scattered throughout the lungs, liver, epicardium and stomach.

Contributor's Morphologic Diagnosis: 1. 3rd to 7th tail vertebrae: Osteomyelitis accompanied with osteolysis, necrogranulomatous, chronic, locally-extensive, severe, with intralesional bacterial colonies of Gram negative rods.

2. Tail, skeletal muscle: Myositis, necrogranulomatous, chronic, locally-extensive, severe.

3. Lungs, liver, heart, stomach: Necrogranulomatous reaction, multifocal, chronic, mild, with intralesional Gram negative rod bacterial colonies (slides not submitted).

Contributor's Comment: *Serratia marcescens*, which belongs to Enterobacteriaceae, is a motile Gram-negative coccobacillus and has been isolated from numerous reptile species. It is a common bacterium in the environment and frequently isolated in soil, water, and food. For human beings, *Serratia marcescens* is mainly an opportunistic pathogen and may cause respiratory, urinary tract, and wound infections. A case of cellulitis of human beings after an iguana bite has been reported. *Serratia* species can acquire resistance against many antimicrobial agents including cephalosporins, macrolides, and many aminoglycosides. Therefore, treatment sometimes is difficult. This organism appears to be part of the normal oral flora of several reptile species; the bacteria in this case were possibly introduced subcutaneously through a bite wound or other traumatic damage to the integument. *Serratia marcescens* has been isolated from subcutaneous granulomas in a green iguana and a northeastern spiny-tailed iguana. However, the pathogenesis of disease in the reptile could be dependent on individual factors, as mice injected intravenously with *Serratia marcescens* eventually clear the infection by the reticuloendothelial system.

AFIP Diagnosis: Bone, vertebra: Heterophilic granulomas, multiple, with periostitis, myositis and fasciitis, bone lysis, and reactive woven bone formation.

Conference Comment: Inflammatory lesions in the bone are classified by the part of the bone affected and include osteitis (inflammation of the bone), periosteitis, or osteomyelitis (involvement of the marrow cavity). The contributor provides a diagnosis of osteomyelitis.[8] Conference participants did not observe the inflammatory process within the marrow cavity, and thus preferred the histologic diagnosis of periostitis to best characterize the bone involvement in the case. Additionally, participants interpreted the most significant histologic lesions as consistent with multiple heterophilic granulomas, with the skeletal changes being secondary to the primary infection.

An interesting aspect of this case observed by the conference moderator is the presence of woven, compact periosteal new bone without prominent osteoblasts. The moderator also pointed out examples of metaplasia of

fibrous connective tissue to bone in the presence of Sharpey fiber-like insertion. Sharpey's fibers are typically seen embedded in bone matrix at the point of tendon insertion into the bone; they are histologically characterized as dense bands of connective tissue emerging from the tendon or ligament which intermingle with the outermost lamellae.[9] Sharpey's fibers are also present in the periodontal ligament where they anchor the alveolar bone to the cementum of the tooth.[9] A fibromatous epulis of periodontal ligament origin with bone-like matrix will have Sharpey's fibers extending into the surrounding connective tissue.[2]

Unlike this case, most cases of inflammation involving bone are classified as osteomyelitis. There are several anatomic and physiologic factors predisposing animals, particularly young animals, to bacterial osteomyelitis; infection often localizes in sites of active endochondral ossification of the metaphyses and epiphyses of long bones and vertebral bodies. Such factors include:[7]

- Capillaries invading the mineralized cartilage make hairpin turns prior to entering the sinusoidal vessels which communicate with medullary veins.
- Capillaries are fenestrated, allowing bacteria to easily leave the vasculature and enter the marrow cavity.
- Sinusoidal blood flow is sluggish and resident phagocytic cells are relatively inefficient.
- Trauma may alter the metaphyseal environment and enhance bacterial infection.

In addition to host factors, several pathogen factors also favor establishment of infection in the marrow. *Staphylococcus aureus* and other bacteria have receptors for bone surface proteins; bone trauma makes these binding sites more available to the bacteria. Many bacteria form a thick mucopolysaccharide glycocalyx which surrounds them and functions to allow tighter adherence to the bone surface, protects the organism from the host immune system, and inhibits uptake of antibiotics. A common finding in osteomyelitis is osteolysis. Cytokines, like tumor necrosis factor, IL-1, and prostaglandin E_2 released from inflammatory cells, activate osteoclasts.[7] Common causes of bacterial osteomyelitis in select species are as follows:[7]

- Equine: *Escherichia coli* (most common in foals); *Streptococcus* spp.; *Salmonella* spp.; *Klebsiella* spp.; and *Rhodococcus equi*
- Bovine: *Salmonella* spp.; *Arcanobacterium pyogenes*
- Canine: Rare; often in dogs that are neutropenic following infection with Canine Parvovirus-1
- Feline: *Staphylococcus intermedius*; other *Staphylococcus* spp.; *Streptococci* spp.; *E. coli*; *Proteus* spp.

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CASE III: S 688/07 (AFIP 3164801). Tissue from a pig

Signalment: 11-year-old, female, Yucatan pig, (*Sus scrofa*).

History: The animal had abrupt hind leg paresis. Radiological and computed tomographic examination revealed osteolysis of thoracic and lumbar vertebrae as well as proximal parts of the second and tenth ribs.

Gross Pathology: All thoracic and lumbar vertebrae had marked osteolysis and replacement of the bone marrow by a soft yellowish to pink mass. The spinal cord was compressed by nodules of the same mass at the second and third lumbar vertebra. The proximal end of the tenth rib had a pathological fracture and a nodule (3 × 1.0 × 0.5 cm) of soft yellowish tissue protruding into the thoracic cavity. Bone marrow of this rib was also replaced by soft yellow to pink tissue.

Laboratory Results: Lymphopenia (3.76 G/l [ref.: 6 – 16.0 G/L]); hypophosphatemia (1.75 mmol/L[ref.: 2.1 – 3.3 mmol/L]).

Histopathologic Description: Rib: The bone marrow is focally infiltrated, effaced and replaced by a non-encapsulated, poorly circumscribed, infiltrative, highly cellular neoplastic mass. Neoplastic cells form solid sheets that are supported by a moderate fibrovascular stroma. Cells are ovoid to polygonal with distinct cell borders, moderate amounts of pale eosinophilic cytoplasm, sometimes with a crescent shaped perinuclear halo. Nuclei are located eccentrically, ovoid, sometimes cleaved, and 2 - 2.5 times the size of erythrocytes in diameter (15-18 µm), with coarsely stippled chromatin and 1 to 3 mostly indistinct nucleoli. There is moderate anisocytosis and marked anisokaryosis. Mitotic rate is 1 to 2 mitoses per high power field with some atypical mitoses. There are multifocal prominent apoptotic neoplastic cells characterized by hypereosinophilia and/or nuclear fragmentation (karyorrhexis). Trabecular and cortical bone is multifocally devoid of osteoblasts and there is mild activation of osteoclasts and resorption of bone. Continuity of the cortical bone is multifocally disrupted by infiltration of neoplastic cells and pathological fractures (not visible in all slides). There is marked periosteal reactive fibroplasia sometimes intermingled with extravasated erythrocytes (hemorrhage) or necrosis. Within the fibrous tissue are multifocal infiltrates of mature lymphocytes. Adjacent to pathological fractures the neoplastic cells multifocally invade the intrathoracic adipose tissue.

Contributor's Morphologic Diagnosis: Rib: Plasma cell myeloma, with pathological fracture, callus formation and medullary cavity fibrosis (not present on all slides), Yucatan pig, porcine.

Contributor's Comment: Plasma cell myelomas (multiple myelomas) are rare neoplasms in animals other than dogs.[4] In the pig they are exceedingly rare.[3,4] Plasma cell myelomas are multicentric neoplastic proliferations of plasma cells originating within the bone marrow and usually secrete large amounts of monoclonal immunoglobulin heavy and/or light chains resulting in monoclonal gammopathy.[1] Most common sites of origin are the vertebrae, ribs, sternum and the skull.[6] An important feature of plasma cell myelomas is invasion of the adjacent bone by activated osteoclasts resulting in skeletal destruction and pathological fractures.[1] Lytic bone lesions within the spongiosa are usually crescent shaped and the corticalis is rarefied.

In humans, diagnostic criteria for plasma cell myelomas are more than 10% clonal plasma cells in the bone marrow, occurrence of monoclonal proteins in the serum and/or urine, and evidence of plasma cell neoplasia associated organ damage. The latter may include hypercalcemia, renal insufficiency, anemia, and lytic bone lesions.[1] Twelve to 15% of cases in people are accompanied by amyloid deposition due to synthesis of immunoglobulin light chains. In this pig, no amyloid deposition was noted. Rare cases of non-secretory multiple myelomas exist in humans,[1] and the present case is apparently also a non-secretory variant. In non-secretory variants, the presence of more than 30% of clonal plasma cells in the bone marrow is a diagnostic criterion.[1]

Clinical signs may include lameness due to bone pain, anemia, renal failure, hyperproteinemia or splenomegaly. Macroscopically, pathological fractures, lytic bone lesions, and nodular, soft, tan masses may be present. Renal failure in plasma cell myelomas is due to hypercalcemia and/or secretion of light chains that are referred to as Bence Jones protein. The latter may pass the glomeruli and result in tubular damage.

Histologically, plasma cell myelomas consist of uniform cells with moderate to marked amounts of densely stained cytoplasm often with a perinuclear halo and a nuclear diameter of 1.5 to 2 (12-15 µm) times the size of red blood cells. Chromatin is dark staining and 1 to 3 indistinct nucleoli may be visible. Mitotic rate is low, and frequency of mitoses is often below that of normal bone marrow.[6,7]

Immunophenotypic characterization of plasma cell myelomas can be challenging because terminally differentiated B-cells lose their typical markers, such as CD20 and CD79α. If they remain immunopositive, a diagnosis of plasma cell myeloma is supported, while in the opposite case the diagnosis cannot be excluded.[1,8] In this case, some tumor cells expressed CD79α, supporting the diagnosis of plasma cell origin. An important differential diagnosis for the histological lesion is solitary osseous plasmacytoma. This can be excluded by the multifocal distribution of the lesion in the case of this pig. However, solitary osseous plasmacytoma can give rise to plasma cell myeloma.[6] In summary, this is a rare case of porcine plasma cell myeloma (multiple myeloma) with associated characteristic bone lesions.

AFIP Diagnosis: Bone, rib: Plasma cell myeloma, intramedullary and extracortical, with lysis of cortical bone, pathologic fracture, and early callus formation.

Conference Comment: Though undecided on the underlying neoplastic process, conference participants agreed the disruption in the cortical bone represented a pathologic fracture. Fractures of normal bone due to application of excessive force are referred to as traumatic, while pathologic fractures occur in abnormal bone due to minimal trauma or normal use. During bone fracture there is damage to the periosteum, cortical bone and soft tissue, resulting in hemorrhage with subsequent hematoma formation. Due to the distance of the fracture ends from the vascular supply, these areas often undergo necrosis characterized histologically as death and loss of osteocytes from their lacunae. Complete disappearance of osteocytes can take as long as to 2 - 4 weeks, and thus the only histologic finding may be osteocyte pyknosis. Macrophages, platelets, proliferating osteogenic tissue and lytic bone release bone morphogenic proteins (BMPs), transforming growth factor-β (TGF-β), and platelet-derived growth factor (PDGF) to regulate callus formation and healing. In the first two days after fracture, there is infiltration by undifferentiated mesenchymal cells from the periosteum, endosteum, and medullary cavity. During this time, the hematoma undergoes neovascularization. As the mesenchymal cells form a loose collagen network, the immature collagen, mesenchymal cells and vasculature begin organizing into granulation tissue. As woven bone is laid down, it forms the primary callus around the fracture to stabilize it and allow time for development of a secondary callus of lamellar bone.[9]

Participants also discussed the pathophysiology of osteolysis seen with myeloma. Neoplastic cells secrete macrophage inflammatory protein-1α (MIP-1α)[illegible] which upregulates the expression of the receptor activator of nuclear factor-κB (NF-κB) ligand (RANKL).[2] The RANKL binds to its receptor on osteoclast precursor cells, resulting in upregulation of NF-κB, which is required for differentiation and survival of osteoclasts.[5] The differentiation of osteoclasts is tightly regulated to prevent excessive osteolysis that could result in potentially life-threatening hypercalcemia; marrow stromal cells are able to block osteoclast precursor differentiation. Stromal cells secrete WNT protein, which binds to osteoblast receptors LPR5 and LPR6 and triggers the activation of the β-catenin pathway and ultimate production of osteoprotegrin.[5] Osteoprotegrin binds to RANK, essentially preventing RANKL binding and osteoclast differentiation.[5]

Participants commented on the slide variability, with the plasma cell neoplasia or bone fracture occasionally missing from individual slides.

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CASE IV: F10/10 (AFIP 3167507). Tissue from a horse

Signalment: 14-year-old, stallion, PRE ("Pura Raza Española"), equine (*Equus caballus*).

History: The horse had left hind limb lameness of four months duration leading up to euthanasia. On initial examination, the lameness was localized to the middle phalanx region, and an abscess of the sole was found (radiographs were not taken). The abscess was surgically drained and the horse was treated with an NSAID (Meloxicam) for one month. The lameness improved with treatment, but the horse was still lame. After an additional one month, a cystic lesion in the center of the middle phalanx was found on radiographs. The horse was rested and a continued NSAID treatment was followed. After an additional two months the cystic lesion was still the same size and the horse was euthanized.

Gross Pathology: The left and right hind legs, including proximal, middle and distal phalanges were examined. A cavity within the bone, measuring 3.5 x 4 x 5 cm, in the center of the middle phalanx of the left hind leg was found. The lesion was divided internally by red septa containing streaks of fibrin and soft fibrous tissue, creating multiple cystic spaces of variable sizes. Pronounced soft tissue was present mainly in the proximal part of the lesion. A mild uneven dorsal periostal border could be palpated. The joints were intact. The right hind leg was normal. Radiographs also show the cystic lesion in the left hind leg middle phalanx.

Histopathologic Description: Tissue from bone, articular cartilage, and subchondral bone of the left proximal middle phalanx: Intact articular cartilage covers a sclerotic subchondral bone of lamellar compact bone structures; focal superficial chondrocyte clusters can be seen in the articular cartilage in some of the sections. The cavity with the bone is characterized by multiple blood-filled spaces of variable sizes. The soft tissue of the lesion in the bone shows large areas of fibrin with adjacent granulation tissue, including neovascularization and fibroblast activity. Also, focal areas of osteoid with reactive trabecular woven bone are present in the loose connective tissue in most of the submitted sections. The border between the lesion and bone shows mild multifocal osteoclast activity and connective tissue with loose strands of fibroblasts and vessels.

Contributor's Morphologic Diagnosis: Bone cyst, unicameral-aneurysmal-like, middle phalanx, left hind leg, equine.

Contributor's Comment: Aneurysmal bone cysts are defined as a destructive expansive lesion in the bone[1]. It is a rare lesion but has mostly been reported in young individuals, both in humans,[2] dogs,[3] cats,[10] cattle[1] and horses.[6,11,12] However, too few cases are described to define a predilection site or age prevalence. A unicameral cyst of bone is a slow growing expansive lesion also reported in young individuals.[14] These cysts may be solitary or multiple. The content of the unicameral cyst contains connective tissue with multinucleated giant cells and hemosiderin-laden macrophages, with foci of reactive bone. Periosteal bone formation is not a feature of this type of cyst.[14]

The aneurysmal cyst is characterized by blood-filled spaces, separated by loose fibrous tissue. The tissue sometimes contains foci of giant cells and hemosiderin-filled macrophages. Hence the soft tissue is similar to the unicameral cyst. Osteoid or reactive bone can also be present in the connective tissue. The typical aneurysmal bone cyst arises from the outer surface of the bone close to the periosteum. The periosteum often shows reactive bone proliferation. An underlying preexisting lesion is always discussed, but seldom identifiable, due to the reactive proliferative granulation tissue. Fibrous dysplasia and neoplasia have been seen in association with aneurysmal bone cysts. An altered blood flow due to trauma has been suggested as a cause.[14] In humans, the aneurysmal bone cysts are mostly reported in the metaphyseal or diaphyseal areas of the long bones -- femur, tibia, humerus and in the spine. It is mostly seen in the immature skeleton, but can be found in adults as well.[7,8] Cysts of the phalanges are uncommon, but bone cysts have been reported,[9] including epidermoid bone cysts.[5]

The present lesion is unusual with reference to the age of the animal and the location as well as the size. The histological appearance is compatible with an aneurysmal cyst as well as a unicameral cyst. The lack of involvement of the periosteum favors a unicameral cyst; however, the multiple blood-filled spaces are more compatible with an aneurysmal cyst. The presented lesion does not show any evidence of fibrous dysplasia, epidermoid cyst or neoplasia. In summary, this is a solitary bone cyst of the middle phalanx with macroscopic appearance of a unicameral cyst. The microscopic features are compatible with a unicameral bone cyst, but also histologically similar to an aneurysmal cyst.

AFIP Diagnosis: Bone, left hind limb, second phalanx (per contributor): Unicameral bone cyst

Conference Comment: Tissue sectioning and orientation presented some difficulties with histologic interpretation for many conference participants. Based solely on the species information and histopathologic evaluation most participants included myelofibrosis and/or myelonecrosis in the differential diagnosis; in the absence of additional information and the histologic findings of hemorrhage, fibrin, granulation tissue and reactive fibroblasts are not inconsistent with necrosis and fibrosis of the marrow space. With the additional clinical information, radiographs, and gross images subsequently made available during conference attendees and the conference moderator essentially agreed with the contributor's interpretation and histomorphologic diagnosis.

This case also was studied in consultation with the AFIP Department of Orthopedic Pathology, since this entity is rarely seen histologically in veterinary species; their differential diagnosis included aneurysmal bone cyst (ABC), unicameral bone cyst (UBC), and ganglion cyst. In the opinion of the orthopedic pathology subspecialists, the histologic findings in this horse are most consistent with a ganglion cyst. Additionally, humans with UBC often respond well to corticosteroid therapy; the history from this horse does not indicate that corticosteroid therapy was attempted. Furthermore, a brief literature did not identify reports of ganglion cysts in veterinary species. The few reports of aneurysmal bone cysts in horses indicate that most animals are euthanized due to lesion recurrence or failure of treatment, which often includes corticosteroids.[6,11,12] In contrast, unicameral bone cysts in horses typically respond well to surgical curettage.[13]

The moderator and participants discussed the differential diagnosis and histopathogenesis for radiographic bone cysts, which includes fibrous dysplasia, subchondral degenerative joint disease (DJD), subchondral osteochondrosis (OCD), unicameral bone cyst, and aneurysmal bone cyst; these entities are summarized in the following chart:[13,15]

Disease	Histopathogenesis	Gross Appearance	Histologic Appearance
Fibrous dysplasia	Possible developmental defect; replacement of bone by expanding mass of fibro-osseous tissue	• Enlarged external contour • Firm with mineralized foci • Many serosanguineous cysts	• Well-differentiated fibrous tissue with regularly spaced, uniformly sized trabeculae of woven bone • Lack of osteoblasts on trabeculae • Osteoclasis
Subchondral DJD	Fissure/clefting of articular cartilage → undermined by synovial fluid → pressure, cytokines → osteoclast activation → lysis	Subchondral cystic spaces and necrosis	• Cystic spaces lined by synovial cell-like membrane • Serous fluid
Subchondral OCD	Failure of endochondral ossification → necrosis → cavitation of retained growth cartilage	Subchondral cystic spaces and necrosis	• Myxomatous matrix with fibrosis • ± degenerate cartilage
Unicameral bone cyst	Unknown; possibly due to decreased venous drainage in areas of active endochondral ossification	• Cysts with serous-like or serosanguineous fluid • Lined by connective tissue • ± pathological fracture	• Cyst wall: Variably dense connective tissue and woven to lamellar bone • Marginal remodeling • ± multinucleate giant cells and hemosiderophages

Aneurysmal bone cyst	Unknown; possible causes include altered blood flow e.g ischemia, hemorrhage, vascular malformation	• Cysts with blood or serosanguineous fluid • ± pathological fracture	• Hemorrhage and hemosiderosis • Cavernous blood-filled spaces • Spaces separated by fibrous, fibro-ossesous, or undifferentiated mesenchymal cell septae • Osteoclast-like multinucleated giant cells

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