Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2013-2014

Conference 19

19 March 2014

CASE I: No label (JPC 4004355).

Signalment: 1-year-old intact female Sprague-Dawley rat, (*Rattus norvegicus*).

History: A one-year-old intact female experimentally naïve Sprague-Dawley rat (NTac:SD) used as a soiled bedding sentinel was noted to have buphthalmia of the right eye and had multiple foci of white tissue within the anterior chamber, in addition to a Y-shaped band of tissue (2mm in diameter) present within the posterior chamber. The vasculature surrounding the pupil was prominent and the anterior chamber was cloudy. Apart from the ocular lesion, the animal appeared to be in good health. The animal

1-1. Eye, SD rat: The right eye was bupthalmic and had multiple foci of white tissue within the anterior chamber in addition to a Y-shaped band of tissue (2mm in diameter) present within the posterior chamber. The vasculature surrounding the pupil was prominent and the anterior chamber was cloudy. (Photo courtesy of: Laboratory of Comparative Pathology, Memorial Sloan Kettering Cancer Center, 1275 York Av Box 270, New York, NY 10065)

1-2. Eye, SD rat: The affected eye on right shows a marked protein effusion filling the anterior chamber as well as a posterior synechia and mineralization subjacent to the lens capsule. Normal eye at left for comparison. (HE 0.63X)

was monitored and the lesion showed no signs of progression. The animal was later euthanized for routine sentinel testing.

Gross Pathology: Gross lesions were observed in the right eye, as described in the history. No other gross changes were observed on complete necropsy.

Histopathologic Description: Right eye: The lens is misshapen and has a wrinkled capsule. Multifocally extensive areas of loss of sub-capsular lenticular fibers (both on anterior and posterior surfaces) and replacement by mineralized debris are evident. Lenticular epithelium is hyperplastic and there is migration of epithelium to the posterior lens surface. Several lenticular epithelial cells are spindle-shaped (fibrous metaplasia).

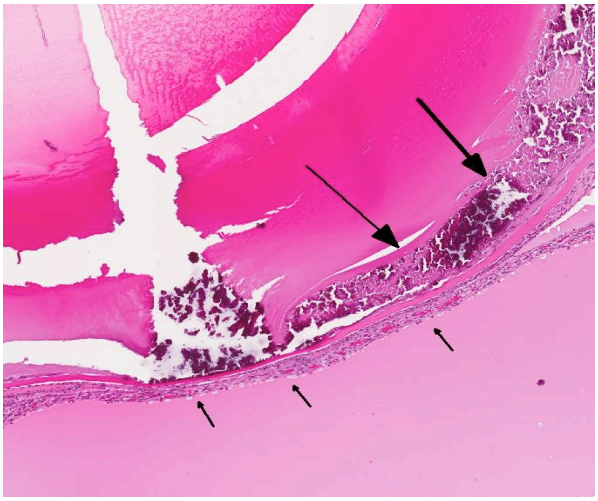
Multifocal adhesions between the lens and posterior surface of the iris (posterior synechiae) are present. Extensive fibrovascular membranes are present and are adhered to the ciliary body, posterior lens capsule, and choroid (cyclitic membranes). The retina shows full thickness atrophy. The iris shows mild vascular congestion. The iris, ciliary body and choroid are thickened by fibroplasia and an inflammatory infiltrate composed of numerous lymphocytes, and moderate numbers of plasma cells, eosinophils, neutrophils and hemosiderin-laden macrophages, with multifocal formation of lymphocytic aggregates in the choroid. Remnant spaces in the posterior chamber that are bordered by cyclitic membranes are filled with eosinophilic homogenous proteinaceous fluid.

The anterior chamber is filled with eosinophilic homogenous proteinaceous fluid (plasmoid aqueous).

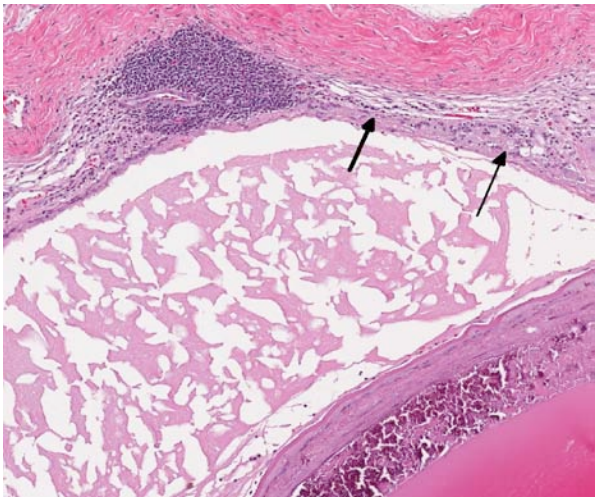
Left eye (section not provided): Within normal limits.

Contributor's Morphologic Diagnosis: Right eye:
1. Marked panuveitis, lymphocytic, with posterior synechiae and cyclitic membranes, chronic.
2. Hypermature cataract, subcapsular, chronic.
3. Retina: Marked retinal atrophy, chronic.

Contributor's Comment: Histopathological changes in the right eye are consistent with advanced cataract, and other changes within the eye suggest phacolysis (lens protein leakage) leading to secondary uveitis (phacolytic uveitis). The pathogenesis is suspected to be leakage of lenticular protein from the lens (even with intact lens capsule) leading to uveal inflammation. Predominant lymphocytic uveitis present in this case is also consistent with phacolysis leading to secondary uveitis. The Y-shaped macroscopic appearance of the aforementioned cataract is similar to the congenital sutural cataract that occurs along the suture lines of the lens in humans and may also be observed as a late change in advanced cataracts of other etiologies. Although



1-3. Eye, SD rat: Higher magnification of the adherence of the iris to the lens capsule (posterior synechia) (small arrows) as well as loss of subcapsular lens fibers with replacement by mineralized debris. (Large arrows). (HE 41X)



1-4. Eye, SD rat: The lens is in direct apposition to the retina at right. At left, the vitreous is markedly diminished and there is severe full thickness retinal atrophy (arrows). Underneath the wrinkled lens capsule, there is fibrous metaplasia of lens fibers adjacent to areas of mineralization.

suture lines are present in both anterior and posterior lens capsules, it is the posterior capsular suture lines that manifest a characteristic Y-shape grossly when cataract forms along its margins. Some forms of non-congenital mature cataracts can progress along suture lines.

Cataracts are commonly associated with aging in various strains, including Sprague-Dawley (SD) rats. No sex predilection for the development of cataracts has been reported in the literature. Capsular cataracts, specifically posterior sub-capsular cataracts, are noted with increasing incidence starting at week 57 of age in SD rats (Week 57- 2.7%, Week 83- 8.5% and Week 110-13.4%).[1] Diffuse opacification of the lens along the posterior suture lines has also been reported in this strain.[1] Anterior cortical striations that can eventually progress to senile cataracts are commonly seen in SD rats between 83 and 110 weeks.[1] It is interesting to note that this case has hypermature cataract in both anterior and posterior subcapsular regions. It is difficult to ascertain the region where the cataract first started. However, based on the reported age-based incidence, it is speculated that the posterior subcapsular region is the first site of cataract formation. It is also possible that both anterior and posterior regions co-evolved the cataractous change independently of one another.

Approximately 3-4% of Sprague-Dawley rats have minor lens lesions comprised of foci of swollen or degenerate lens fibers starting as early as 19-20 days of gestation and these may represent early changes that may eventually lead to cataract.[2] Glaucoma has been described as a complication of advanced cataracts in rats, and the proposed pathogenesis was lens-induced uveitis.[3]

JPC Diagnosis: Eye: Uveitis, lymphoplasmacytic, chronic, diffuse, severe, with cataract formation, drainage angle occlusion, and posterior synechiae.

Conference Comment: Cataract is the most common lens disorder in any domestic species; it can be distinguished microscopically from fixation/sectioning artifact by (in order of occurrence) detection of Morgagnian globules (eosinophilic globules of denatured lens protein), bladder cells (large, foamy nucleated cells that may represent abortive epithelial attempts at new lens fiber formation), lens epithelial hyperplasia and/or posterior migration of lens epithelium (occasionally followed by fibrous metaplasia), and mineralization. Hypermature cataracts often exhibit residual nuclei within lakes of proteinaceous fluid, surrounded by a wrinkled capsule. Cataracts can be inherited (i.e. familial cataracts in dogs) or secondary to anatomic anterior segment anomalies; formation may also be induced by a variety of stimuli, including solar (or other) irradiation, cold, increased intraocular pressure, toxins, nutritional derangements, local inflammation and direct trauma. Most cataracts encountered within veterinary medicine are classified as inherited, post-inflammatory or idiopathic; however, cataract formation due to canine diabetes, galactose accumulation in kangaroos and wallabies raised on cow's milk, arginine deficiency in puppies, wolf cubs, or kittens on milk replacer, dietary deficiencies (in sulfur-containing amino acids, zinc or vitamin C) or solar irradiation in farmed fish and administration of the aminoglycoside hygromycin B in sows, have also been described, although the pathogenesis of these examples is not necessarily fully elucidated.[4] Additionally, as noted by the contributor, cataract formation is a common age-related change in several strains of rats.

In this case, we concur with the contributor's comprehensive histological description as well as the proposed pathogenesis. The formation of age-induced cataracts likely resulted in lens protein leakage (phacolysis), with subsequent phacolytic uveitis, occlusion of the drainage angle, increased intraocular pressure, glaucoma and eventually, full thickness retinal atrophy.

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CASE II: E3236/07 (JPC 3164800).

Signalment: 8-year-old neutered male Cairn terrier, (*Canis familiaris*).

History: Surgical extirpation of the bulbus, further clinical data not available.

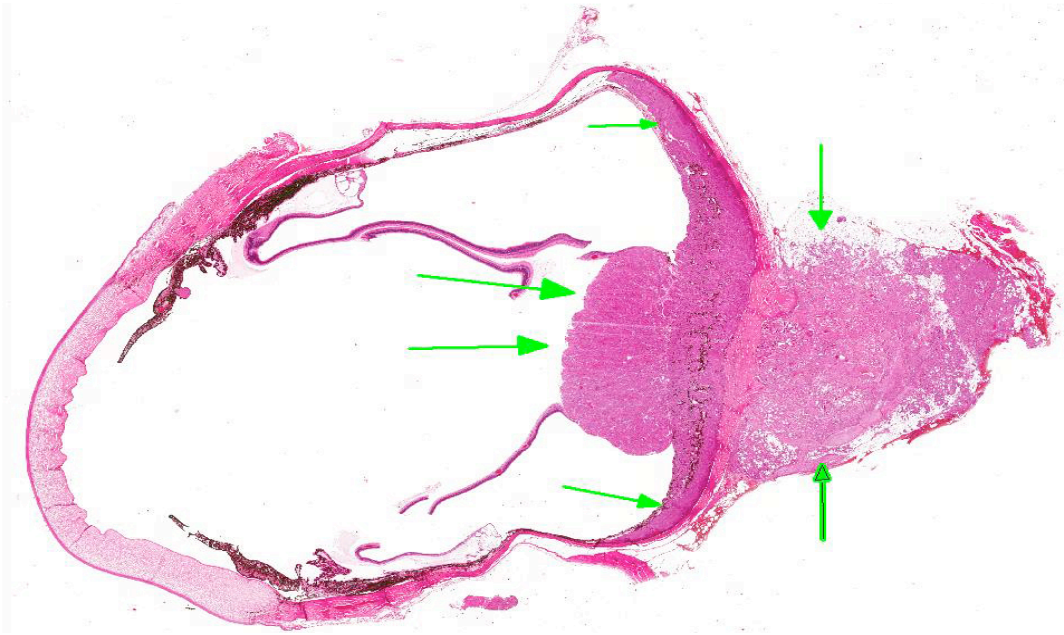
Gross Pathology: None.

Histopathologic Description: Replacing, infiltrating and expanding the optic nerve disc and proximal parts of the optic nerve origin is a moderately circumscribed, densely cellular neoplasm extending bilaterally into the choroid and the retrobulbar adipose tissue. The mass is separated by a thin fibrovascular stroma into nests of closely packed predominantly epithelioid cells or spindle to polygonal cells arranged in loosely interlacing streams and whorls. In areas extending into the choroid variable numbers of melanin-containing cells are intermingled in the stroma. Neoplastic cells have variably distinct borders with varying amounts of eosinophilic cytoplasm, oval to spindle-shaped and occasionally vesicular nuclei with finely stippled chromatin and predominantly one distinct nucleolus. Epithelioid cells forming small nests often show abundant eosinophilic cytoplasm and eccentric nuclei. Mitotic rate is less than one mitotic figure per high power field. Multifocally, especially in extrabulbar parts of the mass are foci of myxoid, cartilaginous or osseous metaplasia. Multifocally, mainly perivascularly, there are few lymphocytes, plasma cells, neutrophils and intermingled with some pigment (hemosiderin) laden macrophages.

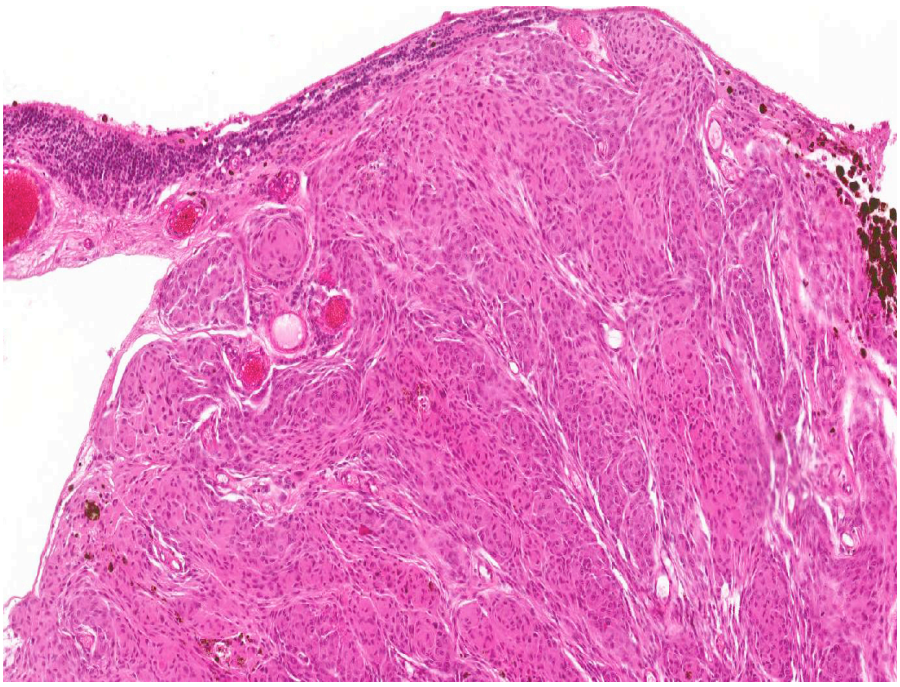
Additionally, segments of the retina adjacent to the tumor are mildly atrophic.

Contributor's Morphologic Diagnosis: Eye, optic nerve: Meningioma, optic nerve type, canine.

Contributor's Comment: In dogs and cats, meningiomas are the most common primary tumor arising in the nervous system.[7] In the dog they occur more commonly in the brain than in the spinal cord[4,7] Those arising in the brain are often localized over the convexities, attached to the falx or the tentorium cerebelli or inside the ventricular system. Rarely they occur retrobulbarly.[3,7] In general intracranial meningiomas are slow growing, discrete, expansile neoplasms and malignant behavior or extracranial metastases are only rarely reported.[1,6] Due to the embryonic origin of the meninges from both mesoderm and neural crest, they can undergo mesenchymal and epithelial differentiation and show highly variable morphological patterns.[7] The current World Health Organization (WHO)



2-1. Eye, dog: A cross section of the globe shows an infiltrative neoplasm expanding the optic nerve, and expanding laterally underneath the detached retina, and protruding into the posterior chamber (arrows) (HE 0.63X)



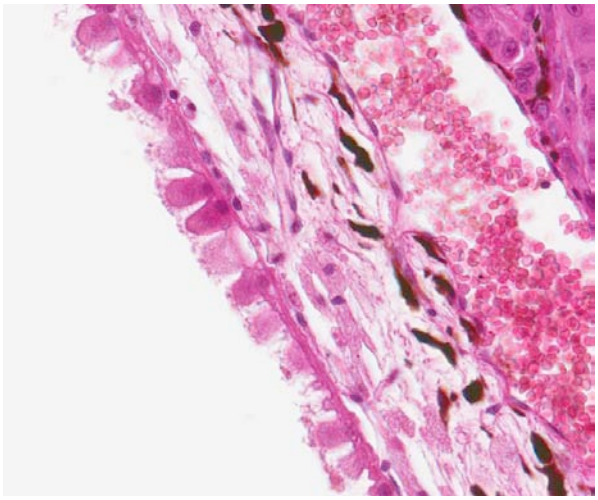
2-2. Eye, dog: Underneath the detached atrophic retina, neoplastic cells are arranged in discrete bundles and whorls characteristic of meningioma. There are aggregates of melanin containing cells, likely from the infiltrated choroid. (HE 140X)

classification of tumors of the nervous system in domestic animals[2] describes nine histological patterns: meningothelial, fibrous (fibrobroblastic), transitional (mixed), psammomatous, angiomatous, papillary, granular cell, myxoid and anaplastic (malignant). Montoliu et al. reviewed 30 cases of meningiomas and divided into transitional, meningothelial, psammomatous, anaplastic, fibroblastic, angioblastic, papillary, microcystic and those types arising from the optic nerve.[5] The latter were characterized predominantly by meningothelial or transitional patterns and contained multiple areas of myxoid, cartilaginous and osseous metaplasia. Because of this distinctive morphology they suggested to include optic nerve meningiomas into the classification as a separate entity. The case presented here qualifies for this type due to localization and histological appearance.

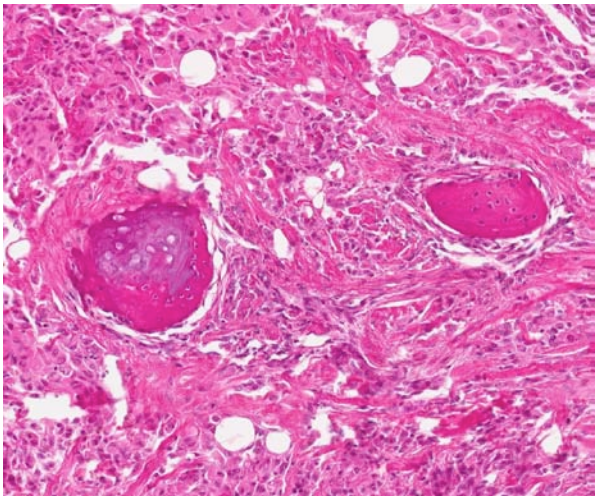
Immunohistochemically, most of the cases stain positive for vimentin, less often also for cytokeratin, pointing to a more mesenchymal and less epithelial differentiation. Expression of S-100 protein and neuron-specific enolase (NSE) is inconstant and rarely a predominant feature.[5]

JPC Diagnosis: Eye, optic nerve: Meningioma with acute neural retinal detachment.

Conference Comment: The contributor provides an excellent summary of canine intra- and



2-3. Eye, dog: The retinal pigmented epithelial cells are markedly hyperplastic ("tombstoned"), indicating that the retinal detachment occurred prior to sectioning. (HE 256X)



2-4. Eye, dog: Scattered foci of metaplastic bone are present within the neoplasm. (HE 180X)

extracranial meningioma. In addition to the distinct neoplastic features described above, participants observed a striking separation of the retinal pigment epithelium (RPE) from the photoreceptors (i.e., neural retina) with diffuse, marked hypertrophy ("tombstoning") and multifocal cystic degeneration of the RPE, as well as pockets of proteinaceous fluid and few neutrophils within the subneural retinal space. There is also mild retinal atrophy, as noted by the contributor. These histopathological findings support an additional diagnosis of neural retinal detachment, which refers specifically to a separation between the neural retina and the RPE. Neural retinal detachment was likely secondary to locally infiltrative neoplastic cells cleaving photoreceptors from their interdigitations with the RPE. Conversely, artifactual retinal separation is a common sequela of formalin fixation, and is distinguished from pathologic retinal detachment by the absence of RPE hypertrophy and absence of fluid and/or inflammatory cells in the subneural retinal space.[8,9]

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CASE III: UW case 1 (JPC 4032969).

Signalment: 17-year-old male neutered domestic shorthaired cat, (*Felis catus).*

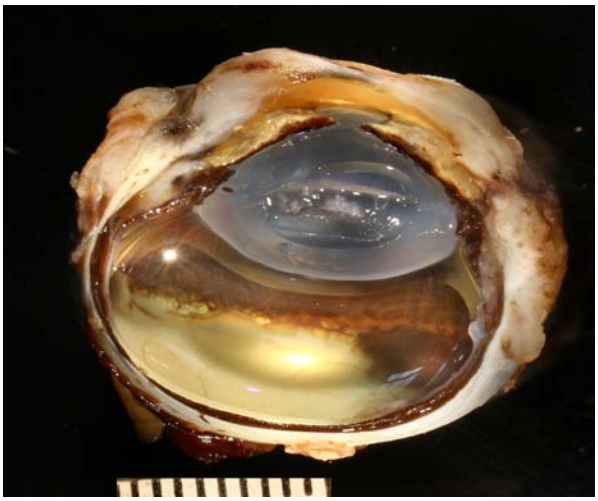
History: The cat presented with a 1-year history of severe conjunctivitis and corneal ulceration with secondary corneal sequestrum formation. Clinically, a collapsed anterior chamber, symblepharon, blepharospasm and protrusion of the third eyelid were observed. Additionally, the cat had chronic corneal disease that was considered a sequel to poorly managed feline herpes virus-related keratoconjunctivitis when it was young. Due to a poor prognosis, the eye was enucleated and sent to the Comparative Ocular Pathology Laboratory of Wisconsin (COPLOW) at the University of Wisconsin-Madison.

Gross Pathology: There is diffuse white to tan opacification and thickening of the peripheral cornea and limbus extending concentrically towards the axial cornea. The most axial cornea surface is depressed and ulcerated, presenting moderate brown discoloration at the periphery and center of the ulceration. On cut section the corneal profile, limbus, equatorial sclera, episclera, and ciliary body stroma are expanded by a white, firm and irregular tissue. The anterior surface of the iris is thickened and irregular. The posterior aspect of the globe is grossly normal.

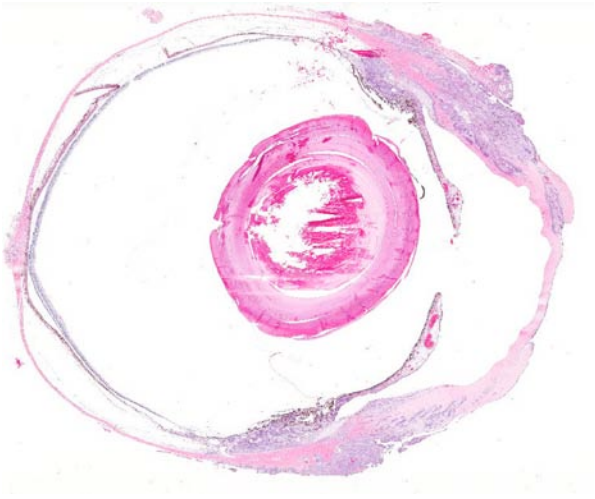
Laboratory Results: Mildly increased intraocular pressure (25mmHg) and positive fluorescein stain in the central cornea.

Histopathologic Description: There is a poorly delineated, highly infiltrative and highly cellular neoplastic tissue infiltrating, expanding and partially replacing the superior and inferior limbus, extending approximately 8 mm into the peripheral cornea, affecting the superficial 2/3 of the stroma. The neoplastic tissue also infiltrates the conjunctival substantia propria, equatorial sclera and episclera, ciliary body stroma, base of the iris and trabecular meshwork causing complete collapse of the iridocorneal angle. A second, distinctive pattern of infiltration is present with the neoplastic cells carpeting the anterior and posterior iris surfaces, the surface of the ciliary body *plicae,* trabecular meshwork beams, and the ulcerated corneal surface, mimicking the corneal epithelium. Neoplastic cells are arranged in cords and nests, sometimes forming anastomosing trabeculae, and are supported by abundant fibrovascular stroma (desmoplastic reaction). Multifocally there is keratinization and sloughing of the neoplastic cells in the center of neoplastic nests. Neoplastic cells present moderate amounts of eosinophilic cytoplasm with variably distinct cell borders, oval nuclei with coarsely stippled chromatin and usually one large central magenta nucleolus. There are 32 mitotic figures in 10 hpf. Cellular pleomorphism is marked with multiple karyomegalic cells and atypical mitotic figures.

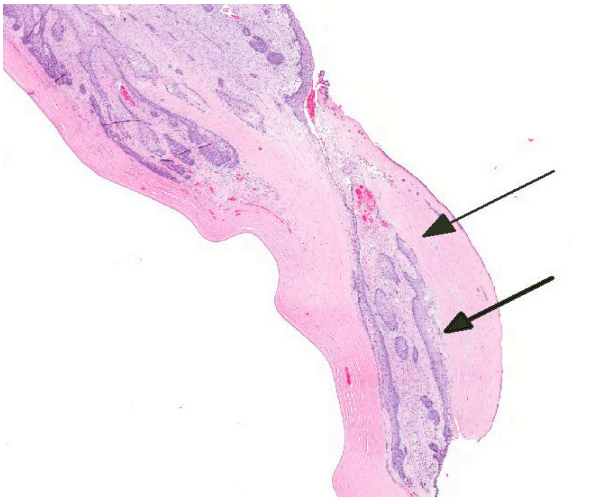
3-1. Eye, cat, sagittal section: There is diffuse thickening of the peripheral cornea and limbus and axial corneal ulceration and brown discoloration. (Photo courtesy of: Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, http://www.vetmed.wisc.edu)



3-2. Eye, cat, sagittal section: Neoplastic tissue infiltrates the corneal, limbus, equatorial sclera and episclera, ciliary body stroma and iris surface. The posterior aspect of the globe is grossly normal. (Photo courtesy of: Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, http://www.vetmed.wisc.edu)



3-3. Eye, cat: The corneal limbus, sclera, uviea, and ciliary body are markedly expanded by an infiltrative neoplasm. (HE 0.63X)



3-4. Eye, cat: Neoplastic cells infiltrate a corneal fissure (arrows). (HE 14X)

Neoplastic cells are also seen infiltrating and completely filling and expanding multiple vascular profiles in the equatorial sclera, ciliary body and iris stroma, and peripheral and peri-papillary choroid. There is diffuse corneal ulceration and marked loss of axial corneal stroma (facet lesion). The peripheral corneal stroma presents focally extensive areas of liquefaction of the corneal lamellae (collagenolysis) with accumulation of fine nuclear debris. There is moderate vascularization of the deep corneal stroma and moderate infiltration of neutrophils. There are diminished numbers of ganglion cells in the inner retina.

Contributor's Morphologic Diagnosis: 1. Eye, Metastatic carcinoma.
2. Cornea, severe and diffuse ulcerative and collagenolytic keratitis with axial facet lesion formation.
3. Retina, Marked and diffuse ganglion cell layer atrophy.

Contributor's Comment: Metastases to the eye are less frequently diagnosed than primary ocular tumors.[1,2,3,4] Despite this, the rich vascularization of the uveal tissue and the immune privilege associated with the intraocular environment favor the globe as a site for metastatic disease.[2] Ocular metastases have been diagnosed in cats with many forms of malignant neoplasia. Pulmonary carcinoma, squamous cell carcinoma of undetermined origin, mammary adenocarcinoma and fibrosarcoma are the most commonly reported.[1,3] There are 4,542 cases of feline ocular neoplasia in the COPLOW collection database. Of those, 580 are metastatic tumors (12%), 423 of which are lymphoma (72%). The remaining 157 metastatic, non-lymphoma cases are described in Table 1.

Table 1. Cases of feline metastatic tumor to the eye on the COPLOW database

	Cases	%
Feline ocular tumors (total)	4542	
Feline metastatic tumors to the eye	580	12% of total cases
1. Lymphomas	423	72% of metastatic cases
1. Non-lymphoma	157	28% of metastatic cases
a. Undifferentiated neoplasia	5	3.1% of non-lymphomas
a. Sarcoma	25	15.9% of non-lymphomas
a. Carcinoma	127	81% of non-lymphomas
- Undifferentiated carcinoma	74	58.2% of carcinomas
- Pulmonary carcinoma	24	18.8% of carcinomas
- Squamous cell carcinoma	24	18.8% of carcinomas
- Mammary carcinoma	3	2.3% of carcinomas
- Anal sac adenocarcinoma	1	0.7% of carcinomas
- Uterine carcinoma	1	0.7% of carcinomas

3-5. Eye, cat: Neoplastic cells carpet the ulcerated corneal surface and multifocally infiltrate the superficial corneal stroma (arrow). (HE 100X) (Photo courtesy of: Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, http://www.vetmed.wisc.edu)

3-6. Eye, cat: Neoplastic cells carpet the anterior and posterior iris surface. (HE 100X) (Photo courtesy of: Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, http://www.vetmed.wisc.edu)

Common morphologic features of metastatic neoplasia in cat eyes include[1]:

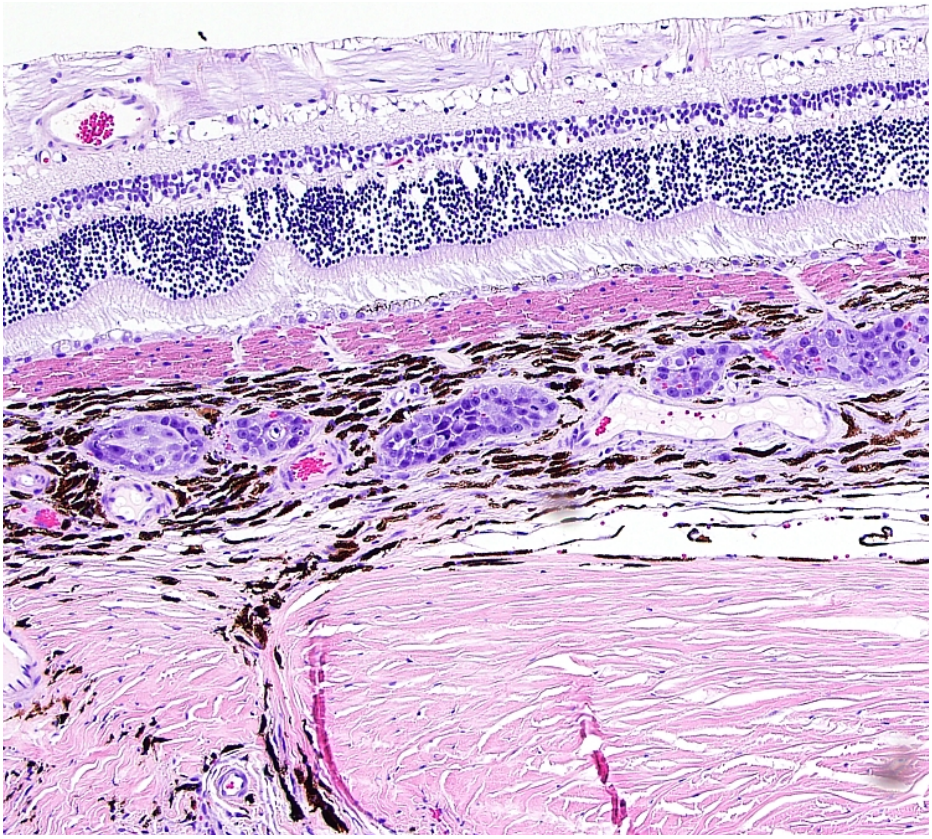
1. Uni- or bilateral uveal metastases.
2. A tendency to affect the choroid more often than the anterior uvea.
3. When the anterior uvea is affected, neoplastic cells line or carpet the surfaces of the iris and ciliary body.
4. Extensive and widespread invasion of blood vessels.
5. A pattern of choroidal infarction with characteristic, wedge-shaped areas of tapetal discoloration and profound vascular attenuation visible on funduscopy.
6. Orbital involvement may accompany involvement of the posterior segment of the globe.

The present case shows most of the previously described common morphologic features of metastatic neoplasia. Of those features, the lining of ocular surfaces and the marked vascular invasion – especially of the choroidal vessels – are the most salient. Interestingly, the neoplastic cells also produce an unusual pattern of carpeting by proliferating over the ulcerated corneal surface, mimicking the corneal epithelium. The absence of the native corneal epithelium and subsequent exposure of the corneal stroma might have facilitated/stimulated neoplastic cells to proliferate in that pattern.

The neoplastic tissue presents classic epithelial morphology with multiple areas developing keratinization of the inner cellular layers. This feature points towards a squamous cell carcinoma, but other undifferentiated carcinomas with squamous metaplasia cannot be ruled out.

Other possible differential diagnoses include pulmonary carcinomas, primary corneo-conjunctival squamous cell carcinomas and mammary carcinomas. Metastatic pulmonary carcinomas tend to form acinar/glandular structures on the uveal tissue and/or present ciliated epithelium carpeting the ocular surfaces. Primary ocular squamous cell carcinomas in cats can invade the intraocular structures, especially the anterior chamber and uvea, but they seldom infiltrate vessels and the posterior aspect of the globe.[4] Metastatic mammary carcinoma is a remote possibility since the cat in this case is male and neutered.

The decrease number of ganglion cells in the retina confirms the clinical diagnosis of secondary glaucoma. In cats, the main histologic feature of glaucoma is loss of ganglion cells without progressive degeneration of the outer retina, as seen in dogs.[1] The majority of glaucomas in cats are secondary to other ocular diseases, most notably chronic lymphoplasmacytic anterior uveitis, systemic hypertension-related intraocular hemorrhages, and intraocular neoplasia.[1,2]



3-7. Eye, cat: Neoplastic cells infiltrate and expand peri-papillary choroidal vessels. (HE 100X) (Photo courtesy of: Department of Pathobiological Sciences, School of Veterinary Medicine, University of Wisconsin-Madison, http://www.vetmed.wisc.edu)

The patient in the present case was lost to follow-up before the identification of a primary tumor.

JPC Diagnosis: Eye, globe: Carcinoma, poorly differentiated with drainage angle occlusion, retinal atrophy, multifocal detachment, ulcerative keratitis with axial facet lesion formation and numerous tumor emboli.

Conference Comment: We thank the contributor for providing this unique, interesting case as well as a comprehensive review of primary and metastatic ocular tumors in cats. The notes on salient histopathology findings in primary versus metastatic ocular tumors are especially relevant. Prior to the conference, the moderator led a particularly informative discussion encompassing normal ocular anatomy and physiology, touching upon the concept (also noted by the contributor) that the abundant uveal vascularization and associated immune privilege of ocular tissue provide a favorable environment for tumor metastasis; however, the moderator pointed out that these conditions are also advantageous for the development of primary ocular tumors. So, while this neoplasm admittedly exhibits similar morphologic features to those described above for metastatic ocular tumors, the moderator suggests that definitive differentiation from a primary tumor is quite difficult, and likely requires identification of the initial tumor at another anatomic location.

Many conference participants tentatively identified this tumor as squamous cell carcinoma (SCC). Ocular involvement of SCC is most common in cattle and horses, but has also been reported in cats and dogs. In all domestic species, SCC involving the ocular surface appears to have a preference for the limbus (corneoscleral junction) which is the transition zone between the corneal and conjunctival epithelial cell populations. The limbus is home to the local stem cell population; stem cells have a high proliferative capacity, are susceptible to the accumulation of oncogenic mutations, and are thought to be the source of many neoplasms. Corneolimbal SCC refers specifically to a neoplasm originating at the limbus with extension into the cornea (as opposed to originating from the corneal epithelium itself).[4] This neoplasm manifests several histologic features suggestive of corneolimbal SCC: neoplastic cells are most numerous in the sclera, ciliary body and limbus, there is fairly prominent intracellular bridging with moderate desmoplasia and there is scattered infiltration of neutrophils; however, participants did not appreciate significant dyskeratosis or formation of keratin pearls, so we are unable to definitively diagnose ocular SCC. The contributor provides a brief, but thorough differential diagnosis for the gross and microscopic lesions in this case.

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CASE IV: Case 1 N092-2012 (JPC 4035683).

Signalment: 1-year-old intact domestic shorthair cat, (*Felis catus*).

History: A recently rescued approximately 1-year-old stray, intact DSH cat, weighing 3.2 kg was presented to the Ross University Veterinary Teaching Hospital (RU-VTH) for routine physical examination and vaccination. A 1 cm smooth, firm to hard, unilateral, non-painful mass was detected on the right mid-mandible. Multifocal areas of ulceration were present on the buccal surface of the gums along the molar portion of the body of the mandible. Despite antibiotic therapy the cat's overall physical condition deteriorated and two months later it was brought back to the RU-VTH for evaluation. The mass was fast growing, reaching 6 cm in its largest dimension. The cat was euthanized due to poor body condition and progression of the lesion despite therapy.

Gross Pathology: Abnormal findings were confined to the right mandible and the regional lymph nodes. The mandible was brittle and could be sliced with the necropsy knife. The right lower gingival mucosa was diffusely red, firm and swollen. The swelling extended to the right sublingual inter-mandibular space. The right submandibular and parotid lymph nodes were markedly enlarged (up to 2 cm in the largest dimension), firm and wet.

Laboratory Results: A core bone marrow biopsy was used for culture and incubated at 37°C in aerobic and anaerobic conditions. Microscopically the cultured organisms were characterized as Gram positive, acid fast negative, filamentous bacteria. Molecular testing of the isolates by amplification and sequencing of the 16S rRNA gene identified the isolates as *Nocardia cyriacigeorgica*.

Histopathologic Description: Mandibular mass: Routine H&E sections from the core biopsy revealed focal new bone formation around areas of osteolysis and inflammatory cell infiltration surrounding large, irregularly-shaped, faintly basophilic clusters of filamentous bacteria rimed by fine eosinophilic amorphous material (Splendore-Hoeppli phenomenon). Bacterial colonies were surrounded by neutrophils, lesser numbers of plasma cells, macrophages, and occasional multinucleated giant cells and fibroblasts at the outermost layer. Anastomosing trabeculae of newly deposited woven bone (bone proliferation) were seen around inflammatory foci.

4-1. Mandible, cat: A 1 cm smooth, hard unilateral mass was present on the right mid-mandible of a 1-year-old cat. (Photo courtesy of: Department of Biomedical Sciences, Ross University School of Veterinary Medicine, St. Kitts, West Indies www.rossu.edu)

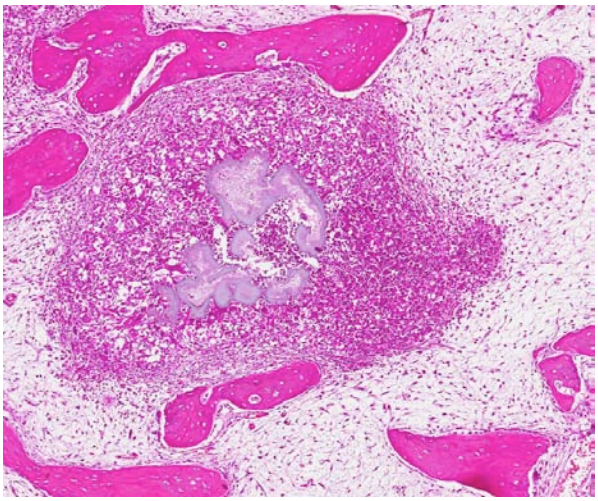
Contributor's Morphologic Diagnosis: Chronic multifocal pyogranulomatous osteomyelitis with intralesional filamentous bacteria.

Contributor's Comment: Mandibular osteomyelitis, also known as "lumpy jaw" in ruminants and other domestic and wild animal species, is uncommon in domestic cats. It is a condition characterized by pyogranulomatous inflammation resulting in bone destruction and remodeling. Lumpy jaw in hoofed animals is believed to occur secondary to oral infection, poor drainage, coarse forage ingestion, dental eruptions and oral abrasions. Common bacterial etiologies for lumpy jaw are *Actinomyces*

bovis in ruminants and *Fusobacterium necrophorum* in kangaroos.[1] Nocardia spp. are aerobic actinomycetes ubiquitous in soil and water, and are known to cause opportunistic infections in terrestrial and marine mammal species.[4] The severe pyogranulomatous mandibular osteomyelitis diagnosed in this cat was the result of infection with a recently described Nocardia species, *Nocardia cyriacigeorgica*. In recent years, *Nocardia* species identification and taxonomy has greatly improved with the availability of molecular methods such as 16S rRNA and hsp65 gene sequence analysis. *Nocardia cyriacigeorgica* is an actinomycete which, since its first description in 2001, has been reported as a causative agent of human disease in Europe, Asia, Canada and the USA.[5] While *Nocardia cyriacigeorgica* infection has not been described in domestic species, it has been reported in a captive beluga whale,[4] and is currently regarded as an emergent pathogen in people.[3] To our knowledge this is the first report of *N. cyriacigeorgica*-induced mandibular osteomyelitis in a cat. Interestingly, gross and microscopic

4-2. Mandible, cat: A dorsoventral view of the right mandibular mass. (Photo courtesy of: Department of Biomedical Sciences, Ross University School of Veterinary Medicine, St. Kitts, West Indies www.rossu.edu)

4-3. Mandible, cat: A core biopsy of the mandibular mass both loss of cortical bone adjacent to periosteal new bone growth (top) and multifocal areas of hypercellularity scattered through the cancellous bone. (HE 0.63X)



4-4. Mandible, cat: Areas of hypercellular within the medulla correspond to pyogranulomas centered on foci of Splendore-Hoeppli material. (HE 48X)

findings of the mandibular lesions caused by this potentially zoonotic bacterium closely resemble those of mandibular actinomycosis (lumpy jaw) in cattle.

JPC Diagnosis: Bone: Osteomyelitis and cellulitis, pyogranulomatous, multifocal to coalescing, marked, with large colonies of filamentous bacteria.

Conference Comment: This case is interesting in that *Nocardia* spp. is not generally classified as a large colony forming bacterium in tissue; *Yersinia* spp., *Actinomyces* spp., *Actinobacillus* spp., *Corynebacterium* spp., *Staphylcoccus* spp. and *Streptococcus* spp. (see WSC 2013-14, conference 1, case 3) are the most common bacteria that form large colonies in tissues in veterinary species. The main etiologic rule-out for the gross and histopathologic findings is *Actinomyces* spp., a gram-positive, non-acid fast filamentous bacteria commonly associated with cutaneous infection secondary to bite wounds and penetrating injuries from grass awns or other foreign bodies. The gross lesions of actinomycosis and nocardiosis are typically identical (cellulitis, abscesses, draining tracts, osteomyelitis), and although it is a more common feature of actinomycosis, both conditions can produce "sulfur granules" (grains composed of necrotic debris, aggregates of bacteria and Splendore-Hoeppli material). Both bacteria are gram-positive, while *Nocardia* spp. is often, but not always, acid fast; if negative, it cannot be differentiated microscopically from *Actinomyces* spp.[2] In this case, filamentous bacteria were both gram-positive and acid-fast; these histochemical staining characteristics, along with the culture results reported by the contributor, support a diagnosis of nocardiosis.

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