Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2022-2023

Conference #4 — 14 September 2022

CASE I:

Signalment:
14-year-old intact female Alpaca (*Vicugna pacos*)

History:
Per attending veterinarian: "Presented with hypernatremia, mild azotemia, decreased albumin, treated last week with IV fluids, electrolytes. Suspect bilateral polycystic kidney disease."

Gross Pathology:
The peritoneal, pleural and pericardial cavities contained approximately 2 L, 1.5 L and 10 mL of clear, yellow watery fluid with scant fibrin strands. The pleural surfaces of the lung lobes contain scant, scattered fibrin strands. The lungs are diffusely wet, heavy and meaty and did not collapse when the chest cavity was opened. The lungs contain enumerable, individual to coalescing nodules ranging from 0.2 cm-2 cm. The nodules are firm and white; some of the larger nodules contain central caseous material.

Laboratory Results:
No laboratory findings reported.

Microscopic Description:
The open alveolar architecture of the lung is nearly diffusely effaced secondary to alveolar filling by numerous macrophages, epithelioid macrophages and fewer multinucleated giant cells, lymphocytes and plasma cells. Randomly scattered conspicuous aggregates of neutrophils (intact and degenerate) randomly interrupt the otherwise monotonous infiltrate by macrophages. When visible, alveolar septa are thickened by congestion approximately 2X expected. Many of the macrophages contain numerous yeast organisms; the yeast organisms were characterized by a 1.0 µm, round to crescent-shaped yeast body surrounded by a variably-sized (1.0-2.0 µm) halo.

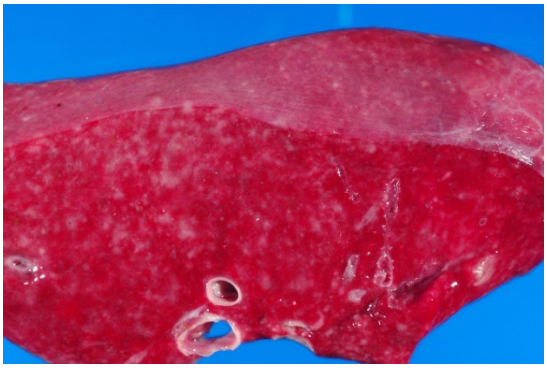

Figure 1-1. Lung, alpaca. The lung is heavy, meaty, does not collapse, and contains numerous white foci measuring 0.2-2.0 cm scattered throughout all lobes. (Photo courtesy of: Department of Veterinary Pathobiology & the Oklahoma Animal Disease Diagnostic Laboratory, Center for Veterinary Health Sciences, Oklahoma State University, www.cvhs.okstate.edu)

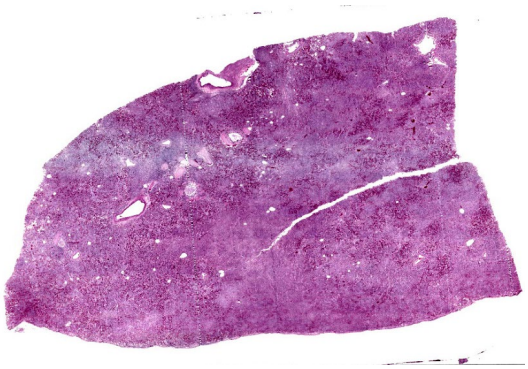

Figure 1-2. Lung, alpaca. There is diffuse consolidation of all lobules within the submitted section of lung. (HE, 5X)

In addition to the lung (provided), sections of the liver and spleen also contained randomly distributed aggregates of macrophages (some with epithelioid morphology and multinucleated giant cells) containing yeast organisms similar to that described in the lung.

Contributor's Morphologic Diagnoses:
Syndrome: Disseminated histoplasmosis

1. Severe, diffuse, granulomatous pneumonia with myriad intralesional yeast organisms consistent with *Histoplasma capsulatum*.
2. Severe, multifocal, granulomatous splenitis with myriad intralesional yeast organisms consistent with *Histoplasma capsulatum*.
3. Severe, multifocal, granulomatous hepatitis myriad intralesional yeast organisms consistent with *Histoplasma capsulatum*.

Contributor's Comment:
This patient originally presented with a history and clinical diagnosis of renal disease. The severe pneumonia, as well as other lesions secondary to histoplasmosis, were a surprise finding at necropsy. After the fact query of the attending veterinarian did not reveal any mention of clinical signs of respiratory disease.

Our institution has a respectable caseload of llamas/alpacas; however, disseminated histoplasmosis has not before been seen, even as an etiology for pneumonias. A literature search revealed a single case report of pulmonary histoplasmosis in a llama.[11] The patient in that report had been recently imported from Bolivia seven months prior; however,

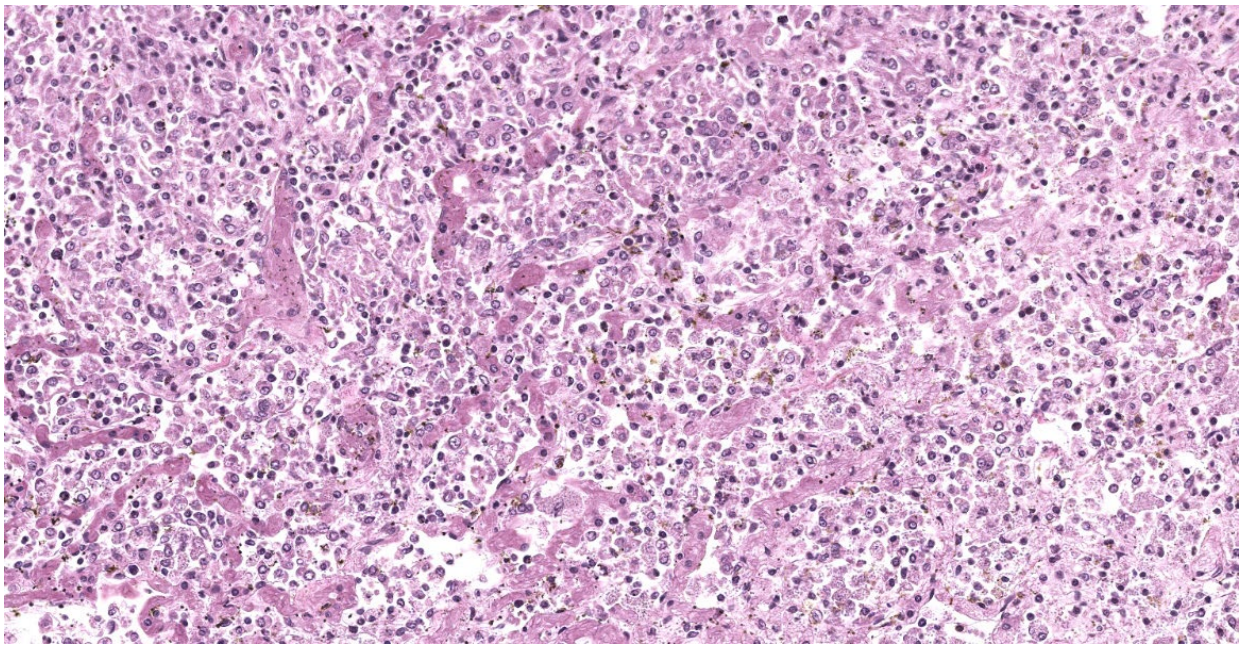

Figure 1-3. Lung, alpaca. Alveoli are filled to bursting with macrophages. At right, alveoli have ruptured and alveolar septa are no longer visible. (HE, 247X)

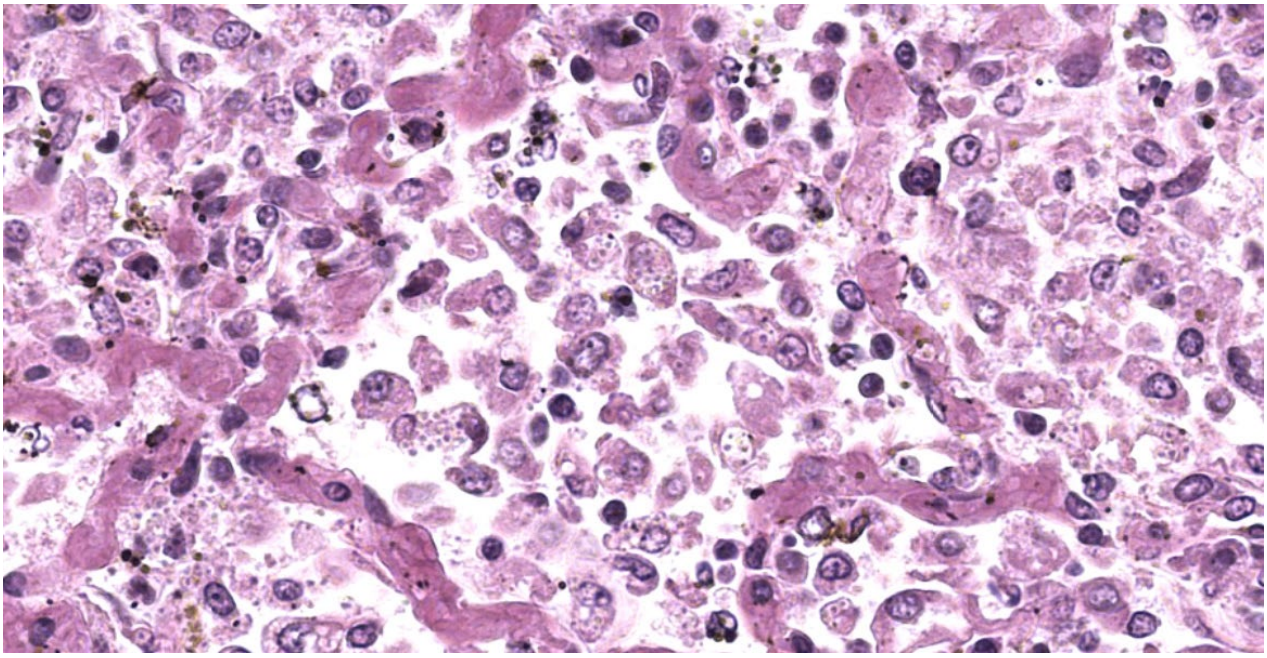

Figure 1-4. Lung, alpaca. Intra-alveolar macrophages contain numerous 2-4 µm round yeasts within their cytoplasm. (HE, 817X)

the patient in this report had spent its entire life in the United States.

Histoplasma capsulatum is a dimorphic fungus commonly found in soil that has been contaminated with bird feces or bat guano.[1] Within the United States, histoplasmosis is most common in the Mississippi, Missouri and Ohio river valleys; however, infections are certainly not uncommon elsewhere in the Midwest.[5] The organism exists in the soil as a mold producing infective microconidia.[1] When inhaled, the microconidia convert to yeast forms that replicate within phagolysosomes of the pulmonary mononuclear-phagocytic system.[1,6] From this initial pulmonary infection, the organism disseminates into other organs by hematogenous (spleen, liver) or lymphatic (lymph node) routes.

Contributing Institution:
Department of Veterinary Pathobiology &
The Oklahoma Animal Disease Diagnostic Laboratory
Center for Veterinary Health Sciences
Oklahoma State University
www.cvhs.okstate.edu

JPC Diagnosis:
Lung: Pneumonia, granulomatous, diffuse, severe with numerous intrahistiocytic yeasts.

JPC Comment:
During the conference, participants discussed the similar histologic morphology of this entity to *Sporothrix schenkii,* and that definitive diagnosis may require speciation through culture, PCR, or IHC.

Histoplasma capsulatum subs. *capsulatum* infects a wide variety of mammals (including humans) and birds, and most infections are likely subclinical or mild due to effective adaptive immunity involving cytokine-mediated macrophage killing and T-cell response.[9] Overt pulmonary or disseminated infections may occur if the animal is exposed to a large dose of infectious microconidia or is immunosuppressed.[1, 9] Dogs and cats are most commonly affected by clinical disease, but a plethora of reports demonstrate that disseminated histoplasmosis can occur in many species, including goats and raccoons, or as seen in this case, an alpaca.[8, 2] Even if an effective immune response is generated, yeast

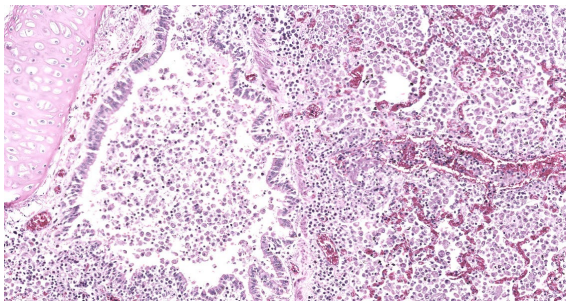

Figure 1-5. Lung, alpaca. Airways (in this case, a bronchiole) are filled with refluxed inflammatory exudate from surrounding alveoli. (HE, 159X)

may enter a state of dormancy and re-emerge when the animal becomes immunocompromised.[1,9] In disseminated infections, *Histoplasma* travels in phagocytic cells to other organs with high concentrations of phagocytes, such as lymph nodes, gastrointestinal tract, spleen, and liver. Spread to the adrenal glands, skin, eye, and bone is also possible.[9]

In most cases, the host develops an appropriate adaptive immune response which controls and eliminates the *Histoplasma* infection. In immunocompetent hosts, the Th1 response is critical in controlling infection.[6] Innate cells initially produce IL-12, which stimulates the production of IFN-gamma mostly by CD4+ T cells.[6] IFN-gamma has a wide range of effects including activation of macrophages, stimulation of intracellular nitric oxide production by macrophages, and regulation of iron and zinc availability.[6] T cells also produce TNF-alpha, which further stimulates nitric oxide production, chemokine production, and increased INF-gamma production.[6] TNF-alpha also restricts expansion and trafficking of regulatory T cells and signals for apoptosis.[6] These proinflammatory cytokines stimulate expression of CCR5, the receptor for chemokines CCL3, CCL4, and CCL5, all of which become upregulated during *Histoplasma* infection.[6] CCR5 activation leads to influx of additional inflammatory cells.[6] These cytokines also activate macrophages to produce microbe-killing agents such as reactive oxygen species (ROS).[12]

The NADPH-oxidase system produces many of these reactive oxygen species, including superoxide, hydroxyl, and peroxide, to neutralize and destroy microbes, and *Histoplasma* has evolved a few tricks to resist ROS destruction. *H. capsulatum* produces two catalases, CatB (M-antigen) and CatP, which create a layered defense by neutralizing extracellular and intracellular ROS, respectively.[12] *H. capsulatum* also produces superoxide dismutases, such as extracellular Sod3 and intracellular Sod1, which add to these defenses.[12] Other mechanisms that *Histoplasma* has evolved to evade non-oxidative host defenses include producing anti-inflammatory IL-4, melanin, and substances which increase intracellular pH.[1]

Other pathogenic *H. capsulatum* species include *H. capsulatum* var. *farciminosum* (HCF) and *H. capsulatum* var. *duboisii* (HCD). HCF, or equine histoplasmosis, causes epizootic lymphangitis (pseudoglanders) in horses and mules.[7] The yeast enters open wounds in the skin and causes swollen lymphatics and chronic, progressive, ulcerative nodules that drain and scar.[7] Less commonly, HCF can cause rhinitis, sinusitis, pneumonia, or keratoconjunctivitis.[7] *H. capsulatum* var. *duboisii* causes African histo-

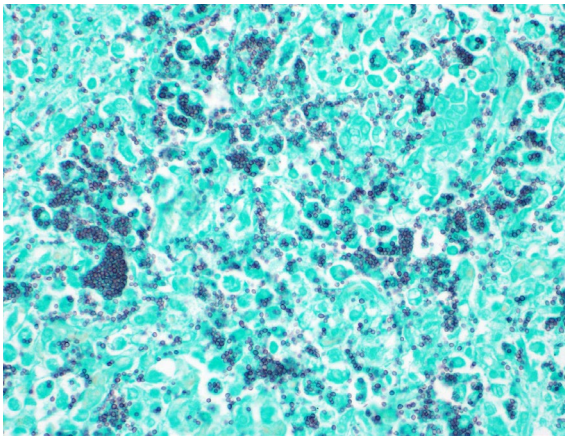

Figure 1-6. Lung, alpaca. A silver stain demonstrates the numerous yeasts present within macrophages. (Gomori methenamine silver, 400X)

plasmosis, which is characterized by granulomatous inflammation within the skin and bone of baboons and humans, though disseminated disease can also occur.[3] A recent report described granulomatous gingivitis due to HCD infection in three baboons.[4]

References:

1. Brömel C, Green CE. Histoplasmosis. In: *Infectious diseases of the dog and cat*. 4th ed. St. Louis, MO, USA: Saunders; 2012: 614-621.
2. Clotheir KA, Villaneuva M, Torain A, Reinl S, Barr B. Disseminated histoplasmosis in two juvenile raccoons (*Procyon lotor*) from a nonendemic region of the United States. *Jour Vet Diag Invest.* 2014; 26(2):297-301.
3. Hensel M, Hoffman AR, Gonzales M, Owston MA, Dick EJ. Phylogenic analysis of *Histoplasma capsulatum* var *duboisii* in baboons from archived formalin-fixed, paraffin embedded tissues. *Medical Mycology*. 2019; 57:256-259.
4. Johannigman TA, Gonzalez O, Dutton JW, Kumar S, Dick EJ. Gingival histoplasmosis: An atypical presentation of African Histoplasmosis in three baboons (*Papio spp)*. *J Med Primatol.* 2020; 49(1): 47-51.
5. Kauffman CA. Histoplasmosis: a clinical and laboratory update. *Clin Microbiol Rev*. 2007; **20**:115-132.
6. Kroetz DN, Deepe GS. The role of cytokines and chemokines in *Histoplasma capsulatum* infection. *Cytokine*. 2012; 58:112-117.
7. Robinson WF, Robinson NA. Cardiovascular System. In: Maxie MG, ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals.* Vol 3. 6th ed. Philadelphia, PA: Elsevier Saunders; 2016: 97-98.
8. Schlemmer SN, Fratzke AP, Gibbons P, et al. Histoplasmosis and multicentric lymphoma in a Nubian goat. *Journ Vet Diag Invest*. 2019; 31(5): 770-773.
9. Valli VEO, Kiupel M, Bienzle D. Hematopoietic System. In: Maxie MG, ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals.* Vol 3. 6th ed. Philadelphia, PA: Elsevier Saunders; 2016: 186-187.
10. Woods JP. Knocking on the right door and making a comfortable home: *Histoplasma capsulatum* intracellular pathogenesis. *Curr Opinion in Microbiol.* 2003; 6:327-331.
11. Woolums AR, DeNicola DB, Rhyan JC, Murphy DA, Kazacos KR, Jenkins SJ, Kaufman L, Thronburg M. Pulmonary histoplasmosis in a llama. *J Vet Diagn Invest.* 1995; **7**:567-569.
12. Youseff BH, Holbrook ED, Smolnycki KA, Rappleye CA. Extracellular Superoxide Dismutase Protects *Histoplasma* Yeast Cells from Host-Derived Oxidative Stress. *PLoS Pathog.* 2012; 8(5): e1002713.

CASE II:

Signalment:

Twelve-year-old, neutered female, domestic shorthair cat (*Felis catus*)

History:

The cat presented with a two month history of anorexia and weight loss. On presentation there was severe alopecia and erythema on the ventral thorax, abdomen, neck, perineum and also extended to the medial aspect of the legs to the paws. The periocular and ear pinna skin also presented with a similar change. Due to the characteristic shiny or glistening appearance of the skin, feline paraneoplastic alopecia was initially suspected. Ultrasound examination was performed with multiple masses detected in the liver and small hypoechoic nodule associated with the small intestinal, pancreas and peritoneum (neoplasia

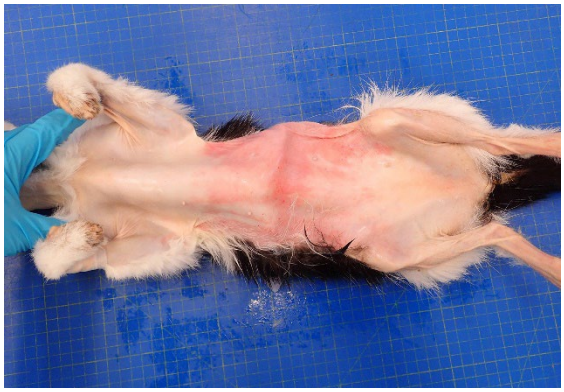

Figure 2-1. Haired skin, cat. Ventral and lateral abdominal skin and that of the extremities is severely alopecic with a glistening and shiny appearance. (Photo courtesy of: University of Liverpool, Institute of Infection, Veterinary and Ecological Sciences, Department of Veterinary Anatomy, Physiology and Pathology, Leahurst campus, Chester High Road, Neston, CH64 7TE, United Kingdom)

considered most likely). As the masses were widespread and the prognosis was poor, the animal was euthanized.

Gross Pathology:
The skin from the sternal to the inguinal regions, extending to the medial antebrachia and to the posterior extremities and partially the lateral abdominal regions, was severely alopecic with a glistening and shiny appearance. Throughout the alopecic skin, poorly demarcated pale red areas (erythema) and rare pale brown crusts were also present. Both periocular and perinasal areas were partially alopecic with increased amount of crusts. The right metatarsal paw pad and the right ventral tarsus showed multifocal ulcers. In the liver, scattered throughout all hepatic lobes, there were multifocal to coalescing, 0.2 to 2 cm in diameter, well demarcated, firm, pale tan nodules showing occasional central umbilication.

Laboratory Results:
No laboratory findings reported.

Microscopic Description:
Haired skin (abdomen)**:** Throughout a multifocally mildly hyperplastic epidermis there are multifocal areas of: intracellular edema, spongiosis, and parakeratosis. In rare foci (not present in all slides), the epidermis is restricted to 1-2, poorly defined, thin layers (epidermal atrophy). The hair follicles are diffusely and markedly reduced in size (atrophy and miniaturization) and contain rare intraluminal eosinophilic tricholemmal keratin (telogen). Adjacent to the atrophied follicles, variably atrophic sebaceous glands and commonly dilated apocrine glands are found. The dermis shows multifocal edema, with mild perivascular to interstitial accumulation of neutrophils, mast cells and extravasated erythrocytes (hemorrhage). Numerous deep dermal and subcutaneous lymphatic vessels (not present in all slides) are markedly dilated by intraluminal accumulation of concentrically arranged, homogenous and acellular eosinophilic material (likely proteinaceous lymph) and rare foamy (activated) macrophages.

Liver: Multifocally infiltrating and effacing the liver, there is a well demarcated, densely cellular, infiltrative and non-capsulated neoplastic proliferation. It is composed of confluent small islands, ribbons and nests of neoplastic cells showing occasionally central

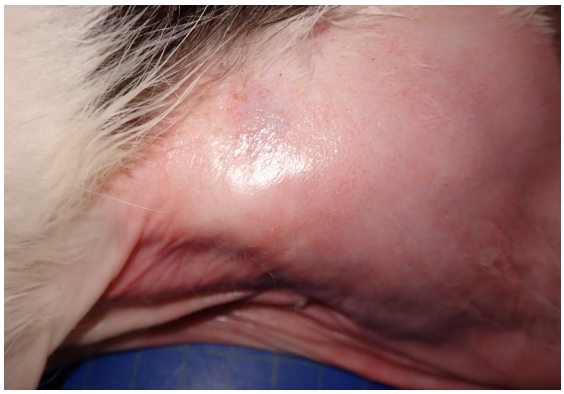

Figure 2-2. Haired skin, cat. Close examination of the shiny appearance to the epilated skin. (Photo courtesy of: University of Liverpool, Institute of Infection, Veterinary and Ecological Sciences, Department of Veterinary Anatomy, Physiology and Pathology, Leahurst campus, Chester High Road, Neston, CH64 7TE, United Kingdom)

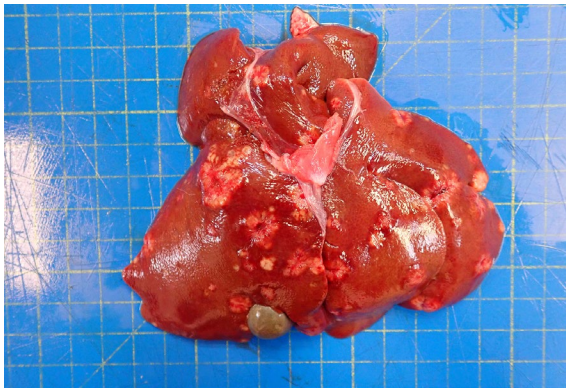

Figure 2-3. Liver, cat. Umbilicated neoplasms are present within all hepatic lobes. (Photo courtesy of: University of Liverpool, Institute of Infection, Veterinary and Ecological Sciences, Department of Veterinary Anatomy, Physiology and Pathology, Leahurst campus, Chester High Road, Neston, CH64 7TE, United Kingdom)

necrotic cores (comedonecrosis) and separated by moderate amount of edematous eosinophilic fibrovascular tissue (desmoplasia). Neoplastic cells are polygonal, variably sized 15-40 µm in length, showing indistinct cell borders, a moderate amount of eosinophilic fibrillary cytoplasm and a single, oval nucleus, bearing vesicular chromatin and 1-2 prominent nucleoli. Anisocytosis and anisokaryosis are moderate and 6 mitoses are observed in 10 HPF (40x objective). Neoplastic islands are also occasionally observed within blood vessels (tumor emboli). Embedded within the fibroblastic stroma, there are hemorrhages and scattered small compressed hepatocytes (compression atrophy). These hepatocytes occasionally have intracytoplasmic finely granular dark brown to green pigment (likely lipofuscin). Centrilobular hepatocytes shows frequently intracytoplasmic lipofuscin (geriatric finding).

Contributor's Morphologic Diagnoses:
Haired skin – severe bilateral ventrally-oriented symmetrical alopecia with glistening appearance with multifocal erythema and crusts.
Haired Skin – Mild multifocal to diffuse epidermal hyperplasia, with miniaturized and atrophic telogen hair follicles and multifocal parakeratotic hyperkeratosis
Haired skin – mild perivascular to interstitial neutrophilic and mastocytic dermatitis, with dermal edema
Liver – cholangiocarcinoma

Contributor's Comment:
The present case was characterized by widespread ventrally oriented bilateral and symmetrical alopecia revealing a shiny and glistening skin, in conjunction with multiple hepatic masses, extending to the pancreas. Histological examination revealed a widespread epidermal thickening with smaller hair follicles, containing very rare trichilemmal keratin. There was also a hepatic carcinoma, whose origin is most compatible with a cholangiocarcinoma. Based on the present findings, a diagnosis of feline paraneoplastic alopecia was made.

Feline paraneoplastic alopecia (FPA) is an infrequent but characteristic cutaneous disorder and has been reported in feline patients with a variety of neoplasms. Usually, FPA manifests between 7 and 16 years of age. It is classically associated with pancreatic carcinomas and bile duct carcinomas; nevertheless, other tumors such as hepatocellular carcinoma,[4]

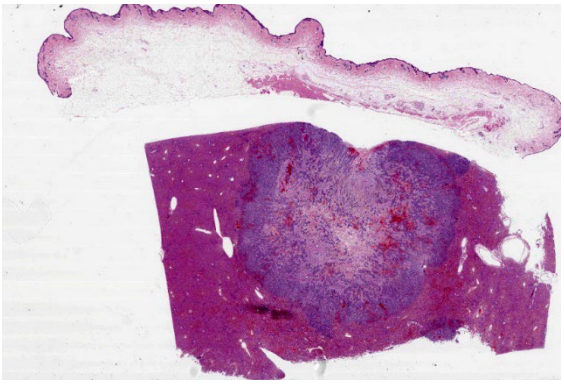

Figure 2-4. Haired skin and liver, cat. A section of haired skin (top) and liver (bottom) are submitted for examination. At subgross magnification, the haired skin has a remarkably paucity of follicles and adnexa, and a large multinodular neoplasm is present within the liver. (HE, 7X)

metastasizing intestinal carcinoma,[3] pancreatic neuro-endocrine and hepatosplenic plasma cell tumor[1] have been associated with this condition.

The characteristic glistening appearance with the mild epidermal hyperplasia and the severe atrophy and miniaturization of the hair follicles are considered key elements in the diagnosis. The skin is shiny, inelastic but not fragile, in contrast to that in hyperadrenocorticism: the latter is characterized by atrophic and telogenized hair follicles with epidermal atrophy rather than the hyperplasia observed in this case.

In FPA, it is reported that the stratum corneum is often missing, likely due to excessive grooming (although a clear evidence for this is lacking). This change, together with the patchy parakeratosis, is what is considered to give the spectacular shiny appearance. In the present case, both parakeratosis and absence of stratum corneum are present and alternating one with the other. Although the stratum corneum is often absent, the absence of the granular layer of the epidermis is inconsistently reported in the FPA reports.[4]

As in other reported FPA cases,[6] crusting, in association with *Malassezia* sp. proliferation was observed in the ear pinna skin but not in the submitted skin sample, and there was also paw pads fissuring and ulceration.

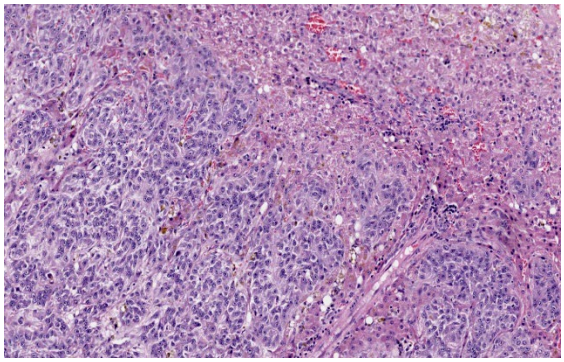

Figure 2-5. Liver, cat. The neoplasm is composed of nests, islands, and trabeculae of epithelial cells on a moderately dense fibrous stroma. (HE, 35X)

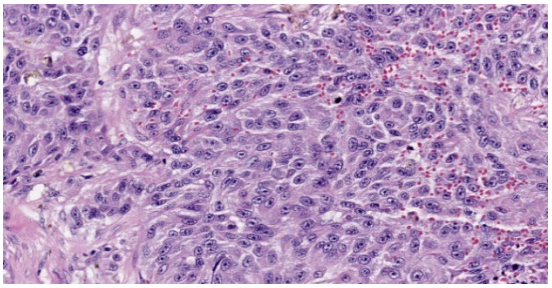

Figure 2-6. Liver, cat. High magnification of neoplastic cells. (HE, 381X)

Adnexae are usually normal or mildly atrophic. In the present case, normal sebaceous glands were intermixed with mildly atrophic ones. The apocrine glands, instead, were diffusely dilated and lined by flattened epithelial cells exhibiting evident suprabasilar cleft-like changes, compatible with either a genuine supra-basilar vacuolar degeneration or artefact.

Another unreported and striking finding was the presence of eosinophilic acellular (Congo red-negative) material in the deep lymphatic vessels, possibly suggestive of a protein rich fluid. There was some discussion about the origin of this change, as they could represent dilated mammary glands/ducts lined by very atrophic epithelial cells.

The hepatic neoplasia was cytologically and behaviorally malignant and consistent with an epithelial origin (i.e. carcinoma). The nodule in the pancreas showed an overlapping morphology with hepatic one, complicating the identification of the origin of the neoplasm. According to the bigger size of the hepatic masses and the histomorphology, a bile duct carcinoma (cholangiocarcinoma) is believed to be more likely. Nevertheless, other tumors, including exocrine pancreatic carcinoma or neuroendocrine pancreatic carcinoma cannot be fully excluded.

The pathogenesis of this cutaneous lesion has not been understood, due to its relative rarity. Considering that all the FPA-related tumors

reported show a variable neoplastic invasion of the liver, it can be hypothesized that some hepatic metabolic derangement are responsible of the cutaneous disorder.

Contributing Institution:
University of Liverpool, Institute of Infection, Veterinary and Ecological Sciences
Department of Veterinary Anatomy, Physiology and Pathology
Leahurst campus
Chester High Road, Neston,
CH64 7TE,
United Kingdom

JPC Diagnosis:
1. Liver: Carcinoma, poorly differentiated.
2. Haired skin, epidermis and adnexa: Atrophy, diffuse, severe, with telogenization of follicles.

JPC Comment:
The contributor lists two differential diagnoses that were discussed by conference participants: pancreatic carcinoma and neuroendocrine tumor. Participants could not definitively determine the cell of origin based on H&E and thus favored the diagnosis of poorly differentiated carcinoma. Additionally, participants remarked on the hepatic stellate cell (Ito cell) hyperplasia present throughout the liver, which may have been secondary to or unrelated to the neoplasm.

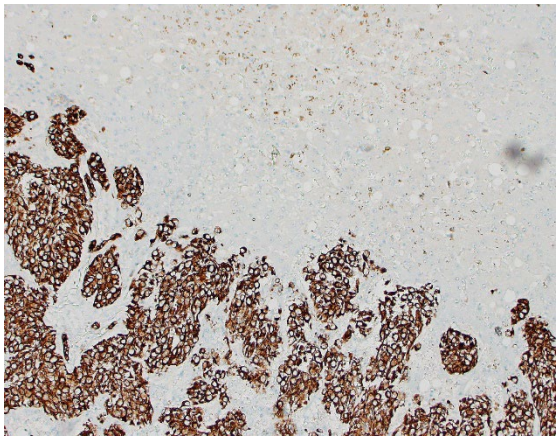

Figure 2-7. Liver, cat. Neoplastic cells are strongly positive for cytokeratins (AE1/AE3, 400X)

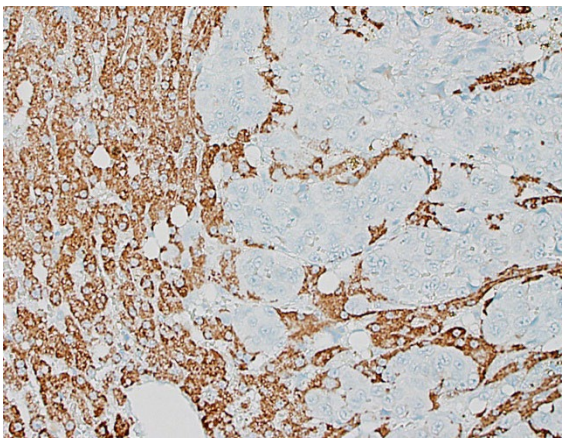

Figure 2-8. Liver, cat. Neoplastic cells are immunonegative for Hep-Par1, a hepatocyte stain. (anti Hep-par1, 400X)

This case is a classic example of paraneoplastic syndrome: the manifestation of a disease in a separate organ system secondary to malignancy elsewhere in the body. While paraneoplastic syndromes in the integumentary system are uncommon in animals, several distinct conditions have been reported.[1] Since integumentary lesions are easily detected by owners and often precede signs of the primary malignancy, paraneoplastic syndromes are frequently the reason for initial presentation of the patient.

Exfoliative dermatitis is another example of paraneoplastic syndrome causing alopecia in cats. This syndrome occurs secondary to thymomas in cats, rarely in rabbits, and anecdotally in a dog, though spontaneous (non-neoplastic) cases occur in cats as well.[5,7] Grossly, there is patchy to diffuse scaling and alopecia, with accumulation of brown waxy material around the claws and mucocutaneous junctions.[5] Histologically, there is variable lymphocytic interface dermatitis and mural folliculitis with orthokeratotic hyperkeratosis, hydropic degeneration of keratinocytes, and decreased to absent sebaceous glands. [5, 7]

Paraneoplastic pemphigus has rarely been reported in dogs, a cat, and a horse and have occurred secondary to sarcomas and thymic lymphomas.[1,5,7] This is a rapidly progressive, severe condition characterized by blistering, erosions, and ulcerations at the mucocutaneous junctions and on mucosal surfaces. Histologically, the syndrome shares features of pemphigus vulgaris, with suprabasilar acantholysis, and erythema multiforme, with a cell-rich lymphohystiocytic interface dermatitis.[5, 7]

Necrolytic migratory erythema, also known as superficial necrolytic dermatitis or hepatocutaneous syndrome, occurs in dogs and rarely in cats secondary to glucagonoma and certain non-neoplastic conditions like diabetes mellitus and hepatic disease.[1, 5, 7] In cats, the condition has also been reported secondary to pancreatic carcinoma, hepatic carcinoid, and lymphoma.[7] Grossly, there is scaling and alopecia with erythema, blistering, and ulceration around the face, pinnae, and pressure points (i.e. elbows). The paw pads are frequently thickened and fissured.[1, 5, 7] Histologically, there is diffuse parakeratotic hyperkeratosis, severe hydropic degeneration and acanthosis within the superficial stratum spinosum, and hyperplasia in the deeper stratum spinosum and stratum basale, imparting a distinct red, white, and blue striped appearance, and there is minimal inflammation.[5, 7]

Nodular dermatofibrosis is another paraneoplastic syndrome of the skin which occurs in German shepherd dogs and occasionally other large breed dogs in conjunction with renal cysts, renal cystadenocarcinomas, and uterine leiomyo-mas.[1, 5] These manifest as multifocal, slow-growing, nodular collagenous hamartomas typically in the subcutis and dermis of the extremities.[1, 5] Other reported paraneoplastic syndromes affecting the skin include necrotizing panniculitis (secondary to pancreatic neoplasia or pancreatitis in dogs, cats, and horses), cutaneous flushing (secondary to pheochromocytomas in dogs), and generalized pruritus (secondary to lymphoma in dogs and horses).[1, 5]

References:

1. Bergman PJ. Paraneoplastic Syndromes. In: Withrow SJ, Vail DM, Page RL, eds: *Withrow and MacEwen's Small Animal Clinical Oncology*. 5th ed. St. Louis, MO: Elsevier Saunders; 2013: 89-90.
2. Caporali C, Albanese F, Binanti D, Abramo F. Two cases of feline paraneoplastic alopecia associated with a neuroendocrine pancreatic neoplasia and a hepatosplenic plasma cell tumour. *Vet Dermatol*. 2016;**27**:508-e137
3. Grandt LM, Roethig A, Schroeder S, et al. Feline paraneoplastic alopecia associated with metastasising intestinal carcinoma. *JFMS Open Rep*. 2015:2055116915621582.
4. Marconato L, Albanese F, Viacava P, Marchetti V, Abramo F. Paraneoplastic alopecia associated with hepatocellular carcinoma in a cat. *Vet Dermatol*. 2007 ;**18**:267-71.
5. Mauldin EA, Peters-Kennedy J. Integumentary System. In: Maxie MG, ed. *Jubb, Kennedy, and Palmer's Pathology of Domestic Animals*. Vol 1. St. Louis, MO: Elsevier. 2016; 586, 603, 691-693.
6. Turek MM. Cutaneous paraneoplastic syndromes in dogs and cats: a review of the literature. *Vet Dermatol*. 2003;**14**:279-96.
7. Welle MM, Linder KE. The Integument. In: Zachary JF, ed. *Pathologic Basis of Veterinary Disease*. 7th ed. St. Louis, MO: Elsevier. 2022: 1209, 1255, 1261.

CASE III:

Signalment:
Adult (unknown age), female, Brazilian hedgehog/Brazilian porcupine (*Coendou prehensilis*)

History:
This porcupine was captured in a transitional region (native forest area on the outskirts of a small town) and sent to the Veterinary Hospital (UFMT) quite dehydrated and with swollen and wrinkled skin on its head. The animal received support treatment, but died the next day.

Gross Pathology:
The animal was submitted to necropsy and showed good conservation status. On the skin of the head (ear, periocular region, lateral face, muzzle and submandibular region), and in the perigenital region there were papules with irregular coalescing plaques, separated by superficial to deep grooves and moderately erythematous. These changes in the periocular region caused eyelid slit occlusion, blocking the view of the eyeball. Additionally, in the nasal and perioral plane region, there were yellowish crusts and a slight superficial erosion of the skin. In the internal examination, no significant alterations were observed.

Figure 3-1. Haired skin, Brazilian hedgehog. Plaques of thickened crusted skin coalesce over the face of this hedgehog. (Photo courtesy of Universidade Federal de Mato Grosso, Faculdade de Medicina Veterinária, Hospital Veterinário, Laboratório de Patologia Veterinária, https:// www.ufmt.br/ufmt/site/, Av. Fernando Corrêa da Costa, nº 2367 - Bairro Boa Esperança. Cuiabá, Brasil - MT - 78060-900)

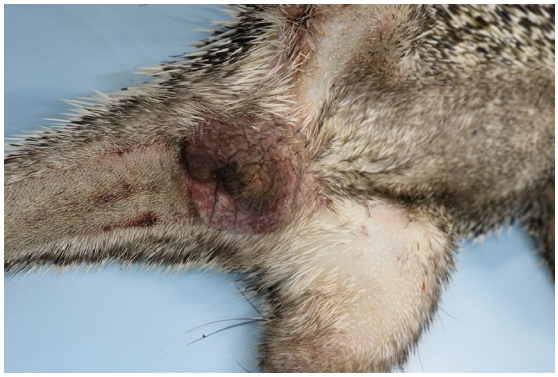

Figure 3-2. Haired skin, Brazilian porcupine. Similar plaques are present on the genitalia as well. (Photo courtesy of Universidade Federal de Mato Grosso, Faculdade de Medicina Veterinária, Hospital Veterinário, Laboratório de Patologia Veterinária, https:// www.ufmt.br/ufmt/site/, Av. Fernando Corrêa da Costa, nº 2367 - Bairro Boa Esperança. Cuiabá, Brasil - MT - 78060-900)

Laboratory Results:
A pan-pox universal PCR practice was performed[9] and subsequent amplicom sequencing, revealing 100% identity with the Brazilian porcupinepox virus (BPoPV).

Microscopic Description:
In the skin section, there are epidermal and hair follicles epithelial sheathing with intense proliferation and thickening (acanthosis). In the epidermis, interdigitations towards the dermis (rete pegs) are frequent. Multifocally, keratinocytes show intracytoplasmic edema and vacuolization (ballooning degeneration). Intercellular edema and mild to moderate, random, multifocal acantholysis are also seen, mainly at the basal and spinous layers, and are often keratinocytes with round/oval, eosinophilic, intracytoplasmic inclusion (Bollinger bodies). In the epidermis and hair follicles, there are multifocal areas of necrosis associated with moderate to severe neutrophil infiltration. There is a diffuse and moderate thickening of the stratum corneum in the epidermis, in which cell contours and finely elongated nuclei are seen, interspersed or paved with basophilic coccoid bacterial colonies (Brown & Hopps methods: gram

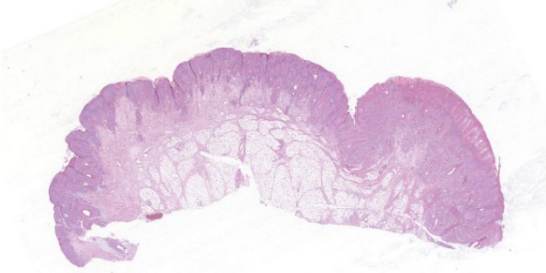

Figure 3-3. Haired skin, Brazilian porcupine. A single section of haired skin is submitted for examination. At subgross magnification, there is diffuse marked epidermal hyperplasia. (HE, 7X)

positive), associated with cellular debris of neutrophils and keratinocytes. In the dermis, from the dermic-epidermic junction to the adipose panniculus there is an infiltration composed of lymphocytes, plasma cells and in multifocal to coalescent areas along with mononucleated inflammatory cells that present distended and eosinophilic cytoplasm with peripheral nucleus. Connective tissue fibers are separated (edema) with a discrete myxoid appearance, especially in the superficial dermis.

Contributor's Morphologic Diagnoses:

1. **Hairy skin, vulva:** Proliferative, necrotic, multifocal to coalescent epidermitis with parakeratotic hyperkeratosis, intracytoplasmic inclusion bodies in keratinocytes and intraepidermal and follicular pustules.
2. **Hairy skin, vulva:** Diffuse, accentuated, and subacute lymphohistiocytic dermatitis.

Contributor's Comment:

Poxvirus is one of the largest and most complex known viruses. It is a double-stranded DNA virus which comprises a wide variety of susceptible species (vertebrates and invertebrates). Historically, it has as its main representative the variola virus (VARV), which causes human smallpox, the most devastating infectious disease in history.[3,11] In the present case, the morphological findings observed in this Brazilian porcupine (*Coendou prehensilis*) are consistent with an infection caused by a new genus of poxviruses belonging to the family Poxviridae, subfamily Chordopoxvirinae. The first report of this infection occurred in 2019 in Brazil, in a free-living Brazilian porcupine that had lesions characteristic of poxvirus infection (There are approximately 1000 km of distance between the case reported by Hora in 2019 and this case). As it is phylogenetically distinct from the other poxviruses previously reported, this poxvirus was named Brazilian Porcupinepox Virus (BPoPV).[6]

Brazilian porcupine (OC) is an arboreal rodent belonging to the Erethizontidae family, found in forests and riparian areas in several South American countries. This animal is more frequently observed in Brazil, where in the last two years have been reports of OC showing characteristic clinical signs of poxvirus infection, associated with high mortality. This situation increased the alert regarding the risk and threat to the conservation of this species.[6]

Macroscopically, the lesions are characterized by wrinkling, thickening and skin erythema of the head, limbs, and genitals.[6] Initially, these lesions appear as papules that coalesce and transform into plaques. Microscopically, the lesions occur mainly at the mucocutaneous junction, and are characterized by proliferative (hyperplasia and hyperkeratosis) and degenerative (ballooning degeneration and intercellular edema) changes in keratinocytes with visualization of intracytoplasmic eosinophilic viral inclusions.[6] These macroscopic and microscopic changes were also seen in this case and are typically related to poxvirus infection.[11]

Other rodents and also lagomorphs are also susceptible to poxvirus infections, but with

clinical manifestations, different from those presented by porcupines. Among them, myxomatosis in rabbits stands out, a fatal disease caused by the myxoma virus (MYXV), a leporipoxvirus belonging to the Poxviridae family that is antigenically associated with the rabbit fibroma virus. [1,4] It is characterized by the presence of cutaneous nodules (myxomas) around the eyes, nose, mouth, ears and genitalia. It can also present in the amyxomatous (respiratory) form, with different degrees of severity.[1,6] Microscopically, skin lesions consist of proliferation of stellate mesenchymal cells surrounded by a mucinous matrix. Intracytoplasmic inclusions are also observed in various cell types, as well as hyperplasia and/or degeneration in keratinocytes.[8]

Another member of the Poxviridae family is the rabbit fibroma virus (Shope), initially considered a benign disease, however, it can cause high morbidity and mortality in newborn animals. It is characterized by flat, mobile subcutaneous nodules that occur mainly on the limbs, feet, ears, muzzle and around the eyes, regressing spontaneously within a few months. Microscopic examination of skin lesions reveals proliferation of mesenchymal cells that become stellate or ovoid with multifocal areas of necrosis and inflammatory infiltrates of mononuclear and polymorphonuclear cells.[8]

Squirrel fibromatosis (SF) is caused by a poxvirus of the genus Leporipoxvirus, subfamily Chordopoxvirinae, and is also closely associated with rabbit fibroma virus. It has been described in red squirrels (*Tamiasciurus hudsonicus*), gray squirrels (*Sciurus carolinensis*) and fox squirrels (*Sciurus niger*). Macroscopically, the disease is characterized by firm, alopecic dermal nodules. Microscopically, typical poxviral lesions, epidermal hyperplasia, ballooning degeneration and intracytoplasmic inclusion bodies are observed, and the proliferation of atypical fibroblasts in the superficial dermis makes it distinct from other infections.[2]

It has been reported in pygmy mice proliferative epidermal lesions on the tail and paws caused by a poxvirus. Lesions appeared

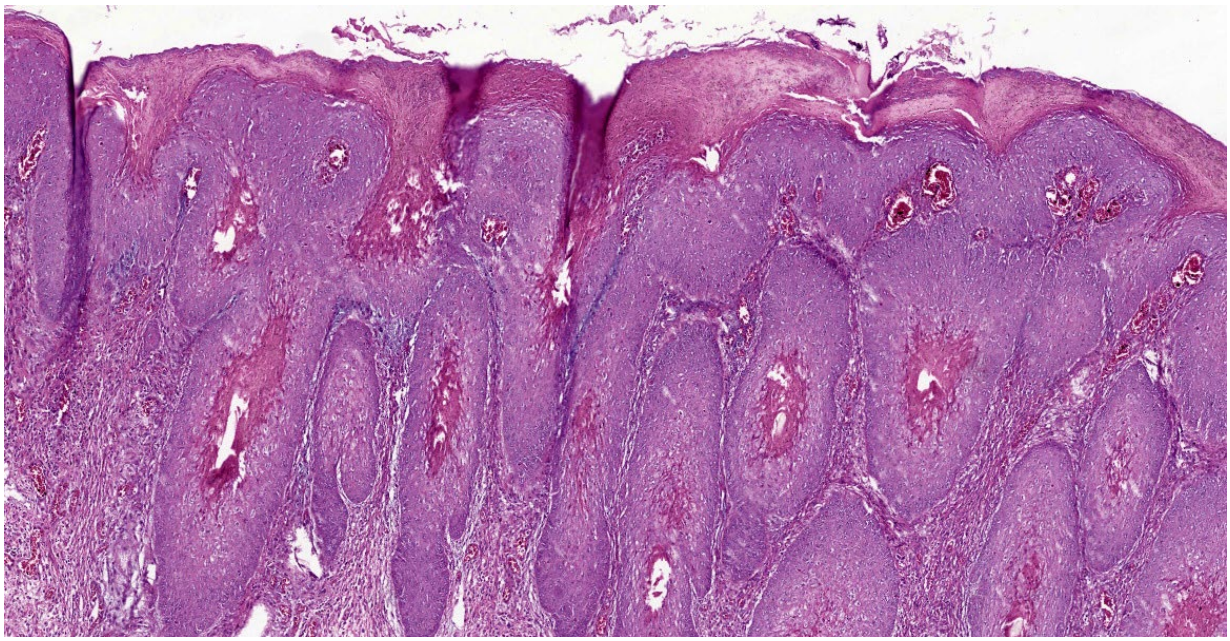

Figure 3-4. Haired skin, Brazilian porcupine. There is marked epidermal hyperplasia, acanthosis and hyperkeratosis which extends down into follicular ostia. (HE, 55X)

as firm, irregular, and pedunculated masses. On microscopic examination, the epidermis presents orthokeratotic and parakeratotic hyperkeratosis, ballooning degeneration of keratinocytes, and intracytoplasmic eosinophilic viral inclusions. Molecular analyzes identified that this poxvirus did not belong to any recognized genus until March 2018, this new species being called Brazospox virus,[5] therefore molecular methods play a fundamental role in the identification and monitoring of the propagation of new poxviruses in wild animals, allowing warnings about the risk and emergence of diseases that represent risks to the conservation of species, especially those that are threatened.

Contributing Institution:
Universidade Federal de Mato Grosso, Faculdade de Medicina Veterinária, Hospital Veterinário, Laboratório de Patologia Veterinária, https:// www.ufmt.br/ufmt/site/, Av. Fernando Corrêa da Costa, nº 2367 - Bairro Boa Esperança. Cuiabá, Brasil - MT - 78060-900

JPC Diagnosis:
Haired skin, epithelium: Hyperplasia, diffuse, severe, with ballooning degeneration, necrosis, and intracytoplasmic viral inclusions.

JPC Comment:
The contributor provides both an informative example of the novel Brazilian porcupine poxvirus and a broad overview of the *Leporipoxvirus* genus. These viruses all belong to the subfamily Chordopoxvirinae, or poxviruses which infect vertebrates.[6] There are ten genera and several newer unclassified viruses within this subfamily.[6] The *Orthopoxvirus* genus contains several poxviruses which are zoonotic or pathogenic to humans, including both the historically devastating and now eradicated variola virus (smallpox)

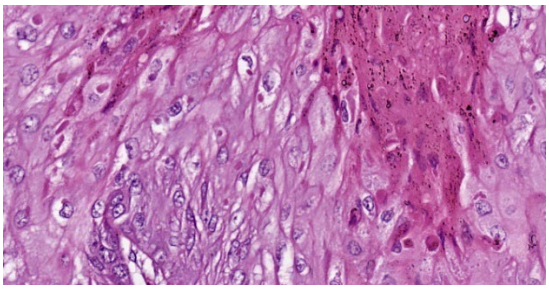

Figure 3-5. Haired skin, Brazilian porcupine. Numerous keratinocytes, often displaying ballooning degenerative changes, contain 2-4 um round intracytoplasmic viral inclusions. (HE, 663X)

and the newer emerging public health threat, monkeypox virus.[6, 12, 16]

Smallpox has affected the human population for millennia, with evidence of smallpox lesions in Egyptian mummies from 1186-1070 BC.[12] Smallpox is estimated to have caused 400,000 deaths annually in Europe in the eighteenth century and up to 4 million deaths in the Aztec and Incan empires after introduction of the virus to the Americas.[12] Initial vaccines were developed in the eighteenth century, and after a widespread eradication campaign, the World Health Organization declared the disease eradicated in the late 1970s.[16] Importantly, smallpox has a very narrow host range and lacks an animal reservoir, which made it susceptible to eradication strategies and contrasts with the wide host range of monkeypox virus.[12]

Monkeypox virus was first identified in cynomologous macaques imported from Africa into Copenhagen, Denmark in 1958.[12, 16] This discovery lead to the somewhat inaccurate naming of the virus, whose largest known reservoir is rodents.[16] Monkeypox infections have been documented in a wide range of animals, including numerous species of mice and rats, prairie dogs, hedgehogs, opossums, wild boar, several monkey and macaque species, orangutans, chimpanzees, and gorillas.[12] The first report of infection in

a human occurred in 1970 in the Democratic Republic of Congo (previously Zaire). Humans can be infected from direct or indirect contact with animals, such as bites, scratches, and the hunting of small animals for bushmeat.[16]

After 1970, case rates slowly increased in Central and West Africa.[16] Some of this spread is attributed to waning population immunity after termination of smallpox vaccination campaigns, which had offered cross protection against other orthopox-viruses; other factors include increased interaction with wildlife, civil unrest, and population dynamics.[16] Sporadic outbreaks outside of Africa occurred due to import of infected animals (United States in 2003) and international travel (UK and Israel in 2018).[16]

The current monkeypox outbreak began in May 2022 and has been designated as a public health emergency of international concern by the World Health Organization.[1, 18] As of September 2, 2022, 51,163 laboratory confirmed cases and 17 deaths have been reported in 102 countries around the world.[1] Transmission occurs through large respiratory droplets and direct contact with skin lesions, and over 95% of reported cases are in men who have sex with men.[1, 18] Clinical signs include fever and lymphadenopathy, with painful skin lesions such as papules, pustules, and ulcers most commonly found in the anogenital area, trunk and limbs, or face.[18]

In the current outbreak, only one case of monkeypox to date has been reported in a companion animal.[14,17] A four year old male Italian greyhound living in a household with two humans infected monkeypox developed mucocutaneous pustules and ulcers.[17] Swabs from the skin lesions were PCR positive for monkeypox and showed 100% homology with the virus isolated from one of the human owners.[17]

References:

1. 2022 Monkeypox Outbreak: Global Trends. World Health Organization. September 2, 2022. Accessed September 4, 2022. https://worldhealthorg.shinyapps.io/mpx_global/
2. Abade dos Santos, FA; Carvalho, CL; Pinto, A. et al. Detection of Recombinant Hare Myxoma Virus in Wild Rabbits (Oryctolagus cuniculus algirus). *Viruses*. 2020, 12:1127.
3. Bangari DS, Miller MA, Stevenson GW et al. Cutaneous and systemic poxviral disease in red (*Tamiasciurus hudsonicus*) and gray (*Sciurus carolinensis*) squirrels. Vet Pathol. 2009,46(4):667-72.
4. Barrett, JW, McFadden, G. Origin and Evolution of Poxviruses. In: Domingo, E, Parrish, CR, Holland, JJ. Origin and *Evolution of Viruses*. Academic Press. 2008:431-446.
5. Bertagnoli S, Marchandeau S. Myxomatosis. *Rev Sci Tech*. 2015; 34(2):549-56.
6. Delhon GA. Poxviridae. In: MacLachlan NJ, Dubovi AJ, eds. *Fenner's Veterinary Virology*. 5th ed. New York, NY: Elsevier. 2017; 157-174.
7. Hodo CL, Mauldin MR, Light JE et al. Novel Poxvirus in Proliferative Lesions of Wild Rodents in East Central Texas, USA. *Emerg Infect Dis*. 2018;24(6):1069-1072.
8. Hora AS, Taniwaki SA, Martins NB, et al. Genomic Analysis of Novel Poxvirus Brazilian Porcupinepox Virus, Brazil, 2019. *Emerg Infect Dis.* 2021:(4): 1177-1180.
9. Hughes AL, Irausquin S, Friedman R. The evolutionary biology of poxviruses. Infect Genet Evol. 2010 Jan;10(1):50-9.

10. Krogstad AP, Simpson JE, Korte SW. Viral diseases of the rabbit. *Vet Clin North Am Exot Anim Pract.* 2005;8(1):123-38.
11. Li Y, Meyer H, Zhao H, et al. GC content-based pan-pox universal PCR assays for poxvirus detection. *J Clin Microbiol*. 2010;48(1):268-276.
12. MacNeill AL. Comparative Pathology of Zoonotic Orthopoxviruses. *Pathogens.* 2022; 11(8):892-914.
13. Marinho-Filho, J., & Emmons, L. 2016. *Coendou prehensilis*. *The IUCN Red List of Threatened Species* 2016: e.T101228458A22214580. https://dx.doi.org/10.2305/IUCN.UK.2016-2.RLTS.T101228458A22214580.en. Downloaded on 28 July 2021.
14. Monkeypox in Animals. Centers for Disease Control and Prevention. August 17, 2022. Accessed September 4, 2022. https://www.cdc.gov/poxvirus/monkeypox/veterinarian/monkeypox-in-animals.html
15. Oliveira JS, Figueiredo PO, Costa GB, et al. Vaccinia Virus Natural Infections in: Brazil: The Good, the Bad, and the Ugly. *Vírus*. 2017; 9(11):340.
16. Peterson E, Koopmans M, Yinka-Ogunleye A, Ihekweazu C, Zumla A. Human Monkeypox Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect *Dis Clin N Am*. 2019; 33: 1027-1043.
17. Seang S, Burrel S, Todesco E, et al. Evidence of human-to-dog transmission of monkeypox virus. *The Lancet*. 2022; 500(10353):658-659.
18. Thornhill JP, Barkati S, Walmsley S, et a. Monkeypox Virus Infection in Humans across 16 Countries – April-June 2022. *The New England Journal of Medicine*. 2022;387(8):679-691.

CASE IV:

Signalment:
17-year-old, female spayed, domestic short-hair cat (*Felis catus*)

History:
The patient presented for evaluation of progressive weight loss and inappetence. Recent increase in seizure activity. Newly diagnosed pulmonary mass, presumptive pulmonary carcinoma. Historical small cell lymphoma, chronic rhinitis, hyperthyroidism, acute cerebral infarction.

Clinical Diagnosis:
1. Historical acute cerebral infarction
2. Stable small cell lymphoma
3. Pulmonary carcinoma
4. Hyperthyroidism
5. Chronic idiopathic rhinitis
6. Acute exacerbation of neurologic signs
7. Progressive weight loss - metastatic disease

Gross Pathology:
The mucosa of the body of the stomach is markedly expanded by irregular, cobblestone-like thickening of the gastric rugae (rule out neoplasia vs proliferative gastritis vs lymphofollicular hyperplasia. The irregular mucosal thickening up to 2.5 mm can be appreciated within the mucosa upon sectioning of the fixed tissue.

Laboratory Results:
Abdominal ultrasound of the stomach was normal.

Microscopic Description:
Two sections of gastric wall from the body/pylorus of the stomach are examined. The mucosa is highly folded and increased in thickness, measuring up to 2 mm. The thickened mucosa comprises increased numbers of

gastric pits lined by abundant mucus containing epithelial cells (mucus neck cells) which are typically lined by a single epithelial cell, but multifocally pile up to 2-3 cell layers thick. Chief and parietal cells are present but comprise a minority of the mucosal area. There are increased numbers of inflammatory cells throughout the lamina propria, with ectatic gastric glands and frequent glandular and luminal nematode parasites. Nematode parasites range from 20-30 um in diameter, with regularly arranged, evenly spaced cuticular spicules. These parasites have platymyarian-meromyarian musculature, a pseudocoelom with a large intestine composed of few multinucleated cells and reproductive structures. Moderately increased amounts of fibrous connective tissue are noted throughout the lamina propria, sometimes concentrically surrounding and separating glands that contain nematode parasites. Inflammation consists of predominantly lymphocytes with fewer plasma cells, macrophages and eosinophils throughout the lamina propria. Lymphocyte aggregates are occasionally present without formation of follicular structures. Multifocally, ectatic gastric glands contain sloughed cells and necrotic cell debris with occasional nematode parasites. The lining glandular epithelium of these dilated glands is multifocally attenuated. The submucosa contains adipose tissue (within normal limits for spp).

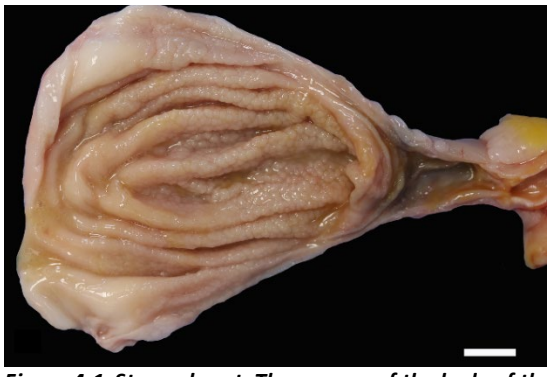

Figure 4-1. Stomach, cat. The mucosa of the body of the stomach is markedly expanded by irregular, cobblestone-like thickening of the gastric rugae (Photo courtesy of Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org)

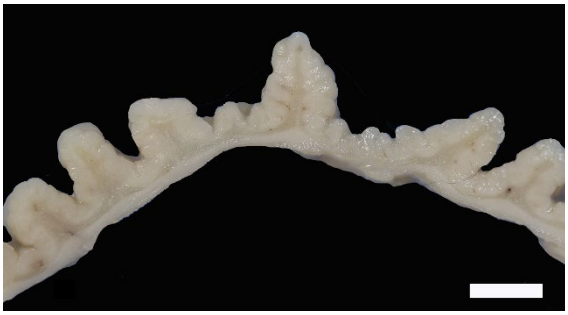

Figure 4-2. Stomach, cat. A cross-section of the gastric mucosa is irregularly thickened up to 2.5mm. (Photo courtesy of Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org)

Contributor's Morphologic Diagnoses:
Stomach: Gastritis, proliferative, lymphocytic, chronic, marked with fibrosis, luminal and glandular nematode parasites (morphology consistent with *Ollulanis tricuspis*)

Contributor's Comment:
The grossly identified cobblestone-like thickening of the stomach mucosa corresponds with proliferative gastritis and nematode parasitism. Numerous nematode parasites observed throughout the mucosa were histologically consistent with trichostronglyes, for which *Ollulanus tricuspis* is given primary consideration.[6] Confirmatory ancillary tests were not performed. *Ollulanis tricuspis* is a small (0.7-1.0 mm length) trichostronglyid nematode with worldwide distribution.[4] This parasite is typically found in the stomach of domestic cats but has been reported in large, non-domestic felids (including captive cheetah, tigers, lions and cougars), dogs, red foxes and pigs.[2,4,5,7,10] *Ollulanis tricuspis* has a direct life cycle, transmitted by ingestion of infected vomitus.[2,4,5,7-10] No paratenic or intermediate hosts have been identified.[5] *O. tricuspis* is larviparous, third stage (L3) larvae developing in the uterus. L3s eliminated in the vomitus are thought to be infective and can remain viable for up to 12 days. A single sample of vomitus can contain 0 to greater

than 170 parasites.[5,7] Feral and colony-raised cats may have a higher likelihood of being infected due to the concentration of numerous cats in a small area.[9] It has been suggested that infected long-haired cats are more likely to transmit the parasite because of more frequent vomiting due to a higher tendency to develop gastric trichobezoars.[8,9]

Infection with this parasite is frequently incidental.[4] The parasite is thought to increase gastric mucus production.[7] Clinical signs, when present include anorexia, weight loss and intermittent vomiting, however heavy infections can cause severe gastritis, neoplastic transformation and rarely death.[4,10] Vomiting has been reported as the most common clinical sign.[4] This patient had multiple concurrent comorbidities, some of which could also present with vomiting (e.g. intestinal small cell lymphoma), however, gastrointestinal signs were not listed as a prominent clinical concern in the historical summary. Despite the large numbers of parasites and prominence of the gastric mucosal proliferation, infection with this parasite was most likely incidental.

In felids with *O. tricuspis* parasitism, the gross appearance of the stomach can vary, depending upon the severity of the infection, ranging from macroscopically normal to grossly evident gastritis with mucosal hyperplasia and rugal thickening.[8] In one study,

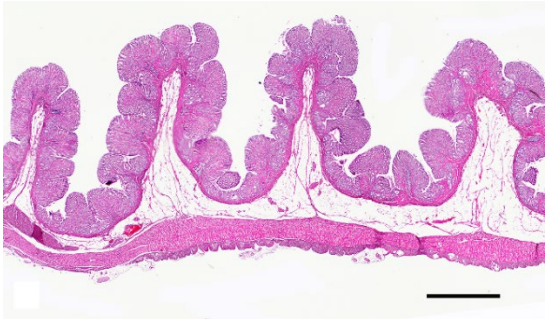

Figure 4-3. Stomach cat. The mucosa is highly folded and increased in thickness, measuring up to 2 mm. (Photo courtesy of Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org)(HE, 100X)

only 1 of 26 cats infected with *O. tricuspis* had grossly visible gastric lesions.[9] Reported histologic lesions include mucosal hyperplasia, mucosal erosion, fibrosis, increased mucosal lymphoid aggregates (some of which display large germinal centers) and increased globule leukocytes.[7,8,9,12] In this case, gastritis predominantly comprised lymphocytes with lymphocyte aggregates but no formation of follicular structures. Increased globule leukocytes were not observed. Mucosal proliferation is attributed to hyperplasia of mucus containing epithelial cells of the gastric pits. Parasites were generally observed within gastric glands as well as the gastric lumen. Fibrosis was also noted, sometimes concentrically surrounding glands with luminal parasites. Fibrosis was more prominent in the deeper portions of the stomach, just superficial to the muscularis mucosa, as has been previously reported.[8]

Other nematode parasites reported in the stomach of cats include *Gnathostoma* sp, *Cylicospirura* felineus, *Physaloptera*, *Cyathospirura* sp, *Aleurostrongylus abstrusus*, *Spirocerca lupi*, *Aonchotheca putorii*, other *Trichostronglyus* spp and oxyurids of prey animals (e.g. mice).[4,5,12] The demonstration of regular cuticular spicules is considered a key distinguishing morphologic feature of adult *O. tricuspis*.[4,6,9] These small parasites can be easily overlooked (both at postmortem examination and clinical examination of vomitus), thus the occurrence may be underestimated, as parasites or eggs are not typically present in feces.[4] Adult *O. tricuspis* usually die due to the high pH of the small intestine and are digested before excretion into the feces.[5] Small worm burdens may lead to difficultly observing or identifying parasites in histologic samples. In studies involving postmortem examination of stomach samples, worms were only identified in half the cats with *O. tricuspis* in three histologic sections, however, all cats had inflammatory changes

consistent with *O. tricuspis* infection.[9] Thus, pathologists should carefully evaluate samples of gastric mucosa in which the typical histologic features of *O. tricuspis* infection are observed. A differential diagnosis in captive cheetah is infection with gastric spiral bacteria (*Helicobacter* spp) which can chronic gastritis.[5] Antemortem methods of diagnosing infections with this parasite include antemortem gastric washings or gastric mucosal scrapings in addition to obtaining endoscopic biopsies. Postmortem peptic digestion of stomach samples can also be performed.[5,7]

Contributing Institution:
Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org

JPC Diagnosis:
Stomach, pylorus: Gastritis, proliferative, chronic, diffuse, moderate, with mucous neck cell hyperplasia, glandular atrophy, and luminal and intraglandular trichostrongyle adults and larvae.

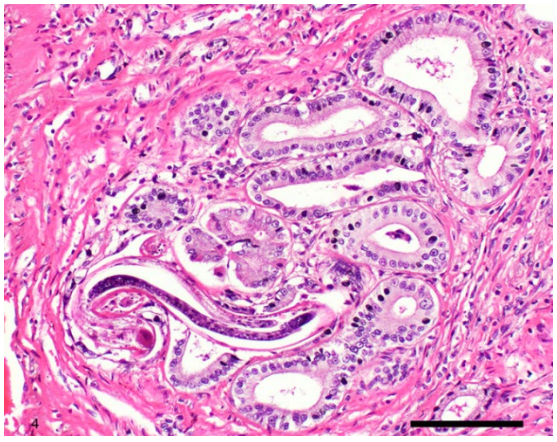

Figure 4-4. Stomach cat. Gastric glands in the deeper mucosa are surrounded by fibrous connective tissue, contain low numbers of a mixed inflammatory population, and cross sections of adult trichostrongyle nematodes. (Photo courtesy of Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org) (HE, 400X)

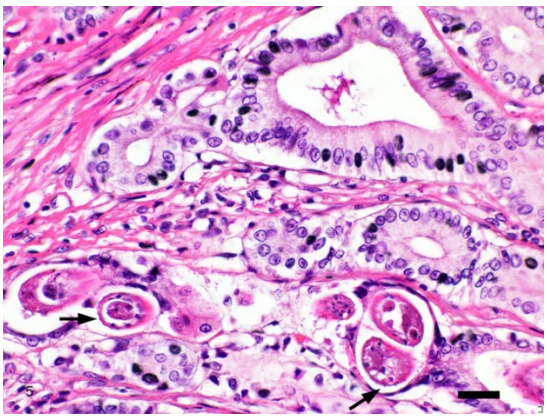

Figure 4-5. Stomach, cat. Cross sections of the nematodes demonstrate evenly spaced cuticular ridges (arrow) and platymyarian-meromyarian musculature. (Photo courtesy of Animal Medical Center, 510 East 62nd St. New York, NY 10065, www.amcny.org) (HE, 400X)

JPC Comment:
The contributor provides a thorough report on this nematode in the stomach of cats. As the contributor mentions, low *O. tricuspis* burdens can make histopathologic examination an insensitive means of detection of the parasite, and the absence of parasites in histologic sections may lead pathologists searching for other differentials. One rare non-parasitic differential which causes similar histologic lesions is chronic hypertrophic gastritis, or Ménétrier's-like disease. In this condition, gastric rugae are diffusely thickened with variable cystic glandular dilation.[1, 11] Histologically, there is mucous cell hyperplasia and atrophy of the oxyntic glands coupled with a mononuclear infiltrate within the mucosa.[1, 11] While Ménétrier's disease and its canine equivalent are rarely reported, there is only a single report of a similar condition in a cat.[1] The patient was a young adult domestic shorthair cat with a history of chronic weight loss and increased appetite.[1] Gastric biopsies showed mucosal hypertrophy with variable cystic glandular dilation, glandular atrophy, fibrosis, and lymphoplasmacytic inflammation.[1] While no evidence of parasitism was observed on histology, the patient in this report was euthanized without necropsy,

so the authors were unable to conduct ancillary testing to rule out *O. tricuspis*. [1]

As the contributor mentions, *Ollulanis* nematodes and eggs are rarely found in feces; thus, a few unique methods can be used to detect infection. Antemortem diagnosis typically involves cytologic examination of gastric fluid collected through gastric lavage or induction of emesis.[3] The specimen is centrifuged or filtered through a Baermann apparatus prior to cytologic examination, which has an estimated sensitivity of 70%.[3] In postmortem specimens, rice-grain sized scrapings collected from various areas of the gastric mucosa are mixed with saline (and KOH if needed) and examined cytologically.[3] Peptide-digestion can also be conducted, but is more laborious and involves everting and soaking the entire stomach in pepsin digestion fluid at 37 degrees Celsius for up to 8 hours and examining the sediment for nematodes.[3]

References:

1. Barker EN, Holdsworth AS, Hibbert A, Brown PJ, Hayward NJ. Hyperplastic and fibrosing gastropathy resembling Ménétrier disease in a cat. *JFMS Open Rep.* 2019;5(2)1-7.
2. Bell AG. *Ollulanus tricuspis* in a cat colony. N Z Vet J. 1984 Jun;32(6):85-7.
3. Bowman DB, Hendrix CM, Lindsay DS, Barr SC. *Feline Clinical Parasitology*. Ames, IO: Iowa State University Press. 2002; 263.
4. Cecchi R, Wills SJ, Dean R et al. Demonstration of *Ollulanis tricuspis* in the stomach of domestic cats by biopsy. *J Comp Pathol* 2006. 134:374-77.
5. Collett MG, Pomroy WE, Guilford WG, et al. Gastric *Ollulanus tricuspis* infection identified in captive cheetahs (Acinonyx jubatus) with chronic vomiting. *J S Afr Vet Assoc.* 2000 Dec;71(4):251-5.
6. Gardiner CH, Poynton SL. *An Atlas of Metazoan Parasites in Animal Tissues*. Washington, DC: Armed Forces Institute of Pathology;1999:22-26.
7. Guy, P A. *Ollulanis tricuspis* in domestic cats – prevalence and methods of postmortem diagnosis. *New Zealand Vet J.* 1984. 32(6):81-84.
8. Hargis AM, Prieur DJ, Blanchard JL. Prevalence, lesions and differential diagnosis of *Ollulanis tricuspis* infection in cats. *Vet Pathol.* 1983. 20:71-79.
9. Hargis, A M, Prieur DJ, Blanchard JL, et al. Chronic fibrosing gastritis associated with *Ollulanus tricuspis* in a cat. *Vet Pathol* 1982. 19: 320-323.
10. Kato D, Oishi M, Ohno K, et al. The first report of the ante-mortem diagnosis of *Ollulanis tricuspis* infection in two dogs. J Vet Med Sci. 2015. 77(11):1499-1502.
11. Uzal FA, Plannter 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. 2013; 53.
12. Veterinary Systemic Pathology Online:https://www.ask-jpc.org/vspo/show_page.php?id=ejYyVGcraFE3alY5cGF-WeXJtdVVzZz09