CASE I: A12-5214 (JPC 4017804).

Signalment: 4-year-old male domestic shorthaired cat (Felis catus).

History: An abdominal mass was palpated in a cat with anorexia and weight loss. The cat was serologically negative for feline leukemia virus and feline immunodeficiency virus. Eosinophilia was detected by complete blood count. At exploratory laparotomy, a solitary, infiltrative, 3 cm x 3 cm x 8 cm jejunal mass was treated by resection and anastomosis. No evidence of metastatic disease was observed grossly or by thoracic radiography. The resected segment of jejunum and a biopsy specimen of mesenteric lymph node were submitted in formalin to the Animal Disease Diagnostic Laboratory at Purdue University.

1-1. Small intestine, cat: The submucosa, muscularis, and serosa are markedly, circumferentially and asymmetrically expanded by fibrous connective tissue throughout which is scattered multiple foci or granulomatous inflammation. (HE 0.63X)

1-2. Small intestine, cat: Necrotic foci contain numerous outlines of non-septate hyphae which have non-parallel walls and measure 6-8 µm in diameter. These foci are surrounded by elongate epithelioid macrophages (below). (HE 340X)
**Gross Pathology:** A solitary, infiltrative, 3 cm x 3 cm x 8 cm jejunal mass was detected at laparotomy.

**Laboratory Results:** Infection with *Pythium insidiosum* was confirmed by PCR and gel electrophoresis on DNA extracted from formalin-fixed paraffin-embedded tissue sections.

**Histopathologic Description:** In a cross-section of resected jejunum, the mucosa was generally spared, except for mild to moderate increase in the number of lamina proprial eosinophils. In contrast, the submucosa and especially the tunica muscularis were almost circumferentially expanded by hypertrophied and hyperplastic fibroblasts in ample to abundant collagenous stroma with diffuse inflammation in which macrophages predominated, but eosinophils were multifocally numerous. The fibroblasts and the macrophages had 0 to 2 mitotic figures per 400x field. The fibroplasia and leukocytic infiltration extended into the serosa and mesentery, but lesional tissue was not evident in the surgical margins of the resection specimen. Although discrete well-organized granulomas were not observed, hyphal ‘ghosts’ were apparent, especially in foci of necrosis with heavy eosinophil infiltration in the outer layer of the tunica muscularis. Hyphae were easier to see with Gomori’s methenamine silver (GMS), and were 2.5-7.5 µm in diameter with nonparallel walls, few septa and few branches. Hyphae and leukocytes were in the wall of a few vessels, mainly arteries. There were increased numbers of eosinophils in sinuses of the mesenteric lymph node biopsy specimen, but granulomatous lymphadenitis was not evident.

**Contributor’s Morphologic Diagnosis:** Jejunum: Eosinophilic granulomatous mural enteritis with sclerosing fibroplasia.

**Contributor’s Comment:** Although the intestinal mass looked like a neoplasm at surgery, the histologic impression was inflammation, with features like those of feline gastrointestinal eosinophilic sclerosing fibroplasia. However, though intrallesional bacteria were found in about half the cases, hyphae were not found with GMS in any of the 25 cats in that multi-institutional study. The presence of hyphae in this case expanded the differential diagnosis to include zygomycosis and pythiosis. Infection with *Pythium insidiosum* was confirmed by PCR and gel electrophoresis on DNA extracted from formalin-fixed paraffin-embedded tissue sections. The location of the lesion and the eosinophilic nature of the granulomatous inflammation were similar to gastrointestinal pythiosis in dogs.

Mammalian pythiosis, caused by *Pythium insidiosum*, is mainly a disease of horses, dogs, and humans in tropical, subtropical and temperate regions of the world. Whereas equine pythiosis is usually a cutaneous infection, dogs are more likely to develop the gastrointestinal form. Most reported feline cases have been cutaneous or subcutaneous, rather than intestinal infections.
However, intestinal pythiosis has been reported in 2 cats.\(^5\) Interestingly, the prognosis after surgical resection of intestinal pythiosis may be much better in cats than in dogs. The invasive nature in most canine cases of gastrointestinal pythiosis hinders complete excision. In the reported cases, both cats became clinically normal after surgical resection of the intestinal mass and treatment with itraconozole.\(^5\) Pythiosis is rare in Indiana, and is less common in cats than in dogs. In this cat, surgical margins were histologically free of hyphae or the eosinophilic and sclerosing inflammation. In addition to surgical resection of the affected jejunal segment, the cat was treated with prednisolone for the peripheral eosinophilia. Five months after excision of its intestinal mass, the owner reported that the cat had gained weight and was seemingly healthy.

**JPC Diagnosis:** Small intestine, submucosa, tunica muscularis, serosa and attached mesentery: Enteritis and peritonitis, granulomatous and eosinophilic, circumferential, chronic, diffuse, severe with marked fibrosis and hyphae.

**Conference Comment:** As noted by the contributor, *Pythium insidiosum* typically produces cutaneous lesions in cats, so with a clinical history of peripheral eosinophilia and palpation of an abdominal mass, pythiosis was not initially suspected. Potential causes of peripheral eosinophilia in a cat include parasitism, hypersensitivity, fungal infection, drug reactions, hyperthyroidism, hypereosinophilic syndrome, gastrointestinal eosinophilic sclerosing fibroplasia and neoplasia, specifically mast cell tumor, T-cell lymphoma, fibrosarcoma, thymoma, various carcinomas and eosinophilic leukemia.\(^6\) Grossly, the jejunal mass was suggestive of alimentary lymphoma, intestinal adenocarcinoma, and feline gastrointestinal eosinophilic sclerosing fibroplasia. One of the most striking histological features in this case is the abundant, circumferential fibrosis, affecting the intestinal submucosa, muscularis and serosa, as well as the adjacent mesentery. This, in combination with the moderate numbers of infiltrating eosinophils, is somewhat reminiscent of feline gastrointestinal eosinophilic sclerosing fibroplasia; however, the presence of hyphae do not fit with this diagnosis.\(^1\)

*Pythium* species belong to the class *Oomycetes* and are found in warm stagnant water, primarily in tropical to subtropical regions. *Oomycetes* are not true fungi, although they also produce characteristic hyphae. In contrast to true fungi, oomycetes have cell walls that contain cellulose and β-glucan but lack chitin, and ergosterol is not a significant component of the cell membrane.\(^4\) Most species of *Pythium* are plant pathogens; however, *Pythium insidiosum* is pathogenic to several mammalian species.\(^4\) The infective stage of the oomycete is a motile, biflagellate zoospore that is chemotactically attracted to injured tissue, such as damaged skin or gastrointestinal mucosa, resulting in the classically described cutaneous or enteric lesions.\(^4\) Microscopically, pythiosis must be differentiated from lagenidiosis and zygomycosis. *Lagenidium* sp. is the only other known pathogenic oomycete, and has rarely been described in dogs; it is morphologically indistinguishable from *P. insidiosum*.\(^4\) Although rarely described in cats and dogs, true fungi belonging to the class *Zygomycetes*, such as *Basidiobolus* and *Conidiobolus* sp., also produce hyphae with rare septae. Occasionally, on H&E stained sections, fungal hyphae are surrounded by a 2.5-25 μm eosinophilic “sleeve,” which helps differentiate zygomycosis from pythiosis and lagenidiosis.\(^4\)

**Contributing Institution:** Purdue University Animal Disease Diagnostic Laboratory: http://www.addl.purdue.edu/  
Department of Comparative Pathobiology: http://www.vet.purdue.edu/cpb/

**References:**

CASE II: 11-37333 (JPC 4009691).

Signalment: 11-year-old female spayed West-Highland white terrier dog (Canis familiaris).

History: This dog had chronic diarrhea for more than 30 days, which was non-responsive to antibiotics. Exploratory surgery revealed numerous small pin-point pale proliferative lesions within the mesentery and on the enteric serosa. The patient was euthanized due to poor prognosis.

Gross Pathology: Four images were submitted along with the biopsy by the referring clinician. These images reveal severely thickened and turgid enteric wall. On cut section (upper-right hand), there is marked transmural edema involving predominantly mucosa. The mucosa is diffusely rough, pink and has Turkish-towel-like appearance due to chyle-filled lacteals. Multiple, pale, pin-point, discrete, raised, and sharply demarcated granulomas are present on the enteric serosal surface and in the mesentery (lower left and right-hand images).

Laboratory Results: Hypoproteinemia.

Histopathologic Description: Small intestine - The lacteals are markedly dilated and the lamina propria is expanded by edema. Lymphatics within the submucosa, adventitia, muscularis, and mesentery are dilated and are surrounded by vacuolated lipid-laden macrophages with necrotic cores, rare neutrophils and fibrous connective tissue (lipogranulomas). Fibrosis, neutrophils, lymphocytes, and plasma cells are scattered within the mesentery.

Contributor’s Morphologic Diagnosis: Small intestine: Severe chronic lymphangiectasia with pyogranulomaticous non-mucosal enteritis and lymphangitis.

Contributor’s Comment: Lymphangiectasia syndrome is a common cause of malabsorption and protein losing enteropathy in dogs. It is characterized by chronic diarrhea, wasting, hypoproteinemia, hypocalcemia, lymphopenia, and hypocholesterolemia. Anorexia, weight loss and steatorrhea are also observed. Yorkshire terriers and Norwegian Lundehunds are predisposed. The lesions of this syndrome grossly resemble an intestinal neoplasm because of the proliferative nature. Patients with this syndrome are often difficult to treat because of the poorly delineated pathogenesis of this condition; typically, these patients have a poor prognosis. The pathogenesis of this syndrome remains unknown. No congenital or acquired cause of lymphatic obstruction is observed in this case. Lipogranulomas are an inconsistent finding considered to be secondary to chronic leakage of lipid-laden chyle. These lesions can secondarily block lymphatics and add to the edema. Malabsorption of lipid from the gut causes diarrhea through the effects of fatty acids on colonic secretion. Hypocalcemia can be due to loss of mineral bound albumin and perhaps due to...
vitamin D malabsorption or binding of calcium with esterified fatty acids. Lipid malabsorption causes hypocholesterolemia, while lymphopenia is due to loss of lymphocyte-rich lymph into the intestine.1

**JPC Diagnosis:** Small intestine, submucosa, tunica muscularis, serosa, and mesentery: Lymphangitis, lipogranulomatous, multifocal to coalescing, severe, with lymphangiectasia and edema.

**Conference Comment:** A distinguishing feature of lymphangiectasia, which is readily apparent in this case, is the even distribution of histological lesions; intestinal lymphatics and lacteals are generally diffusely affected. In contrast, there are few reports focal lipogranulomatous lymphangitis with lymphangiectasia, which manifests as localized masses rather than disseminated intestinal disease. In most of these cases, there is no laboratory evidence of protein losing enteropathy (PLE) and surgical excision appears curative; however, some affected animals do develop signs consistent with PLE, indicating the possibility of disease progression. Both presentations have an unknown pathogenesis and tend to affect older animals, producing vomiting, weight loss, and diarrhea.3

In addition to the idiopathic lymphangiectasia syndrome diagnosed in this case, canine PLE has been associated with alimentary lymphoma, inflammatory bowel disease and infectious agents such as *Giardia, Ancylostoma, Histoplasma, Prototheca* or *Pythium* sp.2 Gross, histological and clinicopathologic findings, which are comprehensively reviewed above, can help differentiate between these conditions; there are also reports of dogs affected with multiple concurrent causes of PLE.
Contributing Institution: University of Illinois Veterinary Diagnostic Laboratory
http://vetmed.illinois.edu/vdl/index.html

References:
**CASE III: 111156-15 (JPC 4018123).**

**Signalment:** 15-year-old female spayed domestic short hair cat (*Felis catus*).

**History:** This cat presented with a history of lethargy, anorexia, and vomiting of bile. Physical exam revealed a 1-pound weight loss within the past 4 months, grade 2-3 heart murmur, and doughy, slightly painful abdomen. Abdominal and thoracic radiographs showed no significant findings. An in-house CBC/serum chemistry/urinalysis panel showed mild azotemia, hypercalcemia, hyperproteinemia, hyperglobinemia and slight increase in ALT. The cat was hospitalized and started on fluid therapy and anti-emetics. Additional clinical samples were then collected and sent out to a commercial laboratory for CBC, routine serum chemistry, urinalysis, serum ionized Ca, serum protein electrophoresis, serum parathyroid hormone related protein (PTHrP) and serum parathyroid hormone (PTH) analyses (see included table). After the results of these tests were known, the owners elected to euthanize the cat upon hearing the presumptive diagnosis (multiple myeloma).

**Gross Pathology:** A partial necropsy was performed by the clinician with no gross abnormalities noted. Samples of femur bone marrow, spleen, kidney, liver and sections of small intestine were collected for histopathological examination.

**Laboratory Results:**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
<th>Reference Range</th>
<th>Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Protein</td>
<td>10.7</td>
<td>5.2-8.8</td>
<td>g/dL</td>
</tr>
<tr>
<td>Globulin</td>
<td>7.4</td>
<td>2.3-5.3</td>
<td>g/dL</td>
</tr>
<tr>
<td>AST</td>
<td>152</td>
<td>10-100</td>
<td>U/L</td>
</tr>
<tr>
<td>AST (ALT?)</td>
<td>155</td>
<td>10-100</td>
<td>U/L</td>
</tr>
<tr>
<td>Urea Nitrogen</td>
<td>52</td>
<td>14-36</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Creatinine</td>
<td>2.6</td>
<td>0.6-2.4</td>
<td>mg/dL</td>
</tr>
<tr>
<td>CPK</td>
<td>1109</td>
<td>56-529</td>
<td>U/L</td>
</tr>
<tr>
<td>Calcium, ionized</td>
<td>2.20</td>
<td>1.16-1.34</td>
<td>µmol/L</td>
</tr>
<tr>
<td>Calcium (verified)</td>
<td>18.3</td>
<td>8.2-10.8</td>
<td>mg/dL</td>
</tr>
<tr>
<td>Protein Electrophoresis, serum</td>
<td>10.7</td>
<td>5.2-8.8</td>
<td>g/dL</td>
</tr>
<tr>
<td>Gamma</td>
<td>4.83</td>
<td>0.50-1.90</td>
<td>g/dL</td>
</tr>
<tr>
<td>PTHrP</td>
<td>0.0</td>
<td>Less than 1.0</td>
<td>pmol/L</td>
</tr>
<tr>
<td>PTH</td>
<td>4.0</td>
<td>4-25</td>
<td>pg/ml</td>
</tr>
</tbody>
</table>

- CBC: WNL
- Platelet count: 56 (LOW); due to platelet clumping.
- Urinalysis (cystocentesis): Light yellow, clear, SG ~ 1.038, pH ~ 6.0, proteinuria (3+), hematuria (3+) and >50 RBC. Glucose, ketone, bilirubin were negative. No casts, crystals or bacteria. WBC and squamous epithelial cells were WNL.
- Urine microalbumin (feline): 7.4 (HIGH) indicating microalbuminuria.

**Histopathologic Description:** Bone marrow:

The bone marrow is 60% effaced and replaced by an unencapsulated, poorly circumscribed, infiltrative, highly cellular neoplasm. The neoplasm is composed of round cells arranged in sheets supported on a pre-existing fibrovascular stroma. Neoplastic cells have fairly distinct cell borders and moderate amounts of eosinophilic cytoplasm. Nuclei are round to oval, occasionally eccentrically placed, with coarsely stippled chromatin and up to three indistinct nucleoli. Mitoses average five per high power field. There is mild anisokaryosis and anisocytosis, and scattered multifocal single-cell necrosis. There are adequate numbers of megakaryocytes and adipocytes.
Contributor’s Morphologic Diagnosis: Bone marrow (femur): Plasma cell myeloma, domestic short hair cat, feline.

Contributor’s Comment: Plasma cell neoplasms originate from terminally differentiated B lymphocytes that have undergone malignant transformation. The two main recognized forms of plasma cell neoplasm in veterinary species are multiple myeloma and plasmacytoma. This case is a classical presentation of multiple myeloma, which refers to diffuse disease and, clinically, is the most important plasma cell neoplasm.

In animals, multiple myeloma is a rare, malignant tumor that arises in the bone marrow. It has a slowly progressive clinical course and sites of metastasis include the spleen, liver, lymph nodes and kidneys. Though rare, it has been reported in horses, cattle, cats and pigs, but it is seen more frequently in older dogs with a mean age of 8-9 years. In cats, the median age is 12-14 years and there is possibly a male predisposition. The cause in domestic animals is unknown, but in people, plasma cell neoplasms are associated with working in agriculture, exposure to petroleum products, and chronic exposure to an antigenic stimulus. There is no evidence that feline immunodeficiency virus, feline leukemia virus, or feline infectious peritonitis virus infections are related to the development of multiple myeloma in cats.

Neoplastic plasma cells usually secrete large amounts of immunoglobulin (Ig), and the hallmark laboratory finding is hyperglobulinemia. This homogeneous protein fraction is often called paraprotein or M-protein.

Diagnosis of multiple myeloma is based on a minimum of two of the following abnormalities:
1. Marked increase in numbers of plasma cells in the bone marrow (at least 30% of the nucleated cells are plasma cells which may be well differentiated to poorly differentiated cells with visible nucleoli, marked anisokaryosis and anisocytosis and multinucleation).

2. Monoclonal gammopathy because of clonal production of Ig or Ig fragments by the neoplastic cells. This is demonstrated by serum electrophoresis and can be characterized further using immunodiagnostic techniques. Most of the Igs migrate in the gamma-region, but some may migrate to the beta-region (particularly IgA and IgM), hence the usage of the term monoclonal gammopathy. Note that monoclonal gammopathy is not specific to multiple myeloma and has been reported in cases of B lymphocyte lymphoma and some nonneoplastic conditions such as canine ehrlichiosis or leishmaniasis.


4. Light-chain proteinuria: Bence Jones proteins are free Ig light chains of low molecular weight that pass through the glomerular filter in the urine. These proteins do not react with urine dipstick protein indicators and are specifically detected by electrophoresis and immunoprecipitation.

Patients with multiple myeloma often present with other pathologic findings including: \(^{1,4-6,12-13}\)

1) hypercalcemia, due to neoplastic cell production of osteoclastic-activating factors (RANKL) resulting in resorption of bone,
2) hemorrhage that is caused by secondary platelet dysfunction due to the binding of the
paraprotein to platelets (decreased aggregation),
3) hyperviscosity syndrome (IgM and IgA dimers
cause an increased viscosity of blood resulting in
tissue ischemia and hemorrhage),
4) cytopenias caused by high numbers of
neoplastic cells displacing normal bone marrow
elements, and
5) renal disease, which develops from
nephrocalcinosis secondary to chronic
hypercalcemia, hypoxic damage from
hyperviscosity, renal toxicity of light chains
and neoplastic cell infiltration into the kidney and/or
renal amyloidosis.

In this rare feline case of multiple myeloma, the
diagnosis was made based on the hallmark
laboratory finding of hyperglobulinemia and
having two out of the four abnormalities for
multiple myeloma: marked increase in numbers of
plasma cells in the bone marrow and monoclonal
gammopathy. In addition, there was metastasis to
t he s p l e e n , k i d n e y a n d l i v e r . Hyperparathyroidism was ruled out based on
PTHrP and PTH laboratory findings within
normal limits.

Acknowledgment: The author thanks Dr. Lynn
Facemire for contributing the clinical case history
and the tissue samples for histopathology.

JPC Diagnosis: Bone marrow: Plasma cell
myeloma.

Conference Comment: In the histopathologic
description, the contributor noted that 60% of the
bone marrow nucleated cell population was
replaced by neoplastic plasma cells, however, in
conference it appeared that plasma cells accounted for a significantly smaller proportion of
bone marrow, and neoplastic cells were largely
confined to one or two foci within the section.
Despite this disparity, conference participants
agreed that plasma cells did constitute greater
than 30% of the nucleated cell population, which,
in combination with the laboratory finding of
hypergammaglobulinemia, supports a definitive
diagnosis of plasma cell myeloma. Evidence of
osteolysis was not reported and there was no
history of Bence-Jones proteinuria, the two other
diagnostic criteria for diagnosing plasma cell
myeloma. Other causes of monoclonal
gammopathy in cats and dogs include lymphoma,
leukemia, amyloidosis, ehrlichiosis, visceral
leishmaniasis, feline infectious peritonitis and
plasmacytic gastroenterocolitis. The azotemia
and proteinuria/microalbuminuria observed in this
case are likely secondary to renal damage, which
is a relatively common finding in plasma cell
myeloma. Hypercalcemia typically occurs due to
neoplastic plasma cell production of osteoclastic-
activating factors, which induce bone resorption
and subsequent release of calcium. The
underlying cause of the elevations in ALT and
AST (both of which are hepatocellular leakage
enzymes) is not clear, but may be related to tumor
metastasis and resultant hepatocellular injury.

Contributing Institution: US Army Medical
Research Institute of Infectious Diseases
Pathology Division
Fort Detrick, MD
http://www.usamriid.army.mil/

References:
1. Fry MM, McGavin MD. Bone marrow, blood
cells and the lymphatic system. In: McGavin MD,
Zachary JF, eds. Pathologic Basis of Veterinary
2. Hanna F. Multiple myelomas in cats. J Feline
3. Imahori S, Moore GE. Multiple myeloma and
prolonged stimulation of reticuloendothelial
4. Kumar V, Abbas AK, Fausto N, Aster JC.
Diseases of white blood cells, lymph nodes,
spleen and thymus. In: Kumar V, Abbas AK,
Fausto N, Aster JC, eds. Robbins and Cotran
Pathologic Basis of Disease. 8th ed. Philadelphia,
PA: Elsevier Saunders; 2009:609-610.
5. Latimer KS. Hematopoietic neoplasia. In:
Latimer KS, ed. Duncan and Prasse's Veterinary
Laboratory Medicine Clinical Pathology. 5th ed.
cytologic analysis of feline myeloma-related
disorders: further evidence for primary
extraduillary development in the cat. Vet
Pathol. 2008;45(2):159-173.
Myeloma-related disorders in cats commonly
present as extraduillary neoplasms in contrast
to myeloma in human patients: 24 cases with
1376-1383.
**CASE IV:** 2013KSUVDL-2 (JPC 4032561).

**Signalment:** 3-month-old mixed breed male puppy (*Canis familiaris*).

**History:** This puppy presented for a complete necropsy following euthanasia. It had a 1.5 week history of myoclonus and tested positive for canine distemper virus on PCR. This puppy was previously vaccinated twice with standard puppy vaccines (DH2PP) and housed with six other puppies who were also positive for canine distemper virus.

**Gross Pathology:** The puppy was thin, had a body condition score of 2/5 and was in fair post-mortem condition. The lungs failed to fully collapse after opening the thoracic cavity. Diffusely, lung lobes were pale pink and rubbery to firm when palpated. Multifocally, there were variably sized, yellow to greenish firm slightly raised areas of consolidation. Sectioned pulmonary parenchyma bulged and oozed small amounts of serous fluid. The trachea contained moderate amounts of serosanguineous fluid mixed with mucus. Teeth were grossly normal.

**Histopathologic Description:** Teeth, alveolar bone and gingiva: Each section has deciduous and developing permanent teeth. In the permanent tooth, ameloblasts lining enamel are multifocally swollen, hypereosinophilic, and have fragmented to vacuolated cytoplasm (degeneration). Frequently, ameloblasts contain intracytoplasmic and intranuclear 3-5 µm diameter, round to irregular, bright eosinophilic inclusions. Syncytia with 5-20 nuclei and abundant eosinophilic cytoplasm are multifocally present and contain similar intracytoplasmic inclusions. Ameloblasts are occasionally disorganized with loss of cell polarity and are piled 5-6 cell layers deep. Rarely, there is individual cell necrosis of ameloblasts characterized by shrunken cells, loss of cellular details and pyknotic nuclei. (The dentin and/or enamel are artifactualy dislocated in some sections.)

Findings in other tissues (not submitted) include necrosuppurative bronchopneumonia, demyelination of cerebellum and brain stem, neuronal degeneration and necrosis of cervical, thoracic, and lumbar spinal cord segments, myocardial degeneration and necrosis, and lymphoid depletion of the spleen, lymph nodes and tonsils. Similar inclusions were present in the respiratory epithelium of the lung and trachea, mucosal epithelium of the renal pelvis and urinary bladder, astrocytes of the cerebrum and cerebellum and neurons of the spinal cord.

**Contributor’s Morphologic Diagnosis:** Teeth, ameloblasts: degeneration and necrosis, multifocal, moderate to severe, with syncytia and eosinophilic intranuclear and intracytoplasmic inclusions.

---

4-1. Lungs, 3-month old dog: At autopsy, the puppy's lungs were rubbery and failed to collapse. This patchy suppurrative interstitial pneumonia is strongly suggestive of canine distemper. (Photo courtesy of: Department of Diagnostic Medicine and Pathobiology, Kansas State Veterinary College of Veterinary Medicine, 1800 Denison Avenue, Manhattan, KS 66506 http://www.vet.k-state.edu/depts/dmp/index.htm)

4-2. Developing permanent tooth (tooth bud), 3-month old dog: Degenerate ameloblasts exhibit marked cytoplasmic swelling and numerous 2-4 µm irregular eosinophilic intracytoplasmic viral inclusions, characteristic of canine morbillivirus. (Photo courtesy of: Department of Diagnostic Medicine and Pathobiology, Kansas State Veterinary College of Veterinary Medicine, 1800 Denison Avenue, Manhattan, KS 66506 http://www.vet.k-state.edu/depts/dmp/index.htm)
Canine distemper virus (CDV) is known to cause systemic disease in dogs, fox, coyotes, ferrets and other animals worldwide due to its ability to infect a variety of cell types, including neuroendocrine, epithelial, mesenchymal, and hematopoietic.\textsuperscript{1,6} CDV is in the \textit{Morbillivirus} genus and is closely related to measles virus and rinderpest virus.\textsuperscript{3,6} The virus is described as a 150-250 nm diameter enveloped virion containing a single negative-sense RNA strand that encodes for various glycoproteins.\textsuperscript{3,6} The H glycoprotein is likely used for attachment to the host cell during initial infection, therefore adequate immune response against H protein may lessen or prevent disease.\textsuperscript{6}

Transmission of CDV occurs via nasal or oral routes where the virus replicates immediately in the lymphoid tissue causing marked immunosuppression.\textsuperscript{1,3,6} Depending on the host response, age and virus strain, the animal will either clear the infection or develop systemic disease. The virus has a propensity to infect epithelial cells in various organs, especially the central nervous system.\textsuperscript{3,6} Dogs with partial immunity can be viremic and shed virus for an extended period of time in secretions; clinical signs in these animals are minor to absent and can later manifest as hyperkeratosis of the foot pad and nose.\textsuperscript{3,6} Disease following vaccination with modified live CDV vaccine has been occasionally reported;\textsuperscript{3,6} however, widespread use of prophylactic vaccination has successfully controlled the disease and is currently uncommon in vaccinated dog populations.\textsuperscript{3} A rare condition caused by CDV infection in mature vaccinated dogs is a progressive chronic encephalomyelitis known as old dog encephalitis.\textsuperscript{1,3,6}

Clinical signs manifest as respiratory, neurologic, and/or enteric disease. Less commonly, young dogs can develop dental lesions, ocular lesions, and neonatal myocardial degeneration and necrosis.\textsuperscript{3} Dental lesions following infection may include necrosis and cystic degeneration of ameloblasts, formation of syncytia, disorganization of ameloblasts, and prominent eosinophilic cytoplasmic viral inclusions.\textsuperscript{3,5} Delayed changes in the enamel occur in animals that survive infection and are described as focal defects in the enamel, which appear as depressions (pits) or well-delineated areas of hypoplasia.\textsuperscript{3,4} This occurs because the virus directly infects ameloblasts and causes disruption of enamel formation.\textsuperscript{4} Other dental abnormalities attributed to CDV include dental impaction, partial eruption, and oligodontia.\textsuperscript{2} In the present case, the puppy was euthanized before gross or microscopic evidence of enamel hypoplasia could be detected.

CDV can be diagnosed by a variety of methods; however, molecular assays such as reverse transcriptase polymerase chain reaction (RT-PCR)
Distinction between field and vaccine strains is possible via nested RT-PCR assays. Postmortem diagnosis is achieved when there is evidence of systemic or CNS disease and the presence of characteristic inclusion bodies supported by positive immunohistochemistry (IHC) or other ancillary tests. Ameloblasts in the present case had intense multifocal cytoplasmic staining for CDV, which correlated with histologic findings. Additionally, cerebrum and brainstem were IHC positive for CDV. In this case, an unequivocal diagnosis of CDV was made due to the spectrum of gross and microscopic lesions seen along with CDV positive ameloblasts and the reported clinical history.

JPC Diagnosis: Developing tooth, ameloblasts; stratum intermedium: Degeneration and necrosis, multifocal, moderate, with eosinophilic intracytoplasmic viral inclusions and multinucleated viral syncytial cells.

Conference Comment: Conference participants agreed that this is an excellent case, providing a unique microscopic view of a lesion that most pathologists have only seen as a gross photograph.

The contributor provides a thorough review of the pathology of canine distemper virus. In addition to canine distemper, measles and rinderpest virus, the genus Morbillivirus comprises peste-des-petits-ruminants virus of goats and sheep, dolphin/porpoise morbillivirus, and phocine distemper virus. Canine distemper virus has a broad host range; besides canids, infection has also been demonstrated in mustelids (ferrets, mink), raccoons, collared peccaries, non-human primates, seals, and felids, including lions, tigers, lynx, bobcat and even domestic cats. The signaling lymphocyte activation molecule (SLAM) is a receptor used by morbilliviruses to invade immune cells. Variations in species specificity and infection of “aberrant” species with canine distemper virus was historically thought to result from amino acid alterations in SLAM and/or the hemagglutinin (HA) protein that binds SLAM; however, recent studies suggest that variability of the hemagglutinin protein is less important in determining infectivity and pathogenicity in various host species than was previously believed. Regardless, CDV has emerged as a potentially devastating pathogen in certain wild felid populations.

Although morbilliviruses are notable for producing both intracytoplasmic and intranuclear viral inclusions, conference participants observed that, in this case, intranuclear inclusions were poorly discernible, possibly as a result of the decalcification process.

Contributing Institution: Department of Diagnostic Medicine and Pathobiology Kansas State Veterinary College of Veterinary Medicine 1800 Denison Avenue Manhattan, KS 66506 http://www.vet.k-state.edu/depts/dmp/index.htm

References: