



WEDNESDAY SLIDE CONFERENCE 2015-2016

Conference 18

23 March 2016

CASE I: 12 599 (JPC 4017817).

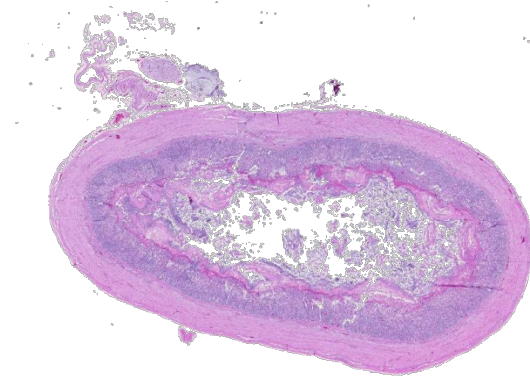
Signalment: 3-week-old female chicken
(*Gallus gallus*)

History: This farm has two groups of 50 chicks each. One group is fed regular, non-medicated feed and the other group is fed organic feed. Twenty-five birds on the organic feed have died. The only clinical sign is a lack of interest in eating. The group fed regular feed is has no clinical signs.

Gross Pathology: The bird is emaciated with no body fat present. The crop and ventriculus contain a small amount of green feed material. The small intestinal mucosa is necrotic.

Laboratory Results: None

Histologic description: The small intestine has diffuse coagulative necrosis of the upper third of the mucosa including the villi, which forms a pseudomembrane over the surface. Numerous gram- positive bacilli are within the necrotic tissue.



Intestine, chicken. Cross section of jejunum in which the proximal 33% of the mucosa is necrotic and brightly eosinophilic. (HE, 6X)

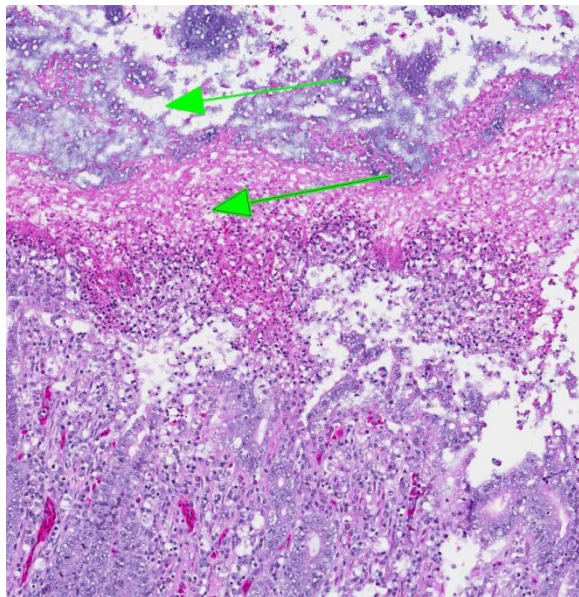
Contributor's Morphologic Diagnosis:
Small intestine: Necrotic enteritis

Contributor's Comment: Necrotic enteritis is an enterotoxemia caused by *Clostridium perfringens* types A and C. The disease affects domestic poultry, primarily birds 2-5 weeks of age, but older birds are also affected.

C. perfringens is normally found in the environment and is part of the normal flora

of birds. Disease occurs following an alteration in the intestinal microflora or a condition that results in damage to the mucosa (coccidia, salmonella, ascarid larva, mycotoxins). Diets high in indigestible, water-soluble, non-starch polysaccharides (wheat, rye, oats, and barley) are risk factors for the disease in birds.³ The organic feed in this case may have contained some of these carbohydrates and would explain why only birds fed this diet were affected.

Necrotic enteritis usually manifests as an acute disease with a sudden increase in flock mortality. There is also a subclinical form of the disease in which birds have reduced weight gain and poor feed conversion ratios due to poor digestion and absorption from the damaged intestinal mucosa.³ This bird was emaciated and may have had the subclinical form of the disease followed by the acute clinical disease terminally.

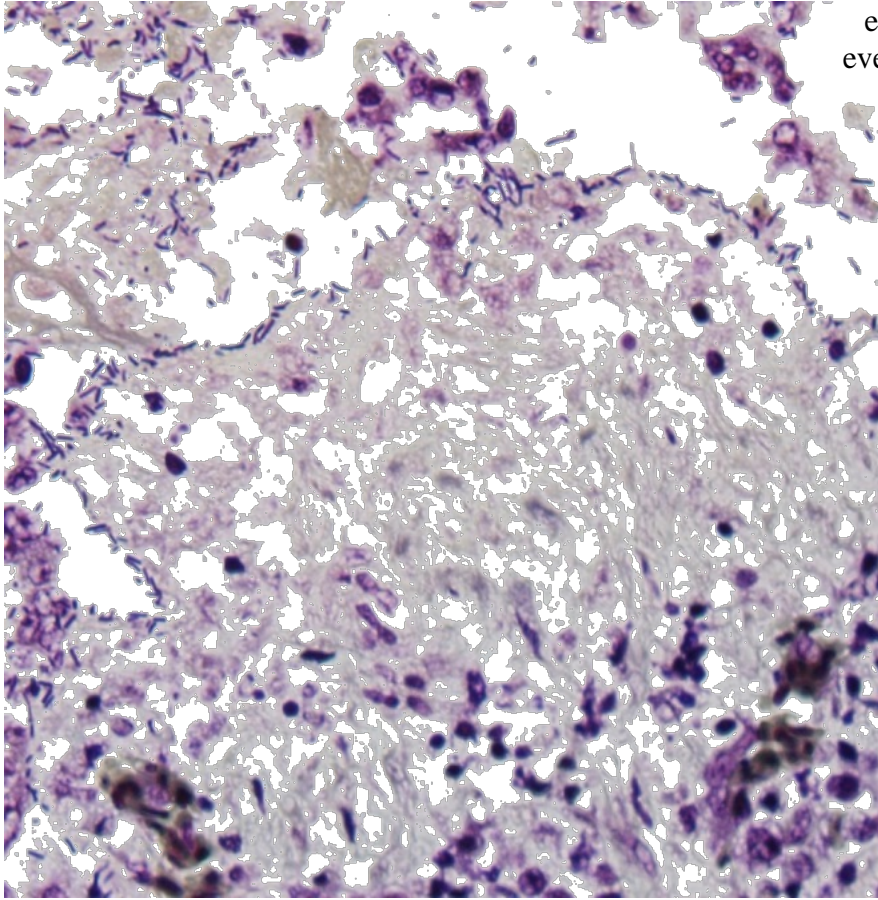


Intestine, chicken. The proximal 33% of the villi are replaced by an eosinophilic coagulum (lower arrow) which is covered by a thick blue layer of bacterial colonies. (HE, 100X)

JPC Diagnosis: Small intestine: Enteritis, necrotizing, circumferential, diffuse, severe with numerous mucosa-adherent bacilli.

Conference Comment: *Clostridium perfringens* is a rapidly growing, gram-positive anaerobe that specializes in tissue destruction and nutrient acquisition classically resulting in extensive necrosis. It has the potential to cause disease in most domestic animal species including cattle sheep, goats, pigs and horses, and often begins as an enterotoxemia, as seen in so-called “pulpy kidney” disease in sheep. The injurious mechanisms of *C. perfringens* are mediated through the actions of many toxins including α , β , ϵ and ι toxins as well as several other degradative enzymes that have cytotoxic effects on endothelial cells, enterocytes, extracellular matrix components and other tissues. The ultimate result is death of enterocytes and/or endothelial cells followed by absorption of toxins into the circulatory system where they can cause cell damage and disease in distant tissues such as the kidney and brain.⁴ *C. perfringens*-induced necrotic enteritis (NE), caused by *C. perfringens* type A (and in some cases) type C, is the most common clostridial enteric disease of poultry. It is most commonly seen in broiler chickens 2-6 weeks of age, but also occurs in many other avian species including turkeys and waterfowl as well as in older broiler chickens. Diagnosis is based on clinical and pathological findings; isolation of the organism and toxin does not prove causation as they can both also be found in the intestine of healthy birds. Other clostridial organisms which can cause disease in birds include *Clostridium colinum* which causes ulcerative enteritis, as well as *Clostridium difficile*, *Clostridium fallax* and *Clostridium baratii*.¹

A key element in the pathogenesis of *C. perfringens* induced NE in chickens is the pore-forming NetB toxin (which has some similarities to *C. perfringens* beta toxin). It creates a hole in the cell membrane that



Intestine, chicken. There are numerous robust bacilli lining the necrotic villi and remaining crypts (at left) and admixed within the overlying cellular debris. (Brown-Brenn, 600X)

results in leakage of cell contents and cell death and is apparently a central factor in disease pathogenesis. Strains of *C. perfringens* positive for the *netB* gene also carry additional virulence genes for toxins, other nutritional/metabolic factors related to fitness, and adhesins, which contributes to their ability to proliferate rapidly and cause disease. It is suggested the NetB toxin is a key initiating factor in the pathogenesis of NE, and may actually target endothelial cells in the lamina propria and not the intestinal epithelium. Key initiating events include colonization of the intestinal mucosa and degradation of the mucous layer, which allows toxins access to the enterocytes.²

Histologic lesions are characterized by extensive mucosal necrosis which may

extend into the submucosa or even the muscularis in severe cases. There is a sharp line of demarcation between necrotic and viable tissue and bacilli are seen trapped in fibrinonecrotic debris.¹ A key histologic feature in NE includes the presence of abundant large *C. perfringens* bacilli at the margin of the submucosa once the superficial mucosa has become necrotic and is sloughed, which may represent biofilm formation and be related to disease pathogenesis or progression.² Gross lesions are typically isolated to the small intestine, but may also be

seen in the ceca. The intestine is thin-walled, gas-distended and filled

with a dark brown, grey, and/or yellow-green fluid, while the mucosal surface is typically covered by a necrotic coagulum. Thickening of the intestinal wall may be seen in chronic cases and some affected chickens may develop cho-langiohepatitis.

The differential diagnosis includes coccidiosis, which may precede NE and can be differentiated by the presence of blood in the intestinal tract (which is not typically seen in cases of NE), and the presence of coccidial organisms. Ulcerative enteritis caused by *C. colinum* and histomoniasis are other diagnostic considerations.¹

Contributing Institution:
College of Veterinary Medicine
Virginia Tech

Blacksburg, VA 24061
www.vetmed.vt.edu

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CASE II: T15-9947 (JPC 4066088).

Signalment: Five-year-old Beagle mix, intact female dog (*Canis familiaris*)

History: The patient suddenly became anorectic, lethargic, and had increased body temperature (105.6°F), high white blood cell count (WBC), and was azotemic.

Gross Pathology: There were multifocal areas of hemorrhage on the epicardium.

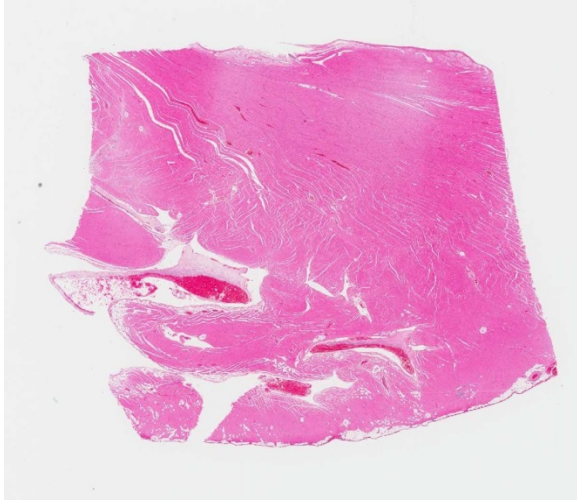
Laboratory Results: Laboratory tests for Lyme disease and *Ehrlichia*, and fluorescent antibody (FA) tests for canine parvovirus

and canine adenovirus were negative. Aerobic culture yielded heavy growth of *Candida albicans* from the intestine and a few colonies from lungs and liver.

Histologic description: Scattered “onion skin” cysts were present between myocardial fibers of the sections of heart. In some sections, multifocal mild to moderate granulomatous to pyogranulomatous myocarditis was observed. Similar cysts were present in the diaphragm, skeletal muscle, pancreas, liver, small intestine and abdominal fibroadipose tissue (sections not included in the slide). Additionally, multifocal areas of necrosis and vascular thrombi were observed in the sections of liver and spleen. Moderate to severe mineralization was present in various tissues including the renal tubules, lungs and intestinal mucosae. Other secondary lesions observed include diffuse, severe amyloidosis in the small intestine, pancreas and renal glomeruli.

Contributor’s Morphologic Diagnosis: Myocardium: “onion skin cysts” (consistent with cysts of *Hepatozoon americanum*) with multifocal mild to moderate granulomatous to pyogranulomatous myocarditis; and dissemination of the cysts to various tissues.

Contributor’s Comment: *Hepatozoon* spp that infect domestic dogs in the United States include *H. canis* and *H. americanum*. *Hepatozoon canis* and *H. americanum* differ in numerous aspects including geographic distribution, definitive tick hosts, sites of merogony and clinical syndromes in canine intermediate hosts, treatment approaches, and regions of 18S rRNA gene sequence. *H. americanum* gamonts are found in circulating leukocytes of dogs, as are those of *H. canis*. Ultrastructural and immunohistochemical evidence indicates that the host cell for *H. americanum* during



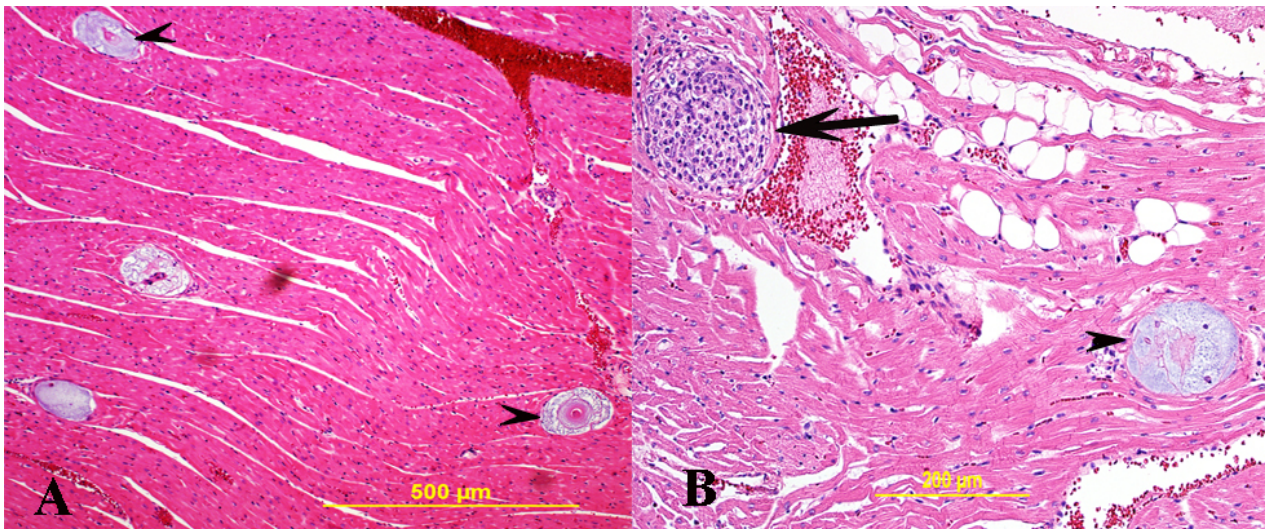
Heart, dog. A cross section of the myocardium is submitted. Small cysts and foci of cellular infiltrates are scattered throughout the section but difficult to pick up at this magnification. (HE, 5X)

merogony and gamogony is a monocyte, rather than a neutrophil, which is considered the favored host cell for *H. canis*. Also, merogony of *H. americanum* takes place in a host cell that is lodged primarily between individual striated muscle fibers whereas the asexual process for *H. canis* occurs in a wide variety of sites, especially in hemolymphatic tissues and visceral organs. The meronts of *H. americanum* are usually found within “onion skin” cysts that are created by layers of mucopolysaccharide-rich material that is apparently elaborated by

the host cell. Such characteristic lesion is not associated with the *H. canis* meront, which is rarely found in muscle and has its own characteristic morphologic feature referred to as a “wheel spoke” arrangement of merozoites within the meront.^{1,4}

Hepatozoon americanum causes American canine hepatozoonosis, which is a highly debilitating, tick-borne disease of dogs mainly in the south-central and south-eastern USA⁴ although documented in other regions of the USA.¹ It is caused by *Hepatozoon americanum*, a protozoan parasite, the definitive host of which is the tick *Amblyomma maculatum*.³ In the United States, *A. maculatum* was traditionally endemic in states bordering the Gulf Coast and several states bordering the Atlantic coast including Georgia, Florida, and the southern portion of South Carolina. However, current data report establishment of the Gulf Coast tick in states farther inland including Oklahoma, Kansas, Arizona, Arkansas, Missouri, Indiana, Kentucky, and Tennessee and additional states along the Atlantic coast including Maryland, Virginia, and West Virginia.^{1,4} Dogs get the disease by ingesting infected ticks.^{3,4}

Clinically, infected dogs are often febrile,



Heart, dog. Sections of myocardium containing scattered “onion skin” cysts (arrow heads) and a focal pyogranulomatous myocarditis (arrow). (HE, 100x). (Photo courtesy of: The University of Georgia, College of Veterinary Medicine, Department of Pathology, Tifton Veterinary Diagnostic and Investigational Laboratory, Tifton, GA 31793, <http://www.vet.uga.edu/dlab/tifton/index.php>)

stiff, lethargic, and depressed. Wasting of body mass, marked in temporal muscles, and periosteal bone proliferation (hypertrophic osteopathy) are documented in dogs with chronic disease. Microscopically, trophozoite within macrophage-like cells in many tissues, mainly in striated muscles, apparently transforms the host cell into a mucopolysaccharide-producing entity that builds structures commonly called “onion skin” cysts. Parasite-containing cysts and lesions can be found in many tissues, but are consistently found in striated muscles.⁴ Adipose and loose connective tissues are less commonly affected; rarely, other organs/ tissues such as lymph nodes, spleen, liver, and pancreas may be affected.^{5,6} Mature meronts of a well-developed cyst of *H. americanum* release merozoites, which

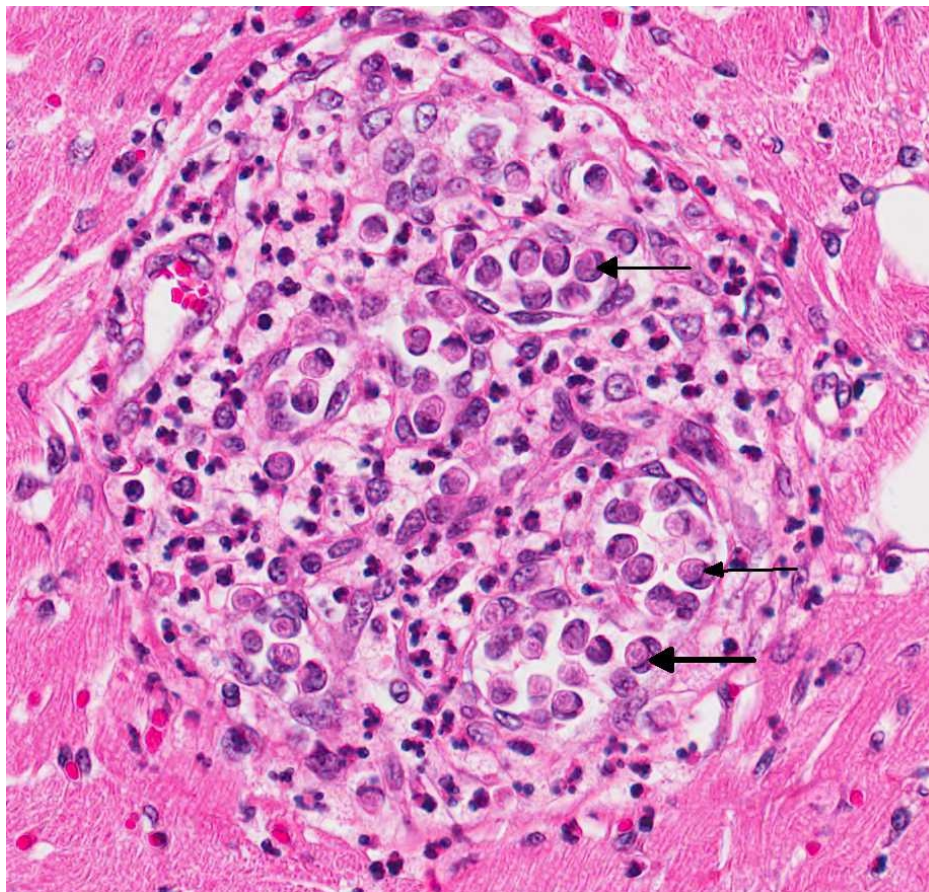
incite local inflammation such as pyogranulomatous myositis, and are associated with a systemic reaction and overt illness.⁴ Dogs may die due to secondary amyloidosis, glomerulonephritis⁸ and associated other secondary lesions such as mineralization.

JPC Diagnosis: Heart: Myocarditis, histiocytic and lymphoplasmacytic, multifocal, mild with apicomplexan cysts and intrahistiocytic and extracellular merozoites.

Conference Comment: Once and infected tick is ingested, the sporocysts excyst and release sporozoites, which penetrate the intestinal mucosa, disseminate systemically, and reproduce asexually (merogony) in cells located within striated muscle.⁴ It is unclear

if the sporozoites travel to target tissues in the extracellular milieu or are ingested by leukocytes and thereupon disseminate hematogenously.¹ The cells, which are parasitized in both the “onion skin” cyst form in striated muscle as well as in peripheral blood, are of monocyte lineage and protect the developing organism from host defenses.³

Merogony results in the production of merozoites that eventually give rise to gamonts that circulate in the blood where



Heart, dog. Foci of pyogranulomatous inflammation represent ruptured meronts, and macrophages often contain phagocytized merozoites (arrows).

ticks can ingest them.⁴ When merozoites are released from the cyst form, they incite a marked, localized, acute inflammatory response that eventually results in formation of a granuloma, but infected mononuclear cells are able to escape the granuloma.³ The cysts are actually located between muscle fibers and contain a host cell, within which is the developing zoite stage. The host cell is surrounded by the lamellated structure composed of muco-polysaccharide in the “onion skin cyst” stage. Collagen fibers, fibroblasts and capillaries may be embedded within or closely associated with the lamellated cyst wall; but inflammatory cells are generally not associated with the large cysts. The developing parasites within the host cell, inside the cyst, bear ultrastructural features of developing apicomplexan trophozoites, although a parasitophorous vacuole is not observed. Both the merozoite asexual stage and the gamont sexual stage may be observed within different macrophages present in the granulomas which form after the tissue cysts rupture.³

As mentioned above, *H. americanum* infection can result in periosteal bone proliferation. Most commonly, periosteal bone proliferation occurs in the diaphyseal regions of proximal limb bones but may also manifest in other locations such as the vertebrae. This finding is in contrast to hypertrophic osteopathy which occurs in the distal limb. Histologically, *H. americanum*-induced periosteal bone lesions are often symmetric, resemble hypertrophic osteopathy, and characterized by trabeculae of woven bone oriented perpendicular to the cortex. The lesions may be widespread and in locations unassociated with presence of the organism, suggesting a systemic effect of the infection as opposed to a local condition.² As compared above, *H. americanum* generally results in more severe disease than *H. canis* and is often fatal.

Infection with *H. americanum* results in a profound neutrophilia and anemia, although the organisms may not be seen on a blood smear. In addition to muscle atrophy and bone pain, other clinico-pathologic findings in affected dogs include hyperglobulinemia, mucopurulent ocular discharge and uveitis. The disease may follow a waxing and waning course over time with periods of relapse correlating with release of merozoites and associated inflammation.^{1,7}

Conference participants described the “onion skin cysts” as 200um in diameter, composed of lamellations of mucinous material, and separating cardiac myocytes. Small characteristic granulomas, present in some slides, were described as foci of macrophages containing tachyzoites which peripheralize the nucleus, with few neutrophils at the margin. A subset of slides also contains small foci of fibrosis, which is populated with low numbers of hemosiderin laden macrophages, lymphocytes and plasma cells. Multifocal areas of hemorrhage are also present. Rare foci of mineralization and myofiber degeneration are present in some sections.

Contributing Institution:

The University of Georgia, College of Veterinary Medicine, Department of Pathology, Tifton Veterinary Diagnostic and Investigational Laboratory Tifton, GA 31793, <http://www.vet.uga.edu/dlab/tifton/index.php>

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CASE III: 14183 (JPC 4069358).

Signalment: Four-year-old, male, crossbreed, feline (*Felis catus*)

History: The cat was admitted to a veterinary facility for lethargy and vomiting. The owner reported that the cat had ingested

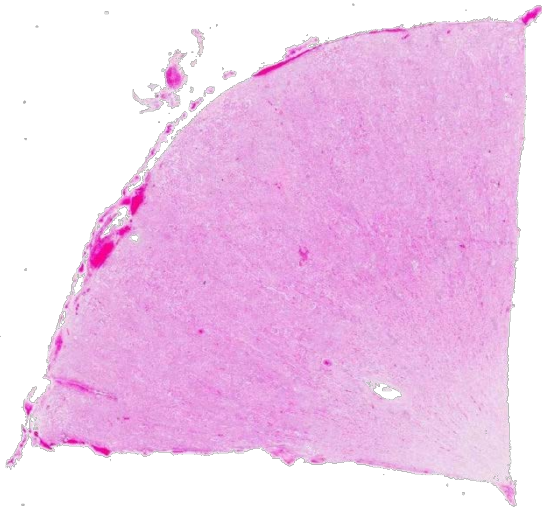
some leaves of lily (*Lilium* sp.). At admission, it was anuric and vomited frequently.

Gross Pathology: Renal congestion with swollen kidneys and perirenal hemorrhages and edema were found. Pulmonary congestion, gastrointestinal congestion, and paleness of the liver were seen. The stomach and intestine was empty.

Laboratory Results: None

Histologic description: In lily toxicosis, severe renal tubular degeneration accompanied by luminal accumulation of cellular and proteinaceous debris is a common finding. Both hyaline and granular casts often occlude the collecting ducts.

The epithelium of most tubules has undergone varying degrees of degeneration and necrosis. Cortical tubules were more severely affected than medullary tubules, and proximal convoluted tubules were more severely affected than straight tubules, thin segments, or ducts. Degenerate epithelial cells had swollen, irregularly vacuolated cytoplasm. Necrotic epithelial cells had granular eosinophilic cytoplasm and either lacked a nucleus or exhibited pyknosis and karyorrhexis. The lumens of many tubules and ducts contained eosinophilic, granular remnants of desquamated, necrotic epithelial cells, granular casts, or homogeneously eosinophilic material (hyaline casts). Lymphocytes and some macrophages had accumulated in the interstitium.



Kidney, cat. A triangular section of renal cortex is submitted. (HE, 5X)

Contributor’s Morphologic Diagnosis:

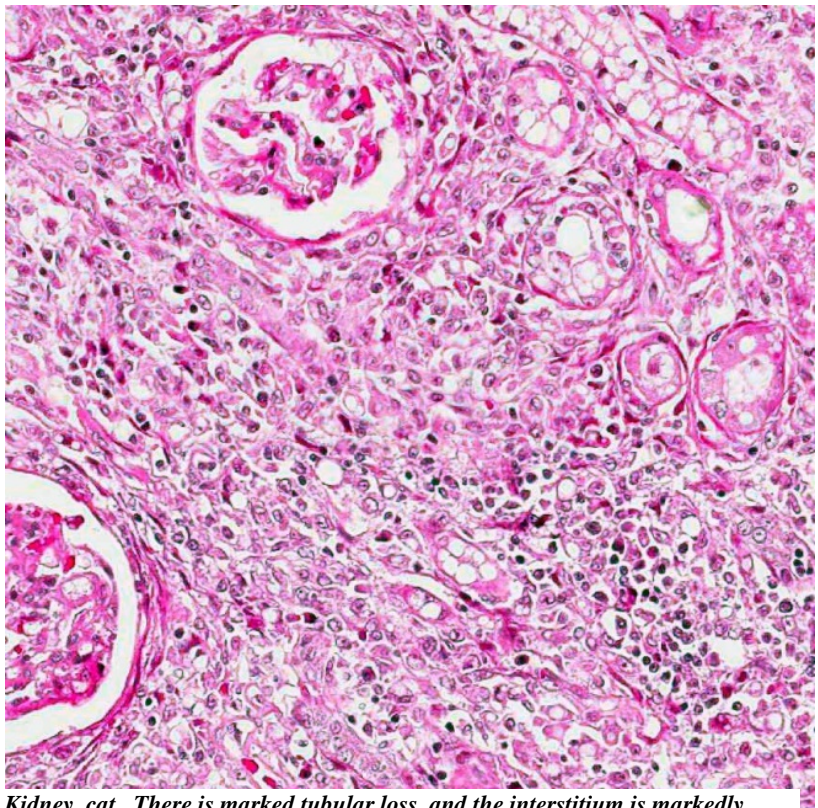
Kidney: Tubular degeneration and necrosis diffuse.

Kidney: Interstitial histio-lymphocytic diffuse subacute nephritis.

Contributor’s Comment: The *Liliaceae*, or lily family, is composed of 280 to 300 genera made up of 4000 to 4600 different species. The numbers vary because botanists differ in how to classify this diversity based on flowering type, ovary position, and distribution. There are ornamental plants within the group (lilies, tulips, hyacinths, daffodils, and amaryllis); food plants (onions, garlic, asparagus, leeks, shallots, and chives); and a variety of toxic species in the family, some of which are quite deadly. It must be remembered that the common name “lily” is applied to many species of multiple

genera within and without this group. *Lilium* plants are mainly sold for indoor use as potted plants or as floral arrangements but are also planted outdoors in flower gardens.⁵

The genera *Lilium* (Madonna lily, white lily, tiger lily, rubrum lily, Japanese show lily, devil lily, Easter lily, trumpet lily, leopard lily, panther lily, stargazer lily, Asiatic lily, wild yellow lily, and Turk’s cap lily) and *Hemerocallis* (the “day” lilies with flowers lasting only one day) are the groups considered potentially nephrotoxic to cats. For the purposes of our discussion, we will limit our investigation to the genera *Lilium* and *Hemerocallis* are which cause nephrotoxicity. Nevertheless, it must be kept in mind that a wide variety of plants are in the lily family or are called “lilies” (and hybrids exist), and within this group there is a similar diversity in the potential toxicological effects.³



Kidney, cat. There is marked tubular loss, and the interstitium is markedly expanded by numerous macrophages and fewer neutrophils, lymphocytes and rare plasma cells. (HE, 100X)

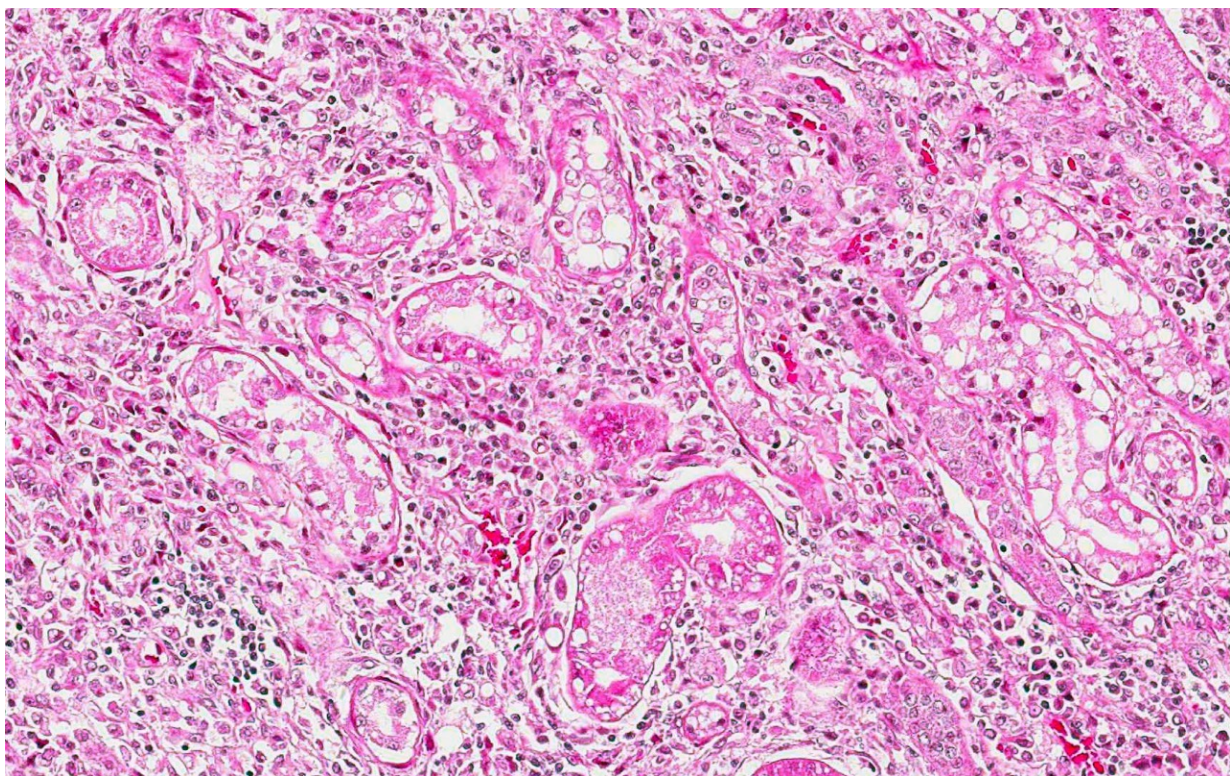
Various members of the *Lileaceae* family of plants can cause acute tubular necrosis in animal species, for example, *Narthedum ossifragum* (bog asodel) in ruminants, several lilies, and their hybrids (*Lilium* spp.)³ Most pet owners know little about the danger these plants pose to cats. Although cats are finicky eaters, for some unknown reason they eat the leaves and flowers of *Lilium* plants. Both leaves and flowers are reportedly toxic. Ingestion of one or two leaves or one whole flower has caused dead in cats.^{3,5}

Cats are really sensitive to ingestion of certain species of lilies; no age, sex, or breed predilection has been identified.³ The mortality rate from Easter lily toxicosis is reported to be as high as 50–100%, depending on the time symptomatic treatment is initiated. High mortality rate is reported if treatment is not initiated before onset of anuric renal failure, which occurs 18–24 hours after exposure.⁵ Nephrotoxic

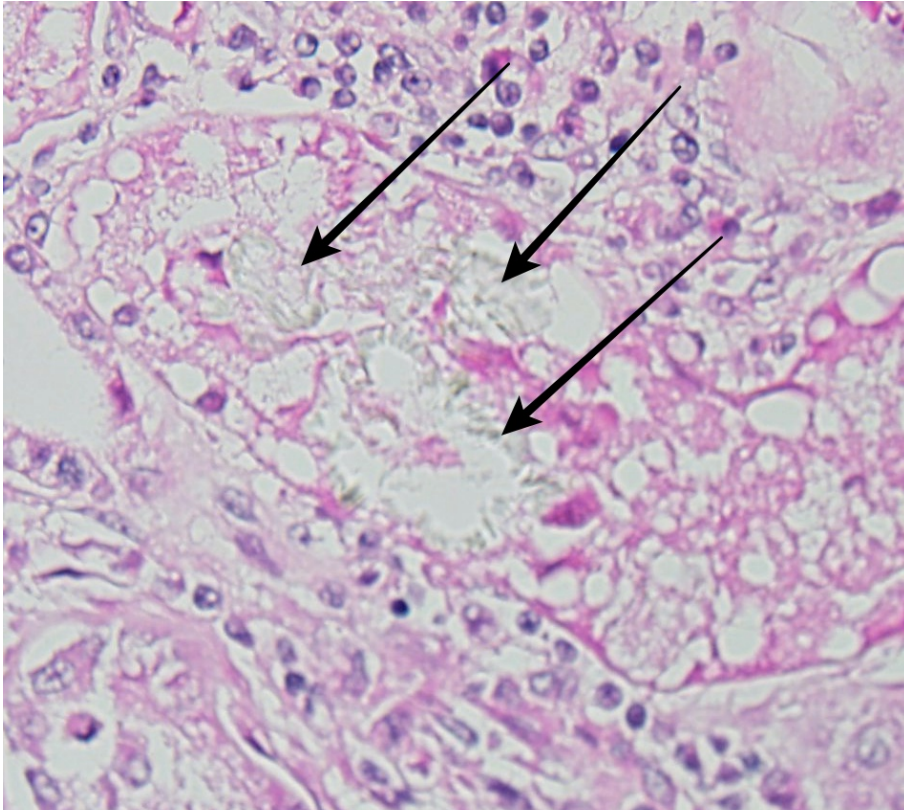
damage cannot be duplicated in rats, mice, or rabbits. In dogs, only vomiting and gastrointestinal signs can be seen after lily ingestion in dogs even when fed large amounts of these plants.³

The exact mechanism of action of lily poisoning, specifically lily-induced nephrotoxicity is unknown. The rapid onset of clinical signs after ingestion of culprit species indicates rapid absorption rate for the poison. The toxins damage renal tubular epithelial cells resulting in cell death and sloughing of damaged renal cells. The insult to the kidney is severe, leading initially to polyuric kidney failure. This polyuric kidney failure leads to extreme dehydration. If this dehydration progresses far enough or goes on long enough, anuric renal failure and complete renal shutdown can develop.³

In this case, microscopic lesions in the kidney were compatible with nephrotoxic tubular necrosis of a few days duration. Nephrotoxic tubular necrosis is not a



Kidney, cat. There is marked tubular loss, and remaining tubules show degenerative changes, including celling into the lumen, the presence of numerous discrete clear vacuoles, brightly eosinophilic cytoplasmic granules. Few epithelial cells are pyknotic and rarely sloughed into the lumen. (HE X)



Kidney, cat. Rarely, degenerating tubules contain birefringent fan-shaped oxalate crystals (arrows) (HE, 400X)

specific diagnosis and can result from a variety of nephrotoxins, such as aminoglycoside antibiotics (e.g., gentamicin), metals (e.g., lead, arsenic, mercury), or metabolites of ethylene glycol.² In this case, the lily was the probable source of the nephrotoxin and the whole renal lesions.

At present, there is no “gold standard” test for analysis and verification of lily ingestion. The most positive confirmations involve the observation of the animal ingesting the lily, compatible clinical syndrome signs, compatible clinicopathological findings, and supportive postmortem lesions in cats that die. Even if postmortem lesions are suggestive of lily poisoning, positive verification of lily ingestion cannot be made unless ingested plant material observed within the gastrointestinal tract. Despite no specific test existing to verify this poisoning, if the index of suspicion for lily intoxication is high,

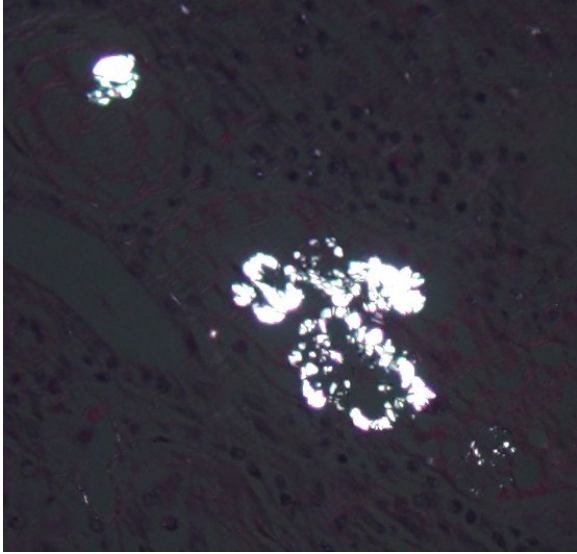
initiation of appropriate fluid therapy should begin to prevent anuric renal failure from developing.³

JPC Diagnosis:
 Kidney: Tubular degeneration, necrosis and, diffuse, marked with loss with mild atrophy and regeneration, marked lymphoplasmacytic nephritis, protein casts and rare oxalate crystals.

Conference
Comment: The contributor has provided an excellent discussion of lily

toxicosis in the cat. Although not commonly described in association with lily toxicosis, pancreatic lesions may also be seen. Changes include cytoplasmic vacuolation affecting the majority of acinar cells which is interpreted as a degenerative change. Pancreatitis has also been reported to result from Easter lily ingestion. Changes in the pancreatic islet cells are not reported.

Seizures are also reported in addition to the renal and pancreatic changes and may occur within 8 hours after exposure.⁵ The flowers of lily plants are more toxic than its leaves but ingestion of either may result in the renal changes described above. Changes within the kidney occur initially in the inner cortex, and as the condition progresses, tubules within the outer cortex succumb to damage as well. Ultrastructural changes include mitochondrial swelling in renal proximal tubule epithelium and the formation of megamitochondria, which may result from either enlargement of individual mit-



Kidney, cat. Luminal oxalate crystals are easily identified, even at lower magnification.) (HE, 400X)

ochondria or fusion of mitochondria. Other ultrastructural changes that have been described include pyknotic nuclei and lipid infiltration.⁵

The conference histologic description included many of the tubular features described above by the contributor. The primary findings in this case are tubule degeneration and necrosis and the inflammation is considered a secondary finding. There was discussion regarding the origin of the inflammation and whether it was a process unrelated to the tubular necrosis, and perhaps present prior to the onset of nephrotoxic tubular changes; however, a consensus opinion was not reached in this regard and thus it was included in the morphologic diagnosis with the tubular changes. Additional features include tubule regeneration and atrophy, mild glomerular changes including thickened parietal and visceral epithelium and low numbers of sloughed epithelium within the urinary space. Low numbers of birefringent crystals are also seen within tubule lumina when viewed under polarized light. The capsule is mildly expanded by

hemorrhage and inflammatory cells. Although mild, the presence of glomerular lesions also lends evidence to another process taking place in the kidney as glomerular lesions are not commonly reported in cases of lily intoxication. Other nephrotoxic plants which affect domestic animal species that were discussed during the conference include *Isotropis* toxicity in ruminants, oak toxicity in ruminants and horses, *Amaranthus retroflexus* (pigweed) toxicity in swine and cattle, *Lantana camara* toxicity in cattle, and oxalate containing plant (i.e. *Rumex* spp., *Oxalis cernua*, *Halogeton glomeratus*, etc.) toxicity in cattle and sheep.²

Contributing Institution:

Animal Pathology Department / Veterinary Diagnostic Laboratory, Veterinary Faculty; Federal University of Pelotas. 96010-900 Pelotas, RS, Brazil.

<http://wp.ufpel.edu.br/sovet/>

<http://www.ufpel.edu.br/fvet/lrd/>

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CASE IV: 0561-15 (JPC 4070541).

Signalment: 9-month-old, intact female Persian cat (*Felis catus*)

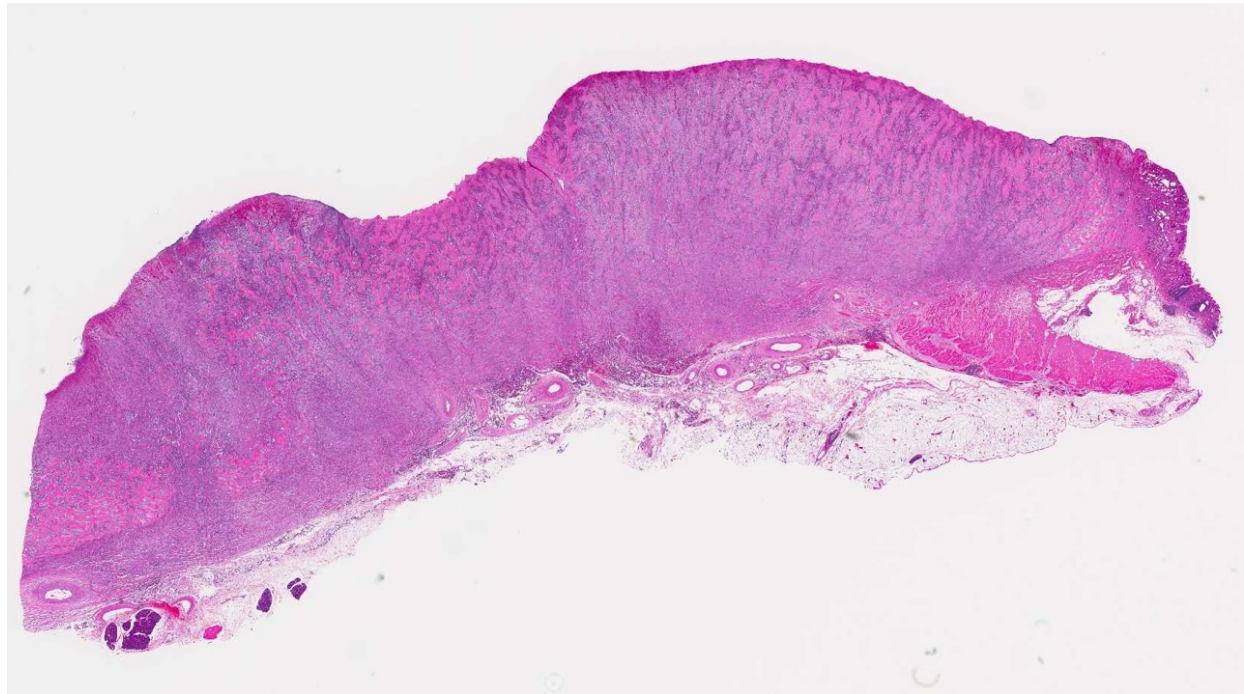
History: The cat had a history of intermittent vomiting and failure to gain weight. Radiographs revealed a mass at the gastric pylorus and an exploratory laparotomy was performed.

Gross Pathology: The gastric pylorus region had thickened wall with roughened

mucosa surface.

Laboratory Results: None

Histologic description: Expanding and effacing the architecture of the gastric mucosa, submucosa and tunica muscularis at the pylorus is a transmural proliferation of a fibroproliferative mass with surface necrosis and ulceration. The lesion affects all layers of the gastric wall, and is comprised of branching and anastomosing cords and trabeculae of dense collagen separated and surrounded by a dense population of fibroblastic cells intermixed with large numbers of eosinophils, plasma cells, regionally dense neutrophils, lesser histiocytes, mast cells and lymphocytes. Toward the serosal surface, the fibroblastic proliferation is necrotic and overlain by edematous, loose fibrovascular proliferation and above described inflammatory cells. There is obliteration of mucosal epithelium, further covered by necrotic cell debris, and dense aggregates of neutrophils that are occasionally centered on small clusters of



Pylorus, cat. The submitted section of pylorus is largely effaced by an infiltrative mass. A small section of pancreas is present in the lower left. (HE 6X).

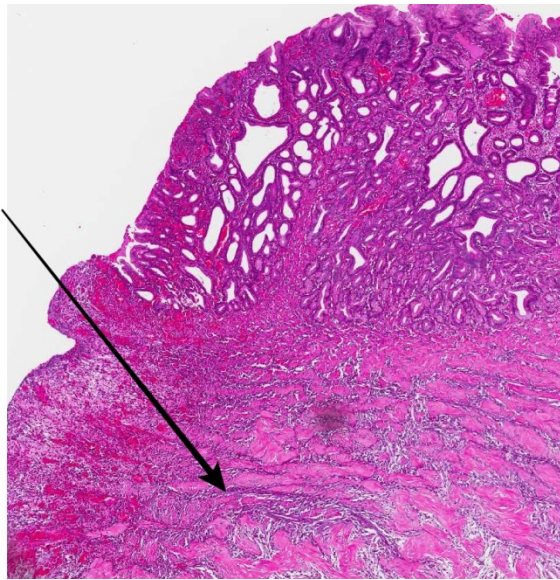
cocci, as well as hair shafts in cross and tangential section .

A Gram stain of the lesion revealed myriad gram-positive rods and gram-negative coccobacilli (often associated with degenerate collagen) on the ulcerated surface.

Periodic acid-Schiff stains failed to demonstrate fungi present within the lesion.

Contributor's Morphologic Diagnosis:

Stomach: 1. Feline gastrointestinal eosinophilic sclerosing fibroplasia
2. Marked surface necro-suppurative gastritis, with intralesional hair shafts and bacteria



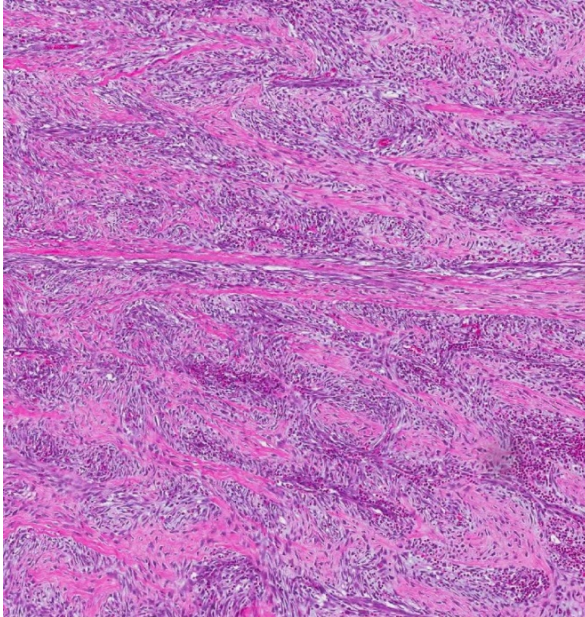
Pylorus, cat. Higher magnification of the interface between the pylorus (top, with dilated glands), and the mass below (arrow). (HE, 45X)

Contributor's Comment: Feline gastrointestinal eosinophilic sclerosing fibroplasia is a recently described disease in cats characterized by a nodular, non-neoplastic, proliferative, fibrosing and eosinophilic lesion that effaces the stomach wall of cats.² The disease tends to affect middle-aged cats and typical clinical signs include decreased appetite, weight loss, vomiting, and diarrhea.³

Reported breeds include Ragdoll, domestic shorthair, domestic longhair, Siamese, Maine Coon, Himalayan, Persian and Scottish fold.^{2,3,4} The disease is most often seen at the pyloric sphincter, ileocecolic junction or colon, often involving the regional lymph node, and can be associated with peripheral eosinophilia.² The etiopathogenesis of this condition is not clearly defined, with migrating foreign body, genetic predisposition and eosinophil dysregulation, herpesvirus infection, and food hypersensitivity are all speculated in the pathogenesis.³

The condition has previously been confused with sclerosing mast cell tumor, which is a neoplasm that tends to occur in the small intestine, unassociated with peripheral eosinophilia and extensive fibroproliferation, and less commonly forms palpable masses in the stomach.³ While bacteria are seen within lesions of feline gastrointestinal eosinophilic sclerosing fibroplasia in some reports, antimicrobial therapy is not effective.² Neither feline coronavirus, feline herpes virus nor any individual bacterial agent have been linked as an etiologic agent.³

A single case report indicated an association between phycomycetes and this disease entity in a domestic cat.⁵ The disease has been reported in United States, Australia, Europe, Japan and New Zealand^{3,4} and this represents this as a first case from Singapore. Prognosis of affected cats is typically grave, and there is no conclusive single conclusive treatment regime.³ Cats treated with prednisolone have a significantly longer survival period and a combination treatment approach of surgical resection, prednisolone, antimicrobial therapy and immune modulation may help improve clinical outcome.³



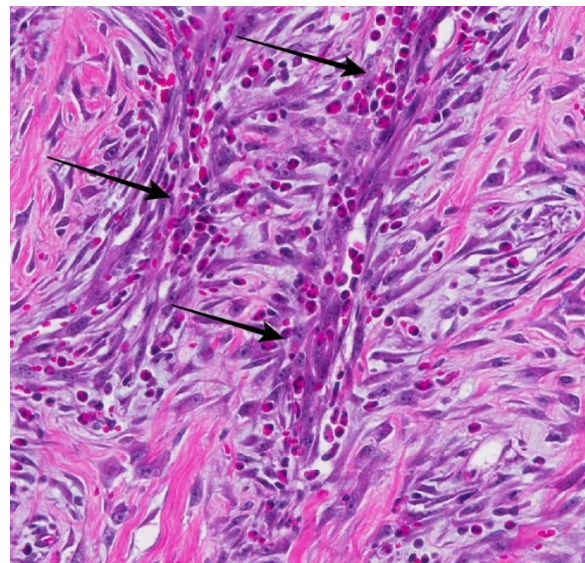
Pylorus, cat. The mass is composed of large numbers of fibroblasts which produce a herringbone pattern of mature collagen. (HE, 200X)

JPC Diagnosis: Stomach: Gastritis, ulcerative, eosinophilic and mastocytic, sclerosing, transmural, severe, with entrapped hair shafts and extracellular bacilli.

Conference Comment: The mass lesion present in feline gastrointestinal eosinophilic sclerosing fibroplasia has been described as hard, non-painful and easily palpable. Upon fine needle aspiration or biopsy the lesions are firm, described as ‘gritty,’ and are heterogeneous when sectioned at necropsy or at time of surgery.³ Histologically, it is not uncommon to find bacteria within the lesions, as seen in this case; fungal organisms and nematode infections have also been associated with these lesions.^{3,5} Secondary infections are proposed to play a role in perpetuation of the inflammatory lesion. The broad trabeculae of fibroplasia intermixed with foci of inflammation is characteristic of the lesion, as conspicuously observed in this case. The histologic differential diagnosis includes fibrosarcoma and mast cell tumor; and malignant

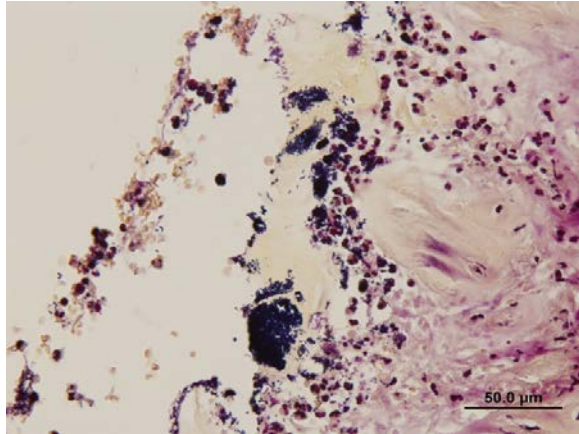
lymphoma is also a consideration at the macroscopic level.

Eosinophils are presumed to play a primary role in the pathogenesis of this fibroplastic lesion. Eosinophils are most commonly called in from the bloodstream in response to chemoattractants, such as in parasitic and allergic conditions, and are often seen as a component of subacute and chronic inflammation. Eosinophils contain several different types of granules, including large specific granules, small granules, primary granules, and secondary granules, which elaborate a wide variety of cytokines, chemokines and degradative enzymes that can perpetuate and enhance the inflammatory response, stimulate fibrosis, and result in significant host tissue damage, including cell and extracellular matrix components. Eosinophil chemottractants originate from a variety of sources such as epithelial cells, parasites, mast cells and eosinophils themselves and include CCL-5 (RANTES), C5a, CCL-11 (eotaxin), IL-4, IL-5 and IL-13.¹ One important mediator is



Pylorus, cat. The mass diffusely contains large numbers of eosinophils (arrows) as its primary inflammatory component. (HE, 400X)

major basic protein, which is present within large specific granules; the protein is toxic to helminths, as well as adjacent host cells, and causes histamine release from mast cells as well as activating neutrophils.



Pylorus, cat. Multifocally, colonies of mixed bacilli are present within the inflammatory mass. (Photo courtesy of: Institute of Molecular and Cell Biology, 61 Biopolis Drive, Proteos Building Level 6 Singapore, (<http://www.imcb.a-star.edu.sg/php/ittid-i-histo.php>)

In this lesion, eosinophils compose a major component of the inflammatory cell population, with mast cells being relatively fewer in number. Extracellular bacteria can be visualized without the aid of Gram stains. Multifocal areas of inflammation, composed of neutrophils, macrophages and multinucleate giant cells, surround free hair shafts.

Contributing Institution:

Advanced Molecular Pathology Laboratory
Institute of Molecular and Cell Biology
61 Biopolis Drive, Proteos
Singapore 138673

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