Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE
2020-2021

Conference 24

28 April, 2021

Joint Pathology Center
Silver Spring, Maryland

CASE 1: 19-0026A (JPC 4139463-00)

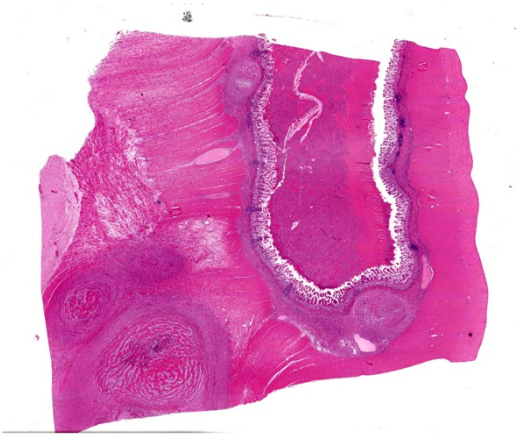
Signalment:
4 year old female entire Ragdoll (*Felis catus)*

History:
Ileocecocolic mass with severely enlarged lymph nodes. Preliminary diagnosis of feline eosinophilic sclerosing fibroplasia based on eosinophils seen on tissue smear. Associated lymph nodes markedly enlarged and purulent discharge present on incision. Ileocecocolic mass resected along with enlarged purulent lymph nodes for histopathology. DDx feline eosinophilic sclerosing fibroplasia vs neoplasia (mast cell tumor, lymphoma, adenocarcinoma, other).

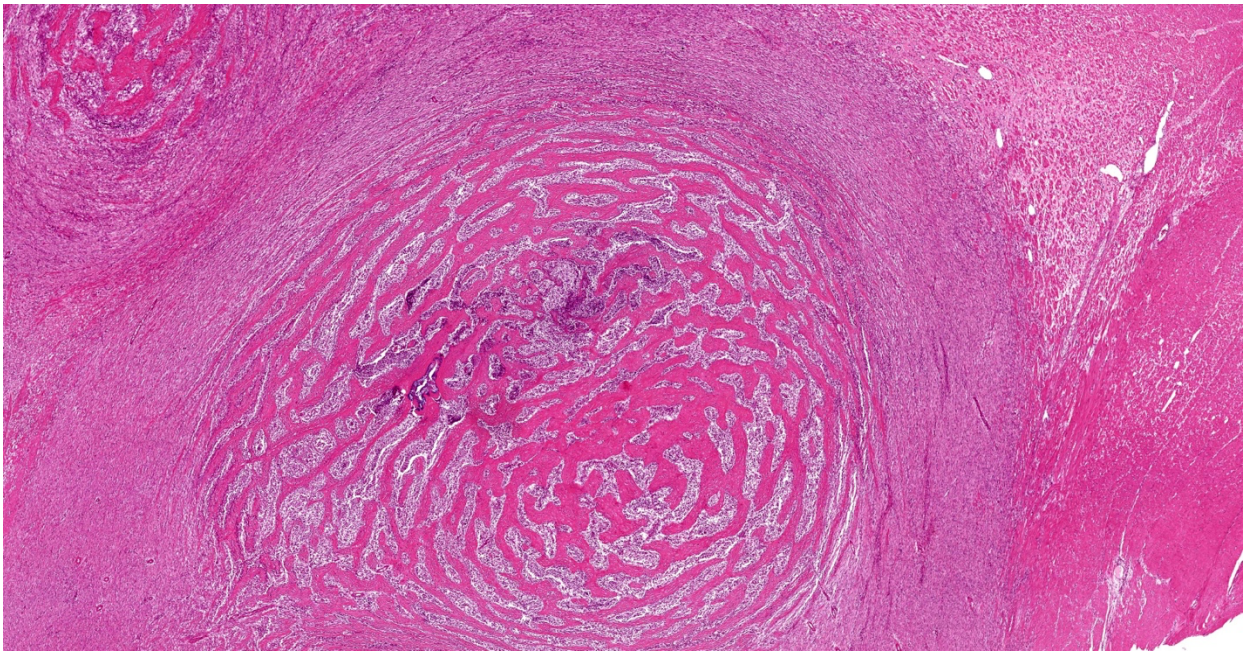
Gross Pathology:
The specimen presented for examination is a section of the ileum, caecum and colon and a mesenteric lymph node. A firm, pale tan-cream, multilobulated mass 120 x 40 x 12 mm is effacing the caecum, ileum and colon. On section, the mass contains soft pale brown-green material surrounded by a thick, cream, firm capsule. The mesenteric lymph node (65 x 58 x 55 mm) is firm, multilobulated, cream-pale tan. On section, the lymph node contains multiple cystic structures which exude viscous brown fluid.

Laboratory results:
RAPID DIFF SMEAR
Mass: Much connective tissue and numerous spindle cells, scattered neutrophils, eosinophils and macrophages, numerous bacterial cocci.
Lymph node: Spindle cells, several neutrophils, scattered macrophages, occasional plasma cell; some cocci are present in neutrophils and the occasional bacterial rod may also be present.

CULTURE (Blood agar, aerobic, anaerobic 37C)
All samples (mass, discharge and node) grew a heavy growth of *Staphylococcus aureus.* The



Ileum, cat: Subgross magnification of the submitted section of ileum. There are multiple pyogranulomas within the submucosa and nodular areas of sclerosing fibroplasia in the muscular tunics (HE, 5X)



Ileum, cat. There are multifocal areas of lytic necrosis scattered randomly throughout the parenchyma, which begin as areas of coagulative necrosis which are then infiltrated by large numbers of neutrophils which become necrotic and add to the cellular debris. (HE, 212X)

sample labeled "lymph node" additionally grew a heavy mixed bacterial population that includes obligate anaerobes.

SENSITIVITY
Susceptible to oxacillin, amoxycillin/clavulanic acid, 1st generation cephalosporins, doxycycline, trimethoprim / sulfonamides, marbofloxacin, enrofloxacin, gentamicin, clindamycin, erythromycin.
Resistant to penicillin, ampicillin.

Microscopic description:
A multifocal proliferative mass composed of thick branching and anastomosing, poorly cellular trabeculae of dense birefringent collagen and plump (reactive) fibroblasts (fibrosis) admixed with abundant degenerate and nondegenerate eosinophils and brightly eosinophilic granular material is expanding and effacing the submucosa, tunica muscularis, serosa and surrounding fibroadipose tissue. The trabecular collagen merges gradually into more typical granulation tissue at the periphery of the lesions. Fewer foamy macrophages, neutrophils and lymphocytes admixed with variably sized foci of cellular and karyorrhectic debris (necrosis), oedema and hemorrhage are scattered throughout the mass. There are rare clusters of cocci. Blood vessels are congested. Numerous lymphocytes, eosinophils and plasma cells admixed with mild oedema and increased amounts of pale collagen and plump (reactive) fibroblasts are infiltrating the lamina propria and extending transmurally through the ileal and colonic wall. The lumen contains cellular and karyorrhectic debris (necrosis) admixed with clusters of basophilic cocci. Occasional ectatic crypts lined by attenuated epithelium contain cellular and karyorrhectic debris (necrosis). There is mild multifocal crypt epithelial hyperplasia, characterized by plump, crowded epithelial cells which pile up, often have overlapping nuclei with frequent mitotic figures. The predominantly eosinophilic inflammation and fibroplasia extend to the colonic surgical margin.

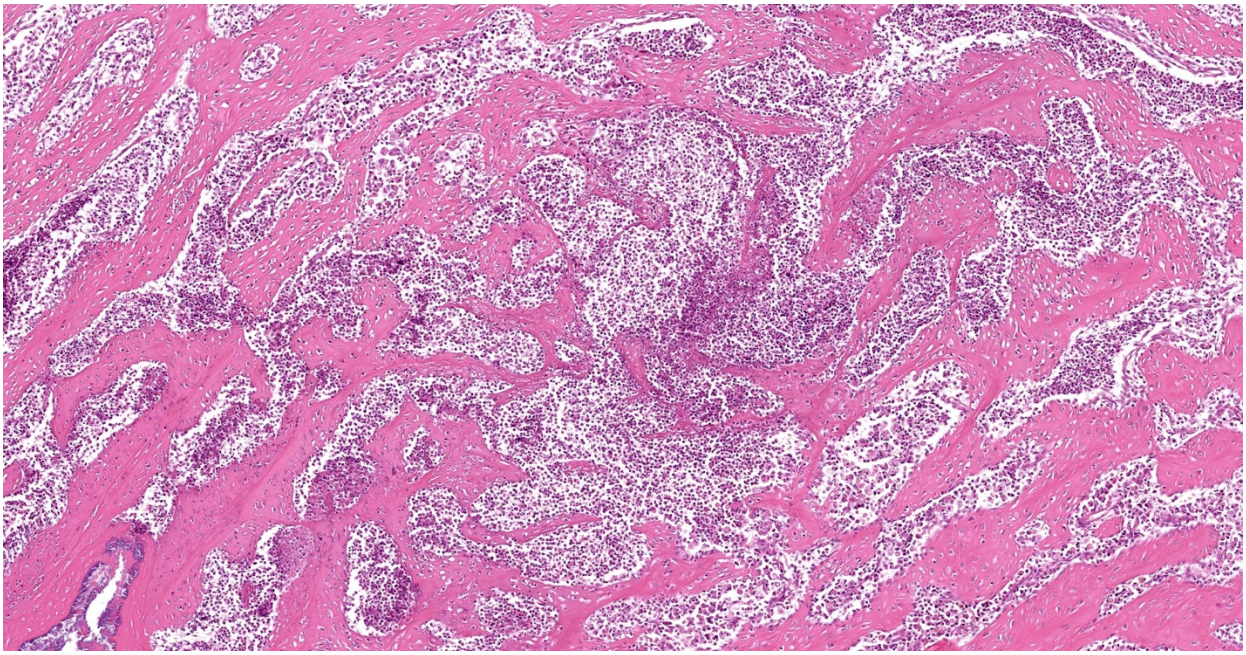
Contributor's morphologic diagnosis:
Ileocecocolic junction, lymph node (not submitted): Eosinophilic sclerosing fibroplasia, with large intralesional colonies of cocci and Splendore-Hoeppli material.

Intestines: Enterocolitis, lymphoplasmacytic, eosinophilic, locally extensive, moderate, chronic, with fibrosis and crypt hyperplasia.

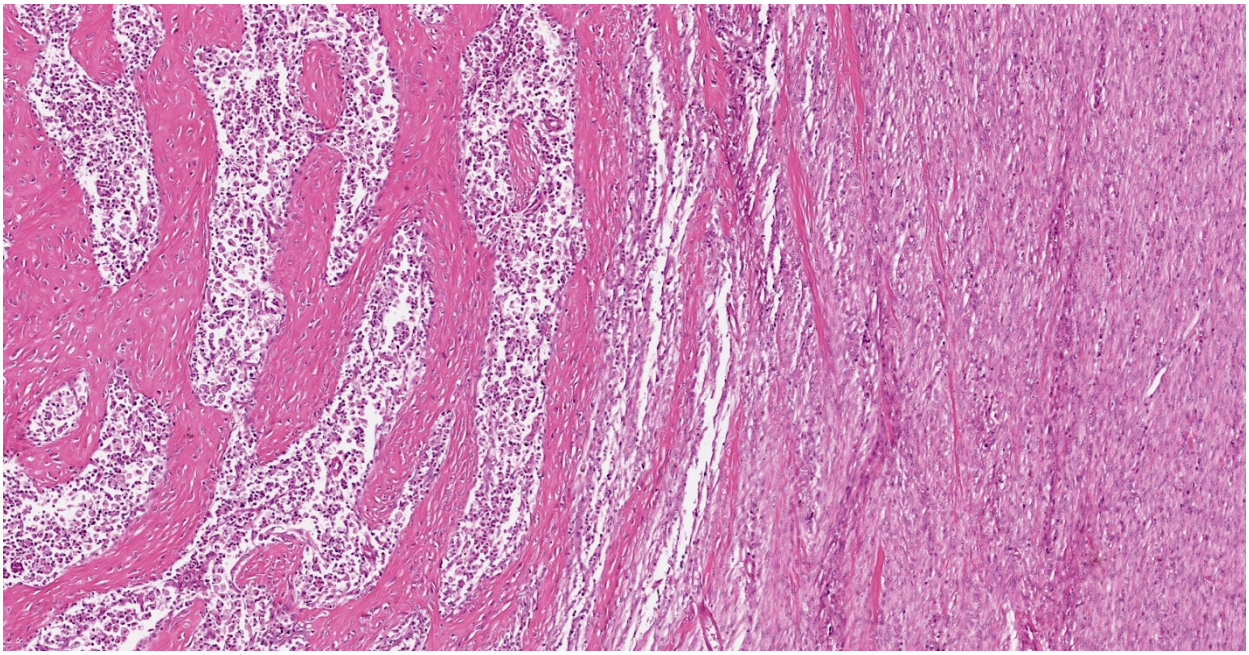
Contributor's comment:
Feline gastrointestinal eosinophilic sclerosing fibroplasia (FGESF) is a feline inflammatory condition which affects the gastrointestinal tract and associated lymph nodes. It is characterized by an intramural, typically ulcerated, multinodular, fibrosing and eosinophilic mass that effaces the wall of the gastrointestinal tract, most commonly at the pyloric sphincter or ileocecocolic junction.[2] The disease primarily affects middle-aged cats, although cats of any age can be affected. FGESF has been reported in domestic shorthairs, Ragdolls, Persians, domestic longhairs, mixed breeds, one Siamese, one Maine Coon, and one Himalayan.[2,8,10] Ragdolls were overrepresented in a review of 13 cases.[8] Typical clinical signs include decreased appetite, vomiting, weight loss and diarrhea.[8] A hard, non-painful abdominal mass is often palpable clinically. During sampling, masses are often described as firm, "gritty", and heterogeneous on section.[5,8] Bloodwork abnormalities associated with the disease include hyperglobulinemia, hypoalbuminemia, peripheral eosinophilia and/or mild peripheral neutrophilia.[2,8,11]

The pathogenesis of FGESF is incompletely understood. It is thought immune dysregulation (genetic predispositions, parasitism, dysbiosis, inflammatory bowel disease or food hypersensitivities leading to eosinophil dysregulation), infections (herpesvirus, bacteria, fungi, *Toxoplasma gondii, Cylicospirura* spp.), and/or migrating foreign bodies may play a role.[4,5,8,9] Secondary infections may also perpetuate the inflammatory response. In cases where intralesional bacteria have been detected (as in this case), it is hypothesized that bacteria could initiate FGESF. However, the role of bacteria is still unclear, and the presence of normal bacterial flora further complicates establishment of an association.[2,8,11] It is likely pathogenesis is multifactorial. The profound inflammatory response noted in FGESF may be related to other eosinophilic diseases in cats (eosinophilic granuloma, indolent ulcer, eosinophilic plaque).

Eosinophils play a major role in the pathogenesis of FGESF. Eosinophils are most commonly associated with parasitic and allergic conditions. They have several types of granules, including small granules, primary granules, and large specific granules (secondary granules).



Ileum, cat. As in the less mature submucosal pyogranulomas, there is often areas of lytic necrosis at the center of the more mature granulomas. (HE, 77X)



Ileum, cat. The sclerosing pyogranulomas are composed of dense anastomosing bands of mature collagen measuring up to 100um in diameter. More centrally (left) bands are separated by loosely arranged macrophages, neutrophils and fewer lymphocytes. Centrifugally (center and right), the inflammatory infiltrate is progressively replaced by myofibroblasts, which outside the areas of necrosis – form dense streams and bundles, infiltrating and effacing skeletal muscle. (HE, 83X)

These granules contain various enzymes, cytokines and proteins that contribute to ongoing inflammation and fibrosis. Specifically, granules contain mediators such as major basic protein (MBP), TGF-α and -β, and Il-1 to IL-6. Eosinophil chemoattractants include histamine, eosinophilic chemotactic factor A, C5a, cytokines (IL-4, IL-5, and IL-13), and chemokines (CCL-5, also known as RANTES, and CCL-11, also known as eotaxin). These chemoattractants are released from epithelial cells, helminths, mast cells, and eosinophils themselves.[2,8,10,11] This chronic inflammation likely contributes to eosinophilic proliferation and fibrosis, resulting in mass formation.

Microscopically, FGESF has a characteristic pattern of densely collagenous and anastomosing trabeculae, large spindle cells (myofibroblasts)[2] and numerous eosinophils.[2,8,10,11] Lesions infiltrate the intestinal wall and, sometimes, regional lymph nodes. There is frequent intestinal mucosal ulceration within affected areas.

The prognosis is guarded and dependent on the ability to completely surgically resect the mass (lesions associated with the pyloric sphincter are unlikely to be completely resected).[2,4,11] There is no consistent treatment regime.[8] A multimodal treatment approach combining surgical resection, prednisolone, antibiotics, and immunomodulatory agents is considered ideal.[8]

Differential diagnoses in cats with abdominal mass(es) and/or mesenteric lymphadenopathy include neoplasia (fibrosarcoma, extraskeletal osteosarcoma, feline sclerosing mast cell tumor, lymphoma, adenocarcinoma), granuloma, and eosinophilic gastritis. Clinically, the presence of an ulcerated mass at the pyloric sphincter or ileocecocolic junction can be misdiagnosed as a neoplasm or granuloma. Microscopically, FGESF needs to be distinguished from other neoplasms, including extraskeletal osteosarcoma, where densely collagenous trabeculae may be misinterpreted as osteoid, and feline sclerosing mast cell tumors, due to the presence of low numbers of well-differentiated, perivascular mast cells admixed with numerous eosinophils.[6]

Contributing Institution:
University of Sydney

https://sydney.edu.au/science/schools/sydney-school-of-veterinary-science/veterinary-science-services.html

JPC diagnosis:
Ileum: Enteritis, pyogranulomatous and eosinophilic, moderate, chronic, multifocal to coalescing, with sclerosing fibroplasia and colonies of cocci.

JPC comment:
The contributor provides a thorough summary of this infrequent disease in cats. As the contributor notes, many cases have been potentially associated with bacteria or fungi, but their role in the development of this disease remains unknown. This disease has a variety of presentations, including a recent case of FGESF confined to the mesentery in a mixed breed cat. The mesenteric nodules were not resectable, but the cat responded to a combination of prednisolone and ciclosporin A. At the time of the report, remission of disease had been achieved, with peripheral eosinophilic resolved, at 689 days post diagnosis. While the pathogenesis is shrouded in mystery, immunomodulatory treatments appear to be efficacious.[7]

While the mesenteric case of FGESF stands alone, a second recently reported case shares a feature that is not typically described: cavitation. A mural lesion located in the proximal duodenum and incorporating the left limb of the pancreas was multilobulated, with pockets of pale colored semi-liquid material that was gritty and contained some solid concretions, consistent with an abscess.[3]

In human literature, and to a lesser degree veterinary literature, describe IgG4-related diseases, with a specific subset of sclerosing diseases. The topic was briefly discussed in Conference 3 this year in regard to sclerosing angiomatoid nodular transformation (SANT) of the spleen. IgG4 is the least common of the four IgG subtypes, does not activate complement, and is a Th2-dependent isotype. IgG4 may also act as a protective, blocking antibody in allergen induced IgE-mediated effector cell activation in parasitic infections. A common presentation in human literature includes a mass lesion in the pancreas, with prominent lymphoplasmacytic inflammation, and abundant fibrosis. These cases usually have elevated serum IgG4 levels, with resulting lesions sometimes causing obstructive jaundice. Similar to feline FGESF, this human disease responds well to steroid therapy.[1] Cats with FGESF may have elevated IgG4 levels, but that parameter has not been reported. This may represent an avenue for additional research.

The moderator emphasized that the most common differentials for a gastrointestinal mural mass would include this entity, FGESF, as well as feline intestinal sclerosing mast cell tumor, gastrointestinal carcinoma, sarcomas, and lymphomas. Within the set of gastrointestinal lymphomas, the most common subtypes in cats include enteropathy-associated T-cell lymphoma (EATL) type I and II, diffuse large B-cell lymphoma (DLBCL), and large granular lymphocyte lymphoma (LGL).

References:

1. Cheuk W, Chan JKC. IgG4-related Sclerosing Disease: A Critical Appraisal of an Evolving Clinicopathologic Entity. *Adv Anat Pathol*. 2010;17(5): 303-332.
2. Craig LE, Hardam EE, Hertzke DM, Flatland B, Rohrbach BW, Moore RR. Feline gastrointestinal eosinophilic sclerosing fibroplasia. *Veterinary pathology*. 2009;46**:** 63-70.
3. Davidson GA, Taylor SS, Dobromylskyj MJ, Gemignani F, Renfrew H. A case of an intramural, cavitated feline gastrointestinal eosinophilic sclerosing fibroplasia of the cranial abdomen in a domestic longhair cat. *J Feline Medicine and Surgery*. 2021;7(1). doi:10.1177/2055116921995396.
4. Eckstrand CD, Barr BC, Woods LW, Spangler T, Murphy B. Nematode-associated intramural alimentary nodules in pumas are histologically similar to gastrointestinal eosinophilic sclerosing fibroplasia of domestic cats. *Journal of comparative pathology*. 2013;148**:** 405-409.
5. Grau-Roma L, Galindo-Cardiel I, Isidoro-Ayza M, Fernandez M, Majo N. A case of feline gastrointestinal eosinophilic sclerosing fibroplasia associated with phycomycetes. *Journal of comparative pathology*. 2014;151**:** 318-321.
6. Halsey CH, Powers BE, Kamstock DA. Feline intestinal sclerosing mast cell tumour:

50 cases (1997-2008). *Veterinary and comparative oncology*. 2010;8**:** 72-79.
7. Kambe N, Okabe R, Osada H, et al. A case of feline gastrointestinal eosinophilic sclerosing fibroplasia limited to the mesentery. *Journal of Small Animal Practice.* 2020;61:64-67.
8. Linton M, Nimmo JS, Norris JM, et al. Feline gastrointestinal eosinophilic sclerosing fibroplasia: 13 cases and review of an emerging clinical entity. *Journal of feline medicine and surgery*. 2015;17**:** 392-404.
9. Ozaki K, Yamagami T, Nomura K, Haritani M, Tsutsumi Y, Narama I. Abscess-forming inflammatory granulation tissue with Gram-positive cocci and prominent eosinophil infiltration in cats: possible infection of methicillin-resistant Staphylococcus. *Veterinary pathology*. 2003;40**:** 283-287.
10. Suzuki M, Onchi M, Ozaki M. A case of feline gastrointestinal eosinophilic sclerosing fibroplasia. *Journal of toxicologic pathology*. 2013;26**:** 51-53.
11. Weissman A, Penninck D, Webster C, Hecht S, Keating J, Craig LE. Ultrasonographic and clinicopathological features of feline gastrointestinal eosinophilic sclerosing fibroplasia in four cats. *Journal of feline medicine and surgery*. 2013;15**:** 148-154.

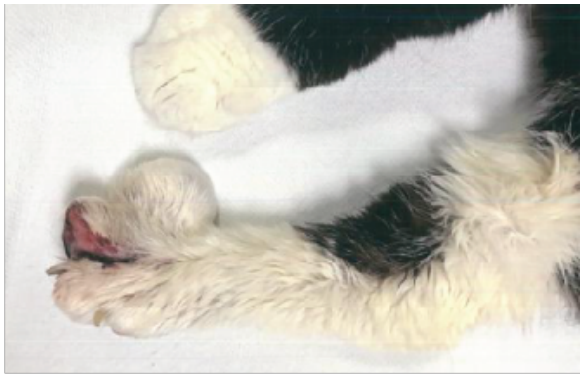
CASE 2: 19F156892 (JPC 4155173-00)

Signalment:
14-year-old female spayed domestic short haired cat (*Felis catus*)

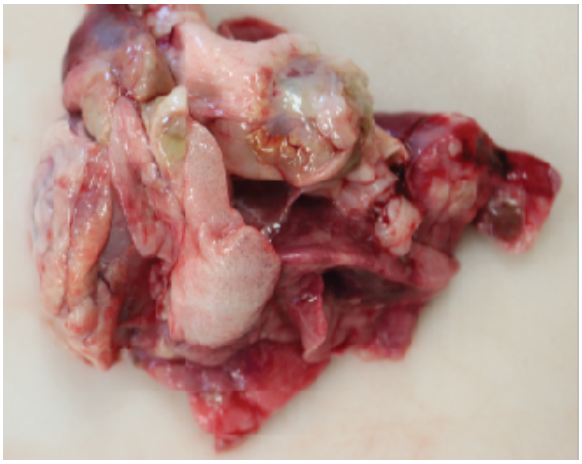
History:
The patient presented with complaints of progressive paralysis in the hind limbs and draining skin lesions of the hind feet and face. The patient had been examined and treated unsuccessfully by veterinarians at three other clinics over the last several months. The patient was an indoor-only cat, was current on vaccinations, was fed a commercial dry cat food, and had moved with her owners to Wyoming from North Carolina.

On physical exam, the patient was thin (3.08 kg) and somewhat depressed but responsive to handling. She was unable to stand on her hind limbs and preferred to rest on her elbows and forearms rather than stand on her front feet. She was afebrile (temp = 100.3 F). Withdrawal and deep pain reflexes were present in both hind legs, but her tail had reduced sensation and her bladder was large and easily expressed. Anal tone was judged to be somewhat reduced. Anisocoria (L > R) was noted. Very firm, nodular swellings of all the digits of the hind feet were present, and the ends of several of the toes were deeply ulcerated and matted with blood and purulent-type discharge. Similar, less dramatic nodular ulcers were present in the front feet and also involved the right upper lip. Additionally, hard, bony masses could be palpated on the left 5th rib and the distal right antebrachium and metatarsal regions. Increased bronchovesicular pulmonary sounds were ausculted diffusely but were particularly prominent in the right cranial and dorsocaudal quadrants. The initial differential diagnostic list included pulmonary hypertrophic osteopathy, metastatic neoplasia, and systemic mycotic disease (including sporotrichosis).

Gross Pathology:
A 14-year-old female spayed domestic short haired cat weighing 3.08 kg was presented for necropsy in excellent postmortem condition with minimal autolysis. The cat was in thin body condition with mildly reduced stores of visceral and subcutaneous adipose tissue. On external exam, there was an open wound with a fistulous draining tract in the skin overlying the right maxillary canine, extending upward to the lateral aspect of the right nostril. The wound was characterized by a peripheral rim of chronic hemorrhage with a central tract extending



Digit cat. The digit is expanded up to 5 x normal and the adjacent digit is swollen as well. (Photo courtesy of University of Wyoming/Wyoming State Veterinary Laboratory http://www.uwyo.edu/vetsci/)



Digit cat. All lung lobes contain nodules of pale neoplastic tissue which when sectioned, oozed a mucinous fluid. (Photo courtesy of University of Wyoming/Wyoming State Veterinary Laboratory http://www.uwyo.edu/vetsci/)

through the subcutis and the underlying musculature. There was loss of the underlying maxillary bone and rostrum, with dark discoloration and loosening of the right maxillary canine in the alveolar socket. The distal aspects of multiple digits on both hindlimbs had similar external wounds with surface ulceration and deep penetrating tracts. The front limbs had less severe ulcerations on the digital surfaces at the junction of the haired skin and the paw pad. Open lesions oozed serous fluid and/or small amounts of purulent exudate. The phalanges were expanded up to 10 times the normal diameter by irregular, circumferential bony proliferations. Additionally, there was similar bony expansion of the right metatarsal bones and the left tibial metaphysis. The mid-bodies of ribs 5 through 7 on the left side of the thorax were focally disrupted by a circular bony lesion with central cavitation.

The thorax contained approximately 10mL of serosanguineous free fluid. All lung lobes were multifocally disrupted by discrete to coalescing nodules that were pale tan to white, solid to cystic or cavitated, and occasionally oozed purulent to mucinous material on cut section. Approximately 60% of the lung parenchyma was affected, and nodules ranged in size from ~3mm to 3cm. Small nodules on the pleural surface had an umbilicated appearance with central depressions and peripheral rims of white discoloration. There was emphysematous change at the borders of the lung lobes. The tracheobronchial lymph nodes were expanded up to 20 times normal and were completely effaced by similar solid to cystic nodules.

Bilaterally, the kidneys had multifocal, irregularly shaped pitted depressions on capsular surface that extended deep into the cortical parenchyma (consistent with chronic infarcts). The liver was diffusely congested and moderately firm. The stomach and small intestines were empty. The distal colon was moderately dilated and contained a large amount of formed feces.

Laboratory results:

Chemistry Panel

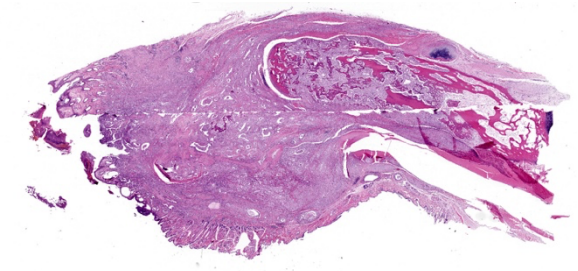
Test	Result	Normal Range	High or Low Units
Total Protein	9.5	5.7 - 8.0	>range g/dl
Albumin	4.7	2.4 - 3.8	>range g/dl
Globulin	4.8	2.4 - 4.7	>range g/dl
A/G Ratio	1	0.6 - 1.1	in range
ALP	21	12.0 - 65.0	in range U/l
ALT (SGPT)	20	8.3 - 53.0	in range U/l
Bilirubin, total	4.4	0.1 - 0.5	>range mg/dl
Glucose	120	61 - 124	in range mg/dl
Cholesterol	160	71.0 - 161.0	in range mg/dl
Amylase	322	371 - 1193.0	<range U/l
Lipase	< 10	0.0 – 76	in range U/l
Creatinine	0.5	0.5 - 1.9	in range mg/dl
BUN	15.4	15.0 - 31.1	in range mg/dl
Sodium	> 250	146.0 - 159.0	>range meq/l
Chloride	> 175	108.0 - 130.0	>range meq/l
Potassium	2.5	3.8 - 5.3	<range meq/l
Calcium	7.5	7.9 - 10.9	<range
Phos	5.5	4.0 - 7.3	in range mg/dl
TCO2	33.1	16.0 - 22	>range
Anion Gap	****	7 - 17	

Hemolysis Moderate

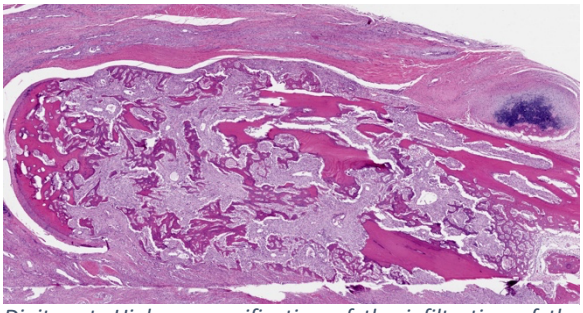
CBC

Test	Result	Normal Range	High or Low Units
WBC Count, Manual	3.6	5.5 - 19.5	<range /microliter
Bands	6	0 - 3	>range %
Neutrophils	75	35 - 75	in range %
Lymphocytes	14	20 - 55	<range %
Monocytes	4	1 – 4	in range %
Eosinophils	1	2 - 12	<range %
Basophils	0	0 - 0.5	in range %
Platelets	109	300 - 700	<range x10e3/ul
Mild Platelet Clumping			
RBC Count	4.93	5.0 - 10.0	<range x10e6/ul
PCV	18.7	30.0 - 45.0	<range %
Hemoglobin	5.8	8.0 - 15.0	<range g/dl
MCV	37.8	39.0 - 55.0	<range fl
MCHC	31.0	30.0 - 36.0	in range g/dl
MCH	11.7	13.0 - 17.0	<range pg
RDW	19.7	14.0 - 19.0	>range %.

Microscopic description:
Distal phalanx: Decalcified sections of the distal phalanx are characterized by marked expansion and effacement of the soft tissue and extensive infiltration and of periosteum and bone by a poorly demarcated, moderately cellular neoplasm comprised of respiratory epithelial cells arranged in variably ectatic glandular structures supported and subdivided by a dense desmoplastic stroma. Neoplastic cells are columnar to cuboidal with variably discernible cilia that line the apical surface. Cells have distinct cell borders, moderate amounts of eosinophilic cytoplasm, and round to oval, basilar nuclei with finely stippled chromatin and one prominent nucleolus. There is marked anisocytosis and anisokaryosis. The mitotic count is 13 per 10 high powered fields, 400x. There are many large, discrete to coalescing cystic structures containing central lakes of eosinophilic secretory material admixed with pyknotic to karyorrhectic debris and lined by a single layer of neoplastic respiratory epithelium. Some cystic structures contain aggregates of degenerate neutrophils. The neoplasm effaces the periosteum and cortical bone and infiltrates the medullary cavity. Spicules of partially necrotic bone are frequently lined by the previously described neoplastic cells and/or less frequently lined by few multinucleated osteoclasts. Within the desmoplastic stroma of the neoplasm, there are moderate numbers of neutrophils, macrophages, and occasional loose aggregates of lymphocytes and plasma cells. The neoplasm markedly expands the subcutis and deep dermis and extends to the superficial dermis multifocally.



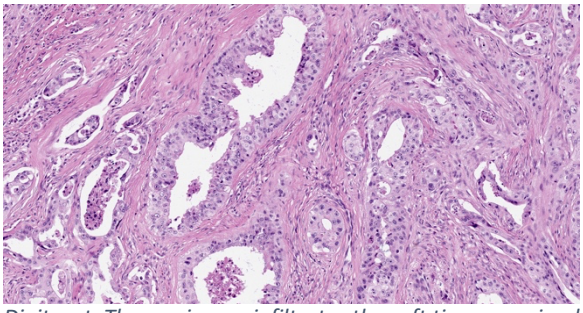
Digit, cat. A sagittal section of the digit with the second phalanx is presented for examination. The third phalanx is not present in this section. The phalanx and soft tissues ventral and proximal to it are expanded and effaced by a neoplasm which in areas makes large cystic glands. (HE, 5X)



Digit, cat. Higher magnification of the infiltration of the second phalanx with neoplastic cells and abundant fibrous tissue replacing marrow spaces, resorption of medullary bone with formation of thin trabeculae of woven bone, and resorption of lamellar bone on the ventral aspect with formation of small amounts of periosteal woven bone. (HE, 24X)

Contributor's morphologic diagnosis:
Bone, distal phalanx: Metastatic bronchogenic adenocarcinoma.

Contributor's comment:
Feline lung-digit syndrome (FLDS) was originally described by Moore and Middleton from a series of three cases in 1982.[9] The main feature was postmortem detection of a primary pulmonary adenocarcinoma, in the face of non-respiratory signs (e.g., dyspnea, coughing, etc).



Digit, cat. The carcinoma infiltrates the soft tissue proximal and ventral to the 2nd phalanx, forming nests, cords, and ultimately pluristratified tubules of various sizes. (HE, 150X)

Two presented with pain and swelling of distal extremities and eventually developed respiratory signs in the following weeks. The third case had non-specific clinical findings (hyporexia and weight loss) and was euthanized the following week due to deteriorating quality of life. The two cases with soft tissue swelling were diagnosed as metastatic adenocarcinoma following antemortem biopsy. A retrospective study of 36 additional cats coined the moniker FLDS in 2000.[7] All cats presented with metastatic digital carcinoma; again, none had respiratory signs.

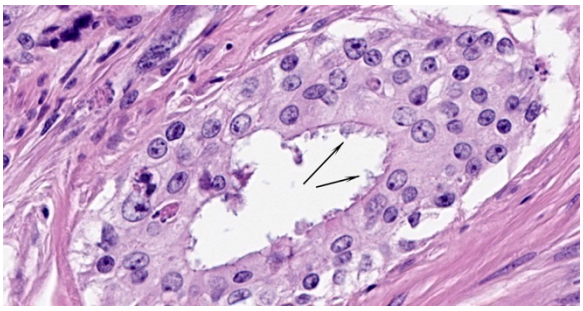
While FLDS is classically acknowledged clinically by metastases to extremities, variations exist. Digits are the most common site, but metastases have been documented in skeletal muscle, bone, eye, and skin.[5,12] The predilection for digit metastasis may be related to the angioinvasive behavior of the neoplasm, and the highly vascular nature of feline digits, which helps to dissipate heat.[5,9] Tumor emboli may mimic aortic thromboembolism (ATE) that is usually attributed to primary cardiac disease. Retrospective studies of 127 cases of ATE identified neoplasia as the cause of 6% of ATE, representing the second most common cause in cats.[8] Ischemia and necrosis of the distal limbs may also manifest as a result of thromboemboli.[11] Ultimately, the size of thromboemboli dictates where they might settle and the pathophysiology.

Diagnosis is most easily accomplished through biopsy or fine needle aspirate of superficial masses and thoracic radiographs depending on the size of the tumor. The primary tumor often escapes detection due to absence of respiratory signs. More modern imaging technique such as computed tomography may be more sensitive in detecting the primary tumor.[12] FLDS is difficult to treat; chemotherapy is not often pursued, as efficacy has not been well documented.[12] Amputation of affected digits or limbs, while performed, is rarely palliative.[7,10] Increased CK may be useful as a marker of metastases to skeletal muscle. Prognosis is poor to grave, even with pulmonary lobectomy. Mean survival time from initial presentation is 34-58 days.[7,13] No breed or sex predilection has been identified.[7]

In general, primary pulmonary tumors are rare in cats. Of these, adenocarcinoma is most common. Eighty-eight percent of carcinomas in digits are the result of metastases from primary pulmonary carcinomas, although squamous cell carcinomas contribute to a fraction of these cases.[13] Lameness is often a common presenting complaint, and lysis of the third phalanx should provide a high index of suspicion;[12] however, other differentials should be considered including bacterial and fungal osteomyelitis. One in eight feline nail and nail bed disorders are neoplastic.[5] Given that other etiologies have better prognoses and generally response to amputation (i.e., bacterial/fungal osteomyelitis) or have a higher mean survival time (i.e., squamous cell carcinoma – 207 days), it is advisable to diagnose or rule out primary pulmonary carcinoma as a cause of clinical signs before pursuing surgery.[7,13]

Contributing Institution:
University of Wyoming/Wyoming State Veterinary Laboratory
http://www.uwyo.edu/vetsci/

JPC diagnosis:
Digit: Metastatic pulmonary carcinoma.



Digit, cat. Neoplastic cells lining tubules occasionally demonstrate cilia (arrows). (HE, 300X)

JPC comment:
When feline lung digit syndrome (FLDS) occurs, one of the most common sites of metastasis is to the dermis on the dorsum of the distal phalanx and under the footpad epidermis.[2]

An important differential to consider is eccrine gland carcinoma.[6] Eccrine adenomas and adenocarcinomas have been documents in dogs, while eccrine tumors are usually malignant in cats.[4] While a common disease in humans, eccrine glands are confined to the footpads of dogs and cats, and this is the only site at which eccrine neoplasia occurs. Importantly, eccrine and pulmonary tumors have different immunohistochemical profiles. Thyroid transcription factor 1 (TTF-1) is expressed by primary pulmonary carcinoma/adenocarcinoma, in addition to napsin A and keratin 7.[3] Approximately 50% of eccrine carcinomas express S100, and about 25% of eccrine and apocrine tumors cells express p63 and has not been documented in metastatic adenocarcinomas in the skin.[3]

Human primary tumors often metastasize but are likely under reported. Approximately 20-70% of patients who died of their malignant disease had histologic evidence of osseous metastasis at autopsy, but only 2% have metastatic lesions to the foot. These lesions are reported to be CK7 and CDX2 (caudal type homeobox transcription factor 2) immunopositive, consistent with bronchogenic adenocarcinoma.[1]

The moderator led a discussion about the most common differentials for digital lesions in dogs and cats. In dogs, the most common include subungual melanoma, subungual squamous cell carcinoma, subungual keratoacanthoma, eccrine carcinoma, soft tissue sarcoma, mast cell tumor, trauma/infection, and lupoid onychodystrophy.[14] In the cat, the most common digital lesions include lung-digit syndrome, squamous cell carcinoma, various sarcomas, plasma cell pododermatitis, and arteriovenous fistula.[15]

References:

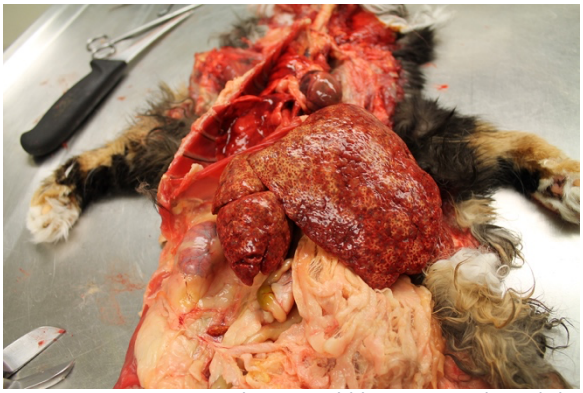
1. Bazrafshan S, Pacheco M, Ortiz JC. Underlying adenocarcinoma of the lung metastasizing to the proximal phalanx of the food causing complex regional pain syndrome. *Journal of the American Podiatric Medical Association*. 2017;107(2):150-154.
2. Caswell JL, Williams KJ: Respiratory system. In: Maxie MG ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*. Vol 2, 6th ed. Philadelphia, PA: Elsevier Saunders; 2016:495-497.
3. Dabbs D. Immunohistology of Skin Tumors. In: *Diagnostic Immunohistochemistry Theranostic and Genomic Applications*. 4th ed. Philadelphia, PA: Elsevier Inc. 4th ed. 2014:414-419, 483-484.
4. Fuentealba C, Illanes O, Haines D. Eccrine adenocarcinoma of the footpads in 2 cats. *Can Vet Jour*. 2000:41:401-403.
5. Goldfinch, N, Argyle, DJ. Feline lung-digit syndrome: unusual metastatic patterns of primary lung tumours in cats. *J Feline Med Surg*. 2012;14(3):202-208.
6. Goldschmidt MH, Goldschmidt KH. Epithelial and Melanocytic Tumors of the Skin. In: Meuten DJ, ed. *Tumors in Domestic Animals,* 5th Ed. Ames, IA:John Wiley and Sons, Inc. 2017;123.
7. Gottfried, SD, Popovitch, CA, Goldschmidt, MH, Schelling, C. Metastatic digital carcinoma in the cat: a retrospective study of 36 cats (1992-1998). *J Am Anim Hosp Assoc*. 2000;36(6):501-509.
8. Hogan, DF, Dhaliwal, RS, Sisson, DD, Kitchell, BE. Paraneoplastic thrombocytosis-induced systemic thromboembolism in a cat. *Journal of the American Animal Hospital Association*. 1999;35(6):483-486.
9. Moore, AS, Middleton, DJ. Pulmonary adenocarcinoma in three cats with nonrespiratory signs only. *J Small Anim Pract*. 1982;23:501-509.
10. Salgüero, R, Langley-Hobbs, S, Warland, J, Brearley, M. Metastatic carcinoma in the ulna of a cat secondary to a suspected pulmonary tumour. *J Feline Med Surg*. 2012:14(6):432-435.
11. Sykes, JE. Ischemic neuromyopathy due to peripheral arterial embolization of an adenocarcinoma in a cat. *J Feline Med Surg*. 2003;5(6):353-356.

12. Thrift, E, Greenwell, C, Turner, A-L, Harvey, AM, Maher, D, Malik, R. Metastatic pulmonary carcinomas in cats ('feline lung-digit syndrome'): further variations on a theme. *JFMS Open Rep*. 2017;3(1):1-8.
13. van der Linde-Sipman, JS, van den Ingh, TS. Primary and metastatic carcinomas in the digits of cats. *Vet Q*. 2000;22(3):141-145.
14. Wobeser BK, et al. Diagnoses and clinical outcomes associated with surgically amputated canine digits submitted to multiple veterinary diagnostic laboratories. *Vet Pathol*. 2007;44(3):355-361.
15. Wobeser BK, et al. Diagnoses and clinical outcomes associated with surgically amputated feline digits submitted to multiple veterinary diagnostic laboratories. *Vet Pathol*. 2007;44(3):362-365.

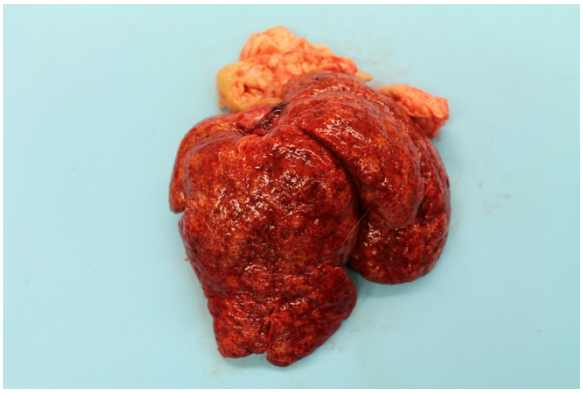
CASE 3: 17-0359 (JPC 4136401-00)

Signalment:
10-year-old, female spayed, domestic longhair cat, *Felis catus*, feline

History:
Presented for a 5-day history of anorexia and lethargy, with two episodes of vomiting 2 days prior to presentation. The cat was not drinking for several days and was reported to be previously healthy.



Liver, cat. Liver in situ. There is mild hepatomegaly and the liver has an enhanced reticular pattern, and numerous pinpoint depression throughout the organ. (Photo courtesy of University of Wyoming/Wyoming State Veterinary Laboratory http://www.uwyo.edu/vetsci/)



Liver, cat. On close inspection, multiple nodules are present within each lobe, and there are numerous foci of necrosis resulting in focal depressions on the liver surface. (Photo courtesy of University of Wyoming/Wyoming State Veterinary Laboratory http://www.uwyo.edu/vetsci/)

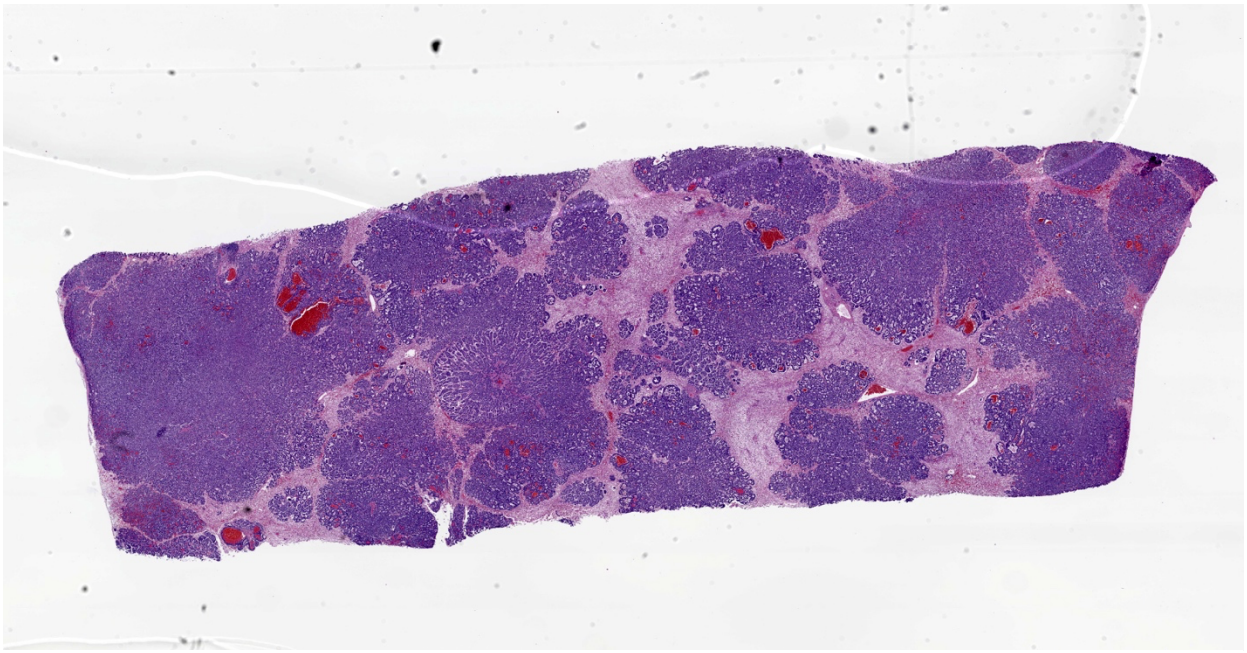
Gross Pathology:
The body was received in good postmortem and fair nutritional condition, with mild diffuse muscle atrophy. The skin, subcutaneous tissues, mucous membranes, and sclera were severely diffusely discolored yellow.

The liver was markedly enlarged (475g; 13.5% of body weight), firm, and mottled red-brown to white-tan with a slightly enhanced reticular pattern. There were too numerous to count irregular pinpoint to 0.2 cm grey depressions that occasionally contained trace amounts of serosanguineous fluid. On cut section, there were multifocal targetoid tan lesions with brown centers ranging from 0.2 to 0.6 cm diameter, almost completely effacing normal parenchyma.

The remainder of the gross examination was unremarkable.

Laboratory results:
None provided.

Microscopic description:
Liver: The normal liver architecture is approximately 80-90% replaced and effaced by an unencapsulated and infiltrative neoplasm composed of polygonal cells arranged in nests, packets, and cords, supported by a fine fibrovascular stroma. The neoplastic cells display



Liver, cat. Subgross magnification of the submitted section of liver shows an infiltrative, multilobular neoplasm effacing 90% of the hepatic parenchyma. (HE, 5X)

occasional attempts at tubule formation and rosettes. Cell borders are distinct, and there is a moderate amount of eosinophilic to finely granular cytoplasm, round to oval often basilar nuclei with finely stippled chromatin and generally one prominent nucleolus. Mitoses are rare at less than 1 per single 400x field. There are small, scattered areas of necrosis and hemorrhage. Remaining small islands of hepatocytes are markedly compressed by the neoplasm and contain single large cytoplasmic lipid vacuoles which often peripheralize the nucleus (lipidosis).

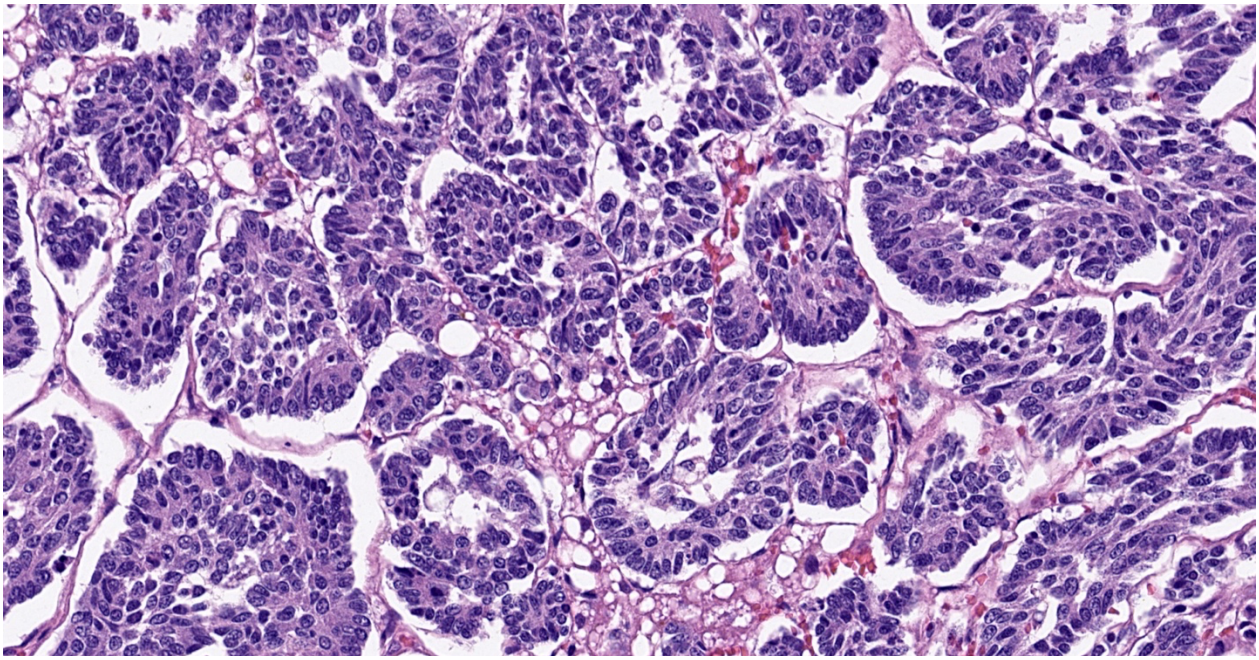
No sites of metastasis were identified.

Contributor's morphologic diagnosis:
Hepatic neuroendocrine carcinoma with severe hepatic lipidosis, domestic longhair, feline.

Contributor's comment:
Neuroendocrine carcinomas (formerly "carcinoids") are malignant neoplasms that arise from the dispersed neuroendocrine system cells. These cells arise from the endoderm during embryogenesis. Neuroendocrine cells belong to a group of cells which secrete both peptide and non-peptide hormones (previously referred to as the amine precursor uptake and decarboxylation (APUD)) group. These cells are important in regulation of gastrointestinal function, and their products include catecholamines and gastrin.

Gastrin-producing tumors lead to gastric hypersecretion and gastric or duodenal ulceration, known as Zollinger-Ellison syndrome.[11,14] Ulcers have been documented in some cats with neuroendocrine carcinoma with hepatic or extrahepatic neuroendocrine carcinoma[15], but were not observed in this case. A recent report describes gastrin immunohistochemical positivity in a feline hepatic neuroendocrine carcinoma.[7] Gastrin secretion by neuroendocrine tumors is well-documented in domestic species.[3,11,14,15] An analogous syndrome in humans, carcinoid syndrome, is characterized by flushing, sweating, diarrhea, vomiting, abdominal pain, and heart failure, but this syndrome has not been documented in domestic animals to our knowledge.[8]

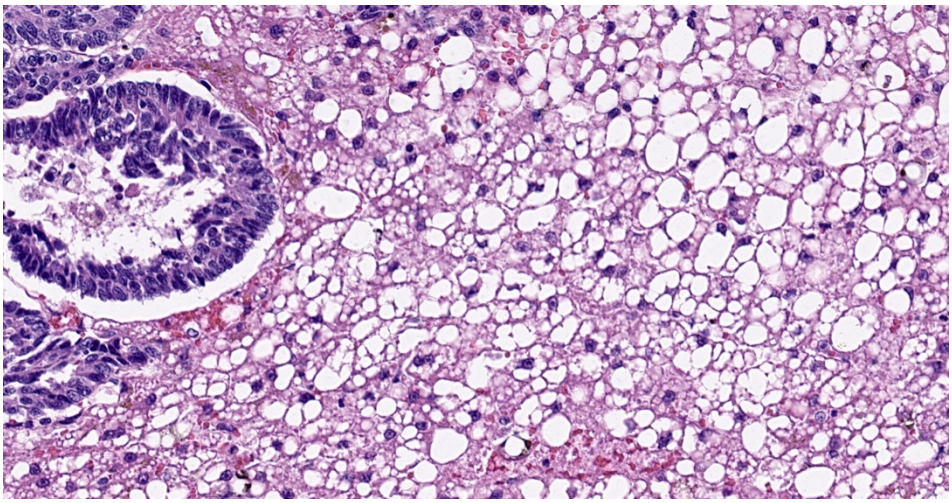
Common primary locations for these tumors in cats and dogs include the gastrointestinal tract, gallbladder, and liver. While they are overall rare in domestic animals, primary hepatic neuroendocrine carcinomas in cats are documented in only a few reported cases.[4,5,7,15]



Liver, cat. The neoplasm is composed of neoplastic polygonal cells with granular basophilic cytoplasm arranged in nest packets and trabeculae on a fine fibrovascular stroma. (HE, 380X)

The present case represents the most common, though non-specific, clinical signs on presentation of cats with hepatobiliary neuroendocrine carcinoma (anorexia, weight loss, vomiting, and hepatomegaly). Most cases reported are mature to senior on presentation, and breeds reported have been variable. Neuroendocrine tumors have also been reported in an African pygmy hedgehog, cow, and others[9,12] and a primary hepatic neuroendocrine carcinoma was recently reported in a baboon.[1]

These tumors typically stain positively with neuron-specific enolase (NSE) and synaptophysin, with variably positivity for chromogranin A.[7,15] A recent report describes gastrin positivity in a feline hepatic neuroendocrine carcinoma[7], further highlighting the potential for Zollinger-Ellison syndrome occurring secondary to tumors outside the gastrointestinal tract.[3,11,14,15] Other useful markers include Churukian-Schenk and Grimelius silver stains to highlight argyrophilic cytoplasmic granules.[11] Immunohistochemistry was not performed in this case; however, the histomorphologic features were considered sufficient for the diagnosis. An important differential diagnosis in this case was cholangiocellular carcinoma, but the frequently observed rosettes and palisading helped to rule out this differential.



Liver, cat. Remaining hepatocytes are swollen by abundant lipid to the point that sinusoidal architecture is effaced. (HE, 380X)

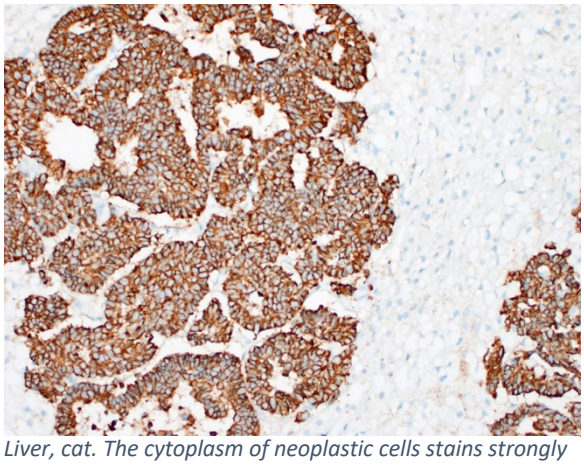
Contributing Institution:
University of Pennsylvania
https://www.vet.upenn.edu/

JPC diagnosis:
Liver: Neuroendocrine carcinoma (carcinoid acceptable).

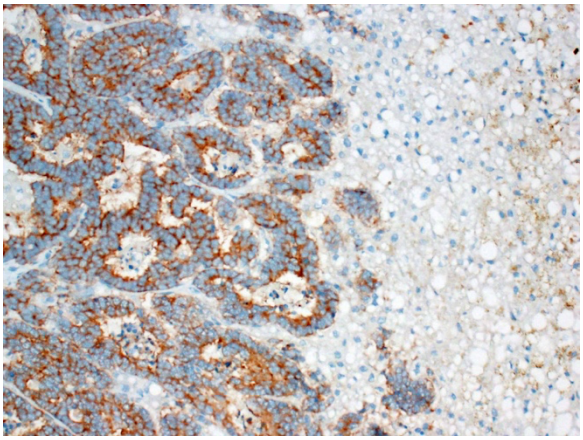
JPC comment:
The moderator led a discussion about nomenclature regarding this entity. In the past, "carcinoid" was used to mean a neoplasm of neuroendocrine origin. However, there is value in being able to convey to a clinician the most likely biologic behavior of the neoplasm. "Carcinoma" is a familiar term for clinicians and conveys a great deal of meaning regarding a diagnosis of malignancy. In this case, the histologic features support a diagnosis of neuroendocrine "carcinoma" and we are confident in sharing that diagnosis with the surgeon or internist.

Neuroendocrine carcinoma is diagnosed infrequently in many species, primarily in the intestine, liver, lung, esophagus, skin, and nasal cavity. Neuroendocrine carcinomas have recently been described in sika deer[16], flamingos[2], a Japanese macaque[6], and bearded dragons.[9]

Neoplasia is rarely reported in bearded dragons (*Pogona vitticeps*), but a recent case of gastric neuroendocrine carcinoma presented with similar clinical signs as mammalian neuroendocrine carcinomas. This neoplasm was poorly differentiated and was not immunoreactive to



Liver, cat. The cytoplasm of neoplastic cells stains strongly immunopositive for chromogranin-A. (anti chromogranin-A, 400X)



Liver, cat. Neoplastic cells demonstrate moderate granular cytoplasmic immunoreactivity to synaptophysin. (anti-synaptophysin, 400X)

chromogranin A, nor gastrin; however, it was immunoreactive for somatostatin, and weakly immunoreactive for NSE.[9]

Unfortunately, there is no standard of care for treatment of these neoplasms. These are often invasive carcinomas, with diffuse infiltration, with limited ability for complete excision. A case of canine hepatic neuroendocrine carcinoma was treated with doxorubicin and metronomic cyclophosphamide treatment, which was tolerated well. The patient lived approximately 15.5 months from initial presentation. However, because these neoplasms are rare, and treatment is not standardized, it is not possible to determine whether the chemotherapy regimen increased this patient's survival time.[13]

References:

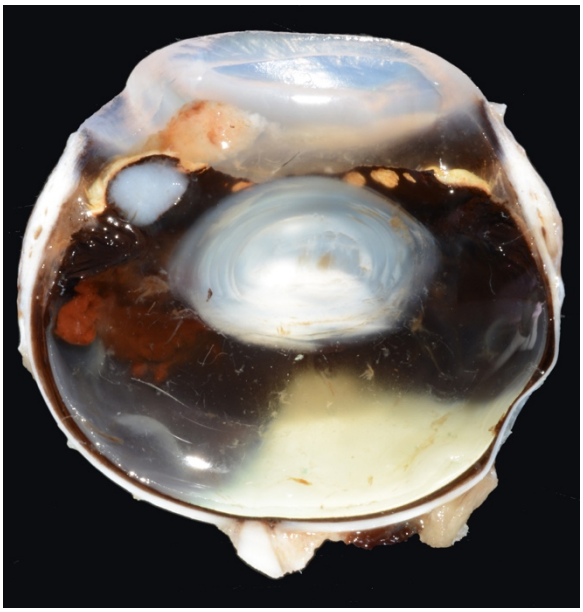
1. Aloisio F, Dick EJ Jr, Hubbard GB: Primary hepatic neuroendocrine carcinoma in a baboon (*Papio* sp.). *J Med Primatol* 38:23-26, 2009
2. Buckles EL. Phoenicopteriformes. In: Terio KA, McAloose D, St. Leger J, eds. *Pathology of Wildlife and Zoo Animals*. San Diego:Elsevier. 2018:692.
3. Cullen JM, Stalker MJ. Liver and biliary system. In: Maxie MG, ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*. Vol 2. 6th ed. St. Louis, MO: Elsevier; 2016:349.
4. Ferreira-Neves, Patricia, et al. "Immunohistochemical Characterization of a Hepatic Neuroendocrine Carcinoma in a Cat." *Journal of Veterinary Diagnostic*

Investigation, vol. 20, no. 1, 2008, pp. 110–114., doi:10.1177/104063870802000125.
5. Head KW, Cullen JM, Dubielzig RR, Else RW, Misdorp W, Patnaik AK, Tateyama S, van der Gaag I. Tumors of the Alimentary System of Domestic Animals, 2nd series.Washington D.C.: Armed Forces Institute of Pathology; 2003:33, 79, 94-96,127-128.
6. Hirata A, Miyamoto Y, Kaneko A, et al. Hepatic neuroendocrine carcinoma in a Japanese macaque (*Macaca fuscata)*. *Journal of Medical Primatology*. 2018;48(2):137-140.
7. Kita, Chiaki, et al. "A Feline Case of Hepatic Neuroendocrine Carcinoma with Gastrin Immunoreactivity." *Journal of Veterinary Medical Science*, vol. 76, no. 6, 2014, pp. 887–890., doi:10.1292/jvms.13-0581.
8. Lips, C. J., et al. "The Spectrum of Carcinoid Tumours and Carcinoid Syndromes." *Annals of Clinical Biochemistry*, vol. 40, no. 6, 2003, pp. 612–627., doi:10.1258/000456303770367207.
9. Lowden LR, Davies JL. Malignant Neuroendocrine Tumor (Carcinoid) of the Spleen in an African Pygmy Hedgehog (*Atelerix albiventris*). *J Comp. Path*. 2016:155:88-91.
10. Lyons JA, Newman SJ, Greenacre CB, Dunlap J. Gastric neuroendocrine carcinoma expressing somatostatin in a bearded dragon (*Pogona vitticeps*). *J Vet Diag Invest*. 2010;22:316-320.
11. Michishita M, Takagi M, Kishimoto TE, et al. Pancreatic neuroendocrine carcinoma with exocrine differentiation in a young cat. *J Vet Diagn Invest*. 2017:29(3):325-330.
12. Michishita M, Takahashi K, Moriya H, Nakamura S, Koyama H, Sako T. Poorly differentiated rectal carcinoid in a cow. *Vet Pathol*. 2007;44:414-417.
13. Morgan E, O'Connell K, Thomson M, Boyd S, Sandy J. Primary hepatic neuroendocrine carcinoma treated with doxorubicin and cyclophosphamide in a dog. *J Am Anim Hosp Assoc*. 2019;55(3):e55305.
14. Munday JS, Lohr CV, Kiupel M. Tumors of the Alimentary Tract. In: Meuten J, ed. *Tumors in Domestic Animals*. 5th ed. Ames, Iowa: John Wiley & Soncs, Inc; 2017:559,568.
15. Patnaik AK, Lieberman PH, Erlandson RA, Antonescu C: Hepatobiliary neuroendocrine carcinoma in cats: a clinicopathologic, immunohistochemical, and ultrastructural study of 17 cases. *Vet Pathol* 42:331-337, 2005
16. Shibata R, Machida Y, Hatakeyama H, et al. Hepatic neuroendocrine carcinoma with metastases to the lymph nodes in a sika deer (*Cervus nippon yakushimae*). *The Journal of Veterinary Medical Science*. 2020; 82(2):193-196.
17. Uzal FA, Plattner BL, Hostetter JM. Alimentary system. In: Maxie MG, ed. *Jubb, Kennedy and Palmer's Pathology of Domestic Animals*. Vol 2. 6th ed. St. Louis, MO: Elsevier; 2016:105-106

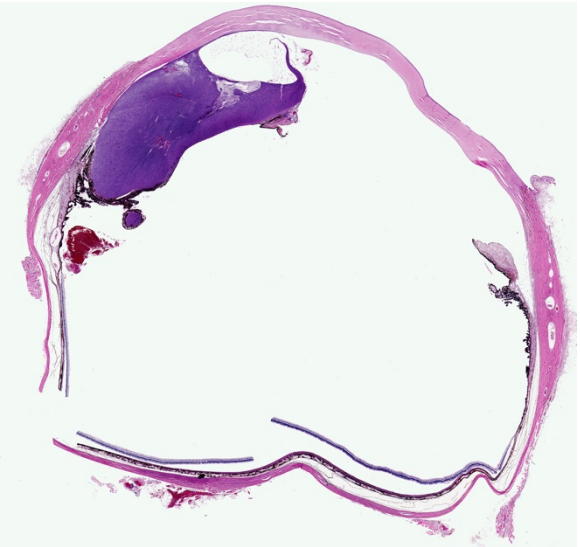
CASE 4: B20-121 (JPC 4152719-00)

Signalment:
12-year old, neutered, unknown sex, domestic shorthair, *Felis catus*, cat

History:
The cat had a tan mass in the lateroventral aspect of the left eye. Fibrin and hemorrhage were reported in the anterior chamber.



Eye, dog. There is a firm tan mass along the posterior surface of the iris, and a focally extensive area of hemorrhage within the posterior chamber. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php)



Eye, dog. A sagittal section of the globe, lacking lens and optic nerve is submitted for examination. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php)

Gross Pathology:
There is a firm tan mass along the posterior surface of the iris. There is red gelatinous material (hemorrhage) in the adjacent vitreous. A small amount of tan material (fibrin) with red flecks (hemorrhage) is in the anterior chamber.

Laboratory results:
None.

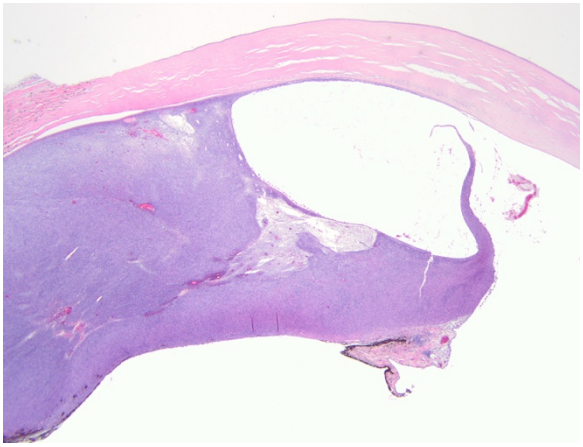
Microscopic description:
Expanding one side of the iris and ciliary body and compressing the iridociliary angle is a well-demarcated mass composed primarily of polygonal cells arranged in nests. The neoplastic cells have moderate amounts of eosinophilic cytoplasm. Nuclei have finely stippled chromatin and indistinct nucleoli. There are 45 mitotic figures in ten 400x fields. In some areas the cells are more spindleoid. In some sections, there are cystic areas within the mass. A periodic acid Schiff (PAS) stain highlights prominent basement membranes around the nest of neoplastic cells. The neoplastic cells are not immunoreactive to MelanA. In some areas the neoplastic cells are weakly immunoreactive to broad spectrum cytokeratin MNF116 or to vimentin. The associated iris leaflet is covered in a pre-iridal fibrovascular membrane. There are aggregates of lymphocytes in the iris stroma and ciliary body. There are varying amounts of fibrin and hemorrhage in the anterior chamber, posterior chamber and vitreous chamber. There is mild peripheral corneal vascularization. The lens is artifactually absent. The retina is multifocally artifactually detached.

Contributor's morphologic diagnosis:
Iridociliary adenoma

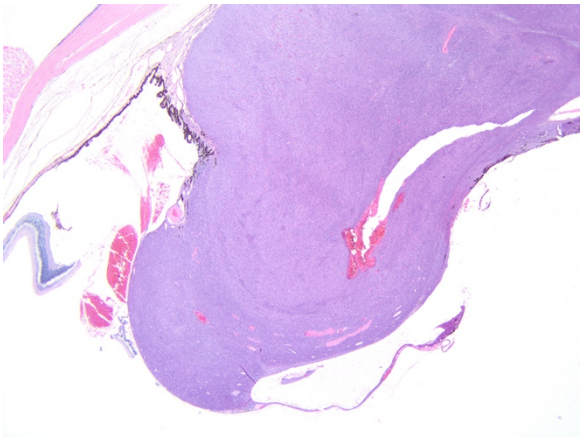
Contributor's comment:
Iridociliary tumors are uncommon in cats, and as in this case, occur primarily in older animals.[3] In dogs and cats, iridociliary tumors are most typically benign,[9] with adenocarcinomas being rarely reported.

Compared to canine iridociliary tumors, which usually have easily recognizable cords of polygonal epithelial cells, the neoplastic cells in feline iridociliary tumors tend to form solid sheets. In some tumors, cystic areas may be common.

The presence of basement membrane around the cells, which as in this case, can be highlighted with a PAS stain[3,9] is helpful in refining the diagnosis and ruling out metastatic carcinomas.[9]



Eye, dog. Higher magnification of the neoplasm demonstrating effacement of the iris and pigment from the ciliary body at the posterior edge of the neoplasm. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php)
(HE, 40X)



Eye, dog. The iris and ciliary body are infiltrated and effaced. There is effacement of the drainage angle and hemorrhage in the posterior chamber. The peripheral retina is detached, and there is hypertrophy of the underlying pigmented retinal epithelium. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php) (HE 60X)

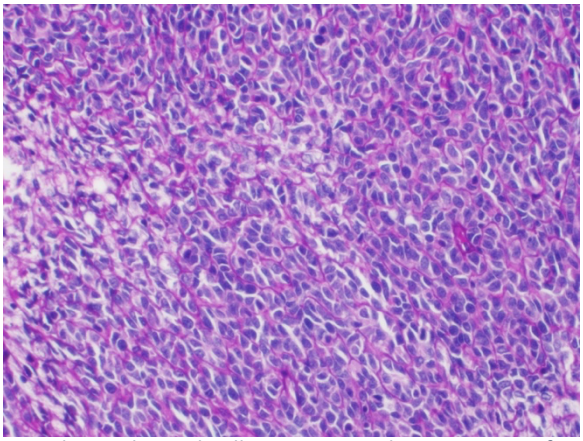
Iridociliary epithelium is derived from neuroectoderm and therefore is typically immunoreactive to the mesenchymal cell marker vimentin,[3,9] and variably immunoreactive to the epithelial marker cytokeratin.[3] Immunoreactivity of neoplastic epithelial cells to vimentin may be useful in differentiating iridociliary tumors from metastatic carcinomas, which otherwise would not be expected to express the vimentin. However, more aggressive iridociliary adenomas may express cytokeratin and or TERT (telomerase reverse transcriptase).[3] Additionally, the neoplastic cells are usually immunoreactive to neuron specific enolase (NSE)[3,9] and variably immunoreactive to S-100.[3]

Contributing Institution:
University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php

JPC diagnosis:
Globe: Iridociliary adenoma.

JPC comment:
The moderator discussed a list of possible differentials with conference participants. Along with iridociliary adenoma/adenocarcinoma, melanoma, post-traumatic sarcoma, severe uveitis, and lymphoma should be considered. Ocular lymphomas were previously presumed to only manifest when an extension of systemic disease. However, more recently, an examination of cases of ocular lymphoma may support a subset of cases that are currently called "presumed solitary ocular lymphoma", or PSOL. These patients did not experience progression of lymphoma following enucleation, and the lymphoma phenotype was not associated with survival.[4,8]

Iridociliary adenomas in the dog and cat, while uncommon, are the second most common primary intraocular tumor. Because these neoplasms are often associated with the formation of a pre-iridal fibrovascular membrane, aqueous outflow obstruction often results in glaucoma. In addition to PAS, vimentin, S100, NSE, and cytokeratin, alcian blue stain may provide additional evidence of epithelial differentiation. These neoplastic cells produce

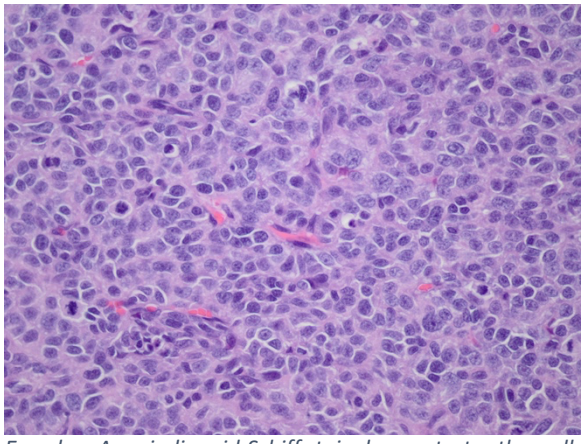


Eye, dog. Polygonal cells are arranged in nests on a fine fibrovascular stroma and exhibit moderate anisocytosis and anisokaryosis, and several mitotic figures are present in this field. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php) (HE, 400X)

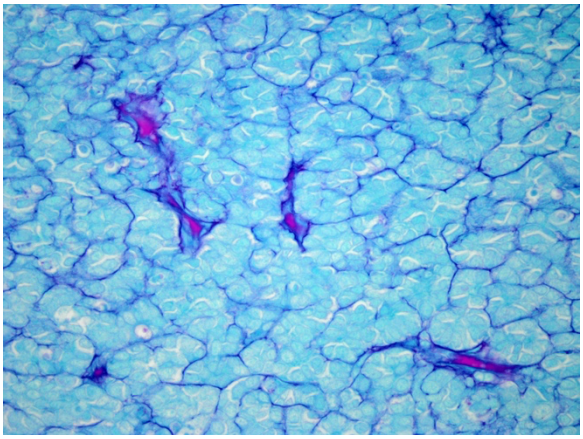
hyaluronic acid, which stains blue with alcian blue, and resists digestion with hyaluronidase.[2]

Analysis of a small sample of canine iridociliary epithelial tumors indicated that surgical excision is difficult, with about half of the patients having recurrence. There are currently no widely accepted treatment guidelines for anterior neoplasms in veterinary species. While human medicine currently favors conservative treatment and globe preservation, the most common treatment for animals is usually enucleation. Determining optimal treatments for veterinary species is limited by the rarity of these cases, limited access to skilled veterinary ophthalmologists, and lack of case follow-up.[1]

There have been a number of reports of iridociliary epithelial tumors in animals other than humans, dogs, and cats. A pleomorphic iridociliary adenocarcinoma was recently reported in a chinchilla (*Chinchilla lanigera*). This animal also had metastasis to its cervical lymph node.[7] A series of four cases of iridociliary neoplasms in rabbits (*Oryctolagus cuniculus*) determined that, while uncommon, this species experiences both iridociliary adenomas and carcinomas.[5] Iridociliary adenoma has also been documented in a Congo African Grey parrot (*Psittacus erithacus*).[6]



Eye, dog. A periodic acid-Schiff stain demonstrates the well-developed basement membranes surrounding neoplastic cells, which is characteristic of this neoplasm. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php) (PAS, 400X)



Eye dog. A periodic acid-Schiff stain (with green counterstain) demonstrates the well-developed basement membranes surrounding neoplastic cells, which is characteristic of this neoplasm. (Photo courtesy of: University of Tennessee, College of Veterinary Medicine, Department of Biomedical and Diagnostic Sciences http://www.vet.utk.edu/departments/path/index.php) (PAS, 400X)

References:

1. Beckwith-Cohen B, Bentley E, Dubielzig RR. Outcome of iridociliary epithelial tumour biopsies in dogs: a retrospective study. *Veterinary Record*. 2014;176(6):147.
2. Dubielzig RR. Tumors of the Eye. In: Meuten DJ, ed. *Tumors in Domestic Animals*, 5th Ed. Ames, IA:John Wiley and Sons, Inc. 2017:908-910.
3. Dubielzig RD, Ketring K, McLellan GJ and Albert DM. The Uvea. In: *Veterinary Ocular Pathology*. 1st ed. St. Louis, MO: Elsevier; 2010: 245.
4. Ota-Kuroki, et al. Intraocular and periocular lymphoma in dogs and cats: a retrospective review of 21 cases (2001-2012). *Vet Ophthalmol*. 2013;1-8.
5. Swisher SD, Klein H, Lennox AM, et al. Four cases of iridociliary tumors in domestic rabbits (*Oryctolagus cuniculus*). *Veterinary Ophthalmology*. 2018;21(6):646-651.
6. Thielen LE, Sledge DG, Hess L. Ocular iridociliary adenoma in a Congo African Grey parrot (*Psittacus erithacus*). *J of Avian Medicine and Surgery*. 2019;33(3):278-284.
7. Ueda K, Ueda A, Ozaki K. Pleomorphic iridociliary adenocarcinoma with metastasis to the cervical lymph node in a chinchilla (*Chinchilla lanigera*). *J. Vet. Med. Sci*. 2019;81(2):193-196.
8. Wiggans, et al. Presumed solitary intraocular or conjunctival lymphoma in dogs and cats: 9

cases (1985-2013). *JAVMA*. 2014;244:460-470.
9. Wilcock BP and Njaa BL. Special Senses. In: *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*. 6th ed. St. Louis, MO: Elsevier; 2016: vol 1:485.