Joint Pathology Center
Veterinary Pathology Services

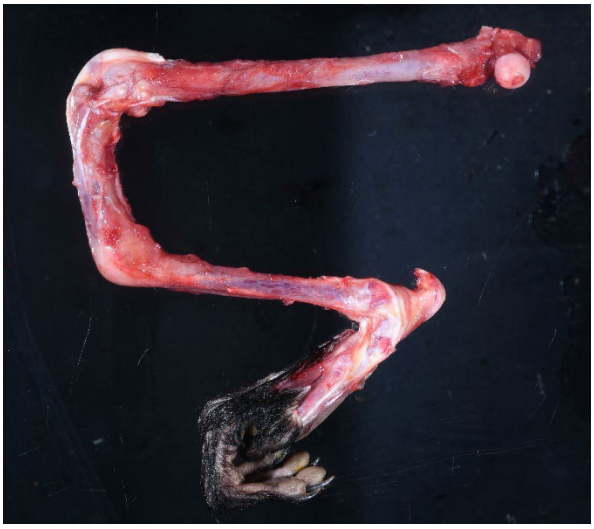
WEDNESDAY SLIDE CONFERENCE 2024-2025

Conference #23 — 9 April 2025

CASE I:

Signalment:
2-year-old male white-faced saki monkey (*Pithecia pithecia*)

History:
A privately owned 2-year-old male white-faced saki monkey (*Pithecia pithecia*) was brought to the University of Tennessee College of Veterinary Medicine's zoo medicine service for hindlimb lameness. Radiographs identified generalized osteopenia and a folding fracture of the right tibia. The monkey had been housed exclusively indoors since birth.



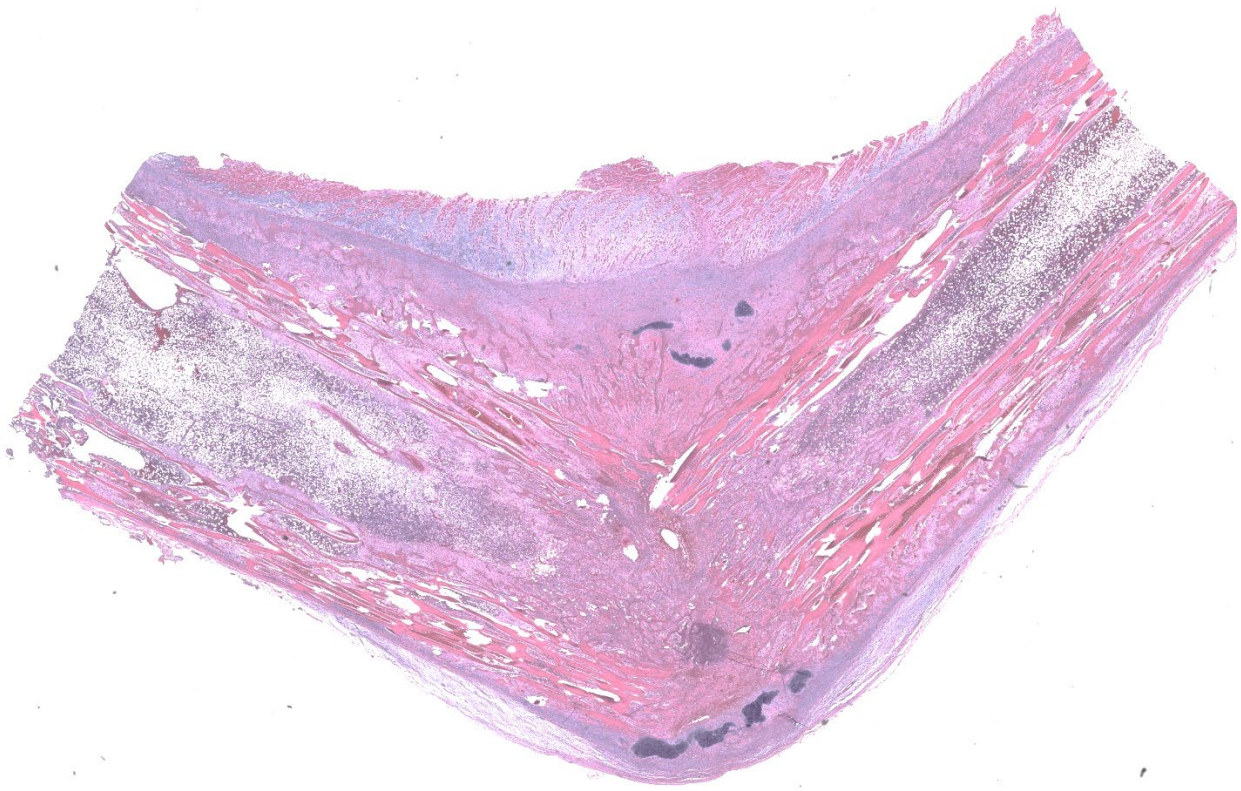
Hindlimb, monkey: There is a midshaft fracture of the tibia. (Photo courtesy of: University of Tennessee College of Veterinary Medicine, https://vetmed.tennessee.edu/)

Gross Pathology:
Midway along the tibial diaphysis of the right hindlimb, approximately 5.5 cm distal to the stifle, was a 3 cm in diameter, circumferential, white, firm, boney proliferation (callus). The tibia and fibula immediately distal to the callus were bent and directed approximately 70 degrees caudally.

On cut section, there was a 2 cm diameter rim of periosteum, skeletal muscle, and subcutis immediately surrounding the callus which was dark red to black (hemorrhage) and had a translucent yellow wet gelatinous appearance (edema). Bone marrow was dark red, soft, and floated in 10% neutral buffered formalin.

Laboratory Results:
A serum chemistry panel identified severely elevated alkaline phosphatase (ALP) at 4167 u/L and mild hypocalcemia with 0.9 mmol/L ionized calcium.

Microscopic Description:
Right tibia: The cortical bone is thin, discontinuous, and replaced by loose fibrovascular tissue (fibroplasia). Fragments of cortical bone are surrounded by fibrovascular tissue and segmentally lined by a single layer of osteoblasts or increased numbers of osteoclasts within Howship's lacunae (resorption). There



Tibia, monkey. There is a midshaft diaphyseal fracture with callus formation. The two ends of the bone are thicker than normal, and there is atrophy of the overlying skeletal muscle. (HE, 8X)

are bands of thick fibrovascular tissue expanding the periosteal and endosteal margins with frequent islands and irregular trabeculae of immature woven bone lined by osteoblasts. There is a focal complete cortical defect and the long axes of bone are positioned at approximately 90 degrees (fracture). At the fracture site, cortical bone is surrounded and separated by the previously described fibrovascular connective tissue mixed with erythrocytes transitioning to basophilic cartilaginous matrix with chondrocytes and irregular trabeculae of woven bone. The marrow cavity has approximately 50% cellularity with megakaryocytes, and erythroid and myeloid precursors of various developmental stages. A lightly basophilic myxomatous matrix extends into and surrounds adjacent skeletal muscle bundles which are frequently small and rounded (atrophy).

Contributor's Morphologic Diagnosis:

Right tibia: Severe chronic diffuse fibrous osteodystrophy with a diaphyseal fracture and callus

Contributor's Comment:

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University of Tennessee College of Veterinary Medicine
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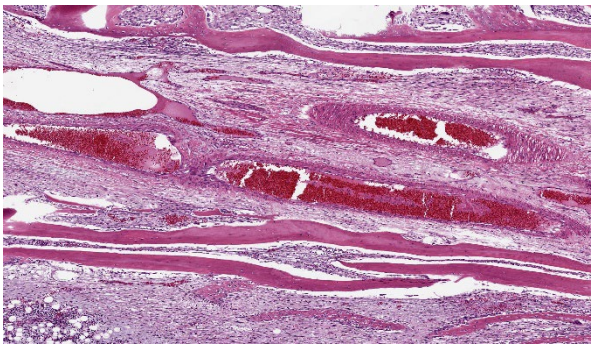
This white-faced saki monkey (*Pithecia pithecia*) had nutritional secondary hyperparathyroidism with fibrous osteodystrophy and a



Tibia, monkey. The cortical bone is no longer compacted, resorbed, and is infiltrate by abundant densely cellular fibrous connective tissue. (HE, 95X)

pathologic tibial fracture. In this case, radiographs also showed a generalized diffuse decrease in radiodensity of all bones, indicating osteopenia.

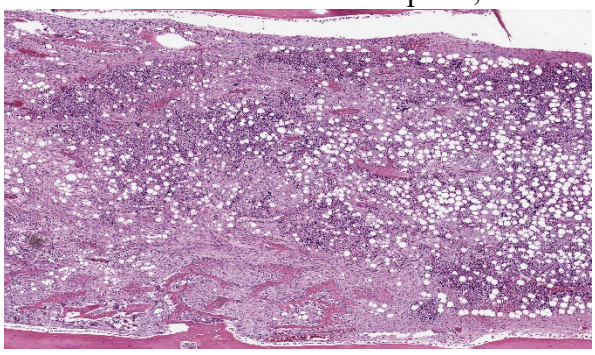
Metabolic bone disease includes multiple morphologic entities which can occur in combination in the same individual. These include rickets, osteomalacia, osteoporosis, and fibrous osteodystrophy, all caused by deficiencies or imbalances in vitamin D, calcium, and/or phosphorous.[1]

Fibrous osteodystrophy is characterized by extensive bone resorption, proliferation of fibrous tissue, and the formation of poorly mineralized immature bone.[1] The pathogenesis includes an elevation of parathyroid hormone (PTH) which may be caused by primary hyperparathyroidism, secondary hyperparathyroidism, or hypercalcemia of malignancy. Primary hyperparathyroidism may be caused by a functional parathyroid neoplasm (adenoma or adenocarcinoma) and secondary hyperparathyroidism may be caused by either renal disease or nutritional imbalances of calcium, phosphorous, and/or vitamin D.

Vitamin D may be obtained from the diet and radiation of the skin with ultraviolet light. Metabolic bone disease is not uncommon in privately owned non-human primates, as their diets may be inadequately balanced, they often receive insufficient exposure to ultraviolet light, and lack supplementation of their diet with vitamin D3 (cholecalciferol).[3] New World monkeys have specific vitamin D requirements to maintain serum calcium levels and are thus exquisitely sensitive to calcium and vitamin D deficiencies.[5] A lack of exposure to ultraviolet light impedes the conversion of 7-dehydrocholesterol in the skin to pre-vitamin D3.[4] Pre-vitamin D3 is then isomerized to vitamin D3 (cholecalciferol). Forms of vitamin D from the diet and skin undergo hydroxylation in the liver, forming 25-hydroxycholecalciferol or 25-hydroxyvitamin D [25(OH)D], which is the form of vitamin D in the circulation. This is then hydroxylated in the kidney by 1α-hydroxylase to form calcitriol (1, 25-dihydroxyvitamin D), the metabolically active form of vitamin D.[2]

Although the diet is unknown, the history of being housed exclusively indoors likely led to vitamin D deficiency and nutritional hyperparathyroidism in this monkey. The parathyroids had diffuse chief cell hyperplasia consistent with secondary hyperparathyroidism. There was no clinical, gross, or histologic evidence of renal disease.

JPC Morphologic Diagnosis: 1. Long bone: Osteoclast-mediated bone resorption,



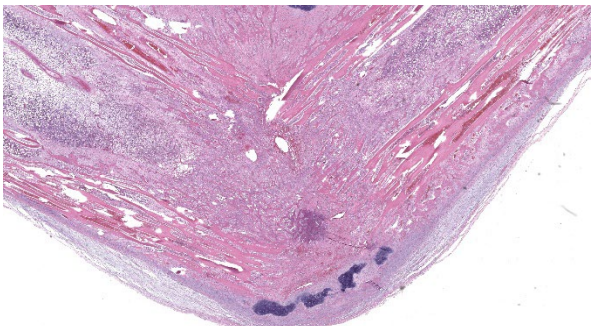
Tibia, monkey. The cortical bone is no longer compacted, resorbed, and is infiltrate by abundant densely cellular fibrous connective tissue. (HE, 95X)

marked, with cortical fibrosis, pathologic fracture, and callus.

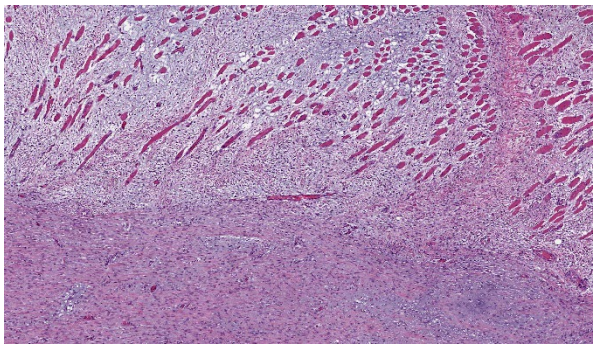
2. Skeletal muscle: Atrophy, multifocal, marked.

JPC Comment: This week's moderator was Dr. Brian Murphy from the University of California at Davis, who selected four bone and oral pathology-centered cases to dazzle conference participants. This first case is beautifully sectioned with a characteristic gross photo that drew an audible reaction from the group. Participants discussed metabolic bone disease at length with Dr. Murphy and used slide features to draw inferences which we faithfully attempt to capture below.

Foremost, evaluation of bone should start first from subgross magnification. While we approach all of our descriptions in this manner, Dr. Murphy emphasized the importance of a careful survey of the cortex, periosteum, endosteum, marrow elements, and surrounding tissue before jumping to higher magnifications. Likewise, evaluation of bone ALWAYS requires radiographs and a detailed clinical history to support interpretation. In this case, the presence of a large, well-developed callus is helpfully centered by the contributor and provides a clue for the apparent right-angle turn in the direction of the bone. That said, the callus is the *effect* and not the *cause* of the lesion in this saki monkey (although it is impressive). Evaluation of adjacent cortical bone reveals the answer, in that it is both wide and lytic with the presence of numerous osteoclasts and fibrous tissue – these features together yield the diagnosis of fibrous osteodystrophy. Dr. Murphy noted that in chronic cases, the presence of osteoclasts may be minimal or absent, though the diagnosis can still be made. The atrophy of skeletal muscle in this case is also distinctive and is itself another effect – we considered the possibility of both disuse and abnormal weight-bearing as contributory factors.



Tibia, monkey. There is a folding fracture of the tibial diaphysis, with periosteal new bone trabeculae oriented perpendicular to the surface of the bone, callus formation with abundant fibrous connective tissue and islands of cartilage, and fibrosis an and atrophy of the overlying skeletal muscle. (HE, 22X)



Tibia, monkey. Above the fracture site, the periosteum is markedly thickened and hypercellular and the skeletal muscle is atrophic and infiltrated by abundant cellular fibrous connective tissue. (HE, 87X)

In addition, evaluation of metabolic bone disease can reveal multiple concurrent processes with overlapping histologic features which the pathologist should expect. In young animals, fibrous osteodystrophy can co-exist with rickets, which warrants consideration of the physis for disorganization and expansion of the zone of hypertrophy as well as evaluation of the metaphysis for unmineralized osteoid.[1] The cortex is generally thickened with unmineralized osteoid along the periosteum. In adult animals, osteomalacia also reflects inability to mineralize osteoid, but there is no

open physis to consider. There may be decreased numbers of thin bony trabeculae and/or cortical thinning.[1] Osteoporosis (a *clinical* syndrome reflecting pain, lameness, and/or bony deformation) may also be superimposed on cases of metabolic bone disease due to microfracture and infraction (fracture without cortical displacement) of bone. Before rendering a final diagnosis, it is helpful to summarize all associated slide features and weigh whether one or more processes is occurring that could explain the constellation of histologic signs.

References:

1. Craig LE, Dittmer KE, Thompson KG. Bones and joints. In: Maxie, MG ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals.* 6th Vol. 1. St. Louis, MO: Elsevier; 2016:60-80.
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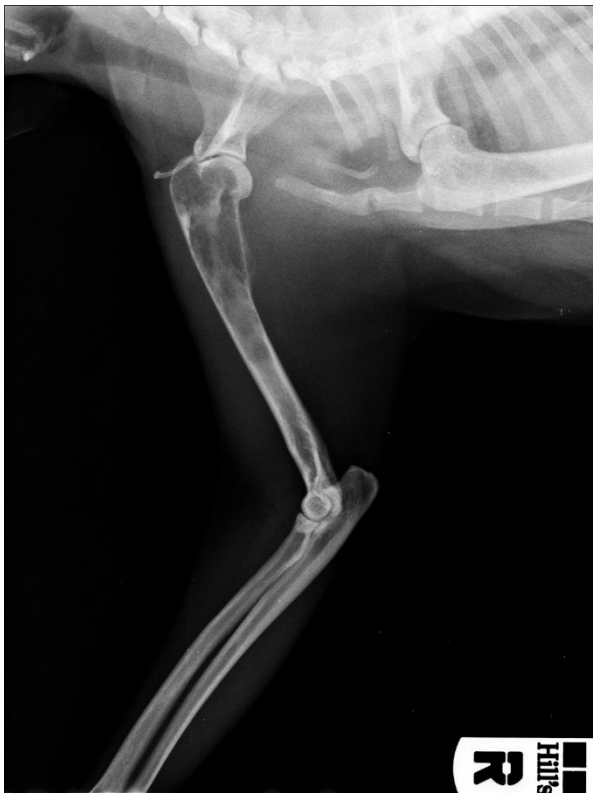
CASE II:

Signalment:

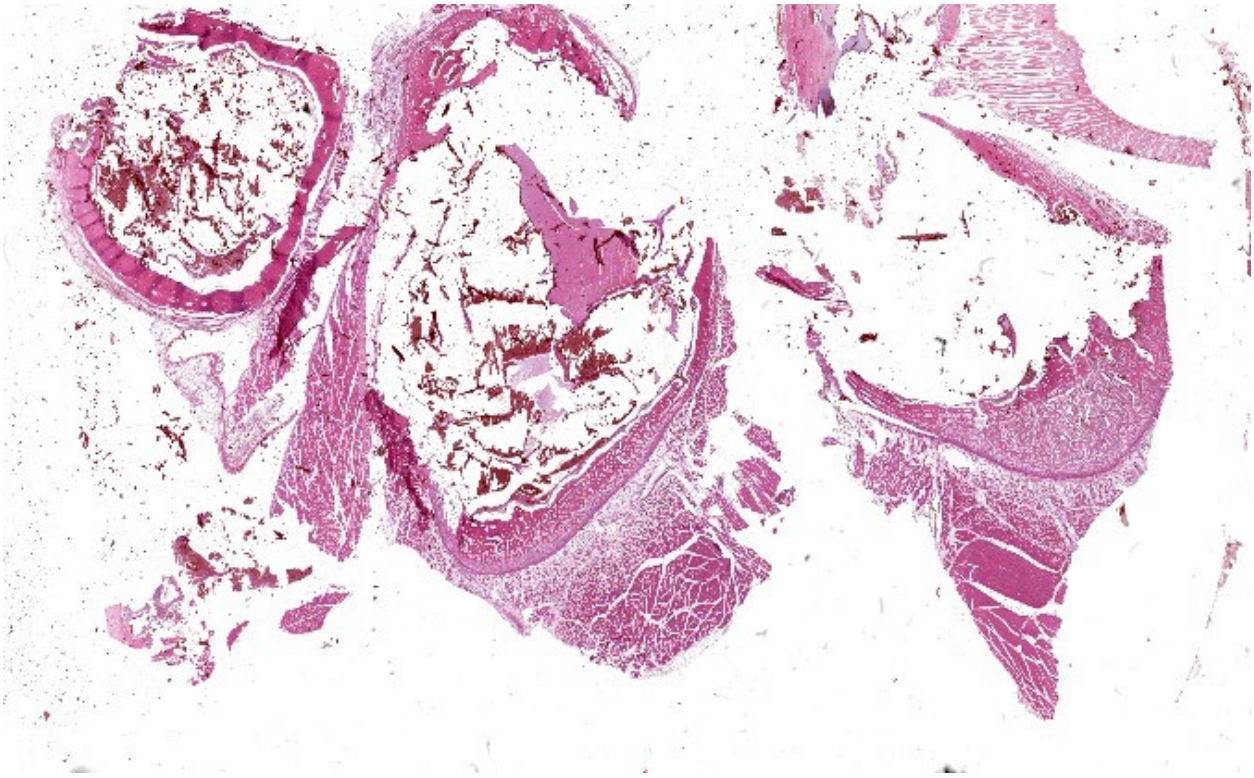
A 7-year-old spayed male domestic shorthair cat (*Felis silvestris catus*)



Humerus, cat: Radiographs reveal a focally expansile lesion and bone lysis in the right third proximal humerus with evident thinning of the cortical bone extending towards the diaphysis. (Photo courtesy of Department of Comparative Biomedicine and Food Science, Viale dell'Università 15, 35020, Legnaro (PD), Italy; https://www.bca.unipd.it/)

History:

A 7-year-old, spayed male domestic shorthair cat, weighing 4.65 kg (body condition score: 5/9), regularly vaccinated and living indoor, was presented to the Veterinary Clinic for evaluation of grade III lameness in the right forelimb. The owner reported that the lameness was observed for a few days following a trauma. Upon presentation, the cat was bright and alert, but exhibited an aggressive behaviour. Physical examination revealed no abnormalities, muscular asymmetry or atrophy were not observed in the forelimbs. The orthopaedic examination indicated moderate pain reaction



Humerus, cat: Three transverse sections of the humerus are submitted for examination. In each section, the medulla is effaced by large blood filled spaces. There is marked periosteal new bone growth in 2/3 sections. (HE, 6X)

upon palpation of the proximal humeral epiphysis and scapulo-humeral joint. The neurological examination was unremarkable. Under anaesthesia, radiography revealed a focally expansile lesion and bone lysis in the right third proximal humerus with evident thinning of the cortical bone extending towards the diaphysis. There was mild focal periosteal reactivity. The lesion was compartmentalized by trabeculae traversing an area of radiolucency, resulting in a mild "soap bubble" appearance. Soft tissue swelling was also observed overlying the region adjacent to the humeral lesion.

Chest and contralateral limbs X-rays were within normal limits. Ultrasound study of adjacent axillary and superficial cervical lymph nodes was also within normal limits.

Fine-needle aspiration (FNA) was performed on the bone lesion. The needle easily penetrated the cortical bone into the medullary canal. Cytologic evaluation of FNA revealed hemo-diluted cytological samples with mild cellularity, primarily consisting of haematopoietic elements, small lymphocytes and occasional small aggregates of round to spindle cells with indistinct cells borders and abundant, basophilic cytoplasm, with oval nuclei, reticular chromatin and prominent nucleoli (figures 3 and 4). The anisocytosis and anisokaryosis were moderate. Finally, rare foamy macrophages were observed.

The cytological diagnosis indicated bone marrow contamination due to the sampling procedure. The presence of occasional mesenchymal elements with moderate atypia could suggest a sarcomatous origin of the lesion, for which histopathological confirmation was recommended.

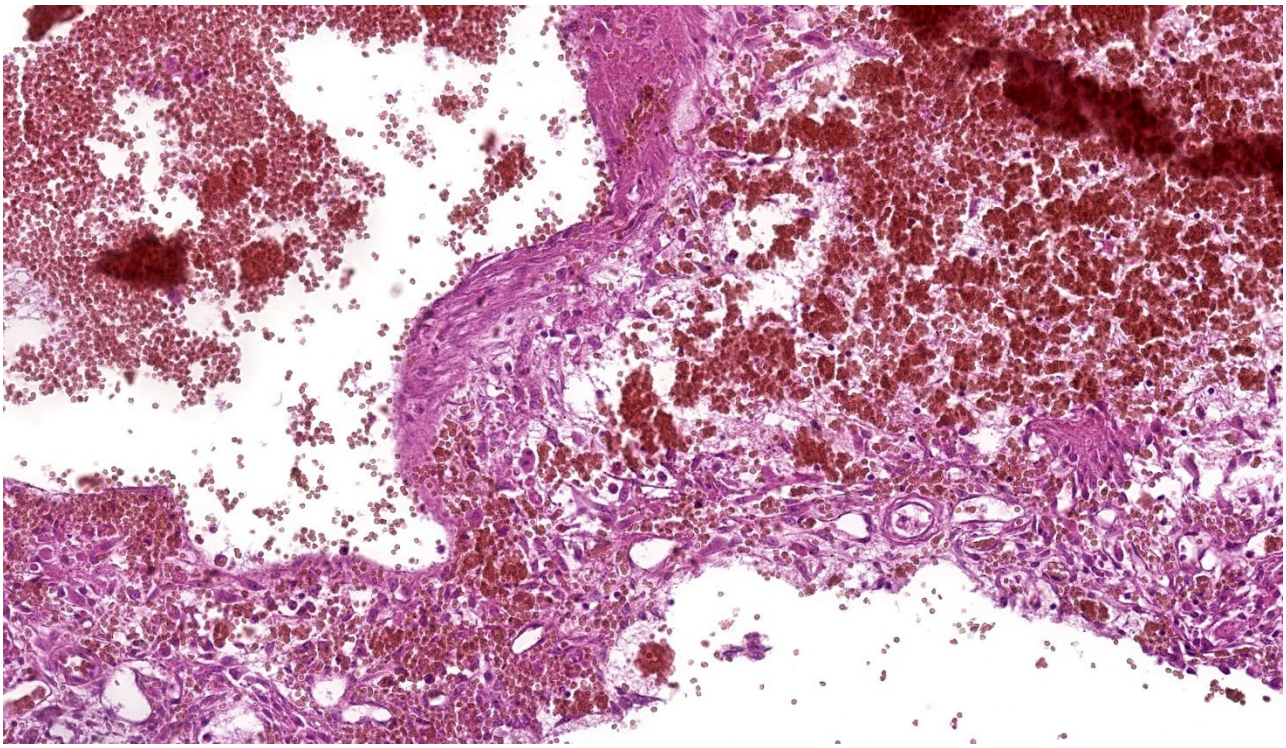
The owner declined the biopsy procedure and provided informed consent for the amputation with scapulectomy and axillary lymph node dissection.

Gross Pathology:

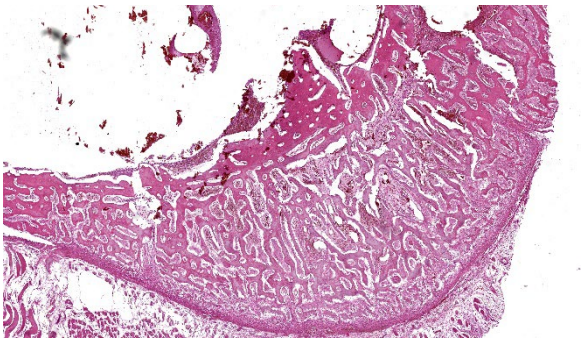
Grossly, an expansile, raised, round nodular lesion measuring about 18 x 12 x 10 mm was present on the third lateral superior proximal humerus. On the cut surface, a cavity full of blood was found within the centre of the bone, expanding the cortex, and internally septated, creating multiple hematic lacunae of variable sizes and cyst-like appearance. A mild periostal thickening, above the cystic lesion was observed. The joints were unremarkable, and no masses were present in the surrounding soft tissue.

Microscopic Description:

Bone and soft tissue from the periphery of the right proximal humerus. Affecting 70% of the sections and located eccentrically in the bone cavity, involving the medullary cavity, and extending into the cortex, a round, well-demarcated, non-infiltrative, non-capsulated mass composed of multiple blood-filled spaces of variable sizes is observed, measuring about 15 x 10 x 8 mm. These spaces contain numerous extravasated red blood cells admixed with eosinophilic, fibrillar, material (fibrin), eosinophilic amorphous material (serous) and are well delimited by septa of variable thickness leaning on spicules of bone (fig. 5). The septa are composed of moderately cellular proliferation characterized by spindle cells with minimal atypia (possible fibrovascular proliferation), multifocally arranged in solid areas (fig. 6). Admixed, mild to moderate proliferation of



Humerus, cat: Blood-filled spaces are separated by fibrous septa which contains variable combinations and concentrations of hemorrhage, siderophages, mixed inflammation, fibroblasts and dense collagen (HE, 381X).



Humerus, cat: In 2/3 sections, the cortical bone is thinned, and there are anastomosing trabeculae of periosteal new bone arising from the hypercellular periosteum. (HE, 381X)

round to oval cells with moderate, eosinophilic, cytoplasm and an eccentric, round, nucleus (possibly osteoblasts, fig. 7) was noticed. Scattered osteoclasts and foamy macrophages with abundant, pink to yellow-brown cytoplasm (hemosiderophages) are observed. The trabecular bone affected by the cystic mass shows, multifocally, irregular margins with shallow pits (Howship's lacunae) occasionally associated with osteoclasts (bone resorption). The rest of bone shows tinctorial alterations, from intense to pale eosinophilic matrix, in which randomly scalloped lines could be observed (new bone deposition). The periosteum appears highly cellular (reactive) while, multifocally, a mild inflammatory infiltrate composed of lymphocytes, plasma cells and rare hemosiderophages is evident. The surrounding skeletal myofibers are separated by optically empty material (edema) and occasionally show a decreased diameter (mild atrophy).

Contributor's Morphologic Diagnosis: Humerus: Focal, monolateral, aneurysmal bone cyst with bone remodelling

Contributor's Comment: Aneurysmal bone cysts (ABCs) are benign, locally expanding bone masses, containing numerous blood-filled or serosanguineous fluid-filled spaces, not usually lined by endothelium, located between bone trabeculae.[8,11] Adjacent tissue to the spaces can vary from well-differentiated fibrous or fibro-osseous tissue to pronounced proliferation of undifferentiated mesenchymal cells admixed with osteoclast-like multinucleated giant cells. ABCs are often locally aggressive, tending to cause lytic bone lesions[12] and destruction of the inner cortical bone layers during expansion.[8] Haemorrhages and hemosiderosis are frequent.[8]

The causes and pathogenesis of ABCs remain unknown;[8] however, they could be consequences of ischemic necrosis, haemorrhage, disruption or shunting of intramedullary blood vessels, or congenital/acquired vascular malformations.[8,11] Local alteration in blood flow has also been thought to play a role.[3] Increased venous pressure may occur secondary to trauma or a tumor, resulting in dilation of the vascular bed and subsequent erosion of bone.[3]

ABCs have been reported rarely in dogs, cats, horses, and cattle,[3] predominantly occurring in the flat bones of the axial[11] and appendicular skeleton.[3] Limited cases are reported in animals to establish age or site prevalence.[3] In cats, ABCs have been described in the scapula,[1,5] pelvis, [9,12] metatarsal bone,[7] humerus,[4] and rib.[2] Radiographically, ABCs appear as expansile, osteolytic lesions contained by a thin, "ballooned" periosteum with an internal "soap-bubble" appearance caused by internal septa. Grossly, ABCs resemble benign bone cysts, telangiectatic osteosarcoma, and hemangiosarcoma.[3] ABCs typically exude blood from the cut surface, and may contain solid areas in addition to multiple blood-filled cysts (multiloculated[3]). Pathologic fracture may be present.[3] Complete resection is the treatment of choice when possible, and carries a favourable prognosis.[12] Other treatment options include surgical curettage with bone grafting, and radiation therapy.[11] Recurrence after complete surgical excision of the aneurysmal bone

cyst (ABC) has not been reported in animals. However, malignant transformation of an aneurysmal bone cyst to a chondrosarcoma has been reported in a dog.[3] In humans, ABC is now considered as a benign locally destructive bone neoplasm.[6]

ABCs must be differentiated from both benign and malignant lesions,[10] such as unicameral bone cyst (UBC),[12] osteosarcoma, hemangiosarcoma, fibrosarcoma, and plasma cell myeloma.[3] One of the major histologic differential diagnosis is telangiectatic osteosarcoma.[1,10] However, we excluded it because nuclear pleomorphism and a high mitotic rate were not features of mesenchymal/associated cells in our case. For the same reason, we have excluded fibrosarcoma, plasma cell myeloma, and hemangiosarcoma. Moreover, we have excluded UBC because it is unicameral, while ABCs are multiloculated[3] as in our case. Finally, fungal infection and osteomyelitis were ruled out due to negative Periodic acid–Schiff (PAS) staining and the very mild inflammatory infiltration. Indeed, acute osteomyelitis are characterized by the presence of fibrin and a dense population of neutrophils and necrotic cells in the primary spongiosa while the presence of neutrophils and plasma cells within the reactive bone and connective tissue supports a diagnosis of chronic osteomyelitis,[3] all features not detected in our case.

Contributing Institution:
Department of Comparative Biomedicine and Food Science, Viale dell'Università 15, 35020, Legnaro (PD), Italy;
https://www.bca.unipd.it/

JPC Morphologic Diagnosis: Long bone: Simple bone cyst (pseudocyst).

JPC Comment: We greatly appreciate that the contributor of this second case included radiographs and accompanying cytology to support case discussion. Although anatomic pathologists may feel some discomfort in interpretating radiographs, the group (and Dr. Murphy) felt it was important to maintain basic competency in recognizing and describing bony changes and using this information to enhance slide evaluation. We agree with the radiologic assessment of bony lysis with at best a mild periosteal reaction in this case, and not an aggressive lesion, which typically combines both bony proliferation and lysis.

Evaluation of this slide provides some challenge due to processing artifact, due to the large blood-filled spaces. The composition and arrangement of spindle cells led some participants to promote the idea that this process resembled a seroma forming within bone (i.e. a response to trauma). It is clear from the current literature that the genesis remains nebulous however.

Lastly, it wouldn't be Wednesday Slide Conference without a good semantic argument and this case offered a perfect minor quibble to occupy at least 5 minutes. While the term "aneurysmal bone cyst" is well established in the veterinary literature, it is also worth mentioning that this is itself a misnomer as there is no lining epithelium present. As such, aneurysmal bone *pseudocyst* probably is more appropriate to the lesion, but we hate making the associated literature even harder to read/categorize. Dr. Murphy muddied the waters further by observing that human literature partially reserves aneurysmal bone cyst for cases with a known genetic component[13] – it is unclear if similar circumstances might apply to the cat in this case. We liked the safety of "simple bone cyst" as an umbrella term and the parallels to human nomenclature, and ultimately combined the two in our

morphologic diagnosis (and eschewed "aneurysm bone cyst" entirely.

References:

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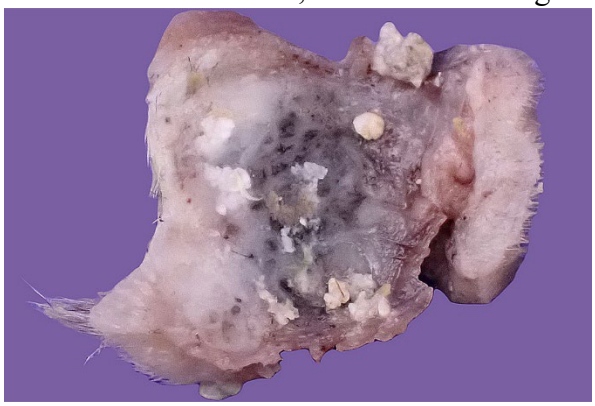
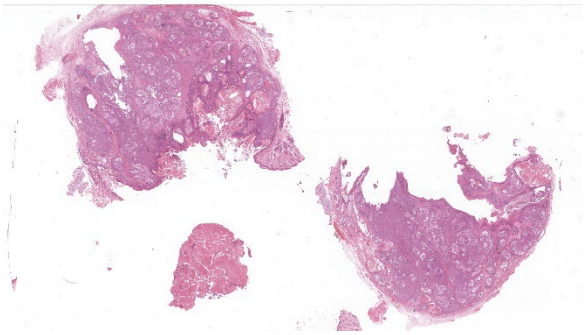
CASE III:

7 years old, female, domestic rabbit (*Oryctolagus cuniculus*)

History: The animal presented with a swelling of the left buccal region, and a firm nodular mass was identified, described as being in



Cheek, rabbit: Buccal/labial skin with embedded approximately ovoid neoplastic nodule. (Photo courtesy of: International Zoo Veterinary Group Pathology, https://www.izvg.co.uk/pathology/pabout.htm)



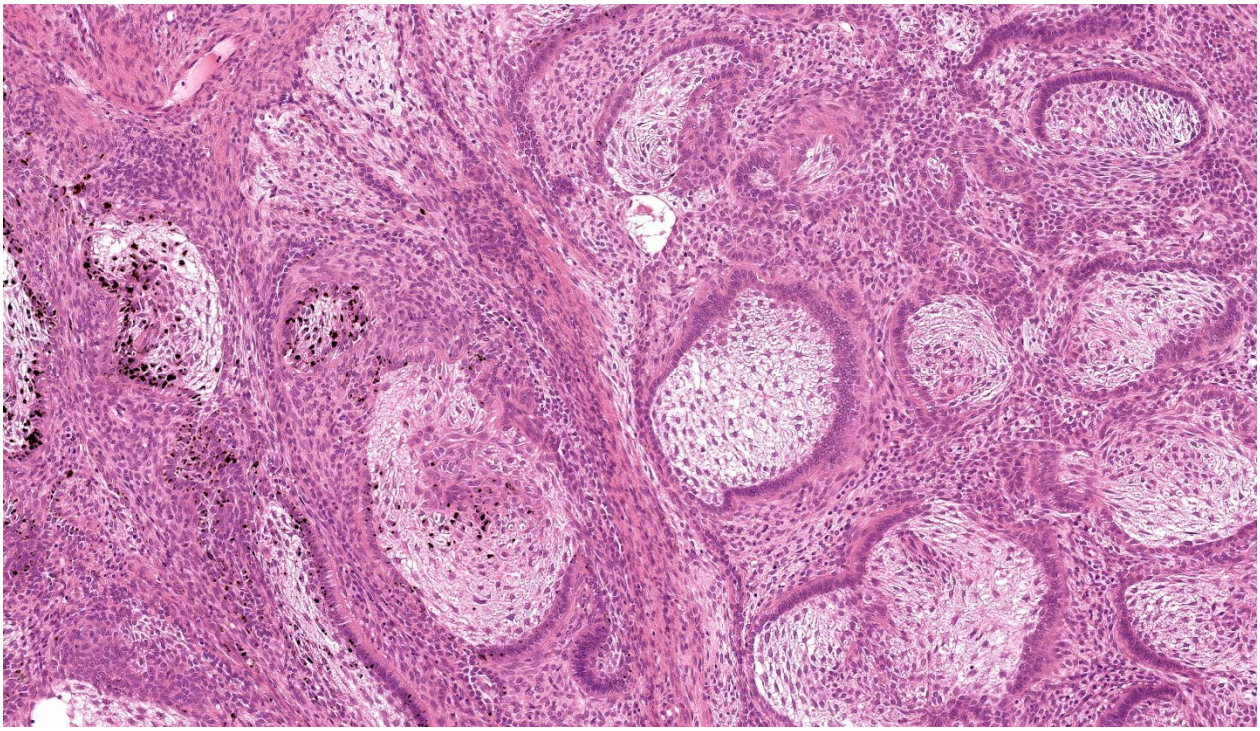
Cheek, rabbit: Multiple sections of a neoplasm are submitted for examination. (HE, 8X)

the lip (not obviously attached to the gingiva/bone). The submitting veterinary surgeon performed an incisional biopsy and a single piece of tissue was submitted for histopathologic examination. Following initial diagnosis, further surgery was undertaken to remove the lesion in its entirety, attached to a small areas of surrounding buccal/labial skin.

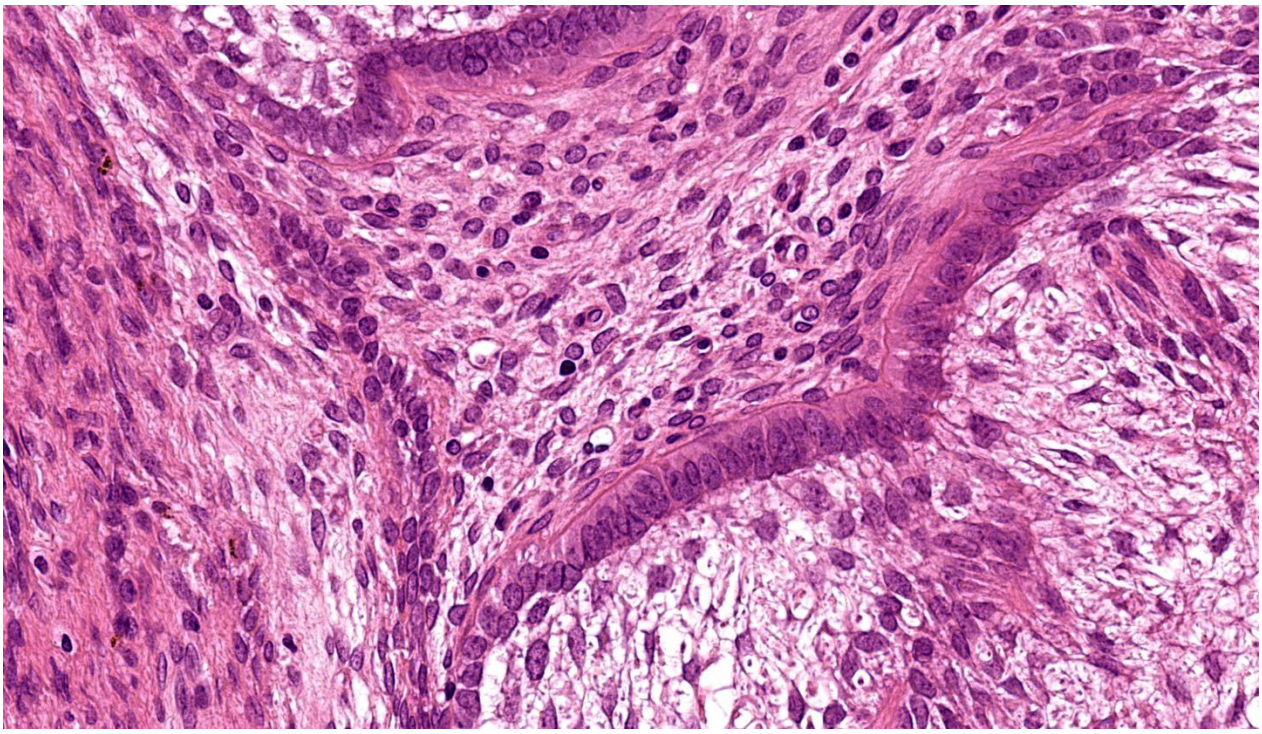
Gross Pathology: The resection specimen was an irregularly ovoid firm nodule (approximately 30 x 25 x 18 mm greatest dimensions) attached to a piece of haired skin (Fig. 1). Incision revealed a relatively well-circumscribed non-encapsulated nodule, with firm to hard, slightly gritty to chalky, grey, cream, and tan mottled cut surfaces (Fig. 2). The lesion required overnight decalcification prior to histological processing.

Laboratory Results:
N/A

Microscopic Description:
Buccal skin: The lesion comprises a relatively well circumscribed non-encapsulated nodular neoplasm expanding within haired skin which forms the lateral margins. The neoplasm is composed of interconnecting is-



1Cheek, rabbit: The neoplasm is composed of thick anastomosing trabeculae of palisading epithelium resembling odontogenic epithelium surrounding loosely arrange mesenchyme reminiscent of dental pulp. (HE, 181X)



2Cheek, rabbit: High magnification of neoplastic epithelium. (HE, 750X)

lands and cords of odontogenic epithelium. Odontogenic epithelium is characterized by peripheral palisading of epithelial cells which have apical nuclei and basal cytoplasmic clearing and central cells which are separated by prominent stellate bridges (Fig. 3). Intracytoplasmic melanin granules are a variable feature within this cellular population, multifocally throughout the lesion. Cellular pleomorphism is moderate. Mitoses range from 0-1 per HPF (per 40x objective), with moderate anisocytosis and anisokaryosis. Odontogenic epithelia frequently form concentric nodules (somewhat reminiscent of Pacinian corpuscles, Fig. 3 arrow) and there are areas of slender anastomosing ribbons. Multifocally, there are cystic structures partially or predominantly lined by palisading odontogenic epithelium which contain dyskeratotic hyperkeratotic debris (Fig. 4). Stratified squamous epithelium with para- and orthokeratotic hyperkeratosis lines further cystic structures, forming an extensive central area of invagination within the neoplasm with coalescent columns of squamous epithelial cells and cystic accumulations of orthokeratotic and parakeratotic debris (Fig. 5). Some of these cystic areas have substantial amounts of heterophilic inflammation with epithelial erosion and ulceration and inflammation extending into the subjacent neoplastic populations. Fragments of mucinous salivary gland are present in the deeper connective tissues (consistent with minor salivary gland/buccal origin). The basal margin of resection comprises compressed striated muscle fibers, including atrophic and regenerative fibers, adipocytes, and varying amounts of fibrosis.

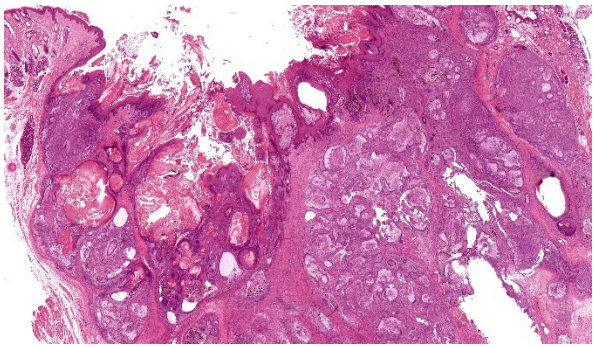
Contributor's Morphologic Diagnosis: Keratoameloblastoma (keratinizing acanthomatous epulis), with focal squamous differentiation, buccal skin.

Contributor's Comment: Histological features are consistent with ameloblastoma, a rare neoplastic entity in rabbits, which has only been described in recent years (since

2009). In total only twelve cases have been described in the literature.[1-7] According to one recent study of odontogenic neoplasms the prevalence of ameloblastoma in rabbits is around 0.24%.[3] As in other domestic species, these are locally aggressive neoplasms and although they are not considered to carry a metastatic risk, they often invade underlying tissues (including alveolar bone) resulting in loss of teeth. Maxillary and mandibular origin have both been described. However, not all typical cases are apparently associated with the cutaneous or mucosal epithelium on clinical inspection, and subcutaneous origin (external to the buccal musculature) has also been described. This may be pertinent to buccal/labial location in this case. Although evidence suggests that these odontogenic-like tumors of the rabbit cheek may be derived from ectopic rests of transformed tooth germ, the histogenesis of these lesions remains unresolved.[2]

If ameloblastomas are therapeutically irradiated, other malignancies including squamous cell carcinoma, fibrosarcoma and osteosarcoma have been reported to occur, in some cases several months to years following treatment, in other domestic species.[8]

Keratoameloblastoma is an uncommon histologic subtype (n=2) amongst the twelve ameloblastoma-like lesions recorded in rabbits to date. This subtype is characterized by keratin formation by ameloblastic epithelium and has also been identified as a rare entity in the human literature.[9] Squamous differentiation (differentiation of neoplastic epithelium towards a keratinizing squamous epithelial phenotype, rather than keratinization arising from ameloblastic cells) has also been recorded in ameloblastoma in rabbit. Whether this has any prognostic significance has not yet been evaluated.



/Cheek, rabbit: The overlying epithelium is markedly hyperplastic and hyperkeratotic. (HE, 28X)

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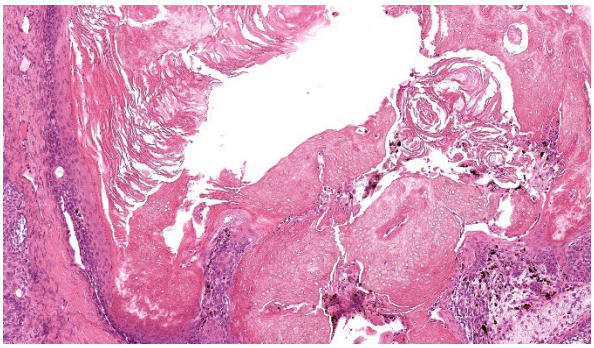
JPC Morphologic Diagnosis: Haired skin: Ameloblastoma.

JPC Comment: This third case presented a bit of a conundrum for the group. While the neoplasm description is straightforward, placing an ameloblastoma in the cheek and/or lip without an apparent source of dental germinal epithelium led us to further explore the idea of an ectopic ameloblastoma (see reference #2 below) or back off this interpretation and use the qualifier of "ameloblastoma-like" to allow for the possibility of another cell of origin. Other similar neoplasms that could mimic ameloblastoma due to overlapping features include trichoblastoma (to include "adamantanoid" trichoblastoma) and basal cell adenoma.[2] The presence of pigment within neoplastic cells is also not typical of ameloblastoma but is a common finding in follicular tumors which gives some credence to the latter theory of this case.



Cheek, rabbit: Higher magnification of keratinizing epithelium with lamellar keratin and ghost cells. (HE, 205X)

Dr. Murphy reviewed the Vickers-Gorlin criteria[10] for diagnosis of ameloblastoma which include hyperchromatic basal cell nuclei, basilar cell palisading and antibasilar nuclear location, and cytoplasmic vacuolation. We also note the prominent, thickened rim (subepithelial band) of hyalinized collagen that blends with the basement membrane (colloquially the Vickers-Gorlin change or Vickers-Gorlin effect[2]) though whether this is a consistent or useful feature of rabbit ameloblastomas was not determined by our discussion.

We also discussed the architectural contrast between the deeper portion of this neoplasm necrotic, ulcerated surface and the multifocal keratinization present at the surface. The contributor lays the case nicely for considering keratoameloblastoma. The most recent WHO classification of benign odontogenic tumors makes no mention of this entity however,[9] which reflects the need to learn more. One aspect of the slide that conforms to keratoameloblastoma that might be overlooked is the abundant dystrophic mineralization of keratin – this is also noted radiographically in more advanced/pronounced human cases.[9]

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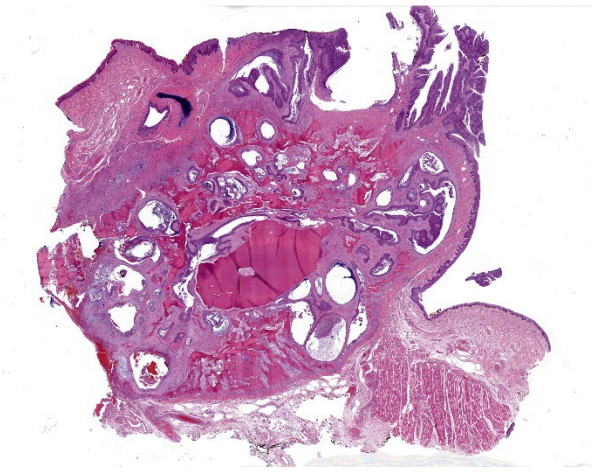
CASE IV:

Signalment: 7 year, spayed female, giant schnauzer, *Canis familiaris*

History: This dog presented to the University of Wisconsin-Madison Veterinary Care for evaluation of an oral mass that was first noted 2 months prior to presentation. Physical exam revealed a pink, irregular mass at the gingiva between teeth 101-102. Computed tomography revealed marked osteolysis of the maxilla associated with the mass and enlarged mandibular and cervical lymph nodes, with no other signs of metastatic disease. A partial maxillectomy was performed and the maxilla was submitted for histologic examination.

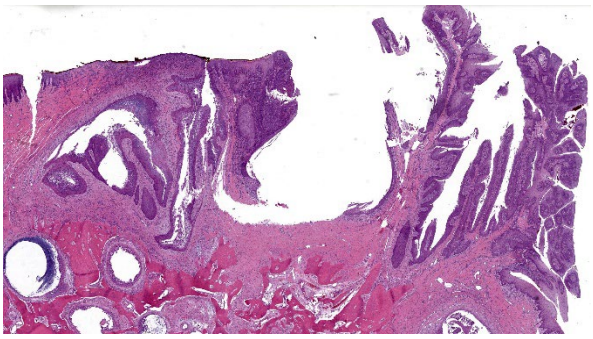


Gingiva, dog: A section of gingiva with an infiltrative cystic and proliferative neoplasm is submitted for examination. The neoplasm forms papillary fronds extending from the gingiva (HE, 8X)

Gross Pathology: The tissue sample submitted for histologic examination consisted of a section of right maxilla including teeth 101-104 and 201. A 0.4 x 1.2 x 1.8 cm pink, soft, exophytic mass expanded the gingiva dorsal to teeth 101-103 and extended to the rostral hard palate. The specimen was decalcified prior to sectioning.

Laboratory Results: A fine needle aspirate and cytology of the enlarged lymph nodes was diagnosed as consistent with lymphoid hyperplasia. A complete blood count was unremarkable. Serum biochemical abnormalities included globulins 3.9 g/dL (2.2-3.5), AST 82 U/L (21-53), ALT 227 U/L (4-87), cholesterol 487 mg/dL (149-319), and triglycerides 261 mg/dL (32-190).

Microscopic Description: Gingiva. Arising from and markedly expanding the hyperplastic gingival epithelium and infiltrating the subepithelial stroma and alveolar bone is an unencapsulated, poorly demarcated, densely cellular exophytic and invasive mass. The mass is composed of neoplastic epithelial cells forming papilliferous projections into the oral cavity supported by a fibrovascular stalk and extending deep to the basement membrane to form nests and trabeculae supported by a moderate amount of fibrovascular stroma. Neoplastic cells are polygonal with distinct cell borders and often prominent intercellular bridges, abundant pale to brightly

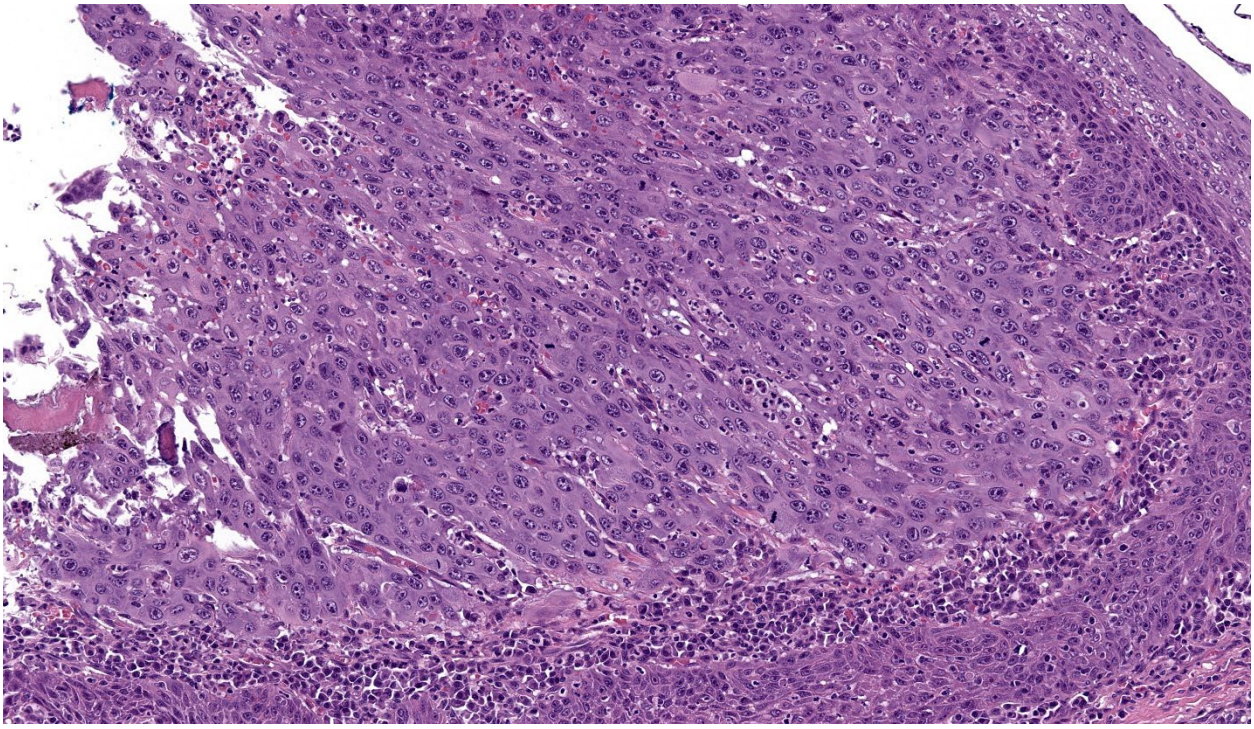


Gingiva, dog: The neoplasm extends outward from the gingival surface, forming both a wide based front (left) or long papillary fronds. (HE, 22X)

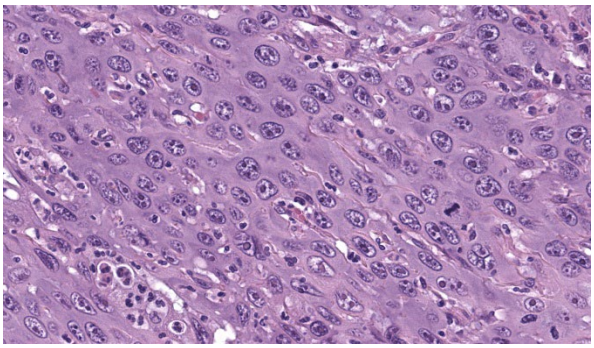
eosinophilic cytoplasm, a round to oval nucleus, finely stippled chromatin, and up to six prominent magenta nucleoli. Anisocytosis and anisokaryosis are marked, there is occasional binucleation, and mitoses range from 2-4 per high-powered field (0.237 mm^2). There is frequent individual cell necrosis and larger foci of central necrosis and vacuolation containing eosinophilic and karyorrhectic debris and neutrophils. The superficial stroma supporting the exophytic mass and its stalk are moderately expanded by clear space (edema) that contains small numbers of neutrophils and macrophages, and the deeper stroma is expanded by multifocal and coalescing regions of hemorrhage and small to moderate numbers of neutrophils that encircle and infiltrate the lobules of neoplastic cells. In regions of alveolar bone invasion, the margins of remaining bone are scalloped and occasionally lined by osteoclasts within Howship's lacunae, and the affected bone contains multiple resting and reversal lines. In more severely affected regions, irregular trabeculae of pale woven bone are deposited on the pre-existing bone and are lined by plump osteoblasts.

Contributor's Morphologic Diagnosis:

Gingiva: Papillary squamous cell carcinoma



3Gingiva, dog: Neoplastic squamous epithelium demonstrates a wide base with an intact basement membrane, a lack of maturation, as well as large nuclei with prominent (HE, 181X)



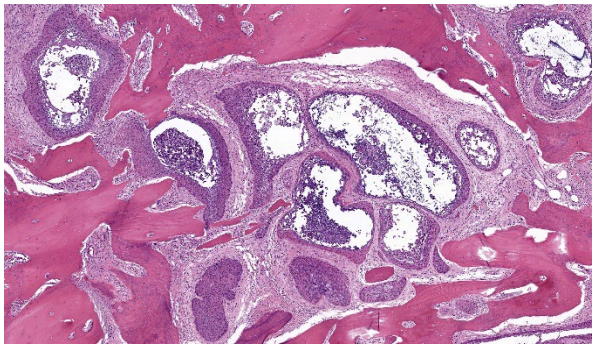
Gingiva, dog: High magnification of neoplastic squamous epithelial cells. (HE, 965X)

Contributor's Comment: This case was diagnosed as a papillary squamous cell carcinoma (PSCC) arising from the gingival epithelium. PSCC is a subtype of oral SCC based on a classification scheme defined by the World Health Organization.[1] In one retrospective study on canine oral SCC, PSCC comprised 6% of cases, compared to the more common conventional subtype which represented 82% of cases.[9] Other subtypes of oral SCC that have been defined in dogs include basaloid, verrucous, adenosquamous, and spindle cell.[1,9] At this time, subtyping is not routinely performed and it is unclear if there is an association between subtype and biologic behavior. In humans, PSCC tends to demonstrate local confinement and more feasible excision, and thus is associated with a more favorable prognosis.[1]

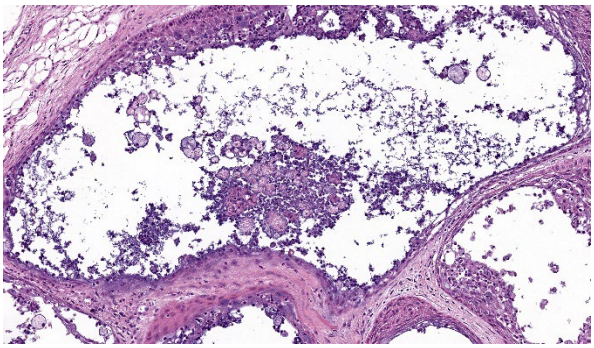
PSCC is differentiated from conventional SCC by the presence of neoplastic epithelial cells forming papillary fronds into the oral cavity, in addition to infiltrating the basement membrane into the subjacent stroma. Invasion beyond the basement membrane and keratinization can be minimal with this subtype, thus complicating the diagnosis in some cases.[7,8] Other histologic features that may be seen with PSCCs include degeneration of apical neoplastic cells and abundant intraepithelial neutrophils.[7] PSCCs can also occur as an intraosseous cavitated cyst within the bone (cavitating pattern), as opposed to the non-cavitating pattern featured in this case.[7,8] Similar to this case, PSCCs appear to have a predilection for the gingiva of the dentate jaws, with the majority occurring on the rostral aspect.[9,10]

Risk factors for development of oral PSCC are not well-defined. This neoplasm has been primarily documented in young dogs,[2,11] however multiple reports have shown that this subtype additionally affects adult and aged dogs, similar to this case.[9,10] While papillomavirus infection has been associated with oral SCC in humans and cutaneous SCC in dogs, studies exploring the association between canine oral SCC and papillomavirus infection have not demonstrated a similar relationship.[1, 3-5] Further, there is no evidence at this time that canine PSCC represents progression of an oral squamous papilloma.

Differential diagnoses in this anatomic location in dogs include canine acanthomatous ameloblastoma (CAA), oral squamous papilloma, and viral papillomas. CAA is differentiated from PSCC by the lack of characteristic papillary formations and by the presence of neoplastic odontogenic epithelium and stroma resembling periodontal ligament. While PSCC can macroscopically resemble oral squamous papilloma or viral papilloma,



4Gingiva, dog: Nests of neoplastic cells infiltrate the underlying alveolar bone. There is central necrosis within some of the larger nests. (HE, 72X)



5Gingiva, dog: There is infiltration of the nests of neoplastic cells with neutrophils, loss of desmosomal attachment, vacuolation and individualization of neoplastic squamous epithelial cells, and central necrosis with abundant bluish cellular material.

both entities can be histologically differentiated from PSCC by the confinement of neoplastic epithelial cells to the basement membrane and lack of cytopathic effects (for viral papillomas).[6]

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JPC Morphologic Diagnosis: Gingiva, incisive bone, and incisor: Papillary squamous cell carcinoma.

JPC Comment: The final case of this conference presents an interesting slide with a few subtle features to discover. Localization of this section to first or second incisor tooth is possible as the nasopalatine canal (incisive canal) is neatly outlined with a sickle of cartilage (lower right corner). Likewise, changes to the incisor tooth merit description as there is apparent lysis of dentin and repair as well as hypercementosis – we interpret the irregular shape and attachment of the tooth as a direct reaction to the neoplasm. We appreciated having a full thickness cross-sectional view to discuss these changes as typical biopsy specimens of this neoplasm are largely superficial.

Conference participants agreed with the contributor's diagnosis of papillary SCC, though discussion of ancillary features and overlap with differential diagnoses still produced a fruitful discussion. The basic structure of this neoplasm is epithelial and we add salivary gland neoplasms as a consideration to the contributor's differential list. CAA and papillary SCC are the most similar, though comedonecrosis (if present) is not consistent with CAA. We also noted several islands of epithelial cells outlined by ribbons of eosinophilic material that lacked osteocytes (dentin-like) which prompted consideration of an odontoma. Other portions of the neoplasm contain woven bone and osteoidal matrix induced by the neoplasm which could be confused with osteosarcoma or osteoinductive squamous cell carcinoma in a more limited biopsy sample. Once again, the value of lesion location, radiographs, and a biopsy sampling that includes the underlying invaded bone is critical for an accurate diagnosis.

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1.