**CASE I:** 10-122 (JPC 4004524)

**Signalment:** Juvenile, female, spayed ferret (*Mustela putorius furo*).

**History:** Approximately six months after arrival from a commercial vendor, this ferret became progressively anorexic with weight loss, diarrhea, and had palpable intra-abdominal masses. There was poor response to IBD-type treatments and the ferret was euthanized.

**Gross Pathology:** An approximately 3 x 3 x 5 cm multi-lobular white-tan mass was present in the area of the mesenteric lymph nodes and surrounding mesenteric fat.

**Histopathologic Description:** Mesenteric lymph node and mesentery: The lymph node and mesenteric fat are effaced by multifocal to coalescing pyogranulomatous infiltrates. There are large central regions of necrosis with admixed degenerate neutrophils and fibrin surrounded concentrically by epithelioid macrophages.
and fibroblasts with fewer peripheral lymphocytes, plasma cells, and rare multinucleated giant cells. Several large arteries are partially or completely occluded by fibrin thrombi and portions of the wall are replaced by inflammatory cells and debris.

Coronavirus immunohistochemistry performed at Michigan State University using a monoclonal antibody against group 1c coronavirus antigen reveals strong positive intracytoplasmic staining of macrophages within the center of pyogranulomas.

**Contributor’s Morphologic Diagnosis:** Mesenteric lymph node and mesenteric fat: Severe multifocal to coalescing pyogranulomatous and necrotizing lymphadenitis, peritonitis, and vasculitis.

**Contributor’s Comment:** The primary differential etiology for this animal from gross and microscopic lesions was ferret systemic coronavirus infection which was subsequently confirmed by immunohistochemistry. Both the ferret enteric coronavirus (FRECV) and the ferret systemic coronavirus (FRSCV) were recently identified as group 1 coronaviruses.\(^3,4\) Ferret enteric coronavirus causes an enteric disease called epizootic catarrhal enteritis (ECE).\(^4\) More recently, a new systemic coronavirus-associated disease closely resembling the granulomatous or dry form of feline infectious peritonitis (FIP) has been reported.\(^1\) Although the similarities in clinical disease and histologic lesions between FRSCV and FIP virus suggest a similar pathogenesis for FRSCV-associated disease and FIP, this has yet to be proven experimentally.

**JPC Diagnosis:** Lymph node: Lymphadenitis, necrotizing and pyogranulomatous, multifocal to coalescing, severe, with mild fibrinoid vasculitis and necrotizing mesenteric steatitis.

**Conference Comment:** Viruses in the family Coronaviridae, genus Coronavirus, are 80-220 nm, enveloped and often spherical (although they can be pleomorphic), with large club-shaped viral spike peplomers (S protein) surrounding an icosahedral core that contains a helical nucleocapsid (N protein). These viruses consist of a single molecule of positive single-stranded RNA.\(^2\) Coronavirus infections have been
reported in many species, including pigs, cattle, horses, cats, frogs, rats, birds, rabbits, ferrets, mink, and mice. The host spectrum of each coronavirus depends on the S protein, which mediates receptor binding and fusion of the virus with the host cell. Coronaviruses use different receptors, including aminopeptidase N, used by several group 1 coronaviruses; carcinoembryonic antigen-related cell adhesion molecule 1 (CEACAM-1), used by mouse hepatitis virus; and N-acetyl-9-O-acetyl neuraminic acid, used by other group 2 coronaviruses. Group 3 coronavirus receptors are unknown at this time; however, heparan sulfate and sialic acid residues may play a role as non-specific attachment factors.\(^2\) Coronaviruses of veterinary importance include:

**Group 1a:**
- Transmissible gastroenteritis virus of swine
- Porcine respiratory coronavirus
- Canine coronavirus
- Feline enteric coronavirus (formerly feline infectious peritonitis virus)
- Ferret and mink coronaviruses

**Group 1b:**
- Porcine epidemic diarrhea virus
- Bat coronavirus

**Group 2a:**
- Mouse hepatitis virus
- Bovine coronavirus
- Sialodacryoadenitis virus of rats
- Porcine hemagglutinating encephalomyelitis virus
- Canine respiratory coronavirus

**Group 3:**
- Avian infectious bronchitis virus
- Turkey coronavirus\(^2\)

In carnivores infected by coronaviruses, disease manifests in one of two ways: infection can be self-limiting enteritis (such as in canine coronavirus, feline coronaviral enteritis, ferret epizootic catarrhal enteritis), or severe systemic disease can occur (such as in feline infectious peritonitis [FIP] or ferret systemic coronavirus infection [FRSCV]).\(^1\) As the contributor noted, pathogenesis for FRSCV is suspected to be similar to that of FIP, based on gross, histologic and immunohistochemical features of the disease.\(^1\) The key feature in FIP is the ability of genetic variants of feline enteric coronavirus to infect macrophages, due to mutations of the S protein and possibly other proteins which alters the tropism of the virus. Strong antibody response (often evidenced clinically as a polyclonal gammapathy) is ineffective at eliminating the virus and cellular immune responses are unable to prevent virus replication in macrophages. The lesions in FIP are often centered on small blood vessels, with vascular injury (necrosis) and leakage of a viscous, protein-rich transudate playing a major role in the wet form of the disease.\(^2\) In this case of ferret systemic coronavirus infection, conference participants noted that, although there was significant slide variation, in some specimens, variable amounts of necrotizing vasculitis are visible. Despite this finding, ferrets generally do not develop the effusive ("wet") form of the disease, as they more often present with lesions consistent with the non-effusive ("dry") end of the disease spectrum.\(^1\)

**Contributing Institution:** Division of Laboratory Animal Resources, University of Pittsburgh
http://www.dlar.pitt.edu/

**References:**
CASE II: UFSM-1 (JPC 4003260).

Signalment: 3- to 4-year-old, female, Murrah water buffalo (*Bubalus bubalis*).

History: Fifty 3- to 4-year-old water buffalo of both sexes were purchased from a farm (farm 1) in southern Brazil and shipped by truck to another farm (farm 2) 300 km away. The buffalo were kept in a holding pen on farm 1 for 12 hours without food or water, immediately prior to being transported for 8 hours to farm 2. As a result, the animals had no food or water for a total of 20 hours. Upon arrival at farm 2, the animals were released into a 200-hectare pasture that already held 200 cattle (*Bos taurus*) that had been there for several months. Ten buffalo died within 24-48 hours of being placed in the pasture. Most of the affected buffalo were found dead, but the owner was able to observe one moribund buffalo that had serous ocular discharge, incoordination, mild bloat, and muscle trembling. The pasture on farm 2 where the 10 water buffalo died had several spots of marshy land where large amounts of a plant later identified as *Baccharis megapotamica* var. *weirii* was found. There was evidence that livestock had been consuming these plants. *Baccharis megapotamica* var. *weirii* was absent from farm 1. A diagnosis of *Baccharis megapotamica* var. *weirii* was made and, to confirm the diagnosis, a susceptible calf (*Bos taurus*) was fed a single dose of 5g/kg/body weight of *B. megapotamica* var. *weirii* harvested from the same site where the buffalo died. Twenty hours after the administration of the plant this calf died with clinical signs and lesions similar to those observed in the naturally poisoned.

Gross Pathology: Necropsy was performed two hours after death. Gross findings in the necropsied buffalo included dehydration and markedly distended rumen with abundant liquid content. There was mild to moderate edema of the wall of the rumen, particularly in the pillars, and diffuse reddening of the mucosa of the fore stomachs, abomasum, and intestine.

Histopathologic Description: Epithelial cells lining the forestomachs displayed coagulative necrosis, the severity of which varied, so that in some segments the more superficial cells of the stratified epithelium were affected, sparing deeper cells. In some instances, these deeper cells had hydropic degeneration. In some other segments, coagulative necrosis affected the entire thickness of the stratified epithelium. Myriads of bacterial aggregates could be observed attached to segments of necrotic epithelial lining. Thrombi were occasionally observed in the submucosal vessels, and neutrophilic infiltrate was evident in some segments of degenerate/necrotic epithelium. Necrosis of the intestinal mucosa was also observed (slides not included). Lymph nodes, spleen, lymphoid aggregates,
and liver were also affected (slides not included). Mesenteric lymph nodes had necrosis of lymphocytes in secondary germinal centers. The subcapsular, trabecular, and medullary sinuses were filled with macrophages, and erythrophagocytosis was conspicuous. Lymphoid necrosis was also observed in the white pulp of the spleen. Gut associated lymphoid tissue and other lymphoid aggregates were not available for histology. Hepatic lesions consisted of intense hepatocellular vacuolization with eosinophilic globules, and marked dilatation of lymphatics in portal triads. The lumina of these lymphatics were filled by faint eosinophilic homogenous material.

**Contributor’s Morphologic Diagnosis:** Rumen, epithelial lining, degeneration and coagulative necrosis, marked, acute, associated with neutrophilic infiltration, bacterial aggregates and submucosal thrombi, water buffalo, female.

**Contributor’s Comment:** The *Baccharis* genus (Asteraceae: tribe Asteraceae) includes nearly 500 species. All are found in the New World with the exception of *Baccharis halimifolia*, which was introduced into Australia from the United States. This species is suspected of poisoning cattle in both countries and proved toxic when administered experimentally to chicks. Another North American species, was toxic to mice and chicks under experimental conditions, and *Baccharis pteronioides* has been associated with cattle poisoning in the southwestern United States. Baccharis *pteronioides* toxicosis was also experimentally produced in hamsters. Both *Baccharis artemisioides* causes disease in cattle in a restricted zone of Argentina northwest of Buenos Aires and southeast of Cordoba.

Nearly 120 species of *Baccharis* have been recorded in Brazil; of those, only *Baccharis coridifolia* and *Baccharis megapotamica* have been proven to be toxic to livestock. Both *B. megapotamica* and *B. coridifolia* are found in southern Brazil, but they occupy different habitats; *B. megapotamica* is found in marshy areas whereas *B. coridifolia* grows in pasturage. Nearly 120 species of *Baccharis* have been recorded in Brazil; of those, only *Baccharis coridifolia* and *Baccharis megapotamica* have been proven to be toxic to livestock. *B. coridifolia* causes disease in cattle in a restricted zone of Argentina northwest of Buenos Aires and southeast of Cordoba.

The two varieties of *B. megapotamica* and *Baccharis coridifolia* cause a severe acute poisoning in livestock characterized by degeneration and necrosis of the epithelial lining of the gastrointestinal tract and necrosis of lymphocytes in lymph nodes, spleen, tonsils, and several lymphoid aggregates. *Baccharis megapotamica*, *B. coridifolia* and *B. artemisioides* contain a series of potent cytotoxic

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2-4. Rumen, Murrah water buffalo: Rumenal papilla exhibit partial to full-thickness mucosal necrosis and are covered by a brightly eosinophilic necrotic coagulum. (HE 40X)

2-5. Rumen, Murrah water buffalo: Epithelial cells between rumenal papilla exhibit ballooning degeneration (arrows), and in more superficial layers undergo necrosis, and pustule formation as a result on infiltration of neutrophils. Numerous bacteria (of little significance in the pathogenesis of this lesion) are present in the overlying crust. (HE 360X)
agents belonging to the macrocyclic trichothecene complex of antibiotics previously believed to be produced only by fungi. These cytotoxic substances were demonstrated to be the toxic principles in these plants. In the case of *B. megapotamica*, the macrocyclic trichothecenes accumulate in the plant as baccharinoids, which are named B1, B2, B3, B4, etc. The B4 baccharinoid is most abundant, but there are also large concentrations of B1-B8. To date, no macrocyclic trichothecenes have been demonstrated in *B. halimifolia*, *B. pteronioides*, or *B. glomerulifolia*.

Spontaneous poisoning by *C. coridifolia* occurs frequently in cattle, occasionally in sheep and rarely in horses. Spontaneous outbreaks involving *B. megapotamica var. weirii* have been reported in cattle, sheep and buffaloes. Typically, the toxicosis in livestock occurs when naïve animals raised in areas free of *Baccharis* spp. are transferred to pastures infested by the plant. The risk of toxicosis increases considerably if the animals are subjected to stress factors as fatigue, hunger, or thirst; cattle that are raised in pastures where *Baccharis* spp. exist will graze it very rarely, if ever.

Livestock will not usually ingest either variety of *B. megapotamica*, but a combination of hunger, dehydration, and lack of familiarity with the plant most likely led the buffalo of this report to the lethal ingestion of *B. megapotamica var. weirii*. In the southern region of Brazil there are reports of spontaneous poisoning by four plants that induce similar disturbances in the gastrointestinal tract and should be included in the differential diagnosis, namely *B. coridifolia*, *B. megapotamica var. weirii*, *Baccharidastrum triplinervium*, and *Eupatorium tremulum*. The toxic principle of the latter two plants is as yet undetermined. Poisoning caused by the first two plants is virtually clinically and pathologically indistinguishable; however, the habitats of *B. megapotamica var. weirii* (marshy areas) and *B. coridifolia* (dry pastureland) differ, and this helps in differentiating between the two intoxications.

Additionally, lymphoid necrosis is reportedly less severe in cases of *B. coridifolia* and *E. tremulum* poisoning and does not occur in the poisoning caused by *B. triplinervium*. Lesions in the forestomachs are much less severe in *B. triplinervium* poisoning than in the poisonings caused by the other three plants. Larger amounts (20-30 g/kg/bw) of *E. tremulum* and *B. triplinervium* must be consumed to induce disease and death in cattle; this translates to much lower mortality ratios for these two plants when compared to *Baccharis* spp. toxicosis. To confirm the diagnosis of poisoning by any of these plants it is important to find evidence of plant consumption. From the standpoint of the morphological aspects of the lesions in the forestomachs, *B. megapotamica var. weirii* poisoning closely resembles ruminal acidosis. However, ruminal acidosis usually follows the ingestion of excess carbohydrate in the form of grain or other fermentable foodstuffs, and is associated mainly with intensive beef and dairy production and not with cattle at pasture. The cause of death in cases of *B. megapotamica* poisoning is unknown. However, since the disease is virtually identical to *B. coridifolia* poisoning, comparisons can be made. *Baccharis*-induced death is believed to be caused by dehydration and acid-base imbalance resulting from fluid loss into the ruminal compartment in a similar manner to what happens in ruminal acidosis. The finding of myriads of bacteria attached to the necrotic ruminal mucosa in cases of *B. coridifolia* and *B. megapotamica* poisoning, even in animals freshly dead, suggests the possibility that bacteremia could play a role in the mechanism of death.

Trichothecenes are terpenoids, which can be divided into two groups: the simple trichothecenes (e.g., deoxynivalenol [DON], diacetoxyscirpenol [DAS], and T-2 toxin) and the macrocyclic trichothecenes (e.g., baccharinoids, roridins, and verrucarins). They exhibit a wide range of biological activity, which includes dermatonecrosis, gastroenteritis, feed refusal, coagulopathy, and immunosuppression. Trichothecenes are also potent phytotoxins, and the macrocyclics are particularly toxic to plants. The T-2 toxin and DAS are highly toxic, causing necrosis of mucous membranes (mouth, pharynx, esophagus, rumen, stomach) on contact similar to lesions produced by plant-associated macrocyclic trichothecene poisoning. Trichothecenes are attributed to ribosomal binding and subsequent inhibition of protein synthesis in actively dividing cells of lymph nodes, spleen, bone marrow, and thymus. Induction of apoptosis in these cells by the trichothecenes is likely to contribute to lesion expression. Changes in cell membrane structure, with resultant lipid peroxidation due to amphiphilic trichothecene molecules, inhibition of RNA and DNA synthesis, and inhibition of mitosis are additionally recognized deleterious effects of T-2 toxin on cells. Although the mode of action of macrocyclic trichothecenes in *B. megapotamica* on subcellular levels is not completely determined, macrocyclic trichothecenes are believed to act by compromising protein synthesis by inhibiting the peptide bond formation step, and it is fair to assume that mechanisms associated with all types of trichothecene toxicoses are similar. Interesting results that could...
shed some light on the pathogenesis of Baccharis-induced toxicosis stemmed from experimental B. pteronioides poisoning in hamsters.\(^{18}\) Hamsters in the highest dosed group (200 mg) developed multiple hemorrhagic infarcts in the liver and kidney, with severe hemorrhagic enteritis and severe necrotizing vasculitis with vascular thrombosis of hepatic and renal vessels associated with fibrin thrombi in glomerular capillaries. The authors of the hamster study compared their findings to those of bacterial endotoxin-produced vasculitis and infarction.\(^{18}\)

The diagnosis of B. megapotamica toxicosis in the buffalo of this report was made based on the characteristic acute clinical disease, the presence of the plant in large amounts in its characteristic habitat, and the experimental reproduction of the disease by feeding the plant present in the pasture to a calf. Baccharis megapotamica var. megapotamica and var. weirii had been previously experimentally fed to calves and lethal doses were determined to be between 3 and 4 g/kg/bw for var. megapotamica and 1 g/kg/bw for var. weirii.\(^{20}\) Fatal poisoning was acute with both varieties. The most important postmortem findings were edema of the ruminal wall along with congestion of the rumen, abomasum, small intestine, cecum, and colon. Histologically, the rumen showed necrosis characterized by pyknosis and karyorrhexis of epithelial cells, mainly of the stratum spinosum. Lymphoid tissue (spleen, lymph nodes, Peyer’s patches) showed necrosis characterized by pyknosis and karyorrhexis of the lymphoid cells. Thus, the disease observed in the spontaneous outbreak in buffalo was essentially the same as described previously in cattle and sheep.\(^{6,14,20}\)

**JPC Diagnosis:** Rumen, mucosa: Necrosis and hydropic degeneration, diffuse, acute, severe.

**Conference Comment:** The contributor provided an excellent and thorough discussion of Baccharis-induced toxicosis. Conference participants noted moderate slide variation, with several sections exhibiting neutrophilic inflammation and pustule formation in the mucosal epithelium, and few slides containing occasional submucosal fibrin thrombi. Participants debated whether the lesions in the ruminal mucosa represent a necrotizing rumenitis; however, participants ultimately agreed that inflammation was not the primary feature, and thus favored the morphologic diagnosis of “necrosis” over “necrotizing rumenitis.”

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**References:**


**CASE III: 05-1595 (JPC 3031293).**

**Signalment:** Nine-year-old owl monkey (*Aotus* sp.).

**History:** Acute onset of weakness and depression with hypothermia, weight loss and anemia (PCV =18%). The animal responded slightly to palliative therapy but then was found dead.

**Laboratory Results:** PCV = 18%.

**Gross Pathologic Findings:** At necropsy the animal was in poor body condition. The scent gland was enlarged and both kidneys were pale, firm and pitted.

**Histopathologic Description:** Small and medium sized arteries of the pancreas and duodenum are infiltrated and disrupted by low numbers of neutrophils, macrophage, and lymphocytes. Vessel walls are often necrotic and expanded by abundant fibrin and hemorrhage. Occasionally the entire vessel is replaced by fibrin and necrotic debris that completely occludes the vessel lumen (thrombus). Often the tunica intima is proliferative. The tunica adventitia and perivascular connective tissue contain moderate numbers of macrophages, fewer lymphocytes and fibroblasts. Both in the duodenum and more extensively in the pancreas there is coagulative necrosis. Multifocally pancreatic lobules contain tubules and ducts that are surrounded by a loosely arranged, proliferative, edematous stroma. Other tissues affected in this case with a necrotizing arteritis include the heart, gallbladder, jejunum, and adrenal gland.

**Contributor’s Morphologic Diagnoses:**
1. Pancreas; duodenum: Arteritis, fibrinonecrotic, multifocal, marked, with coagulative necrosis.
2. Pancreas: Mesenchyme proliferation, peritubular and periductal, multifocal, moderate.

**Contributor’s Comment:** In humans polyarteritis nodosa (PAN) is a systemic vasculitis of small and medium-sized arteries, most often affecting young adults. It typically involves renal and gastrointestinal vessels with a predilection for branching points but spares the lungs.\(^5\) It has been reported in rats, mice, dogs, cats, pigs, and non-human primates, specifically cynomolgus macaque.\(^4\) In rats it typically involves the mesentery, pancreas, and testis of aged Sprague-Dawley rats, with a higher incidence in males.\(^3\) In dogs it is most often reported in beagles, referred to as beagle pain syndrome, affecting vessels of the mediastinum, cervical spinal cord, and heart.\(^2\) To our knowledge, this is the first case involving an Aotus monkey. The tissues affected and histologic characteristics of the lesion make it similar to the case previously reported in a cynomolgus.\(^4\) The lesion typically involves a necrotizing vasculitis with transmural infiltration by neutrophils, eosinophils and fewer macrophages often with fibrinoid necrosis of the vessel wall. Eventually the vessel wall is replaced by a fibrous thickening. In humans renal involvement is often the cause of death. Interestingly approximately 30% of humans with PAN have hepatitis B antigen in the serum. Characteristically various stages of chronicity exist simultaneously, even within the same vessel.\(^5\) The pathogenesis of PAN is unknown but is
suspected to be immunological. Patients with PAN have elevations of serum interferon- gamma and interleukin-2. Immunohistochemistry showed inflammatory cell infiltrates are mainly macrophages and CD4+ T cells.\textsuperscript{4} Clinical response to immunosuppressive therapy further supports an immunologic-based pathogenesis. In this case the histologic lesions in the pancreas and duodenum are typical of PAN. Within the pancreas, however, there are lobules that contain tubules, and to a greater extent ducts, that are surrounded by a loosely arranged, edematous stroma. In more severely affected areas this stroma appears proliferative. To our knowledge this change has not been reported in association with PAN. We speculate that these areas are proliferative due to the many cytokines and growth factors being released in the local area from the extensive necrosis and inflammation. Why only peritubular and periductal areas are affected is not known and other possible explanations for this morphologic characteristic cannot be excluded.

**JPC Diagnosis:**

1. Duodenum: Arteritis, proliferative and necrotizing, chronic, multifocal, severe, with mucosal necrosis.

2. Pancreas: Arteritis, proliferative and necrotizing, chronic, multifocal, severe, with acinar necrosis, atrophy and loss and ductal hyperplasia.

**Conference Comment:** The contributor provided an excellent review of polyarteritis nodosa. The conference moderator noted the presence of autolysis of the common bile duct, and cautioned students not to mistake this for a focus of lytic necrosis. Participants
noted the areas of necrosis within the duodenum and pancreas correspond to areas of arteritis. The occurrence of abundant stroma within the pancreas that the contributor described and speculated to be due to cytokines and growth factors in areas of inflammation and necrosis led to discussion of the induction of mesenchymal tissue due to acinar loss. This phenomenon that occurs during acute and chronic pancreatitis is thought to be due to the release of TGF-β (which acts as the main stimulator), TNF-α, IL-1 and IL-6, and PDGF (which acts as the main mitogen), from acinar cells, inflammatory cells and platelets. These factors induce the activation and proliferation of periacinar myofibroblasts (aka pancreatic stellate cells) by inducing them to transform from their fat-storing phenotype to their matrix-producing phenotype, which plays a role in tissue repair and result in pancreatic fibrosis.¹

Contributing Institution: Walter Reed Institute of Research/Naval Medical Research Center
http://wrair-www.army.mil
http://www.nmrc.navy.mil

References:
CASE IV: S11-686-v11 (JPC 4019872).

Signalment: 12-year-old mixed breed female spayed cat.

History: This cat had a lumpectomy in November of 2010. One month later, regrowth was found, and the mass had grown fast since. Mastectomy was recommended and performed on July 7, 2011. At operation, pyometra was detected and an OHE was also performed. The uterus was submitted for examination along with the ovaries.

Gross Pathology: The uterine horns and body were submitted in formalin. The uterus was bilaterally swollen and the uterine horns multifocally enlarged. Bilaterally, ovaries were shrunken and interpreted to be atrophic. Upon sectioning, the uterus was diffusely and bilaterally thickened, had a cystic nature, and the lumen was filled with inspissated chocolate-colored material.

Histopathologic Description: Uterus: Expanding the endometrium and encroaching upon the lumen is a well-demarcated, unencapsulated, poorly circumscribed, infiltrative, moderately cellular neoplasm. Neoplastic cells form florid papillary and micropapillary projections into the lumen; neoplastic cells are supported by a moderate fibrous stroma. Neoplastic cells are cuboidal to columnar with indistinct cell borders and a moderate amount of finely granular eosinophilic cytoplasm. Nuclei are round to oval with finely stippled chromatin and 1-2 basophilic nucleoli and there is mild anisocytosis. Mitotic figures are rare. Throughout the neoplasm, there are multinucleated neoplastic cells with dense, hyperchromatic nuclei. These giant cells range up to 250 µm in diameter. The uterine lumen and spaces between papillary projections are filled with brightly eosinophilic cellular and basophilic nuclear debris, admixed with small amounts of hemorrhage and mineral. Within the underlying endometrium, there are numerous mildly ectatic glands containing bright red secretory material.

Contributor's Morphologic Diagnosis: Uterus: Endometrial adenocarcinoma, giant cell variety.

Contributor's Comment: Epithelial malignancies of the uterus are considered to be rare in domestic species. In domestic species, uterine adenocarcinoma is most commonly seen in the cow, but has also been reported in the mare, ewe, bitch, and queen. In the bitch and queen, uterine malignancies constitute less than 1% of all neoplasms. In the ox, uterine carcinomas are solitary, often scirrhous neoplasms which invade the endometrium and myometrium, and often metastasize to the iliac and sublumbar lymph nodes, and ultimately to the lung and liver. Endometrial adenocarcinoma has been reported rarely in the queen. In the largest review of 13 uterine neoplasms arose in the endometrium; one of these was a mixed Mullerian neoplasm. Myometrial invasion was variable in these cases, and carcinomatosis was noted in three, and pulmonary metastasis in one. Only two of the cats with endometrial adenocarcinoma had disease-free intervals longer than five months. Neoplastic cells are immunopositive for cytokeratin, vimentin, smooth muscle actin, COX-2, beta catenins, progesterone and estrogen receptors and caveolin-1. In laboratory species uterine adenocarcinomas are most commonly reported in the rabbit and mouse. In the mouse, endometrial carcinomas are infiltrative neoplasms which invade the endometrium and myometrium, may occlude the uterine lumen, and may metastasize to distant sites. Squamous differentiation is seen with endometrial adenocarcinoma in the B6C3F1 mouse, usually in association with chemical administration. Uterine adenocarcinomas are considered to be the most common spontaneous neoplasm in the rabbit, usually seen in animals four years or older. In this species, multiple neoplasms may arise in both horns of the uterus and metastasize readily to the peritoneal cavity and ultimately to lungs and viscera. In humans, a variety of endometrial carcinomas have been diagnosed, based on the predominant cell-type (serous, clear cell, and poorly-differentiated endometrial carcinoma). One of the many variants of poorly-differentiated endometrial...
carcinoma in the human is the endometrial giant cell carcinoma which morphologically resembles the neoplasm of this case. In a limited number of cases in one study, visceral metastasis was seen in one of five individuals. The presence of giant cells is of special interest in this case. In addition to the human cases listed above, giant cells have been rarely reported in endometrial carcinoma in domestic species, with one reported in the bitch.

JPC Diagnosis: Uterus: Endometrial carcinoma.

Conference Comment: The contributor provided a very good summary of endometrial carcinoma in various species. Interestingly, in women, post-menopausal hormone replacement (estrogen) is understood to be a risk factor for developing endometrial adenocarcinoma. Other species in which endometrial adenocarcinomas have been reported (i.e. rabbits, cats) are induced ovulators, which can result in extended periods of estrogen stimulation similar to post-menopausal women receiving estrogen replacement therapy. Rabbits have a high incidence of uterine adenocarcinoma, with 79% of females affected after 5 years of age. The lower prevalence of uterine adenocarcinoma in cats may be attributable to the common practices of either neutering females, or breeding intact queens, thus reducing the number of individuals that experience the prolonged increases in estrogen. In women, there are estrogen-dependent and estrogen-independent adenocarcinomas, of low and high grade, respectively. In one study, feline tumors with marked nuclear atypia and metastasis usually did not express estrogen receptors, suggesting that estrogen independence may indicate a worse prognosis.

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