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Department of Veterinary Pathology
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Conference Moderator: Dr. Matthew Starost, DVM, PhD, DACVP
National Institutes of Health
Bethesda, MD

CASE I – H-7645 (AFIP 3031560).

Signalment: ~30-year-old, male, rhesus macaque (*Macaca mulatta*), nonhuman primate.

History: Submitted for diagnostic workup were heart and lung tissues. Per the clinician, the animal was found lethargic with labored breathing and swelling of the ventral neck. Auscultation revealed harsh lung sounds and audible wheezing. There was a foul odor from the oral cavity with mucus and purulent material. Symptomatic treatment was unsuccessful and the monkey was euthanized.

Gross Pathology: At necropsy, the clinician found a pocket of purulent material in the ventral neck. The lungs were congested and most lobes had fibrous adhesions to the thoracic wall. The dorsal surfaces of the lungs contained several yellow/tan, 0.5-1.5 cm oval and slightly depressed foci that on sectioning were cavitated and gritty. Similar areas were found within the lung parenchyma. A small lung lobe was atelectatic, dark red, and firm. Coronary disease was suspected in the heart.

Histopathologic Description: Lung sections are characterized by dilated, chronically inflamed airways; the presence of parasites; and, pleural inflammation and fibrosis. Affected airways vary from 3-5 mm in width/length with lumens up to 2000 μ in diameter; have thickened walls (up to 500 μ) with mixed infiltrates of mononuclear cells (lymphocytes, macrophages, plasma cells), segmented cells (eosinophils, neutrophils), and/or macrophages containing golden-brown, anisotropic pigment; and, often contain the profile of a parasite (with jointed appendages) consistent with lung mites (presumably genus *Pneumonyssus*). Focally, this process involves the pleural surface with chronic inflammation and fibrosis. Peripheral to the latter,

the lung is congested, edematous, and occasional fibrin thrombi are observed within blood vessels.

Contributor's Morphologic Diagnosis: Lung: bronchiolitis/bronchiectasis, chronic-active, multifocal, severe with lung mites and pleural inflammation and fibrosis.

Contributor's Comment: Gross and microscopic lesions are consistent with the presence of lung mites (pulmonary acariasis). Although not confirmed in this case, lung mite infection in the rhesus and other macaques is usually attributed to *Pneumonyssus simicola*.[1] In addition to the severe chronic-active inflammatory process associated with the mites, adjacent lung tissues had areas of acute, severe pneumonia and vasculitis and sections of ventricular myocardium had mild cardiomyopathy (slides not submitted). Taken together, the lung lesions suggest a severe lung infection with secondary pneumonia and vascular problems. The role, if any, of the heart lesion could not be determined.

To our knowledge, lung mites are considered an uncommon finding in today's rhesus monkey colonies. Reported to occur in up to 100% of wild or imported rhesus monkeys, import restrictions and the routine use of anthelminthics (e.g., ivermectin) in colony health programs probably explain the lack of reports in recent years.[1] Also, the fact that the infection is usually subclinical and not a significant factor in colony management may account for the low reporting.

While subclinical disease is most common, secondary and severe infections can occur.[1] However, severely infected monkeys may not be detected until necropsy or may only develop coughing and dyspnea.[1,2] Exceptions to the latter scenarios in the rhesus are complications such as pneumothorax and pulmonary arteritis.[1] In other macaques, lung mite-induced dyspnea and pneumatocele have been reported in the pig-tailed macaque (*Macaca nemestrina*).[3,4] Massive infections leading to death have also been reported in the pig-tailed monkey, the douc langur (*Pygathrix nemaeus nemaeus*), and proboscis monkey (*Nasalis larvatus orintalis*).[1] Although we had access to only limited tissues from this animal, we believe this case may represent the exceptional scenario where lung mite infection and associated complications lead to death.

AFIP Diagnosis: Lung: Bronchiolitis, granulomatous and eosinophilic, multifocal, marked, with bronchiolectasis, abundant anisotropic yellow-brown mite pigment/excrement, and adult mites, etiology consistent with *Pneumonyssus simicola*, rhesus macaque (*Macaca mulatta*), nonhuman primate.

Conference Comment: Conference participants agreed that the lung mites in this case were most likely *Pneumonyssus simicola*. Several species of mites in the genus *Pneumonyssus* infect the respiratory system of Old World primates. *Pneumonyssus simicola* is recognized as the genus and species found in rhesus monkeys.[1]

The exact life cycle is unknown. It is believed that the entire life cycle can be completed in the lungs as all stages of *P. simicola* (adults, eggs, larvae) can be found there. Transmission is most likely by direct contact. Mites feed on host erythrocytes, lymph, and pulmonary epithelial cells. Infection rarely causes clinical disease in immunocompetent animals. Secondary infections may occur due to altered bronchiolar epithelium and impaired mucociliary clearance.[1] As pointed out by the contributor, clinical signs vary from none to clinically significant infections with heavy infestations resulting in coughing, sneezing, and dyspnea.

Typical gross findings include discrete, 1-7 mm in diameter, yellow or gray cystic foci ("mite houses") present throughout the lung parenchyma.[1]

Typical light microscopic findings include arthropods with a chitinized cuticle, jointed appendages, striated musculature, a body cavity, digestive tract, and reproductive structures; golden brown refractile mite pigment; granulomatous bronchiolitis and peribronchiolitis; alveolar emphysema; bronchiolar smooth muscle hyperplasia; and interstitial fibrosis.[1,5]

Conference participants briefly reviewed other parasites of the respiratory system to include those listed below.[1,6,7,8, 9]

NASAL PASSAGE/SINUS

1. *Oestrus ovis* (nasal bot) – sheep
2. *Linguatula serrata* (pentastome) – dogs
3. *Pneumonyssus caninum* (arthropod) – dogs
4. *Anatrichosoma* sp. (nematode) – nonhuman primates
5. *Halicephalobus deletrix* (nematode) – horses
6. *Syngamus laryngeus* (nematode) – cat, cattle
7. *Cephenemyia* sp. (arthropod) – wild cervids
8. *Rhinophagia* sp. (arthropod) – Old World monkeys

COMMON LUNGWORMS

1. *Metastrongylus* sp. – (bronchi, bronchioles) swine
2. *Protostrongylus rufescens* – (bronchioles) sheep, goats
3. *Muellerius capillaris* – (alveoli) sheep, goats

4. *Filaroides osleri* – (trachea, bronchi) dogs
5. *Filaroides milksi/hirthi* – (bronchi, bronchioles, alveoli) dogs
6. *Capillaria aerophila* – (trachea, bronchi) dogs, cats, foxes
7. *Syngamus trachea* – (trachea) birds
8. *Angiostrongylus vasorum* – (pulmonary arteries) dogs, foxes
9. *Angiostrongylus cantonensis* – (pulmonary arteries and capillaries) rats
10. *Dictyocaulus filaria* – (bronchi, bronchioles) sheep, goats
11. *Dictyocaulus viviparus* – (bronchi, bronchioles) cattle
12. *Dictyocaulus arnfieldi* – (bronchi, bronchioles) horses, donkeys
13. *Aelurostrongylus abstrusus* – (bronchioles, alveolar ducts) cats
14. *Otostrongylus circumlitis* – (bronchi, bronchioles) pinnipeds
15. *Parafilaroides decorus* – (bronchi, bronchioles) pinnipeds

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CASE II – 05-0314 (AFIP 3028754).

Signalment: 4-week-old Labrador Retriever, canine.

History: This puppy was unable to nurse, unable to defecate and had difficulty in breathing for 2 days. The clinical signs progressed to generalized flaccid paresis. The puppy was treated by antibiotics and prednisone with no improvement and then died one week after the appearance of the clinical signs. All other puppies in litter were normal.

Gross Pathology: No significant lesions were described by the referring veterinarian who performed the necropsy; however, the submitted formalin-fixed muscles had patchy white streaks.

Laboratory Results:
1. Immunohistochemistry for *Toxoplasma spp.* on muscle sections was positive.
2. Pure culture of hemolytic *E.coli* was isolated from the spleen and lung of this puppy.

Histopathologic Description: Affecting 80% of the submitted skeletal muscle sections, there was myofibrillar necrosis and fibrosis with a massive multifocal to coalescing infiltration of lymphocytes, histiocytes, plasma cells, and fewer neutrophils. Myriads of protozoal zoites (2-3 microns with no visible cyst wall, and present in aggregates of 4 to >100 zoites) were present amid the inflammatory cells. Both the liver and heart had random multifocal areas of necrosis characterized by cellular loss and aggregation of neutrophils. No significant lesions were present in the sections examined from lung, thymus, lymph node, kidney, spleen, and gastrointestinal tract. Brain and spinal cord were not available for examination.

Contributor's Morphologic Diagnosis: Skeletal muscles: Myositis, lymphohistiocytic, necrotizing, with muscle regeneration and myriad tachyzoites and protozoal cysts.

Contributor's Comment: The differential diagnoses for protozoal skeletal myositis in dogs include *Neospora caninum*, *Toxoplasma gondii*, and *Sarcocystis canis*. The immunohistochemistry was positive when muscle sections from the current case were stained for *Toxoplasma* sp. Toxoplasmosis caused by *Toxoplasma gondii* is one of the most common protozoal diseases affecting domestic animals. Felids are the only definitive host. Felids and other mammals act as intermediate hosts. Infective stages for both the final and intermediate hosts are the oocysts, which are produced only by felids, tachyzoites and tissue cysts are present in different

organs of the intermediate host particularly the skeletal muscles.[1] The infection is maintained between intermediate hosts by facultative homoxenous transmission without the need of oocyst production. Transplacental transmission is important in cats, sheep, and goats; however, the importance of transplacental infection in dogs is still unknown. Other minor modes of transmission include transfusion of fluids or transplantation of organs. Disseminated toxoplasmosis is a rare primary disease in adult dogs and is commonly seen in puppies and immunosuppressed adults and is characterized by lymphoplasmacytic to histiocytic inflammation virtually in any organ but particularly in brain, skeletal muscles, heart, and liver.[2] In addition to toxoplasmosis, the submitted puppy had a colisepticemia.

AFIP Diagnosis: Skeletal muscle: Myositis, pyogranulomatous, diffuse, marked, with myocyte degeneration, necrosis, regeneration, and numerous protozoal cysts, Labrador Retriever, canine.

Conference Comment: Most infections with *Toxoplasma* go unrecognized. Clinical manifestations of disease occur most frequently in young animals or the aged. In dogs, toxoplasmosis is often triggered by immunosuppression, such as that caused by canine distemper virus. Necrosis is the predominant histologic lesion. In disseminated infections lesions include multifocal necrotizing interstitial pneumonia, focal necrotizing hepatitis, myocarditis, splenitis, myositis, encephalitis, and ophthalmitis.[3,4]

Toxoplasma gondii can infect a wide variety of animals. New World monkeys and Australian marsupials are the most susceptible, whereas Old World monkeys, rats, cattle, and horses are highly resistant.[5] The most common expressions of *Toxoplasma* in cats are pneumonia, encephalitis, and pancreatitis. In sheep and goats, toxoplasmosis most commonly causes necrotizing cotyledonary placentitis, with characteristic 1-2 mm diameter white foci of inflammation, necrosis, and mineralization.[4,6] In humans, toxoplasmosis is a common complication in immunosuppressed patients and can cause disseminated and often fatal parasitemia in the human fetus.[2]

Conference participants discussed *Neospora caninum* as a differential diagnosis for this lesion. *Neospora* is nearly identical in appearance to *Toxoplasma* and induces similar lesions, particularly in the central nervous system (CNS). *Neospora* has a thicker cyst wall and cysts are restricted to the CNS whereas *Toxoplasma* cysts are thin-walled and can be found in multiple tissues. Although there are morphologic differences between the two protozoa, differentiation by light

microscopy is unreliable and electron microscopy or immunohistochemistry are required. Ultrastructurally, *Toxoplasma* tachyzoites are within parasitophorous vacuoles and have 4-6 rhoptries whereas *Neospora* tachyzoites do not develop within parasitophorous vacuoles and have numerous rhoptries.[4]

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CASE III – 04-0417-1 (AFIP 2936168).

Signalment: 8 month, male, Bengali, Cat.

History: This animal with growth delay (1.8 Kg on presentation time) presented with sudden prostration and anorexia. Clinical neurological exam revealed a severe proprioceptive deficiency with suspicion of central nervous system or cervical cranial affection. The cat was euthanized four days later and necropsy performed.

Gross Pathology: Brain: Severe dilatation of lateral ventricles (stars) and dilatation of the fourth ventricle (arrow) associated with thickening of meninges in the ventral surfaces of the brain (arrow head).
Laboratory Results: Magnetic Resonance imaging analysis: Severe hydrocephalus.
CSF analysis: Pleocytosis with predominance of polynuclear neutrophils.
Serological exam for FIP: positive at 1/16000.
Hemogram: Leucocytosis (70% polynuclear neutrophils; 30% lymphocytes).

Contributor's Morphologic Diagnosis: Cortex sections at the level of lateral ventricles: Severe pyogranulomatous periventriculitis characterized by a partial effacement of ependymal lining by a heavy infiltrate of histiocytes and lymphocytes associated with reactive astrocytes ("gemistocytes"). This lesion was closely associated with perivascular cuffing in the adjacent neuroparenchyma.

Slides are from various localizations: Size of the ventricular cavities varies with slides. Furthermore, some slides present edematous choroid plexus fragments with granulomatous infiltrate.

Contributor's Comment: Feline infectious peritonitis (FIP), first described in 1963 as a chronic fibrinous peritonitis, was identified in domestic as well as in wild *felidae* all over the world. This disease is due to a coronavirus that affects most frequently cats younger than 3 years of age.[1] Recent evidence supports the idea that FIP virus has evolved as a mutation of FECV (Feline Enteric Coronavirus), a common and not serious disease in the cat.[1,3]

FIP has been subdivided into two forms:
- the classical effusive form with peritoneal and/or pleural fluid effusions
- the dry form characterized by pyogranulomatous lesions in various visceral organs.

Clinical signs of the effusive form are chronic fever, anorexia, weight loss, depression and abdominal distention. The dry form is more chronic and frequently induces ocular signs and 25% of cats develop a neurologic form of the disease with spastic paresis, ataxia, nystagmus and balance loss.[2,4]

Gross lesions of FIP in the CNS may be subtle with thickening and opacity of meninges in the ventral surfaces of the brain and ventricular dilatation, usually of the fourth ventricle and less frequently lateral ventricles. Histopathologic lesions consist of meningitis, ependymitis, periventriculitis, choroiditis with dense infiltrate of lymphocytes, plasma cells, neutrophils and macrophages. Meningitis is generally more severe on the ventrocaudal surfaces of the brain and the inflammation may extend into cranial nerve roots as well as in the neuropil with perivascular cuffs and glial nodule formation. In the periventricular area inflammation is accompanied by

reactive astrocytes and accumulation of cellular debris may cause obstruction of the cerebrospinal fluid flow and then hydrocephalus.[2,4] FIP meningoencephalitis is one of the most common inflammatory disorders of the CNS in the cat.[4]
Physiopathology :
Once ingested or inhaled, FIP virus replicates in macrophages that travel to regional lymph nodes; a viremia results of active replication allowing virus-laden macrophages to be deposited in endothelium of blood vessels. If the cat cannot develop a cell mediated immune response, the effusive form develops accompanied by pyogranulomatous vasculitis. A partial cell mediated immune response can also occur allowing a slower viral replication and formation of classical granulomas observed in the dry form of the disease.[1]

The way of entry of the virus in the CNS is probably hematogenous via macrophages. There is no evidence of replication of the virus in vascular basement membranes or in the cells of the neuropil.[2] Mechanisms of the disease are primarily immune mediated, involving humoral and cell immunity with massive complement activation.[3,2] Apparently some antibody production occurs locally in the CNS in response to locally replicating virus.[2]

Remarks on FIP diagnosis:
Pre-mortem diagnosis is based on the leucocytosis with neutrophilia, mild to moderate non regenerative anaemia, and increased plasma protein concentration. CSF examination reveals elevated protein concentration and extensive pleocytosis. Serological analysis can be made (ELISA or IFA) but doesn't permit to distinguish safely virulent or avirulent strains. Similarly the use of RT-PCR for coronavirus doesn't allow distinguishing FIP from FECV. The combination of clinical signs, historical factors and laboratory values is important.[1]

Generally, post-mortem histopathological analysis allows one to obtain a conclusive etiological diagnostic.

AFIP Diagnosis: Brain, cerebrum: Ventriculitis and periventriculitis, granulomatous, diffuse, moderate, with lymphocytic perivasculitis, Bengali, feline.

Conference Comment: The contributor provides an excellent overview of feline infectious peritonitis virus. In addition to the slide variability addressed by the contributor, there was also more neutrophilic inflammation in some sections. The inflammatory process in cases of FIP meningoencephalitis is focused on the inner and outer surfaces of the CNS. Recognition of this surface-related pattern is useful in differentiating FIP from other forms of encephalomyelitis in the cat.[4] Recent

literature suggests that activated monocytes play a central role in the development of FIP vasculitis.[5]

Conference participants discussed the definition of vasculitis and what histomorphologic features must be present to diagnose a vasculitis. Many participants felt that there must be fibrinoid necrosis of vessel walls, inflammation, and/or apoptotic or necrotic cellular debris within a vessel wall to call a vasculitis. Evidence of damage to the vessel wall such as hemorrhage, fibrin, edema, and thrombi around and within the affected vessel lend support to the diagnosis of a vasculitis. Jubb & Kennedy states that "vasculitis is characterized by the presence of inflammatory cells with and around blood vessel walls with concomitant vessel wall damage as indicated by fibrin deposition, collagen degeneration, and necrosis of endothelial and smooth muscle cells."

Other Coronaviruses include those listed below.[7,8,9]

Bovine coronavirus (winter dysentery)	Bovine	Gastroenteritis, coronavirus implicated
Canine coronavirus	Canine	Enteritis
Feline coronavirus (FIP)	Feline	Peritonitis, pneumonia, meningoencephalitis, panophthalmitis; granulomatous vasculitis
Feline enteric coronavirus	Feline	Diarrhea in kittens
Mouse hepatitis virus (MHV)	Mouse	Hepatic necrosis, enteritis, encephalomyelitis; syncytia formation
Porcine transmissible gastroenteritis (TGE)	Porcine	Gastroenteritis
Porcine hemagglutinating encephalomyelitis virus	Porcine	Vomiting, wasting and encephalomyelitis (usually no diarrhea)
Porcine epidemic diarrhea	Porcine	Gastroenteritis (western Europe, similar to TGE)
Rat coronavirus	Rat	Rhinitis, tracheitis, pneumonitis in young
Rat sialodacryoadenitis virus	Rat	Sialodacryoadenitis, porphyrin released from damaged harderian gland, squamous metaplasia of ducts
Avian infectious bronchitis	Chickens	Tracheobronchitis, nephritis
Bluecomb (turkeys)	Turkeys	Enteritis, cyanosis of the comb
Rabbit coronavirus	Rabbits	Enteritis, myocarditis
SARS virus	Humans	Severe Acute Respiratory Syndrome
Epizootic catarrhal enteritis (ECE)	Ferrets	Profuse, green mucoid diarrhea in adults; thought to be a coronavirus

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CASE IV – 06-A-025 (AFIP 3031275).

Signalment: 6 years/308 days old adult female, rhesus macaque, *Macaca mulatta*, nonhuman primate.

History: This animal experienced a three kg weight loss since September 2005. She was removed from an outdoor corral for an unthrifty appearance, diarrhea and difficulty ambulating in January 2006. Physical examination revealed cachexia, abdominal distension, mild kyphosis, atrophy of the pelvic limb musculature and contracture of the joints. There was minimal response to supportive and therapeutic care. Humane euthanasia was performed and she was submitted for necropsy.

Gross Pathology: The animal was cachexic and there were no visible stores of subcutaneous or visceral adipose tissue. The mesenteric lymph nodes were

moderately enlarged. The mucosa of the small intestine was raised, thickened, rugose and exhibited a terry cloth appearance (Fig. 1). The cecum and colon were markedly dilated, flaccid and reddened and contained abundant green fluid feces (Fig. 2). The large intestinal mucosa was diffusely reddened with thickened mucosal folds. There was mild kyphosis and the medial condyles of both femurs were moderately eroded.

Laboratory Results: *Campylobacter coli* was isolated on one of two fecal cultures performed in January 2006. One of two fecal parasitology screens demonstrated flagellates. The remaining screen was negative.

Histopathologic Description: The lamina propria is diffusely expanded with an abundant amount of amorphous, acellular, pale eosinophilic material that widely separates the villous stromal cells and the intestinal glands. Villi are mildly and multifocally blunted and fused. Multiple lacteals are moderately dilated. There are scattered aggregates of low numbers of neutrophils in the villous tips.

Contributor's Morphologic Diagnoses:
Small intestine: Amyloid deposition, lamina propria, diffuse, severe with multifocal mild villous blunting and fusion, rhesus macaque (*Macaca mulatta*).
Mesentery: Atrophy, adipose tissue, diffuse, severe.

Contributor's Comment: The profound weight loss in this animal is attributed to severe amyloid enteropathy. The deposits stained light orange with the Congo red method and demonstrated green birefringence under polarized light (Fig 3). There were abundant deposits of amyloid in the lamina propria of the small intestine with minimal to moderate involvement of the stomach, cecum, colon, liver, spleen, adrenal gland, mesenteric lymph nodes, mammary gland, and renal medulla. A moderate, chronic-active, proliferative typhlocolitis was present. The amyloid deposits in the small intestine with consequent malabsorption of nutrients and protein loss and the typhlocolitis account for the emaciated body condition and diarrhea noted clinically. Underlying conditions that presumably led to systemic amyloidosis include typhlocolitis, osteoarthritis and spondyloarthropathy.

Amyloidosis is a heterogeneous group of diseases characterized by the extracellular deposition of insoluble protein in various tissues with consequent compromise of normal function. Ultrastructurally, the deposits are composed of protein fibrils assembled in antiparallel β-pleated sheets. The deposition of amyloid protein A (AA) occurs in reactive or secondary amyloidosis and is associated with infectious and noninfectious chronic inflammatory conditions. Its precursor, serum amyloid A (SAA) is an acute phase protein produced primarily by the liver.[1,11] Functions ascribed to this protein include a role in cholesterol transport and metabolism as well as both anti- and proinflammatory activities.[13]

The pathogenesis of reactive systemic amyloidosis is poorly understood. SAA is produced under the control of cytokines such as interleukin-1, interleukin-6 as well as tumor necrosis factor-α released during inflammation.[14] Increased levels of SAA are common with chronic inflammation but amyloid deposition usually does not occur. In individuals that do develop amyloidosis there is limited or defective proteolysis of SAA with formation and deposition of insoluble AA protein. Proposed mechanisms include failure of degradation due to excessive levels of SAA relative to enzyme, an intrinsic proteolytic enzyme defect or a structural anomaly in the SAA molecule making it resistant to degradation.[1] Pressure atrophy of surrounding tissue occurs with progressive accumulation of amyloid.

Reactive systemic amyloidosis is not an uncommon disease in rhesus macaques and has been reported in several species of nonhuman primates including common marmosets, squirrel monkeys, pigtail macaques, Celebes macaque, cynomolgus macaques, a stumptailed macaque, baboons, a mangabey and chimpanzees.[2-10,12,13] Underlying conditions include chronic enterocolitis, osteoarthritis, chronic vascular catheterization, and retroperitoneal fibromatosis associated with Type D retroviral infection.[3-5,8,10,12] The gastrointestinal tract, liver, adrenal gland, renal medulla and spleen are sites often affected. Lymph nodes, thyroid gland and gallbladder may also be affected.

Clinical signs are related to the site affected and the amount of amyloid deposited. They include weight loss, diarrhea refractory to treatment, hepatomegaly and splenomegaly. A protein losing enteropathy may be seen with enteric amyloidosis. Laboratory findings may include elevated levels of SAA, hypoproteinemia, hypoalbuminemia, hypergammaglobulinemia, and elevated liver enzymes with hepatic involvement.

Although gross lesions are often absent, the liver and/or spleen may be extraordinarily enlarged, pale, waxy and firm. Prominent splenic nodules may be observed on sectioned surface with white pulp involvement. The intestinal mucosa may be thickened and either pale or hyperemic.

Histologically, amyloid is an acellular, homogeneous to finely fibrillar, lightly eosinophilic extracellular material. AA amyloid deposits stain pale orange with the Congo red histochemical method and demonstrate green birefringence under polarized light. Typically, these deposits do not stain as prominently in nonhuman primates when compared to those in canine tissues.[3] In nonhuman primates, AA amyloid is most often deposited in the space of Disse in the liver, the lamina propria of the gastrointestinal tract, the corticomedullary junction of the adrenal gland, either the red or white pulp of the spleen and the renal medullary interstitium. The small intestine is the segment of the gastrointestinal tract most

often and severely affected. Other than marmosets, the renal glomeruli are rarely involved.[2-10,13] Progressive amyloid deposition results in atrophy of adjacent tissues.

AFIP Diagnosis: Small intestine, lamina propria: Amyloidosis, diffuse, marked, with moderate villar blunting and fusion, and lymphangiectasia, rhesus macaque (*Macaca mulatta*), nonhuman primate.

Conference Comment: The contributor provides an excellent overview of reactive systemic amyloidosis in nonhuman primates.

Amyloidosis has been classified several different ways to include the following:

1. Primary versus secondary
2. Systemic (generalized) versus localized
3. Combination of the above

Systemic amyloidosis is also divided into 1) primary amyloidosis (immunocyte dyscrasia) and 2) secondary amyloidosis (reactive systemic amyloidosis).[15]

Reactive systemic amyloidosis is the most common form of amyloidosis in animals with amyloid being deposited in the kidney, liver, spleen, and lymph nodes. The spleen is the most frequent site of amyloid deposition in systemic reactive amyloidosis and occurs in the periarteriolar lymphoid sheaths and red pulp. The most functionally important deposition of amyloid occurs in the renal glomeruli of aged dogs resulting in proteinuria.[15]

AL amyloid consists of immunoglobulin light chains, is monoclonal, and secreted by plasma cells in immunocyte dyscrasias. This is the most common form of amyloidosis in humans, but does not commonly occur in animals.[15]

Localized amyloidosis involves a single organ or tissue and occurs in the nasal vestibule or rostral portion of the nasal septum and turbinates of horses and in the pancreatic islets of cats.[15]

β-Amyloidosis involves the extracellular accumulation of amyloid-β protein (Aβ) and is characteristic of Alzheimer's disease in humans. Amyloid- β protein has also been identified in the brains of aged dogs with highest concentration in the frontal cortex.[15]

Contributor: Oregon National Primate Research Center, http://onprc.ohsu.edu

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