CASE I — 07L-1736 (AFIP 3066074).

Signalment: 6-week-old, female, Bulldog, canine

History: This animal is from a litter of 5 puppies which had recurrent diarrhea and chest problems from birth. Three siblings had died in a period of 9 days. Death was described as sudden, occasionally preceded by rigidity and vocalisation. The mother was fully vaccinated.

Gross Pathology: The heart was diffusely pale and moderately enlarged and a mild pericardial effusion was observed. The lungs were markedly and diffusely oedematous and the liver was severely congested.

Laboratory Results: Immunohistochemistry for canine parvovirus was performed on sections of myocardium, lung, stomach, small intestine, colon, liver, pancreas, gall bladder, spleen, thymus, and bone marrow. Positive immunolabelling was observed in the intranuclear inclusion bodies of the cardiac myocytes.

Histopathologic Description: Conference slides vary and include sections of left ventricle, septum and right ventricle but similar histological changes are consistently seen throughout.

There is moderate to severe, multifocal to coalescing, interstitial, predominantly lymphocytic and histiocytic infiltration with occasional scattered plasma cells and neutrophils, together with mild to moderate interstitial fibrosis. The myocardial fibers exhibit moderate diffuse anisocytosis and multifocal loss of striation, with cytoplasmic eosinophilia and occasional fragmentation. Multifocally, single, large (up to approximately 20x40 µm), homogeneous and occasionally stippled, basophilic, 

1-1 Heart, dog. Cardiomyocyte nuclei contain basophilic inclusion bodies which obscure and peripheralize chromatin (arrows). (H&E 400X)
mostly elongated, intranuclear inclusion bodies (fig. 1-1) are observed in myofibers. In the cells containing inclusion bodies, the nuclear chromatin is clumped at the nuclear membrane.

**Contributor’s Morphologic Diagnosis**: Heart, myocardium: Myocarditis, diffuse, moderate, lymphohistiocytic, necrotizing, subacute to chronic, with intranuclear inclusion bodies, Bulldog, canine.

**Contributor’s Comment**: Canine Parvovirus (CPV) is a non-enveloped single-stranded DNA virus grouped informally in the Feline Parvovirus subgroup of the genus Parvovirus (*Parvoviridae* family).6,16

*Parvoviridae* are amongst the smallest DNA viruses, the virion being 18 to 26 nm in diameter, and are composed entirely of protein and DNA.11 The lack of fatty components, typically present in viral envelopes, makes these viruses stable under diverse environment conditions and difficult to eliminate through disinfection. They can however, be inactivated by bleach, formalin and sunlight.7

The host range is one of the widest, the subfamily Parvovirinae infecting vertebrates, including humans and the subfamily Densovirinae infecting insects.

CPVs infect domestic dogs and several species of wild canids, including coyotes, bush dogs, gray wolves, raccoon dogs and manged wolves. Presently two autonomous parvoviruses are known to infect dogs: CPV type 1 and CPV type 2.

CPV type 1 was initially named Minute Virus of Canines and was first identified in 1970.1 It was proven to cause enteritis and diarrhoea in neonatal canines. It appears to be highly related to the Bovine Parvovirus14 and is antigenically unrelated to CPV type 2. To date, only few cases have been reported.

On the other hand, CPV type 2 appeared as a pandemic disease and presented characteristics of an epidemic infection affecting dogs of all ages. Although there is no specific data to support this, we can assume from the low mortality rate, that death was mostly restricted to canines less than 4 months old.3 It was first detected in 1978 but is estimated to have emerged up to 10 years before.10

CPV type 2 is thought to result from mutations of feline panleukopenia parvovirus (FPV), with which it shares more than 98% of the DNA sequence4 or from a closely related carnivore parvovirus.12 CPV type 2 was found to be unable to infect cats although it was able to replicate *in vitro* in feline cells.13 As opposed to this, FPV was found able to replicate *in vivo* in the canine thymus but unable to replicate *in vitro* in canine cultured cells.

The CPV type 2 strain was soon replaced, worldwide, by two new lineages: CPV2a, identified in 1980, that later gave rise to CPV2b, identified in 1984, both with the added ability to replicate in cats and produce clinical signs in experimentally infected cats.12,18 In Italy, Vietnam and Spain, a third type, CPV2c has been identified.10 This antigenic drift is accompanied by successive replacement of prevalent strains by newer serotypes.13 This is exemplified by the gradual disappearance of CPV2b from the dog population in Italy6,10 and the replacement of CPV2a by CPV2b in the UK.5

The mutations occur at the level of the VP1/VP2 gene (encoding capsid proteins) and the new serotypes have an improved binding ability to its receptor, the canine transferrin receptor.17

CPVs require host cells to be in the S-phase to replicate as they are unable to induce it. They replicate within the nuclei of infected cells and are highly dependent on the cellular function.11

Pathology and clinical signs are dependent on the time of infection and which cells are in a highly mitotic rate at that particular moment within the host. Infection occurs oronasally and disease develops after 3 to 10 days of incubation.6 After faeco-oral infection, the virus is taken up by the epithelium over the tonsils and Peyer’s patches. In 1 to 2 days after experimental inoculation, the virus can be found in the mesenteric lymph nodes. Further dissemination of virus particles into other central or peripheral lymphoid tissues occurs via infected lymphoblasts. Following the lysis of infected cell, viruses are released and contribute to elevate the viremia which is only terminated if neutralising antibodies appear, typically 5 to 7 days post infection. Moderate pyrexia usually occurs.2

If the infection takes place up to two weeks postnatally and the puppies do not have sufficient neutralising antibodies, nonsuppurative myocarditis is the most common condition. On the other hand, if infection occurs later than these two weeks, due to the fast replication of the epithelia of the small intestines and bone marrow granulopoiesis, hemorrhagic gastroenteritis with lymphoid depletion is the pathological picture. The two forms of the disease rarely occur at the same time in an individual
or group of animals. When nonsuppurative myocarditis occurs, it is usually detectable between the third and eighth week of life, but can be asymptomatic until animals are six months old. Puppies frequently succumb to sudden death but can also present symptoms of congestive heart failure due to myocardial scarring or conduction failure. Grossly, the main findings are cardiomegaly and lesions in the myocardium, more pronounced in the left atrium and left ventricle. Pericardial and pleural effusions, ascites and hepatomegaly can also be observed. In the myocardium lesions are pale and streaky and often accompanied by multifocal petechial. Microscopically, single, homogeneous, basophilic or amphophilic, round to elongated, intranuclear, Feulgen-positive inclusion bodies are observed. The chromatin is clustered at the nuclear membrane. Inclusion bodies are more frequent in late incubation, before extensive exfoliation (in the intestinal form) or infected cell lysis. In animals 4 to 7 weeks old, separation of the thin myocytes by extracellular edema, histiocytes, fibroblasts and fibrous tissue is seen. Myocytes appear granulated and with fragmented cytoplasm. In animals 6 to 9 weeks old, inflammation is more severe and mainly lymphoplasmacytic. In juvenile animals, 14 to 24 months old, inflammation is milder, histiocytes and fibroblasts are more frequent, and fibrosis more extensive.

AFIP Diagnosis: Heart: Myocarditis, lymphohistiocytic, chronic, multifocal, moderate, with necrosis and loss and basophilic intranuclear inclusion bodies, Bulldog (Canis familiaris), canine.

Conference Comment: The contributor gives an excellent review of canine parvovirus type 2. Canine parvovirus requires actively dividing cells for replication. Lesions of canine parvovirus, such as those of intestinal crypt cells and lymphoid cells, reflect this dependence on actively dividing cells (radiomimetic). The viral genome does not include DNA polymerase, so the virus depends on DNA polymerase expressed during the S phase of the cell cycle for transcription of viral DNA.

Intranuclear inclusions are usually observed late in the incubation phase and prior to the lysis or exfoliation of the cells. Therefore it is possible that intranuclear inclusions may not be seen in samples submitted for histopathology.

Other potential causes of myocarditis in canines include:

Viral: Morbillivirus (canine distemper)
Parasitic: Neo spora caninum, Trypana soma cruzi, Toxoplasma gondii
Rickettsial: Rickettsia rickettsii, Ehrlichia ca nis, Ba r-тонella elizabethae
Fungal/Algae like: Prototheca sp.
Spirocheatal: Borrelia burgdorferi

Other parvoviruses in animals include porcine parvovirus (SMEDI); feline parvovirus (feline panleukopenia); rat parvovirus (Kilham rat virus); minute virus of mice; goose parvovirus; and two genetically and antigenically distinct parvoviruses in mink (mink enteritis virus, which causes similar lesions as feline parvovirus, and Aleutian mink disease virus, which causes immune complex glomerulonephritis and arteritis).

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References:

CASE II – 1 (AFIP 3065544).

Signalement: Juvenile (approximately 8-12 months), Male intact, DSH, Felis catus, cat

History: This was a free living cat from a cattery of the city of Milan. The cat was found dead and sent for a full necropsy.

Gross Pathology: Elevated numbers of fleas were found in the hair coat. The cat was anemic. All central metacarpal and metatarsal pads were swollen (figs.2-1 and 2-2) and softened. The chin had grossly visible comedoes consistent with feline acne.

In the abdominal cavity renal lipidosis and hyperemia of most organs was evident.
In the thoracic cavity severe pulmonary edema and severe constrictive cardiomyopathy were present.

**Laboratory Results:** None

**Histopathologic Description:** The normal microanatomical structures of the dermis and the underlying adipose tissue are variably effaced to completely obscured by a perivascular to diffuse infiltrate of mature plasma cells. Variably abundant Mott cells (fig. 2-3) with Russell bodies and rare binucleated plasma cells can be seen. Occasional mature small lymphocytes, neutrophils and macrophages are also present.

The epidermis is hyperkeratotic, irregularly hyperplastic and occasionally characterized by infiltration of plasma cells. Superficial erosion or serocellular crusting characterizes some of the sections.

Additional microscopic findings:
- Hepatic lipidosis, diffuse membranous glomerulonephritis, renal tubular hyaline casts and diffuse tubular lipodosis.

**Contributor's Morphologic Diagnosis:** Severe multifocal to diffuse chronic lymphoplasmacytic pododermatitis.

**Contributor's Comment:** Feline plasma cell pododermatitis is a rare disease of unknown pathogenesis. It is clinically characterized by soft and spongy swelling of multiple foot pads. Breed, age, or sex predilections have not been noted. The central metatarsal and metacarpal pads are most consistently involved. The lesion is generally painless but lameness may develop secondary to ulceration and extensive hemorrhage. The cause and pathogenesis of feline plasma cell pododermatitis are still unknown however, the marked plasma cell infiltrate, consistent hypergammaglobulinemia and response to immunosuppressive (i.e. glucocorticoids) or immunomodulating (i.e. tetracyclines) therapy suggest an immune dysfunction. In some cats concurrent plasmacytic stomatitis, renal amyloidosis or immune-mediated glomerulonephritis have been reported. In some cases, spontaneous remission of the lesions occurs, whereas in others there is a seasonal exacerbation of the disease. Recurrence in warm weather may support an allergic origin. Doxycycline monohydrate has been reported to produce partial or complete clinical remission in more than half of the cases. The response of feline plasma cell pododermatitis to doxycycline is possibly due to its immunomodulatory effects, but since doxycycline has also antibacterial activity an infectious etiology has also been suggested. In a recent study, no infectious agent has been demonstrated by anti-BCG immunohistochemistry and by PCR assays for *Bartonella* spp., *Ehrlichia* spp., *Anaplasma phagocytophilum*, *Chlamydophila felis*, *Mycoplasma* spp., *Toxoplasma gondii*, and Feline herpesvirus 1 (FHV-1), further supporting the non-

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2-1 Footpad, cat. The metacarpal pad is diffusely swollen.
2-2 Footpad, cat. The metacarpal pad is diffusely swollen.

*Photographs courtesy of the Dipartimento di Patologia Animale, Igiene e Sanità Pubblica Veterinaria, Sezione di Anatomia Patologica e Patologia Aviare, Facolta’ di Medicina Veterinaria, Milano, Italy*  
[http://www.anapatvet.unimi.it](http://www.anapatvet.unimi.it)
infectious hypothesis. A possible link between feline plasma cell pododermatitis and concurrent feline immunodeficient virus (FIV) infection was suggested in one study, but the role of the virus remains controversial. Plasma cell pododermatitis has been also treated with wide surgical excision of the affected footpads, suggesting that other factors are probably involved.

Histologically, lesions are characterized by large numbers of plasma cells, occasionally in a predominantly perivascular pattern. The dermis and often the underlying adipose tissue of the pawpads are diffusely infiltrated with plasma cells. Russell body-containing plasma cells (Mott cells) are often conspicuous. Binucleated plasma cells and mitoses have also been described. The epidermis is acanthotic with variable erosion, ulceration, and exudation. Neutrophilic infiltration is variable, but neutrophils can be up to 50% of the infiltrate and their presence is not dependent upon ulceration. Eosinophils are rare. Edema of the dermis, deep perivascular tissue, or interlobular septa of the fat pad may be seen. Blood vessels are often prominently dilated and congested, and hemorrhage may be present.

AFIP Diagnosis: Footpad: Pododermatitis, plasmacytic, chronic, diffuse, marked with fibrosis, domestic short hair (Felis catus), feline.

Conference Comment: There is slide variation with multifocal erosions and/or ulcerations in some sections but not in others, as well as variable amounts of fibrosis.

Mott cells are plasma cells that contain large eosinophilic, amorphous globules (Russell bodies) within their cytoplasm. These Russell bodies are composed of immunoglobulin (g globulin). Characteristic features of plasma cells on a transmission electron micrograph include an eccentric nucleus, alternating areas of electron dense heterochromatin, and electron lucent euchromatin forming a “cart-wheel” pattern, a prominent Golgi apparatus (the “perinuclear hol” seen in light microscopic section), abundant rough endoplasmic reticulum (cytoplasmic basophilia in light microscopic section), and few mitochondria.

Conference participants discussed the concurrent findings of plasmacytic stomatitis, immune-mediated glomerulonephritis, and renal amyloidosis that are occasionally seen in animals with plasmacytic pododermatitis. AA amyloid (reactive systemic amyloidosis) is the most common form found in animals, where AL amyloid (Immunoglobulin-derived amyloidosis) is the most common form in humans. In cats, amyloid in the kidney is most commonly deposited in the interstitial spaces of the medulla with relative sparing of the glomerulus. In most other animals, amyloid is primarily deposited in the glomerulus. However, in familial amyloidosis, the amyloid is primarily deposited in the renal medullary interstitium in the Shar Pei dog and the glomerulus in the Abyssinian cat, while it is primarily deposited in the liver in Siamese cats.

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http://www.anapatvet.unimi.it

References:
4. Dias Pereira P, Faustino AM: Feline plasma cell podo-

CASE III – 04-2071 (AFIP 3063516).

Signalment: 5-year-old, female Quarter horse

History: Large (15 cm diameter), ulcerative skin lesion on ventral midline

Gross Pathology: This 15 cm diameter, ulcerated, crater-like mass in the skin has a 3 cm thick fibrous wall extending through the subcutis. Within the ulcerated surface, 1 mm yellow granules are seen (kunkers) (fig. 3-1)

Laboratory Results: Pythium insidiosum was cultured from the cutaneous wound and the presence of P. insidiosum DNA was confirmed by PCR

Histopathologic Description: The mass is mostly fibrovascular connective tissue containing a diffuse inflammation of eosinophils, lymphocytes and plasma cells. Distinct foci of coagulative necrosis (fig. 3-2) are present circumscribed by a thin rim of macrophages. Within the necrotic foci are hyphae (fig. 3-3) that are negatively stained and show only a clear space outlined by the hyphal wall. The hyphae are 10 microns in width with non-parallel sides and rare septation. A Gomori’s methenamine silver (fig.3-4) stain outlines the hyphal wall.

Contributor’s Morphologic Diagnosis: Skin: chronic, ulcerative and fibrotic dermatitis with multifocal caseous granulomas and intralesional hyphae

Contributor’s Comment: The gross appearance, location of the lesion, and the hyphae within the lesion are most consistent with an infection by Pythium insidiosum. The organism was cultured from the lesion and confirmed with PCR. Pythium is a water-born organism classified as an Oomycete in the kingdom Protista. The organism requires a water environment with decaying vegetation to maintain its life cycle and temperatures between 30 C and 40 C for reproduction. Infective zoospores are produced and invade damaged plant or animal tissue. Animals acquire the infection with prolonged exposure to freestanding water containing the Pythium organism.

Cutaneous disease in horses is the most common infection seen in animals, but infection is reported in many other animal species and in other locations, such as the intestinal and respiratory tracts. Cutaneous lesions usually occur on the distal extremities or ventrum, areas most likely to be in contact with stagnant water.
The zoospores produce an ulcerative lesion that rapidly expands to a large mass of granulation tissue containing draining sinus tracts. Distinct yellow to tan masses, 2-10 mm in diameter, form within the sinus tracts and are known as “kunkers”. Kunkers represent areas of tissue necrosis containing hyphae and necrotic eosinophilic inflammation.

**AFIP Diagnosis:** Haired skin: Dermatitis and panniculitis, pyogranulomatous and eosinophilic, focally extensive, severe, with ulceration, vasculitis, and few hyphal structures, Quarter Horse (*Equus caballus*), equine.

**Conference Comment:** There is significant slide variation with some sections having prominent vasculitis with fibrin thrombi.

*Pythium insidiosum* and *Lagenidium* sp. are aquatic dimorphic water molds of the kingdom Protista. *Lagenidium* sp. have only been described in dogs. The infective stage of pythium is a biflagellate zoospore that is attracted chemotactically to injured tissue. Upon contact with host tissue the zoospores lose their flagellae and form germ tubes to allow penetration and invasion of tissue.

Histologic features of pythiosis are granulomatous inflammation with foci of liquefactive necrosis and extensive fibrosis with eosinophilic coagula. Circulating monocytes are recruited from the circulation by several chemotactic stimuli such as C5a, TGF-α, and platelet derived growth factor. The tissue macrophages are then activated primarily by IFN-γ, or by endotoxin.

*Pythium* sp. stain well with GMS but do not stain well with PAS. Fungal hyphae or hyphal-like structures are distinctive between various entities; the key diagnostic features are provided in table 1.

Eosinophils are a prominent feature of equine pythiosis. Residents discussed the four primary differentials for eosinophilic and granulomatous dermatitis in a horse:

1. **Pythiosis** – Hyphal-like structures, negative images on H&E that are highlighted with GMS stain, necrotizing vasculitis
2. **Habronema** – Nematode larvae within eosinophilic granulomas
3. **Mast cell tumors** – Monomorphic population of mast cells surrounding eosinophilic granulomas
4. **Eosinophilic collagenolytic granulomas** – Usually centered on collagen bundles

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3-2 Subcutis, horse. Eosinophilic granuloma. (H&E)

3-3 Subcutis, horse. Multifocally, the granulomatous inflammation is admixed with the outlines of hyphal structures with non-parallel walls and rare septation. (H&E)

Photomicrographs courtesy of the College of Veterinary Medicine, Virginia Tech, Blacksburg, VA, 24061

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CASE IV - Case 1 (AFIP 3027389).

Signalment: Feline, Domestic shorthair cat, 5 years, neutered male

History: The cat had a subcutaneous, mobile, non-painful mass located in the interscapular region, which was surgically excised and submitted for histopathological evaluation. It was reported that the cat had been previously vaccinated in this area including administration of a rabies vaccine.

Gross Pathology: None available

Laboratory Results: None available

<table>
<thead>
<tr>
<th>Species</th>
<th>Hyphael type</th>
<th>Septate</th>
<th>Width</th>
<th>Branching</th>
<th>Walls</th>
<th>Misc</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Aspergillus sp</em></td>
<td>Hyphae, +/- fruiting bodies</td>
<td>Regularly septate</td>
<td>2.5-4.5 um</td>
<td>Acute angle, dichotomous</td>
<td>Parallel walls</td>
<td>Conidia not seen in tissue</td>
</tr>
<tr>
<td><em>Candida sp.</em></td>
<td>Hyphae, pseudo-hyphae &amp; budding yeast</td>
<td>septate</td>
<td>3-6 um</td>
<td>Irregular branching</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pseudallescheria boydii</em></td>
<td>Hyphae with conidiophores</td>
<td>septate</td>
<td>5 um</td>
<td>Less acute, highly branching, intertwined</td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Pythium insidiosum</em></td>
<td>Hyphal like structures</td>
<td>Rarely septate</td>
<td>2-9 um</td>
<td>Irregularly branching</td>
<td>Non-parallel</td>
<td>Kunkers or leeches</td>
</tr>
<tr>
<td><em>Zygomycetes</em></td>
<td>May occur as 5-30um chlamydoconidia</td>
<td>Few septae</td>
<td>3-25 um</td>
<td>Non-dichotomous irregular branching</td>
<td>Non-parallel</td>
<td>Mucor sp., Basidiobolus sp., Rhizopus sp.</td>
</tr>
</tbody>
</table>
Contributor’s Comment: The tumor was diagnosed as a vaccine-associated fibrosarcoma based on the reported location in the interscapular region, the history of previous vaccine injections in this area together with the typical microscopic features characteristic of this type of fibrosarcoma. Microscopic features of vaccine-associated fibrosarcomas include subcutaneous location, peripheral lymphocytic aggregates, intraliesional large histiocytes with intracytoplasmic bluish-grey material and areas of micro-cavitation.2,8

Feline vaccine-associated sarcomas (FVAS), also known as post-vaccine and vaccine-induced sarcomas, are most commonly associated with the administration of killed feline leukemia (FeLV) and rabies vaccines.11,15 The tumors are located in the subcutis of the common vaccination sites e.g. dorsal neck, interscapular region, dorso-lateral thorax, hindleg and dorsal lumbar region.3,7,8 The most common type of vaccine-associated sarcoma is the fibrosarcoma8, which was observed in this case. Other sarcomas which have been reported in a similar setting include rhabdomyosarcomas 8, osteosarcomas 8, chondrosarcomas8, malignant fibrous histiocytomas and myofibroblastic sarcomas.5

Fibrosarcomas are composed of spindle cells arranged in interlacing bundles, are located in the dermis and/or subcutis and are often circumscribed, but can have infiltrative margins. In vaccine-associated fibrosarcomas, spindle cells are admixed with histiocytoid cells and scattered multinucleated giant cells.8,16 Microscopic features differentiating feline vaccine-associated fibrosarcomas from

Histopathologic Description: Haired skin; The subcutis contained a well-demarcated, unencapsulated mesenchymal tumor composed of interlacing streams and bundles of neoplastic spindle cells, separated by fibrovascular stroma. The neoplastic cells had indistinct borders and a scant amount of pale eosinophilic cytoplasm. Most neoplastic cells contained a single, ovoid to elongated, vesicular nucleus with one to several, prominent basophilic nucleoli. Anisocytosis, anisokaryosis and cellular pleomorphism were moderate. Mitoses (fig. 4-1) ranged from 2-6 per high power dry field. Scattered multinucleated neoplastic cells were observed. Multifocal nodular aggregates of lymphocytes and fewer plasma cells were present at the tumour periphery, located mainly perivascularly, and also in the adjacent subcutis. Clustered macrophages (fig. 4-2), which contained intracytoplasmic bluish-grey granular material (interpreted as possible phagocytosed vaccine adjuvant) were present in the tumour, at the tumor margin and within the deeper subcutis.

In some sections, the tumor contained poorly defined, variably-sized irregularly-shaped cystic cavities. The cystic cavities contained eosinophilic material, cellular debris, foamy macrophages, mildly basophilic fluid and/or red blood cells.

Contributor’s Morphologic Diagnosis: Haired skin, subcutis; Fibrosarcoma with nodular lymphocytic and histiocytic infiltrates and presence of bluish-grey material within intralesional histiocytes (suspected vaccine-associated sarcoma)

4-1 4-2

4-1 Subcutis, cat. The neoplastic cells have a high mitotic rate (arrows). (H&E 400X)
4-2 Subcutis, cat. Infiltrating macrophages often contain intracytoplasmic, amphophilic granular material interpreted to be vaccine material (star). (H&E 200X)
non-vaccine associated fibrosarcomas include prominent inflammation (peripheral lymphocytic aggregates), presence of large histiocytic cells with intracytoplasmic bluish-grey material and areas of cavitation. In comparison to nonvaccine-associated fibrosarcomas, vaccine-associated fibrosarcomas are considered to have a higher degree of cellular pleomorphism and more inflammation. The bluish-grey intrahistiocytic material contained aluminum by electron probe x-ray microanalysis. Aluminium hydroxide is a common adjuvant used in killed feline leukemia (FeLV) and rabies vaccines. In feline VAS, a positive correlation was observed between increased number of neoplastic multinucleated giant cells and higher tumor grade, whereas the tumor grade was not influenced by the degree of inflammation.

The average age of cats with vaccine-associated fibrosarcoma is younger (with a median age of 8 years) than the age of cats affected by non-vaccine associated fibrosarcomas (with a median age of 11 years). Feline vaccine-associated fibrosarcomas are locally invasive and aggressive with a high rate of local recurrence and more rare metastases to draining lymph nodes, mediastinum and lungs.

Although the exact pathogenesis of vaccine-associated sarcomas is unknown, an association between persistent antigenic stimulation, chronic inflammation and/or wound healing and neoplastic transformation of primitive mesenchymal cells resulting in soft tissue sarcomas is suspected.

After subcutaneous injection of rabies vaccine, focal granulomatous injection-site reactions often with central necrosis, peripheral lymphocytic aggregates and presence of globular grey-blue material within the cytoplasm of some macrophages have been reported. The growth factors FGF-b and TGFα, which are involved in wound healing and neoplastic transformation of mesenchymal cells, are expressed by tumor cells in feline VAS. Based on ultrastructural and immunohistological studies, myofibroblasts which are involved in wound healing, have been identified in feline VAS.

Platelet-derived growth factor (PDGF) plays a role in the migration and proliferation of fibroblasts. By using VAS cell lines, it was shown that neoplastic cells of VAS express the Platelet-derived growth factor receptor (PDGFR-β) and that inhibition of this receptor inhibited cell growth. Mutations of the tumor suppressor gene p53, which are genomic alterations involved in tumorigenesis, have also been identified in feline VAS. In addition, over-expression and altered expression of the P53 protein, which is most commonly caused by mutation of its gene, have been detected in feline VAS.

Feline vaccine-associated sarcomas and feline posttraumatic ocular sarcomas are similar in morphology and pathogenesis: both tumors can be composed of a spectrum of sarcomas suspected to arise within a background of persistent inflammation or wound healing.

Sarcomas associated with vaccination sites have also been reported in ferrets and dogs. Microscopic features of these tumors are similar in all species.

AFIP Diagnosis: Haired skin, subcutis: Fibrosarcoma, domestic short hair (Felis catus), feline.

Conference Comment: The contributor provides a thorough overview of feline vaccine-associated sarcomas. Conference participants discussed the cell cycle as well as the four classes of regulating genes (growth promoting genes, growth inhibiting tumor suppressor genes, genes that regulate apoptosis, and genes involved in DNA repair) and how defects in any of these genes may lead to uncontrolled cellular proliferation and tumorigenesis.

Sarcomas in cats have also been associated with subcutaneous administration of long acting drugs and with the presence of foreign materials, such as non-absorbable suture or microchips. Ocular sarcoma may develop following ocular trauma.

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References:
6. Hendrick MJ, Dunagan CA: Focal necrotizing granulo-