



WEDNESDAY SLIDE CONFERENCE 2017-2018

Conference 13

3 January 2017

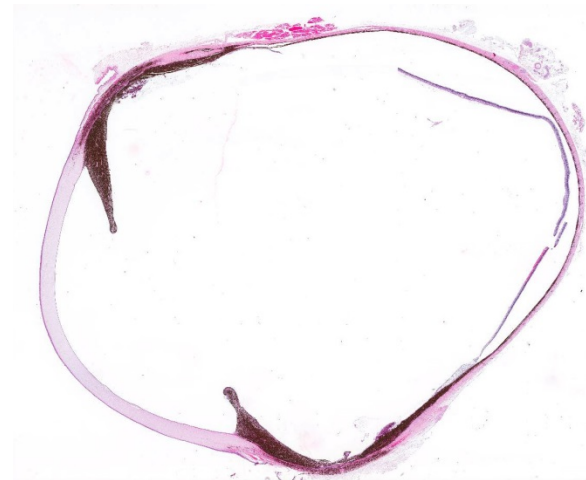
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CASE I: 14/327 (JPC 4050462).

Signalment: 12 year-old, male, Cairn terrier, *Canis familiaris*, canine.

History: The dog was examined at the veterinary school at Norwegian University of Life Sciences due to eye problems and was diagnosed clinically with ocular melanosis/melanocytic glaucoma bilaterally but more extensive in the right eye. Eye examination revealed right side buphthalmos +2, right side moderately mydriatic irresponsive pupil, left side iatrogenic miosis, IOP 37/23, diffuse endothelial edema; right side +2-3 and left side +1-2, vitreous prolapse right side and posterior lens luxation, and dorsally ectatic and black pigmented sclera was noted. Black pigmentation also involved conjunctiva. Attempts at controlling the intraocular pressure in the right eye was not successful, and the right eye was enucleated. The

owners were informed that lesions also in



Eye, dog. A cross section of the globe demonstrates thickening of the iris with pigment laden cells that expand the adjacent uvea and infiltrate the sclera. (HE, 5X)

the left eye most likely would progress.

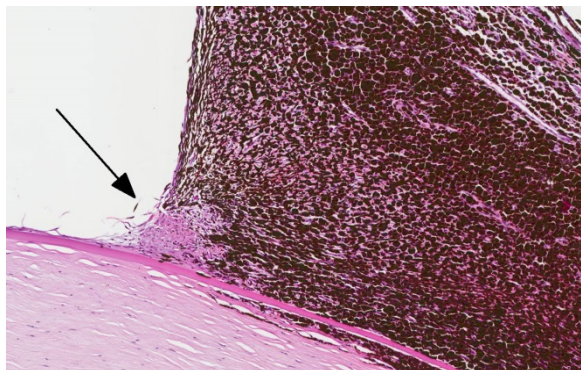
Gross Pathology: An enucleated right eye was received for histopathologic evaluation. The globe measured 2.5 cm in diameter. In

the medial canthus of the eyelids, there was a 3mm exophytic tumor with a black surface. The third eyelid was diffusely black without discernible thickening of the tissue. In the globe there were four slightly bulging areas in the anterior portion of the sclera, each 3-4 mm in diameter, with black discoloration of the surface of the sclera, and trans-scleral black discoloration on the cut surface. Anterior vitreous prolapse was not obvious after sectioning of the eye and the lens was detached (thus not included in the sections). A few small opaque areas were detected in the periphery of the lens.

Laboratory results:

None provided.

Microscopic Description: In the iris, ciliary body and filtration angle there was a diffuse infiltration of large round plump pigmented cells. Close to the filtration angle, the cells also focally infiltrated the cornea, between Descemet's membrane and corneal stroma. At the anterior portion of the sclera, at the level of iris and ciliary body, there was transscleral infiltration of pigmented cells with separation and loss of scleral connective tissue. Pigmented cells also extended into episclera in some areas. The pigmented cells had abundant cytoplasm



Eye, dog. The iris root is markedly thickened pigment-laden macrophages. The drainage angle (arrow) is closed by few spindle and pigment-laden cells admixed with a collagenous matrix. (HE, 144X)

with numerous dark brown granules that was bleached by potassium permanganate and a central or peripheral round vesicular nucleus with a small nucleolus. The mitotic index was <1 per 10 HPFs, and minimal anisocytosis and anisokaryosis. The retina was detached (artifact). There was degeneration and loss of neurons in the ganglion layer, moderate thinning of the inner granular layer and mild multifocal fusion of inner and outer nuclear layer in the retina. In the anterior and posterior chambers a pale blue material (vitreous) with some free pigmented cells.

In the lens (not submitted) there was multifocal degeneration of stroma on the anterior side and swollen lens fibers (Morgagnian globules) and large eosinophilic swollen cells (bladder cells).

On the rim of the eyelid from medial canthus there was a focal hyperplasia of sebaceous glands with lobules of well differentiated glandular tissue surrounding a centrally located duct (not submitted). In the surrounding dermis in this area and diffusely in the medial conjunctiva, including the third eyelid, there was multifocal to confluent infiltration of pigmented cells as described above.

The globe was re-embedded in a standard size tissue block, and this caused an artificial dorsoventral flattening of the globe.

Contributor's Morphologic Diagnosis:

Eye: Ocular melanosis with secondary glaucoma.

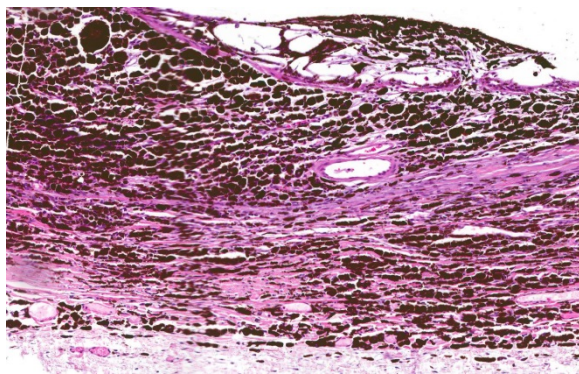
Contributor's Comment: The lesions in this specimen are consistent with the condition called ocular melanosis of Cairn terriers. In a study describing the clinical presentation of 114 Cairn terriers diagnosed with ocular melanosis, the earliest lesions was dark-colored thickening of the iris root followed by scleral/episcleral pigment

plaques, release of pigment into the aqueous and deposition in the drainage apparatus, especially ventrally.³ In advanced cases, secondary glaucoma develops, and 3 of the 114 dogs developed uveal melanocytic neoplasms.³

Ocular melanosis is characterized by diffuse infiltration of plump pigment-laden cells mainly in anterior segments of the eye including the iris, ciliary body, sclera/episclera overlying the filtration angle and the peripheral deep layers of the cornea, but posterior segments may also be involved.⁴

An important differential diagnosis is uveal or limbal melanocytoma in the dog, as the pigmented cells infiltrating ocular tissue in ocular melanosis are histologically similar to such tumor cells. However the growth pattern is reported to be different; in ocular melanosis the pigmented cells infiltrate diffusely in the tissues, as opposed to uveal or limbal melanocytomas in which the tumor cells are expected to result in an expanding mass.⁴

The origins of the pigment-laden cells have been controversial, and the main cell population has been described to be dominated by either melanophages or melanocytes. Van de Sandt et al⁶ described the ultrastructural morphology of most of



Eye, dog. The choroid at left, sclera (bottom), and peripheral retina (upper right) are all infiltrated and expanded by pigment-laden macrophages. (HE, 120X)

the cells to be consistent with melanophages and some cells appearing to be melanocytes. In this paper, the specific origin of ocular tissue chosen for electron microscopy study was not indicated. In another study⁴ where iridal and ciliary body tissue was ultrastructurally investigated, the main cell population was described as melanocytes containing melanosomes in stage III or IV of development, but some cells that probably represented melanophages were also observed. Both Van de Sandt et al⁶ and Petersen-Jones et al⁴ reported the cells to be negative for the common melanocyte marker Melan A. However, Petersen-Jones et al⁴ described most but not all cells to be immunohistochemically positive for HMB45, an antibody that recognizes gp100, which is a melanosome organelle specific marker localized in stage II and III melanosomes. Some cells were also positive for MITF, a melanocytic nuclear transcription factor. Most eyes contained some pigmented cells positive for CD18 suggesting they were macrophages that had engulfed pigment, but in 1 globe which was markedly inflamed, out of 8 globes investigated immunohistochemically, there were abundant CD18 positive pigmented cells.⁴

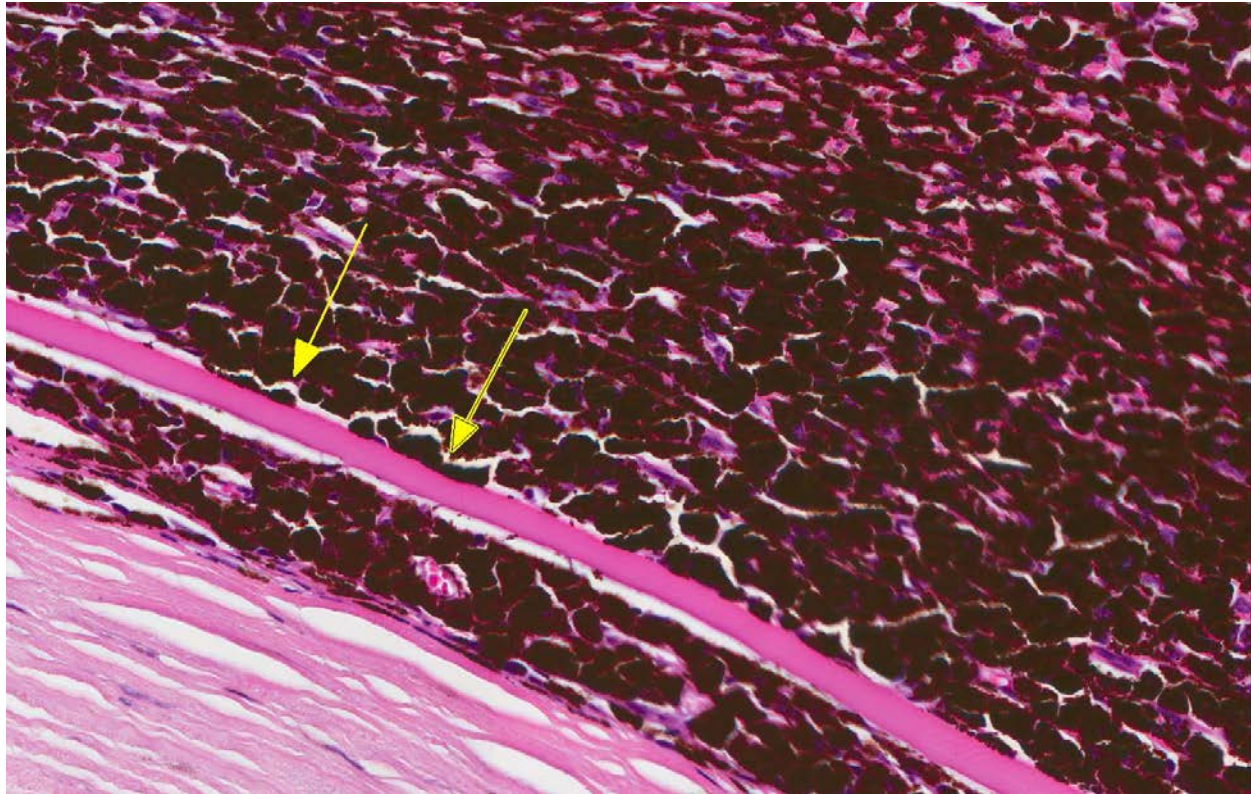
The cause of the disease is unknown. The disease is reported to be inherited with a possible autosomal dominant mode of inheritance.³ In one study examining 11 potential candidate genes, none of the selected candidate genes were likely to be the gene locus for ocular melanosis in Cairn terriers.⁷

JPC Diagnosis: Globe, anterior uvea, choroid, and sclera: Melanosis with anterior synechiae formation and drainage angle occlusion with mild to moderate diffuse retinal atrophy, Cairn terrier, canine.

Conference Comment: Ocular melanosis, also known as pigmentary glaucoma, most commonly occurs in the Cairn terrier breed and results in excessive pigmentation of the uvea which disrupts the contour of the uvea particularly prominent at the iris base, anterior ciliary body and limbal sclera. The pigmented cells have been identified through electron microscopy and immunohistochemistry to be melanocytes or melanophages (described in more detail above). The thickened limbal scleral and episclera can give the impression of neoplasia; however, melanocytoma (the most likely differential) can be distinguished from melanosis by the presence a regional mass that compresses adjacent tissues. In contrast, melanosis is more diffuse and often bilateral in the Cairn terrier. Ocular melanosis has also been identified in other breeds such as the Boxer and Labrador Retriever, and in these breeds is clinically

and morphologically similar, varying only in the distribution. In other breeds, melanosis is usually unilateral and composed predominately of melanophages based on limited electron microscopic studies.²

The eyelid and brow may also be involved, in which the condition is known as oculodermal melanocytosis, which correlates with a high risk for melanoma in Caucasian patients.² In dogs, there have been occasional reports of melanocytoma or malignant uveal melanoma occurring in eyes simultaneously affected with melanosis. A recent article¹ reports a Golden Retriever with diffuse ocular melanosis and extension into the bulbar conjunctiva and orbital space forming a pigmented, necrotic mass diagnosed as a limbal melanocytoma. Remarkably, there was also a pigmented mass in the third eyelid of the opposite eye that was also diagnosed as a melanocytoma.



Eye, iris and peripheral cornea. Large pigment-laden macrophages efface iridal architecture and infiltrate the cornea underneath Descemet's membrane (yellow arrows). (HE, 400X)

Cases such as this give weight to the belief of some pathologists that ocular melanosis is merely diffuse melanocytoma.²

Ocular melanosis results in a slowly progressive chronic glaucoma associated with compression of and accumulation of pigmented cells within the filtration angle and scleral venous plexus. Free melanin granules are often present and are phagocytized by local macrophages and trabecular endothelial cells within outflow tracts. Secondary glaucoma of this nature is not responsive to medical or surgical treatment because melanophages and melanocytes continue to proliferate and eventually abrogate the treatment by obstructing whatever therapeutic intervention was initiated.⁵ In humans, ocular melanosis occurs rarely and results in unilateral heterochromia of the iris and a darkened choroid.

Canine glaucomas are classified based on the following criteria: possible cause (primary, secondary, or congenital), gonioscopic appearance of the filtration angle, and duration or stage of disease. Primary glaucomas are characterized by intra-ocular pressure (IOP) increases without any concurrent disease; these are often hereditary in certain breeds (reported in over 45 breeds, of which the most notable are Beagle, Basset Hound, Welsh springer spaniel and Great Dane) and can occur bilaterally. Primary glaucomas often occur due to pectinate ligament dysplasia or consolidation of ligaments into sheets (mesodermal dysgenesis) or abnormal metabolism of the trabecular cells of the outflow system or pupillary blockage. Secondary glaucomas result from increased IOP associated with concurrent ocular disease, such as uveitis, lens luxations, intumescent cataracts, phacolytic or clastic uveitis, hyphema, intraocular neoplasia or

melanosis, which obstruct aqueous outflow pathways. Several breeds are predisposed to lens luxation, most commonly Fox Terrier, Sealyham Terrier, Border Collie, Tibetan Terrier, Cairn Terrier, Welsh Corgi, and Jack Russell Terrier. In Jack Russell Terriers, Miniature Bulldogs, and Lancashire Heelers, a mutation of the ADAMTS17 gene has been associated with lens luxation. Finally, in congenital glaucoma increased IOP is caused by multiple anterior segment anomalies resulting in decreased aqueous humor outflow and develops soon after birth. Congenital glaucoma is exceedingly rare in dogs, whereas, primary (breed-related) and secondary glaucomas are most common.⁵

Conference participants described peripheral anterior synechiae (Descemet's membrane extends into the ciliary body), ectropion uveae due to a thin pre-iridal fibrovascular membrane, and evidence of secondary glaucoma (thin sclera and retina). The moderator discussed a proposed grading scheme that has not been published yet for ocular melanosis: increased melanin-containing cells (grade I), increased melanin-containing cells and distortion (grade II), and melanin-containing cells increased and invading sclera (grade III).

Contributing Institution:

www.nmbu.no

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CASE II: K13-8163-B (JPC 4070254).

Signalment: 8 year-old castrated male Saint Bernard, *Canis familiaris*, canine.

History: Firm, non-pruritic, non-seasonal, longer than a year infiltrative disease within the eye; discrete symmetrical, 1-5 cm (an enucleated globe was received for histopathologic evaluation).

Gross Pathology: None.

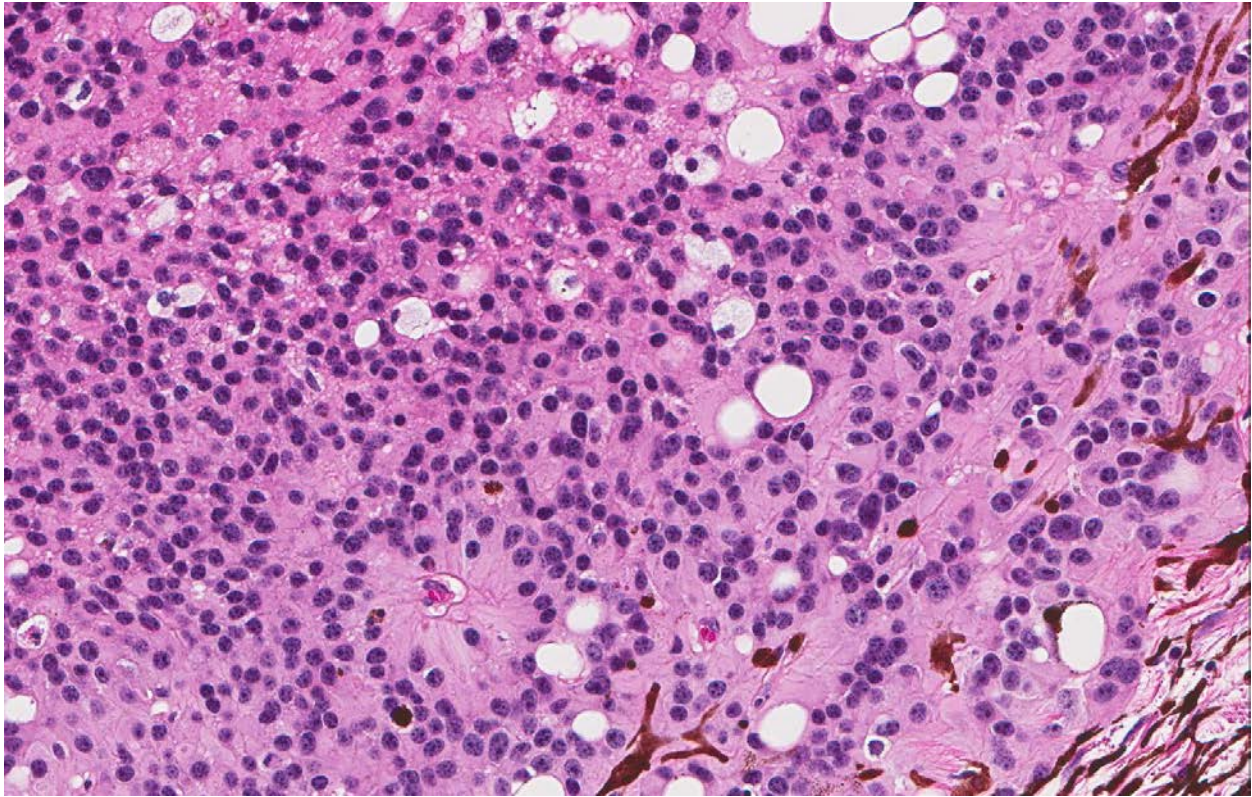
Laboratory results:



Globe, dog. At subgross magnification, there is a large, pigmented, densely cellular neoplasm arising from the ciliary body, effacing the anterior and posterior chambers and displacing the lens backward. There is extensive hemorrhage the anterior and posterior chambers as well as within the optic nerve at left. (HE, 6X)

None provided.

Microscopic Description: The slide contains a partial cross section of a canine globe. The globe has an unencapsulated mass arising from the ciliary body within the anterior uveal tract between the iris and lens. The mass is composed of tightly packed sheets and cords of polygonal cells and supported by a very fine vascular stroma. Neoplastic cells have indistinct cell borders, moderate to abundant eosinophilic cytoplasm and oval nuclei with finely stippled chromatin. Pseudorosettes and occasional large bone formation are present. There is moderate anisokaryosis and anisocytosis. Mitotic figures are 7 in 5 HPF. There are variably-sized cavitated spaces containing blood or eosinophilic material and melanophages throughout the mass. The mass is not invading the sclera but is filling the iridocorneal angle and displacing the lens posteriorly. There is abundant hemorrhage filling the posterior and anterior chamber occasional associated to hematin-laden macrophages and fibrosis. The retina exhibits atrophy of the nerve fiber and ganglion cell layers. The lens has few eosinophilic spherical globules (Morgagnian globules) and bladder cells within



Globe, dog. Neoplastic cells are polygonal with distinct cell borders and abundant eosinophilic granular to vacuolated cytoplasm. Nuclei are variably sized with finely clumped chromatin and 1-2 basophilic nuclei. There are large areas of hemorrhage and necrosis throughout the mass.

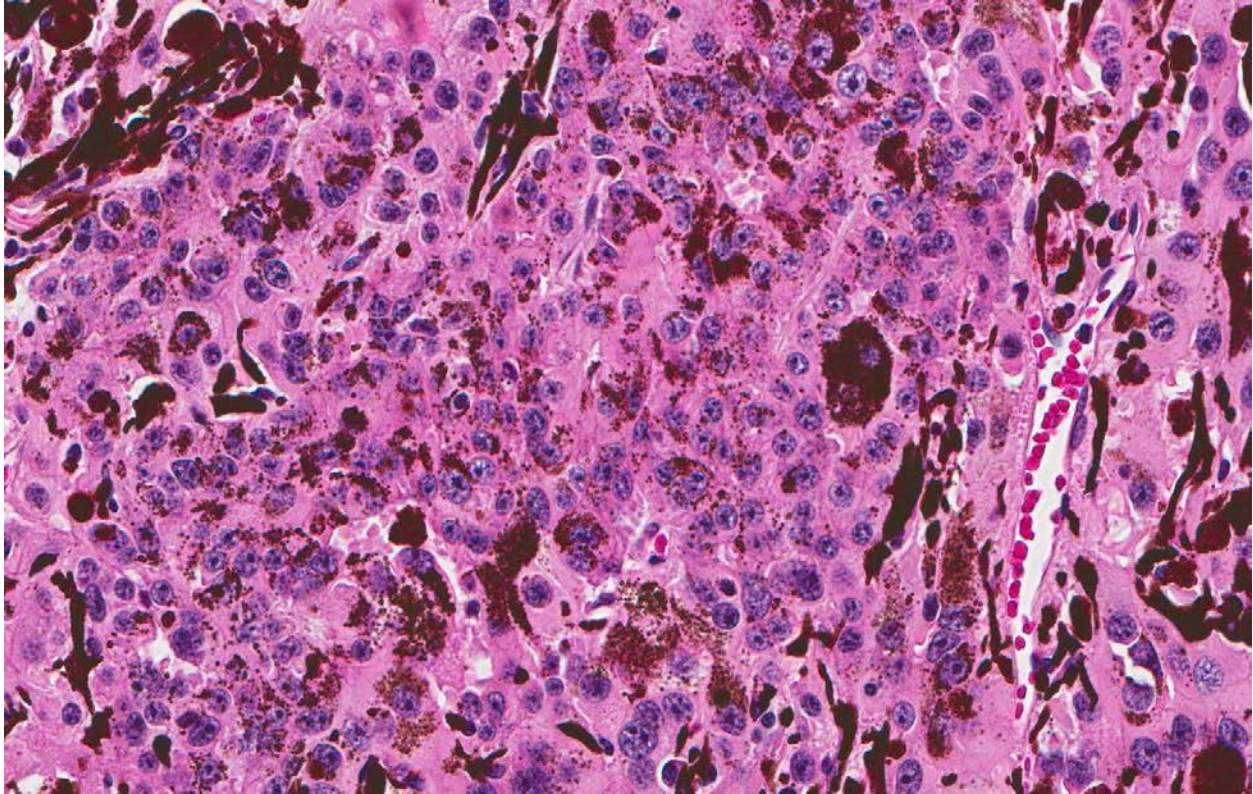
subcortical areas. The special stain PAS reveals a complex network of delicate PAS positive basement membranes surrounding groups of neoplastic cells.

Contributor's Morphologic Diagnoses:

1. Eye: Pigmented iridociliary adenoma.
2. Eye: Secondary glaucoma and retinal atrophy with cataractous change.

Contributor's Comment:
 Histopathological features are most consistent with a benign iridociliary adenoma in this case. The tumor is considered benign because is not invading the sclera or choroid, and lacks cellular pleomorphism. Iridociliary adenomas and adenocarcinomas arise from the pigmented or non-pigmented epithelium of the ciliary body and iris, which are of neuroectoderm

origin.^{2,7} They are the second most common primary intraocular tumor of dogs, occasionally seen in cats and infrequently seen in other species.^{2,5} In general, morphologic patterns for iridociliary epithelial tumors include papillary, solid, palisading ribbons or ribbon-cord, tubular, cystic and anaplastic. The most common secondary abnormality detected with these tumors is glaucoma.⁵ However; other complications include uveitis, cataract, loss of vision and, less frequently, retinal detachment, lens luxation and corneal decompensation.¹ Although, iridociliary adenocarcinomas are extremely rare and usually do not metastasize, metastasis is a late stage phenomenon and unlikely in the absent of extensive scleral invasion.⁸ Iridociliary epithelial tumors, benign and malignant, can be diagnosed based on histopathological features; however,



Globe, dog. In an extensive area of the mass, neoplastic cells also contain dark brown globular intracytoplasmic pigment.

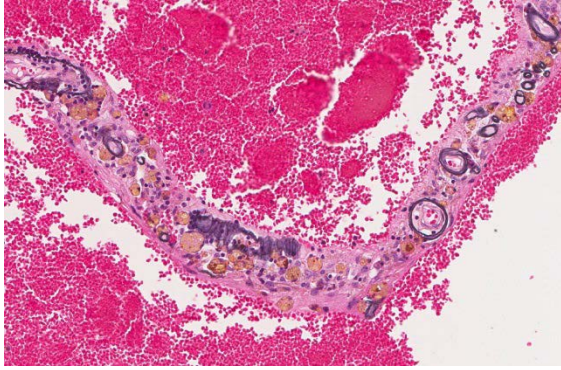
adenomas were indistinguishable from adenocarcinomas by biopsy in one study.¹ Additionally, these tumors almost always retain abundant basement membrane production that can be accentuated with PAS staining.³ A unique characteristic is the positive staining for vimentin and negative for cytokeratin in adenomas.⁶ The cells also stain for S-100 and neuron-specific enolase.⁶ On the other hand, the malignant version is vimentin and cytokeratin AE1/AE3 positive.⁸

JPC Diagnosis:

1. Globe: Pigmented iridociliary adenoma with drainage angle occlusion, hyphema and subretinal hemorrhage, and retinal detachment and atrophy, Saint Bernard, canine.
2. Retina, vessels: Ferrugination, multifocal, severe.

Conference Comment: Iridociliary epithelial tumors are of neuroectodermal origin and arise from the epithelial cells of either the iris or ciliary body. Primary iridociliary epithelial tumors generally exhibit one of the following criteria: noninvasive growth of epithelial cells that extends into the aqueous adjacent to the iris or ciliary body, pigmented epithelial cells, or thick basement membrane structures on the cell surface.

The incidence of benign (adenoma) and malignant (adenocarcinoma) iridociliary epithelial tumors are about equal; however, ocular melanomas are about twice as common as iridociliary tumors and are the most frequent primary intraocular tumor in the dog. Adenomas are easier to distinguish from melanomas because they are often limited to the ciliary body, whereas, adenocarcinomas, like melanomas, are characterized by a more invasive growth



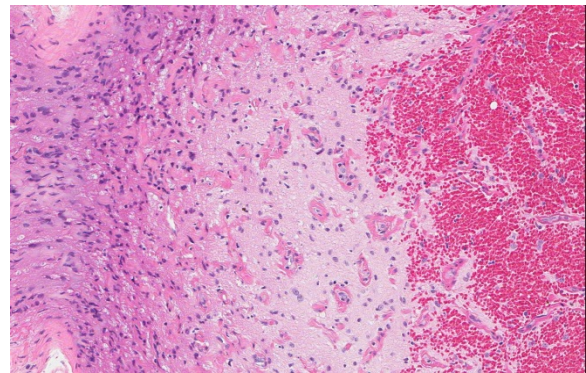
Globe, dog. The detached retina is floating in the markedly hemorrhagic vitreous. The markedly atrophic retina has lost nuclei within all layers. Vessel walls are mineralized, and the retina contains hemosiderin-laden macrophages.

pattern, may extend through the iris base or pupil and are potentially metastatic. The typical microscopic growth patterns of iridociliary adenoma and adenocarcinoma are described by the contributor above. The key microscopic difference between the two depends on extension into the sclera and the presence of anaplasia. If present, these features support a diagnosis of iridociliary adenocarcinoma.

Interestingly, these tumors often appear non-pigmented grossly, regardless of the extent of microscopic pigmentation. In addition to the immunohistochemical characteristics noted above, Alcian blue can often be used to identify hyaluronic acid secretions, which are commonly associated with cells of iridociliary epithelial origin.⁴ Historically, tumors of the ciliary body have been induced in laboratory beagles via intravenous injection of ²²⁶Ra and ²²⁸Ra. These tumors were not identified as of neural crest origin, ruling out melanoma, and were assumed to represent unique radium-induced neoplasms arising from the pigmented epithelium of the ciliary body.⁴

The conference moderator also discussed the significance of the location of new vessels within the corneal stroma. Vascularization

of the deep corneal stroma (as seen in this case) tends to be associated with intraocular disease, while more external vessel formation is typically due to corneal trauma. Additionally, a prominent cyclitic membrane was noted by conference participants, arising from the ciliary body and extending to the posterior aspect of the lens. Finally, conference participants discussed the extensive hemorrhage within the posterior segment of the eye. Although the reason for this is unclear, some



Globe, dog. There is marked hemorrhage in the optic nerve (right), and edema centrally which separates degenerating nerve fibers. (HE, 256X)

participants postulated that the patient was hypertensive, while others suggested the possibility of trauma to a non-sighted eye. Of note, within the retinal remnant vessel walls often appear deeply basophilic and are highlighted with Prussian-blue stain, which suggests accumulation of iron-containing material, a process known as “ferrugination”. This could be associated with the chronic hemorrhage noted above.

Contributing Institution:

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 Department of Agriculture
 Consumer and Industry Services
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<http://www.tn.gov/agriculture>

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CASE III: 719/16 (JPC 4095576).

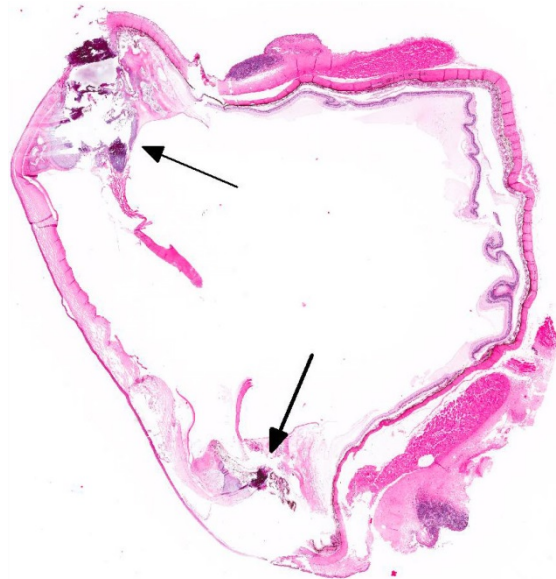
Signalment: Adult, female, *Cavia porcellus*, guinea pig.

History: The animal stems from a large colony kept in a zoo and was euthanized due to an overall poor body condition. At necropsy the ocular lesion was an incidental finding.

Gross Pathology: On external examination the left eye presented with an irregularly shaped, well-demarcated whitish-grey mass at the limbal region of the iris, which encircled the pupil entirely. On cut section there was a marked thickening of the ciliary body with a bone-like structure and projections extending into the anterior chamber. Otherwise the eye was unremarkable.

Laboratory results:

None provided.



Globe, guinea pig. The globe is artifactually flattened in the anterior-posterior plane. The ciliary body contains well-formed spicules of bone. (HE, 6X)

Microscopic Description: Eye: Expanding and replacing the stroma of the ciliary body and the iris is a proliferation of regularly formed lamellar bone containing multiple central cavities filled by hematopoietically active bone marrow. The bone is partially surrounded by a fine fibrous layer. Multifocally in the subepithelial connective tissue of the bulbar conjunctiva there are nodular infiltrates composed of large numbers of lymphocytes and few plasma cells.

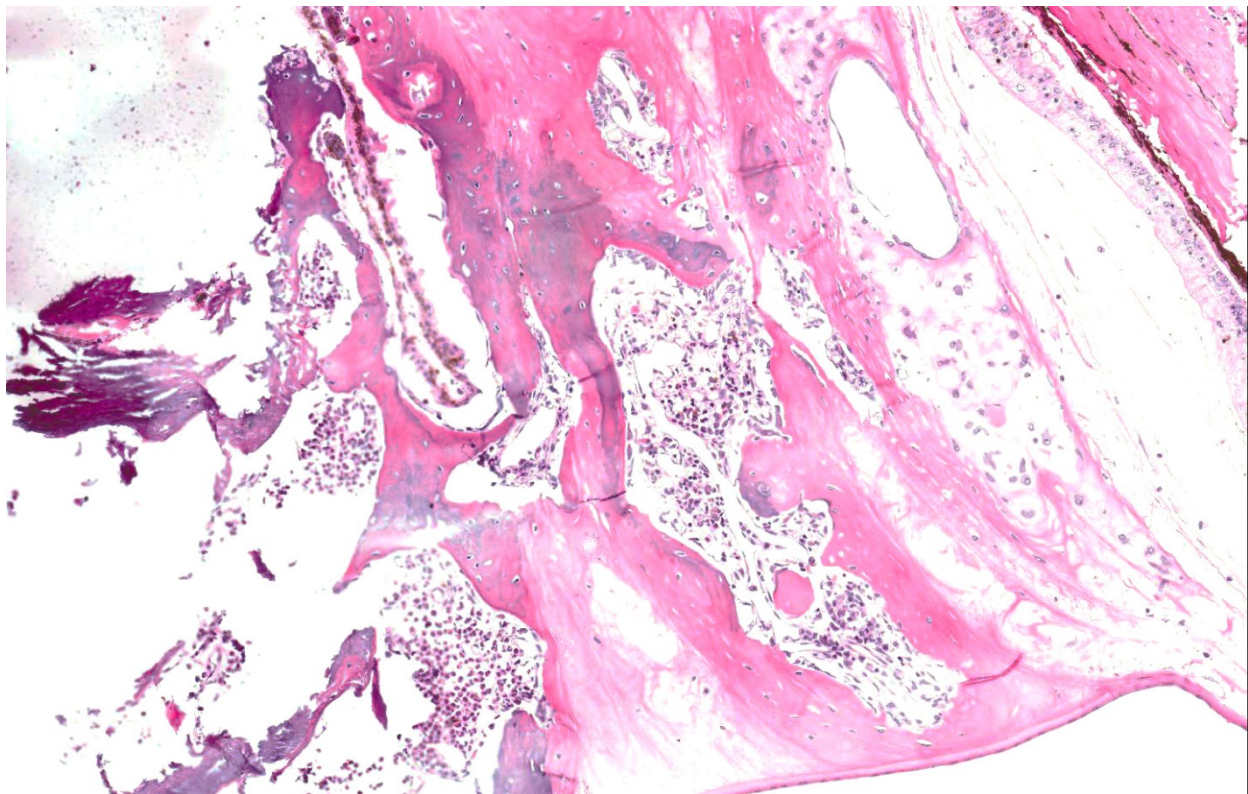
Contributor's Morphologic Diagnoses:

1. Eye: Heterotopic bone formation of the ciliary body.
2. Eye: Lymphoplasmacytic conjunctivitis, multifocal, chronic, mild.

Contributor's Comment: Heterotopic bone

formation, also known as osseous choristoma, is a sporadic, usually incidental finding in the eye of guinea pigs.^{5,10} Heterotopic bone formation of the ciliary body can be found in young as well as aged guinea pigs of both sexes and it might occur uni- or bilaterally.^{10,12} In general, affected animals don't show any clinical symptoms, however, development of secondary open-angle glaucoma by blockage of the iridocorneal filtration angle has been reported with chronic exposure keratitis being the most notable associated sequelae.¹⁰ Other authors on the contrary found no elevation of the intraocular pressure inside eyes displaying heterotopic bone formation of varying degrees compared to unaffected eyes.^{8,12}

The etiology of this condition has not been fully determined yet. Bone in the eye can



Globe, guinea pig. The spicules of bone within the ciliary body are mineralized (at left) and at right contain marrow elements. (HE, 84X)

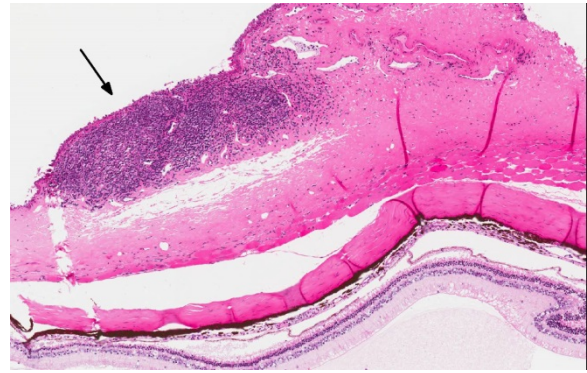
arise within metaplastic or neoplastic processes particularly in phthisic eyes.⁵ In most affected guinea pigs, however, no previous ocular trauma or disease has been reported.^{5,10,12} Due to their slow-growing nature and well-differentiated appearance, they originally have been classified as choristoma, which is defined as histologically normal tissue arising in ectopic positions and considered a benign congenital neoplasm, therefore resulting of an incorrect embryogenesis.⁷

It has also been noted that the role of the ciliary epithelium in transporting and concentrating plasma ascorbic acid into the aqueous humor might be a pivotal factor for development since ascorbic acid positively influences trabecular bone formation by modifying the expression of several bone matrix genes in osteoblasts.^{1,13} Osseous metaplasia and mineralization are common findings in other organs of guinea pigs, especially the lungs.⁸

Similar ocular lesions have also been described in other species including dogs and also humans.⁶ In humans the location differs in that mainly choroidal structures are affected.^{5,11}

JPC Diagnosis: Eye, anterior uvea: Osseous choristoma (heterotropic bone) with fibrovascular membrane formation, drainage angle occlusion, iris bombe, and diffuse mild retinal atrophy, *Cavia porcellus*, guinea pig.

Conference Comment: There have been several reports within the past 30 years detailing individual cases of osseous choristoma in guinea pigs with little additional information about this benign lesion which is considered an embryologic remnant that is left behind and grows as the animal ages.^{2, 3, 4, 5, 6, 10, 12}



Conjunctiva, guinea pig. There are numerous lymphocytes and fewer plasma cells within the conjunctiva. HE, 84X)

Bone is a normal feature of the eyes, particularly the sclera of birds and some reptiles, but not of the eye of mammals. Osseous metaplasia may result from trauma. Additionally, bone may develop as ossification within a pre-existing choroidal hemangioma.⁵ These causes can be ruled out by an otherwise normal ocular anatomy and no evidence of pre-existing vascular lesions or ocular trauma.

Osseous choristomas within the ciliary body appear microscopically as replacement and elevation of ciliary body tissue with mature bony spicules surrounded by a thin fibrous envelope. Frequently, the bone will contain vascular spaces and hematopoietically active bone marrow.⁵

Guinea pigs are particularly susceptible to ectopic mineralization, possibly related to the high calcium content of commercial guinea pig diets and alfalfa. In addition to heterotropic bone formation within the ciliary body of the eye, guinea pigs may develop ectopic ossification within the lungs and urolithiasis from high calcium within urine. Like rabbits, guinea pigs' main mode of calcium homeostasis is renal excretion, thus, chronic renal disease predisposes animals to ectopic mineralization.⁹ Ectopic

mineralization is different that an osseous choristoma, which is mature bone in an abnormal location.

In addition to the findings listed above by the contributor, conference attendees identified peripheral anterior synechiae, posterior synechiae, thinning of the sclera, and multifocal atrophy of the ganglion cell layer. Microscopic evidence for glaucoma was considered, and there was spirited discussion related to the cause, whether it was due to the pre-iridial fibrovascular membrane or compression of the trabecular meshwork by the osseous choristoma. Additional discussion centered on the presence of numerous lymphocytes within the conjunctiva and as to whether they represented true conjunctivitis or mucosal-associated lymphoid tissues which is commonly found at this site in older rodents.

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CASE IV: NE 17-399 (JPC 4101750).

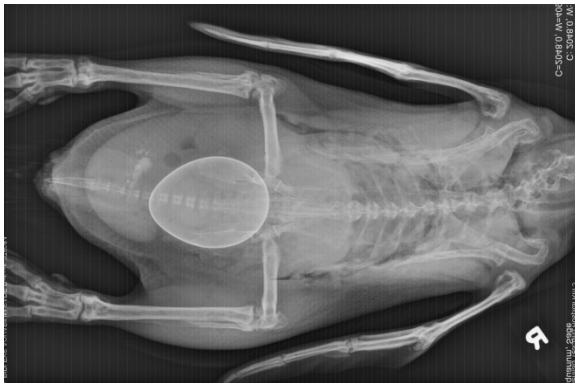
Signalment: 8.5 year-old, female, African black-footed (jackass) penguin (*Spheniscus demersus*).

History: This penguin was presented for acute inability to walk 2 days after laying an egg. Radiographs showed a large shelled egg in the coelom and diffuse osteopenia compared to an age-matched, control penguin. She was treated with calcium, butorphanol, meloxicam, enrofloxacin, and subcutaneous fluids, but died several hours later.

Gross Pathology: The body was in good nutritional condition (body condition score 3/5). The ribs were irregular, soft and serpentine, and cut easily with a scalpel blade. Both the left and right parathyroid glands were enlarged; the left measured 9x4x1.5mm and the right measured 10x4x1.5mm. There was an 89.7g egg in the oviduct near the cloaca. The eggshell was pale blue-green and hard. There was a complete fracture of the spine at the synsacral-thoracic junction with associated hemorrhage.

Laboratory results:

None provided.



Whole body radiograph, penguin. The cadaver displays diffuse osteopenia as well as a well formed shelled egg within the uterus. (HE, 6X). (Photo courtesy of: University of Tennessee College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences, 2407 River Drive, Room A205, Knoxville, TN 37996, https://vetmed.tennessee.edu/departments/Pages/biomedical_diagnostic_sciences.aspx)

Microscopic Description: The hematopoietic and adipose tissue of the marrow of the scleral ossicles is variably replaced by fibroblasts and osteoclasts. The numerous osteoclasts and their Howship's lacunae are forming a scalloped endosteal margin and thin cortex.

Contributor's Morphologic Diagnoses:

Scleral ossicles: Marked osteolysis with fibroplasia (fibrous osteodystrophy).



Ribs, penguin. The ribs are irregular, twisted, and cut easily with a scalpel. (Photo courtesy of: University of Tennessee College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences, 2407 River Drive, Room A205, Knoxville, TN 37996 https://vetmed.tennessee.edu/departments/Pages/biomedical_diagnostic_sciences.aspx)

Contributor's Comment: This was a case of nutritional secondary hyperparathyroidism with widespread fibrous osteodystrophy and vertebral fracture. The lesions in the scleral ossicles were also present in the femur, ribs, and vertebrae (all other bones examined).

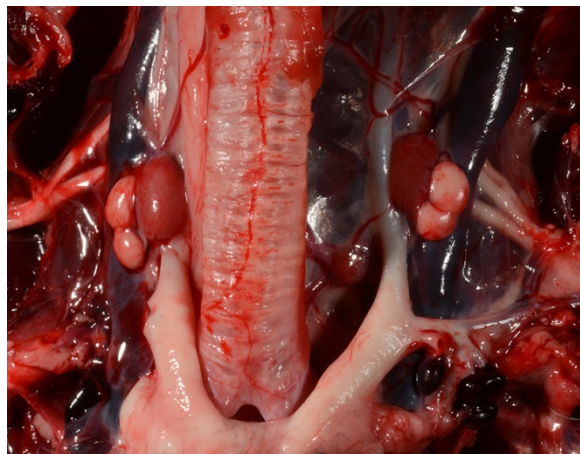
This penguin was part of an indoor colony at an aquarium. The diet consisted of capelin and a daily avian multivitamin. At one time this bird was supplemented with calcium carbonate during times of egg production, but due to her habit of only laying a single egg per season, the supplementation was discontinued. It is common for penguins to lay two eggs per clutch. After the death of

this bird, serum from other birds in the collection was tested for calcium and vitamin D3 levels; both were low and the birds are now supplemented.

Nutritional hyperparathyroidism and fibrous osteodystrophy has been reported in juvenile penguins.¹ It also occurs in laying hens, where the physiology of parathyroid hormone (PTH) is like that in mammals. PTH responds to hypocalcemia by stimulating osteoclasts (directly and indirectly via osteoblasts) to remove bone.³ The response is especially rapid in birds, where in response to PTH, osteoclasts increase their cell spread area by 40% within 2-4 minutes.³ Osteoclasts also increase their ruffled border and acid production in response to PTH.³

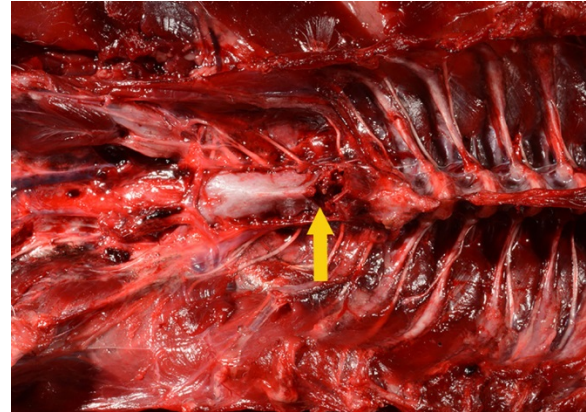
JPC Diagnosis: Eye, scleral ossicles: Osteolysis, diffuse, severe with fibroplasia (fibrous osteodystrophy), African black-footed (jackass) penguin (*Spheniscus demersus*).

Conference Comment: Fibrous



Parathyroid glands, penguin. Bilaterally, the parathyroid glands are markedly enlarged. (Photo courtesy of: University of Tennessee College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences, 2407 River Drive, Room A205, Knoxville 37996 https://vetmed.tennessee.edu/departments/Pages/biomedical_diagnostic_sciences.aspx)

osteodystrophy is a metabolic bone disease characterized by bone resorption with proliferation of adjacent fibrous tissue and poorly mineralized immature bone. This condition is due to chronically elevated plasma parathyroid hormone (PTH) or hyperparathyroidism and occurs in horses, pigs, dogs, cats, ferrets, goats, reptiles, and non-human primates (sheep and goats are



Vertebral column, penguin. There was a complete fracture of the spine at the synsacral-thoracic junction (yellow arrow) with associated hemorrhage. (Photo courtesy of: University of Tennessee College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences, 2407 River Drive, Room A205, Knoxville, TN 37996, https://vetmed.tennessee.edu/departments/Pages/biomedical_diagnostic_sciences.aspx)

relatively unaffected). PTH can be elevated due to any one of the following: functional parathyroid gland adenoma (primary hyperparathyroidism), hypercalcemia of malignancy (production of parathyroid hormone-related peptide (PTHrP)), reduced renal clearance of phosphate and thus low calcium due to their inverse relationship (renal secondary hyperparathyroidism), dietary deficiency of calcium, excess of phosphorus, or in association with vitamin D deficiency (nutritional secondary hyperparathyroidism).²

Primary hyperparathyroidism is characterized by autonomous secretion of PTH resulting in persistent hypercalcemia and hypophosphatemia (due to increased

urinary secretion of phosphate). This clinical pathology finding distinguishes primary from secondary hyperparathyroidism. In all cases of secondary hyperparathyroidism, plasma total calcium concentrations are normal or slightly decreased. Animals with primary hyperparathyroidism often suffer from polyuria and polydipsia, generalized muscle weakness, and widespread mineralization of soft tissues including nephrocalcinosis, which may result in the death of the animal even before skeletal changes are evident. Hereditary and familial primary hyperparathyroidism has been reported in German shepherd puppies and Keeshond dogs, respectively. Hypercalcemia of malignancy due to elevated PTHrP is most common in lymphoma and apocrine gland adenocarcinoma of the anal sac.²

Renal secondary hyperparathyroidism develops when impaired glomerular filtration leads to decreased excretion of phosphate. Hyperphosphatemia and is more common in dogs and cats. Subsequently, hypocalcemia develops (due to complexing of calcium with phosphate) which stimulates the release of PTH. Additionally, the hypocalcemia is exacerbated by released of FGF23 from osteocytes (triggered by hyperphosphatemia) with increases renal excretion of phosphate and suppresses 1α -hydroxylase which leads to decreased production and breakdown of $1,25(\text{OH})_2\text{D}_3$. Adult dogs with renal failure are most commonly affected with renal secondary hyperparathyroidism, but, as mentioned above, skeletal lesions are usually not as clinically important as the manifestations of uremia.²

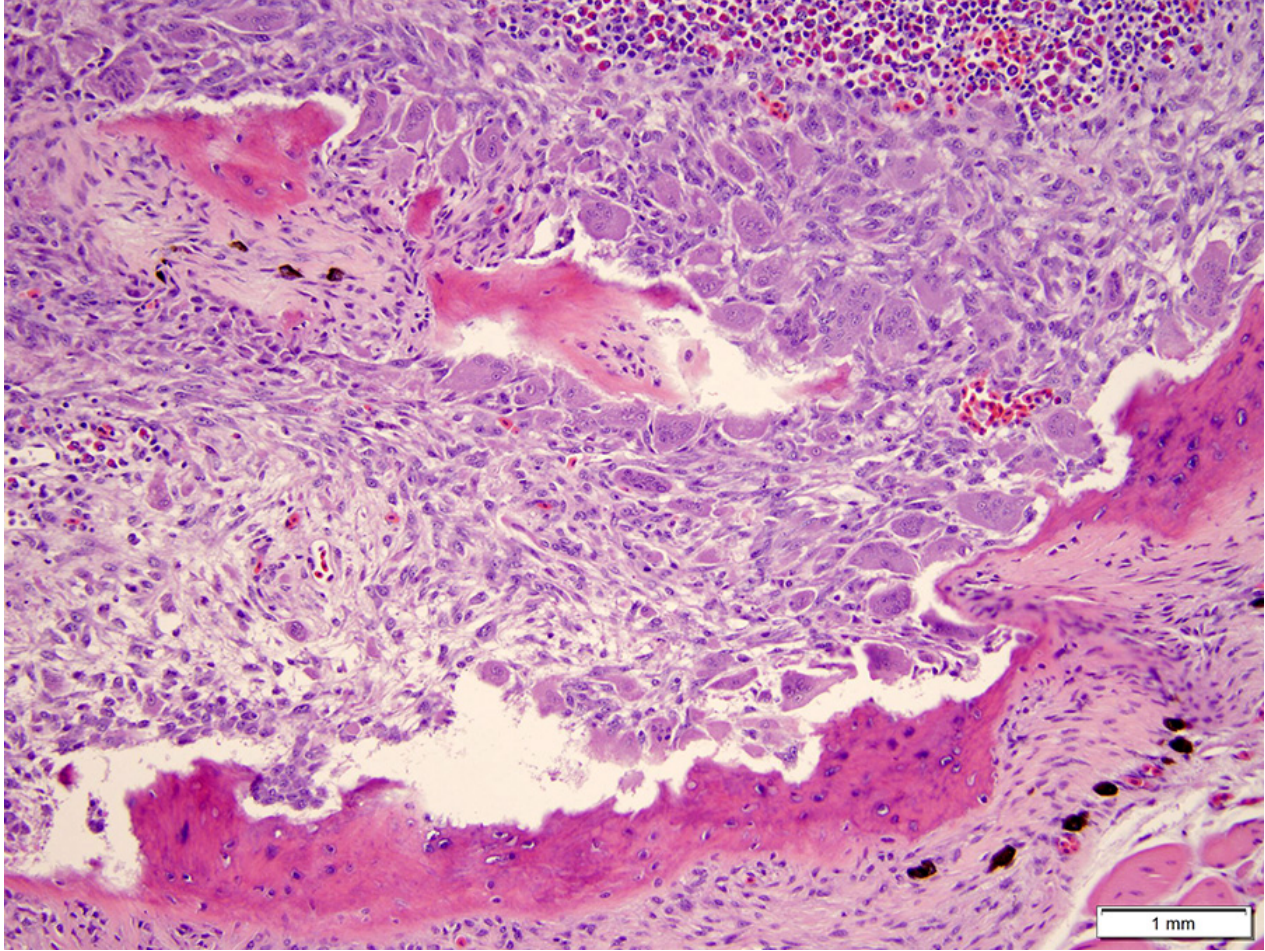
Finally, nutritional secondary hyperparathyroidism is most commonly caused by diets with low calcium and a high concentration of phosphorus. In most



Globe, penguin. The scleral ossicles (arrows) are prominent; one scleral ossicle (two arrows) is thickened and hypercellular. (HE 5X)

species, this affects primarily young, rapidly growing animals except in horses that are extremely sensitive to the effects of high phosphorus. In horses, nutritional secondary hyperparathyroidism, colloquially known as “bran disease” usually occurs after several months of a maintenance diet high in grain or tropical grasses high in oxalate, such as: *Setaria sphacelata*, *Cenchrus ciliaris* (buffel grass), *Brachiaria mutica* (para grass), *Digitaria decumbens* (pangola grass), *Pennisetum clandestinum* (kikuyu grass), and *Panicum* spp. These are dangerous because oxalate binds calcium and makes it unavailable for absorption. The characteristic gross finding in horses is “big head” or bilateral enlargement of the maxilla and mandible.² In captive birds with fibrous osteodystrophy, nutritional imbalances in calcium, phosphorus, and vitamin D are often compounded by inadequate amounts of unfiltered sunlight, which provides ultraviolet light required for birds to make vitamin D. The lighting conditions of the penguin in this case are unknown.

Contributing Institution:



Scleral ossicle, penguin. (100X) The lamellar and trabecular bone of the scleral ossicle is markedly decreased and has a scalloped edge. The cellular contents of the marrow spaces is replaced by a combination of osteoclasts (often in Howship's lacunae on the remaining bone) as well as plump fibroblasts. A small amount of marrow is present at upper right. (Photo courtesy of: University of Tennessee College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences, 2407 River Drive, Room A205, Knoxville, TN 37996, https://vetmed.tennessee.edu/departments/Pages/biomedical_diagnostic_sciences.aspx)

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