**CASE I:** T2319/13 (JPC 4035545).

**Signalment:** Juvenile male castrated domestic shorthair cat (*Felis catus*).

**History:** A juvenile stray cat was found in neglected condition in the spring of 2012. The animal had diarrhea and an ulcerative stomatitis as well as many endoparasites and a marked ectoparasitosis (fleas and mites). Serological testing revealed an infection with feline lentivirus (FIV virus). Kept in an animal shelter, the condition of the cat improved with still occasional episodes of stomatitis. In summer 2012, a pedunculated mass on a forepaw was removed surgically. In spring 2013, the cat showed severe facial dermatitis, otitis, and the mass at the paw had recurred. Suspecting a malignant neoplasm, the tumor tissue, including the claw, was resected and submitted for histopathological examination.

1-1. Footpad, cat: A polypoid mesenchymal neoplasm arises from the haired skin and pawpad. (HE 0.63X)

1-2. Footpad, cat: The moderately cellular neoplasm is composed of spindle cells arranged in vague bundles. The overlying epithelium is moderately hyperplastic and forms deep rete ridges. There is mild orthokeratotic hyperkeratosis overlying the neoplasm. (HE 38X)
**Gross Pathology:** A 2.5 x 2 x 1.5 cm mass close to a claw, partially covered by skin, was submitted. The mass had an irregular cauliflower-like surface. The consistency was firm and the color on the cut surface was grey-white throughout.

**Laboratory Results:** Detection of papillomaviral DNA (PCR): positive
[Institute of Hygiene and Infectious Diseases of Animals, Justus Liebig University Giessen]
Detection of FeSarPV (PCR): positive
[Institute of Virology, Justus Liebig University Giessen]

**Histopathologic Description:** Skin, claw: Protruding from the superficial dermis and elevating the overlying epidermis, there is a moderately cellular, well-demarcated, lobular and pedunculated, expansively growing, unencapsulated neoplasm composed of spindle cells arranged haphazardly in interweaving bundles and streams within moderate amounts of collagen and sparse vessels. Neoplastic cells are spindle shaped, have indistinct cell borders, and a moderate amount of fine fibrillar, pale eosinophilic cytoplasm. Nuclei are oval to elongated with finely stippled, occasionally vesicular chromatin and a single, variably distinct nucleolus. Mitotic rate is very low (<1 per 10 high power fields). Cells show mild anisocytosis and anisokaryosis. Occasionally, neoplastic cells are arranged perpendicular to the dermal-epidermal interface. Interspersed within the spindle cells, there are moderate numbers of well-differentiated mast cells (3-4 per high power field). The overlying epidermis is hyperplastic with occasional papillary projections, acanthosis and spongiosis, elongated, thin, often branching rete ridges, and moderate orthokeratotic and parakeratotic hyperkeratosis.

**Contributor’s Morphologic Diagnosis:** Skin and claw: Feline sarcoid, feline, (*Felis domesticus*).

**Contributor’s Comment:** Feline sarcomas are also known as feline fibropapillomas. They most often occur in young male cats at various sites of the skin (e.g. pinna, lip, nose, digits, tail, gingiva). They can be ulcerated and cats can harbor one or several of these tumors. Recurrence often occurs;
metastasis has not yet been described. Feline sarcoïds share many similarities with sarcoïds in equine species regarding their etiology, clinical outcome, morphology, and prognosis.

Different papillomaviruses are suspected to be responsible for feline sarcoïds. The feline sarcoïd associated papillomavirus (FeSarPV) is similar to BPV-1, OvPV-1 and BPV-2. The genome of FeSarPV shows high homology with the genome of papillomaviruses of different ruminants. Some of these papillomaviruses are classified as members of the genus \textit{Deltapapillomavirus}. In contrast, the host specific papillomaviruses of cats, causing papillomatous plaques and real papillomas, are members of the genus \textit{Lambdapapillomavirus}. Infection of horses or cats by ruminant papillomaviruses is therefore regarded as cross-species papillomavirus infection.

For a recent classification of animal papillomaviruses, see Rector and van Ranst, 2013.

Sarcoïds are also described in lions. A possible mode of infection of large felids may be the consumption of bovine carcasses that had not been skinned.

Viral papillomas caused by feline papillomavirus (FdPV-1) are rarely found in domestic cats. These lesions are most likely associated with different forms of immunodeficiency in stray cats often in association with FIV infection. Feline papillomatous plaques, often caused by FdPV-2, sometimes undergo malignant transformation to squamous cell carcinoma (SCC). In one report, Human papillomavirus type 9 was identified using molecular biology.

Predisposing factors of feline sarcoïds are the behavior of rural cats. Contact with ruminants is occasionally mentioned. Numerous cases of sarcoïds are reported from areas with dairy industry (e.g. New Zealand, Minnesota). However, many interspecies contacts or modes of virus transmission are possible. A recent study demonstrated detection of feline sarcoïd PV genome sequences within different bovine skin samples.

Additional factors that favor the development of sarcoïds in cats are in discussion, for example, trauma. Interestingly, as in the presented case, FIV infection is reported in cases of feline sarcoïds and can play a role in the pathogenesis of the disease.

Tumors most often occur in young male cats. They are solitary or multiple skin nodules that measure up to 2 cm and can be pedunculated or ulcerated. Predilection sites are the skin at the ears, lips, tail or paws. Their consistency is firm.

Histomorphology of feline sarcoïds is identical to equine sarcoïds. Characteristically they show proliferating fibroblasts covered by hyperplastic epidermis. Differentials are fibrosarcoma, histiocytic sarcoma, other spindle cell sarcomas, peripheral nerve sheath tumor and amelanotic melanoma.

Feline sarcoïds often show local recurrence after surgery. Often, relapses show a marked increase in growth rate.

The presented case shares most of the characteristics described for that entity. Three months after surgery, the health status of the cat was good, and there were no signs of tumor recurrence.

\textbf{JPC Diagnosis:} Haired skin and footpad: Feline fibropapilloma (sarcoïd).

\textbf{Conference Comment:} Papillomavirus (PV) belongs to the family \textit{Papillomaviridae} (formerly \textit{Papovaviridae}); it is a non-enveloped, icosahedral virus with double stranded DNA that is resistant to high temperatures, low pH, lipid solvents and detergents. Infection occurs via direct/indirect contact with entry through cutaneous abrasions, and virus replication is intimately linked to the growth and differentiation of epidermal and mucosal squamous epithelial cells. Papillomaviruses are divided into 16 genera (Alpha, Beta, Gamma, Delta, Epsilon, Zeta, Eta, Theta, Iota, Kappa, Lambda, Mupa, Nupa, Xipa, Omikron and Pipapapillomvirus) on the basis of DNA sequence/genome, host range and biological properties. The most important genera in veterinary medicine include the following.
• **Alpha** (α): Oncogenic “high risk” mucosal types that cause benign mucosal/cutaneous lesions
• **Beta** (β): Cutaneous PVs that rarely cause lesions without immunosuppression
• **Delta** (δ): Cause benign fibropapillomas in ungulates; unique ability to infect multiple species (e.g. Bovine papillomavirus (BPV)-1 and -2 affects both cattle and horses)
• **Epsilon** (ε): BPV-5 and -8; cause both fibropapillomas and true papillomas
• **Lambda** (λ): Associated with skin lesions in the dog and cat; *Felis domesticus* PV1 (FdpV-1) and canine oral PV (COPV)
• **Xipa** (ζ): Bovine papillomaviruses (BPV)-3, -4, -6, -9 and -10; restricted to cattle and cause true, cutaneous squamous papillomas

Papillomaviruses are usually host specific, with a strong tropism for cutaneous and mucosal squamous epithelium, where they typically induce the formation of benign squamous papillomas or fibropapillomas. These tumors tend to spontaneously regress as a result of cell-mediated immunity; however, some PVs can undergo malignant transformation, leading to locally aggressive tumors such as equine sarcomas, or invasive squamous cell carcinomas (ISCC).3,7,10

In cats, FdpV-1 and -2 infection, in combination with solar-induced p53 mutation and papillomavirus-induced inhibition of keratinocyte apoptosis, may lead to uncontrolled cell proliferation, progressing to Bowenoid in situ carcinoma (BISC) and, less commonly, SCC. Additionally, as noted by the contributor, papillomavirus DNA has been localized to proliferating fibroblasts suggesting an association between feline fibropapillomas (sarcomas) and PV. As in cats, cutaneous PV infections in dogs can generate viral plaques that may subsequently progress to ISC or ISCC; pugs, miniature schnauzers and immunosuppressed dogs are predisposed. Although Canine oral papillomavirus (COPV) infection is not associated with cutaneous neoplasia, vaccination with a live COPV vaccine may result in cutaneous ISCC.10

There are currently ten different papillomaviruses described in cattle.14,20 BPV-1 and BPV-2 cause fibropapillomas, while BPVs-3, -4, -6, -9 and -10 are epitheliotropic and induce true cutaneous squamous papillomas. BPV-5 and BPV-8 appear to have a dual pathology, causing both fibropapillomas and cutaneous squamous papillomas. Bracken fern (*Pteridium aquilinum*) contains immunosuppressants and a number of mutagens; in cattle that have ingested bracken fern, BPV-4-induced alimentary papillomas may progress to SCC, while transforming protein E5 associated with BPV-2 or -4 may synergize with ptaquiloside to produce bladder cancer.14 See table 1 for a summary of select papillomaviruses and their affects on various species.
Table 1: Select papillomaviruses in domestic animal species.\(^3,6,7,10,14,20\)

<table>
<thead>
<tr>
<th>Species</th>
<th>Skin lesion</th>
<th>Papillomavirus Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cat</td>
<td>Feline viral plaque progressing to BISC +/- ISCC</td>
<td>FdPV-1,-2,(^\lambda(1))</td>
</tr>
<tr>
<td>Cat</td>
<td>SCC</td>
<td>FdPV-2, novel δ</td>
</tr>
<tr>
<td>Cat</td>
<td>Feline sarcoid (feline cutaneous fibropapilloma)</td>
<td>FeSarPV BPV-1,-2, novel δ</td>
</tr>
<tr>
<td>Dog</td>
<td>Canine pigmented viral plaque progressing to ISC and SCC</td>
<td>CfPV-3,-4, novel δ</td>
</tr>
<tr>
<td>Dog</td>
<td>Endophytic papilloma and SCC in immunosuppressed dogs</td>
<td>CfPV-2, novel δ</td>
</tr>
<tr>
<td>Dog</td>
<td>Oral papilloma and vaccine-induced cutaneous SCC</td>
<td>COPV (^\lambda)</td>
</tr>
<tr>
<td>Horse</td>
<td>Equine sarcoid (equine cutaneous fibropapilloma)</td>
<td>BPV-1,-2, δ</td>
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<tr>
<td>Horse</td>
<td>Equine penile papillomas, ISC &amp; SCC</td>
<td>EcPV2</td>
</tr>
<tr>
<td>Ox</td>
<td>Cutaneous fibropapilloma</td>
<td>BPV-1,-2, δ</td>
</tr>
<tr>
<td>Ox</td>
<td>Both fibropapillomas and squamous papilloma</td>
<td>BPV-5,-8, Epsilon ((\epsilon))</td>
</tr>
<tr>
<td>Ox</td>
<td>Cutaneous squamous papilloma</td>
<td>BPV-3,-6,-9,-10, Xi ((\xi))</td>
</tr>
<tr>
<td>Ox</td>
<td>Squamous papilloma of alimentary tract &amp; urinary bladder</td>
<td>BPV-4, Xi ((\xi))</td>
</tr>
<tr>
<td>Ox</td>
<td>Co-carcinogen with bracken fern (ptaquiloside) to induce urinary bladder neoplasms</td>
<td>BPV-2, δ</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bull (young)</th>
<th>Papilloma/ fibropapilloma of glans penis</th>
<th>BPV-1, δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ox</td>
<td>Squamous papilloma</td>
<td>BPV-7, novel δ</td>
</tr>
<tr>
<td>Cotton-tail rabbit</td>
<td>Cutaneous SCC</td>
<td>CRPV Kap pa ((\kappa))</td>
</tr>
<tr>
<td>Western barred bandicoot</td>
<td>Cutaneous papillomatosis &amp; SCC (digits, lips)</td>
<td>BPCV-1, novel δ</td>
</tr>
<tr>
<td>Egyptian fruit bat</td>
<td>Basosquamous carcinoma</td>
<td>RaPV-1, novel δ</td>
</tr>
<tr>
<td>Natal multimammate mouse</td>
<td>Keratoacanthoma and SCC</td>
<td>MnPV Lota ((\iota))</td>
</tr>
<tr>
<td>European harvest mouse</td>
<td>Sebaceous carcinoma</td>
<td>MmPV Pi ((\pi))</td>
</tr>
</tbody>
</table>

**Contributing Institution:** Institut fuer Veterinaer-Pathologie, Justus-Liebig-Universitaet Giessen
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http://www.uni-giessen.de/cms/fbz/fb10/institute_klinikum/institute/pathologie

**References:**
6. Lange CE, Tobler K, Lehner A, et al. EcPV2 DNA in equine papillomas and in situ and


CASE II: 10058-12 (JPC 4018119).

Signalment: Six-month-old male castrated German short-haired pointer dog, (Canis familiaris).

History: Three punch biopsies were submitted from a patient with a 4 month history of alopecia and scaling. The submitting veterinarian reported initial presentation was on the nose and above the eyes. It progressed to the ears and ventrum. Therapy consisting of dermatologic shampoos gave mild relief of clinical signs. Little response was noted with omega-3 fatty acids nor with vitamin E. There was a recent development of pruritus.

Gross Pathology: None.

Histopathologic Description: In sections of haired skin examined, there are multiple changes of the dermal epithelium and follicular epithelium as well as the superficial dermis. Changes in the dermal epithelium include moderate orthokeratotic hyperkeratosis with colonization with rare bacterial cocci. Basilar hydropic degeneration (Civatte body formation) is present in the stratum basal, mural follicular epithelium and less commonly in the stratum spinosum. Moderate numbers of the cells of the stratum basale exhibit apoptosis. Few exocytic lymphocytes are seen within the epidermis. A focal area of separation of the epidermis from the underlying dermis is noted (dermoepidermal clefting-not present in all sections). One section has a mild lichenoid infiltrate of lymphocytes. Follicular changes include similar changes as seen in the epidermis as well as ectasia of the follicles due to mild hyperkeratosis. The dermis is characterized by mild superficial edema, moderate multifocal pigmentary incontinence, and very mildly increased numbers of lymphocytes. Formal hair is frequently present in all stages including anagen. Sebaceous glands are unaffected by inflammatory changes.

Contributor’s Morphologic Diagnosis: Mild, diffuse, subacute to chronic, lymphocytic and apoptotic basilar epidermitis and folliculitis.

Contributor’s Comment: The lesions present, the breed of the patient, and the age are all
consistent with a diagnosis of exfoliative cutaneous lupus erythematosus of the German shorthaired pointer. This is an autosomal recessive subclassification of lupus erythematosus.\(^4\)

This disease was first reported in 1992 under the name of “Hereditary lupoid dermatosis of the German Shorthaired Pointer.”\(^3\) In a relatively recent study, 17 patients were evaluated. The lesion distribution among the sexes was approximately 2:1 (female:male).\(^1\) Young dogs were affected with a mean of 10 months of age (1.8-48 months). Prominent clinical findings in the study were initially scaling (100%), alopecia (76%), crusting with or without ulceration (52%), generalized lymphadenopathy (32%), follicular casts (28%), mild pruritus (28%), and intermittent pyrexia (12%). Lesion distribution early in the course of the disease was reported at the muzzle, pinnae, and the dorsal trunk. The distribution progressed to the limbs and ventral trunk with 52% of the dogs displaying generalized disease.

Clinical pathologic changes included lymphopenia (3/17), hyperglobulinemia (4/17), mild thrombocytopenia (4/17), and lack of antinuclear antibodies in all 17 patients.\(^1,5\) Bryden et al additionally reported anemia.

Histologic findings reported parallel the microscopic findings in our case. They include a moderate to marked lymphocytic interface dermatitis, diffuse hyperkeratosis, basal keratinocyte vacuolation and individual necrosis, exocytosis of lymphocytes into the epithelium, with the interface dermatitis and hyperkeratosis being the most common findings.\(^1,5\)

Primarily CD3 + lymphocytes were identified in the inflammatory infiltrate in the deep epidermis, superficial dermis, hair follicular infundibula, and surrounding sweat glands.\(^3\) In greater than half of the dogs examined, indirect immunofluorescence detected the presence of IgG specific to the follicular basement membranes and specific against sebaceous glands.\(^1\)

Some patients receiving immunomodulatory therapy additionally had generalized demodicosis.\(^5\) Noncutaneous findings consisted of peripheral lymphadenopathy, colitis, eosinophilic and lymphoplasmacytic enteritis.

A recent study evaluating the genetic heritability of this disease showed an autosomal recessive pattern of inheritance due to singular nucleotide polymorphism of an as-of-yet unidentified gene.

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2-2. Skin, German Shorthaired Pointer: The basal epithelium contains several apoptotic basal cells (“Civatte bodies”). (HE 400X)
Histologic differential diagnoses include sebaceous adenitis, lupus-like drug reactions, lupus erythematosus and erythema multiforme. Sebaceous adenitis can be differentiated from the above condition by a lack of an interface dermatitis. Lupus-like drug reactions are reported commonly to otic preparations placed topically and may have a similar histologic appearance. Other forms of lupus erythematosus can be differentiated by the breed and age of the patient and decreased intensity of an inflammatory infiltrate when compared to discoid lupus erythematosis. Erythema multiforme has a similar distribution, is more ulcerative than exfoliative, has a mixed lymphocytic and histiocytic interface dermatitis, may have apoptosis in all levels of the epidermis, and generally occurs in animals greater than one year of age.

JPC Diagnosis: Haired skin: Dermatitis, interface, cell-poor, diffuse, mild, with basal epithelial degeneration and necrosis, pigmenary incontinence and loss of sebaceous glands.

Conference Comment: The contributor provides a complete review of exfoliative cutaneous lupus erythematosus of the German shorthaired pointer, and in a well-constructed description of the microscopic findings, mentions that sebaceous glands are generally spared; however, conference participants observed that they appear decreased in number. The moderator pointed out that while loss of sebaceous glands is not a finding specific for this condition, it is consistent with interface dermatitis, because as inflammation progresses along the epidermis and follicular infundibula, the normal organization of adnexal structures is disrupted. Additionally, as noted by the contributor, a recent study detected the presence of IgG antibody against sebaceous glands in many of these cases.

Lupus erythematosus occurs in two distinct forms in animals: Systemic lupus erythematosus (SLE), which affects multiple tissues, occasionally including the skin; and cutaneous or discoid lupus erythematosus (CLE/DLE), in which lesions are localized to the skin. There is some controversy over the designation of DLE; some pathologists prefer the term “generalized chronic cutaneous lupus.” Exfoliative cutaneous lupus erythematosus (ECLE) of the German shorthaired pointer is a unique form of CLE.

In addition to humans, systemic lupus erythematosus (SLE) is recognized in mice, non-human primates and various domestic animals. SLE is characterized by the loss of B- and T-cell tolerance to self-antigens, resulting in polysematic inflammation. Patients with SLE produce autoantibodies against a range of nuclear and cytoplasmic components of the cell, including histones, double-stranded DNA, nonhistone proteins bound to RNA, and nucleolar antigens. Autoantibodies and self-antigen complexes deposit within glomeruli, blood vessels, skin and joints, inciting a type III hypersensitivity reaction. To a lesser extent, tissue damage is induced by antibodies directed toward self-antigen on erythrocytes, leukocytes and thrombocytes initiating a type II hypersensitivity reaction, or cell-mediated immunity (type IV hypersensitivity). As a result of all of these variables, SLE generates a wide spectrum of clinical presentations and is often referred to as “the great imposter.” Affected patients may exhibit a combination of renal disease (glomerulonephritis, interstitial nephritis, vasculitis, and proteinuria), polyarthritis, skin lesions, hematologic disorders, respiratory, or neurologic dysfunction.

Although the definitive cause of SLE remains unknown, numerous endogenous (genetic, hormonal, metabolic, immunologic) and exogenous (drugs, ultraviolet light, infectious agents) factors have been implicated in its pathogenesis. In NZB/W mice, one of the most common strains used in models of SLE, multiple genes have been shown to contribute to the development of SLE, including major histocompatibility complex (MHC) and several non-MHC genes. Recent research has also shown that SLE patients often have hypomethylated DNA, which may lead to an anti-MHC class II response and apoptosis of MHC class II antigen presenting cells. In addition to loss of phagocytic cells, genetic deficiencies of complement components may lead to decreased clearance of apoptotic debris and circulating immune complexes, which is another predisposing factor for SLE. Sex hormones, nutrition and both humoral (via autoantibodies) and cell-mediated immunologic factors also contribute to SLE. In dogs, abnormalities in cellular immunity result in lymphopenia characterized by a high CD4+:CD8+
ratio. In normal dogs this ratio is less than 2, while it may reach as high as 6 in dogs with SLE. Additionally, cutaneous disease in affected dogs is exacerbated by ultraviolet light, which may be related to tissue damage and inflammation resulting in elaboration of IL-1, IL-1, IL-2, IL-6, and TNF-β and further damage to the epidermis.\(^2,7\) Alternatively, UV radiation may render DNA immunogenic.\(^7\) Interestingly, ECLE in German shorthaired pointers occurs/progresses without the influence of ultraviolet light.\(^5\) In humans, drugs such as hydralazine, procainamide and D-penicillamine are also associated with SLE, while in animals, drug exposure is a suspected trigger, but specific drugs have not been implicated.\(^7\)

In domestic animals, lupoid skin disorders, such as CLE, are most frequently seen in the dog, often localized to the nose. “Lupus-specific” histopathological features include hyperkeratosis, epidermal atrophy, basal cell vacuolar degeneration or necrosis (“Civatte bodies”), basement membrane thickening, mononuclear cell infiltration at the dermoepidermal interface and subepidermal cleft formation. Gross lesions range from alopecia to ulcerative dermatitis.\(^2,5\) On the other hand, skin disorders associated with SLE are non-specific and may not display the lupus specific findings enumerated above.\(^5\)

**Contributing Institution:** Veterinary Diagnostic Center
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nvdlsl.unl.edu

**References:**
CASE III: 6069-12 (JPC 4018118).

Signalment: 4-year-old female spayed domestic short hair cat, (Felis domesticus).

History and Gross Pathology: A 4-year-old spayed female domestic short-haired cat presented with weight loss of 3.5 lbs over the past several months. The cat lived indoors and had no major previous health problems, but recently the owners felt the cat had appeared agitated and possibly painful. On presentation the cat weighed 7.5 lbs and appeared quiet, alert, and responsive although was easily stressed and began to pant. Physical examination was unremarkable with the exception of a fractured tooth and a tooth with an enamel defect. A CBC with manual differential count was performed and the cat had a mature neutrophilic, lymphocytic, and monocytic leukocytosis. A chemistry panel revealed an elevated GGT and slightly elevated sodium. A urinary tract infection was noted on urinalysis. Heartworm testing, FeLV, and FIV were negative and total T4 was normal. The referring veterinarian recommended radiographs, ultrasound, and screening for a variety of infectious diseases, which the owner declined at the time. The cat was sent home on clindamycin 25 mg capsules, for treatment of the urinary tract infection, with the option for adding buprenorphine and high calorie diets with appetite stimulants. The cat returned to the clinic 6 weeks later for euthanasia due to further decline. While restraining the cat for euthanasia the cat was unruly and appeared to be in pain. After euthanasia a technician went to move the cat by its scruff, and the skin over the dorsal thorax tore forming a large flap. A section of skin and liver was collected and submitted for histological evaluation.

Laboratory Results:

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<tr>
<th>Parameter</th>
<th>Value</th>
<th>Reference Range/ Units</th>
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<tr>
<td>HCT</td>
<td>37.1</td>
<td>30.3-52.3%</td>
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<tr>
<td>HGB</td>
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<td>MCV</td>
<td>49.5</td>
<td>35.9-53.1 fL</td>
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<td>MCH</td>
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<td>11.8-17.3 pg</td>
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<td>MCHC</td>
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<td>RDW</td>
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<tr>
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<td>%</td>
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<tr>
<td>%Eos</td>
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<td>151-600 K/µL</td>
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FeLV negative

3-1. Haired skin, cat: After euthanasia a technician went to move the cat by its scruff, and the skin over the dorsal thorax tore forming a large flap. (Photo courtesy of: Veterinary Diagnostic Center, University of Nebraska-Lincoln, Lincoln, NE. nvdlhs.unl.edu)
FIV negative
Heartworm negative

Chemistry

<table>
<thead>
<tr>
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<td>BUN</td>
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<td>CREA</td>
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<td>BUN/CREA</td>
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<td>PHOS</td>
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<td>Ca</td>
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<td>100-1400</td>
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<tr>
<td>Na</td>
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<td>150-165 mmol/L</td>
</tr>
<tr>
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<td>3.5-5.8 mmol/L</td>
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<td>Na/K</td>
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<tr>
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</tr>
<tr>
<td>TT4</td>
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<td>µg/dL</td>
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</tbody>
</table>

Urinalysis (collected off counter)

- Color: bright yellow
- Appearance: clear
- SpGr (refractometer): >1.050

Test strip

- Urobilinogen: normal
- Glucose: negative
- Ketone: negative
- Bilirubin: negative
- Protein: 100 mg/dl
- Nitrate: negative
- Leukocytes: 3+
- Blood: negative
- pH: 6.5 on strip, 7.4 on meter
- Specific gravity: 1.02

Sediment

- WBC: 1-2/hpf
- RBC: rare
- Epithelial cells: occasional
- Casts: Waxy (one seen)
- Crystals: triple phosphate
- Bacteria: cocci 2+

Histopathologic Description:
Skin: Two sections of haired skin are examined. The sections consist of epidermis and dermis, with normal appearing hair follicles. The epidermis is thin and ranges from 1-2 cell layers thick, and has diffuse mild orthokeratotic hyperkeratosis. The dermis is severely atrophied and there is loss of a majority of the dermal collagen. The remnant collagen is loosely packed and interspersed with small to moderate numbers of lymphocytes, plasma cells and mast cells. The erector pili muscles within the specimen are prominent.

Liver: The cytoplasm of nearly all of the hepatocytes is expanded by several small, distinct, clear cytoplasmic vacuoles (lipid). The swollen hepatocytes have compression of the associated
sinusoids. Moderate numbers of hepatocytes, often within the periacinar region have intracytoplasmic green-brown pigment (hemosiderin).

**Contributor’s Morphologic Diagnosis:**

1. Dermal atrophy, diffuse, chronic, severe.
2. Hepatic lipidosis, diffuse chronic, moderate to severe.

**Contributor’s Comment:** Acquired skin fragility syndrome has long been recognized in the cat. The gross and histologic lesions are consistent with the condition feline skin fragility syndrome (FSFS). The pathogenesis of the syndrome is unknown; however, it is typically associated with a hyperglucocorticoidism, diabetes mellitus, or excessive use of progestational compounds. It has been seen in conjunction with severe liver disease, including hepatic lipidosis. This cat did have hepatic lipidosis. However, it is unknown whether this was a primary condition or secondary to some other systemic illness that resulted in anorexia as has been reported previously. Ehlers-Danlos syndrome was considered to be one of the differential diagnoses by the submitting veterinarian. Ehlers-Danlos syndrome was ruled out due to the severe dermal atrophy, being more consistent with acquired skin fragility syndrome. Dermis is of normal thickness and lacks attenuation of dermal collagen seen in Ehlers-Danlos syndrome. Another case of dermal atrophy in a cat reports the occurrence after treatment of the cat with phenytoin, but no mechanism was established. It is important to note, phenytoin is metabolized in the liver. Not all cases of FSFS are related to endocrine or hepatic disease. There is a report of fragile skin due to cutaneous histoplasmosis. In that case, the epidermis was attenuated and there was dermal edema. Fibrinoid necrosis of blood vessels in the subcutis with granulomatous inflammation was reported.

Skin fragility cases have been reported associated with a variety of concurrent diseases. However, the mechanism for this syndrome has yet to be determined. Clinical cases of FSFS should be an
indication of concurrent disease and further evaluation of cases should be performed.

**JPC Diagnosis:**
1. Haired skin: Epidermal, dermal, and follicular atrophy, diffuse, severe.
2. Liver, hepatocytes: Lipidosis, diffuse, severe.

**Conference Comment:** As there was some difficulty in distinguishing glycogen from lipid type hepatocellular vacuolar change, initial conference discussion focused on the histological differences between these two processes. In general, lipid-type vacuolar degeneration produces hepatocytes with discrete globules which may coalesce into a single large vacuole that peripheralizes the nucleus, while glycogen-type vacuolar degeneration causes significant cell swelling with indistinct vacuolar boundaries and fine, feathery cytoplasm (see WSC 2013-2014 conference 13, case 1 for a more detailed summary as well as an example of glycogen-type change). Unlike dogs, steroid hepatopathy is uncommon in cats, even those with hyperadrenocorticism. Additionally, cats suffering from hepatic lipidosis typically exhibit micro- or macrovesicular hepatocellular vacuolation, rather than a single large vacuole that peripheralizes the nucleus.4 Thus in this case, hepatic lipidosis is a more likely diagnosis than glycogen-type hepatocellular degeneration. There was also some debate regarding the origin of the golden-brown granular material noted multifocally within Kupffer cells. Initially, some participants speculated that this was bile pigment, lipofuscin or ceroid, but histochemical staining for iron identifies the material as hemosiderin. The significance of the iron is not evident in this case.

Conference participants went on to discuss the differential diagnosis for the histological skin lesions. Ehlers-Danlos syndrome is reported (albeit rarely) in cats, and results in hyperextensible skin; however, severe, diffuse attenuation of dermal collagen is not a characteristic feature. Additionally, acquired feline skin fragility syndrome (FSFS) typically presents in middle aged to older cats, while Ehlers-Danlos occurs in young animals.4 Electron microscopy (not performed in this case) is also a useful tool in diagnosis of Ehlers-Danlos syndrome, which classically demonstrates enlarged, fragmented collagen fibrils.3 Similarly, ultrastructural studies in cats with FSFS reveal disorganized, tangled, variably sized collagen fibrils, although fibrils are not generally fractured.4 Paraneoplastic alopecia secondary to pancreatic/biliary carcinoma was also suggested as a possible rule-out. While this condition is associated with follicular atrophy, the dermis is unaffected and epidermal hyperplasia, rather than atrophy, is the most frequent microscopic characteristic; furthermore, the footpads are often involved and skin fragility is not reported, which aids in differentiating this condition from FSFS.9

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CASE IV: 2011905671 (JPC 4018075).

Signalment: Age unknown castrated male mongrel dog, (*Canis familiaris*).

History: A solitary subcutaneous mass was surgically excised from the perianal region.

Gross Pathology: The mass was approximately 6 mm in diameter with a red surface. The cut surface (after fixation) was smooth, firm and white.

Histopathologic Description: The well-circumscribed dermal/subcutaneous mass is adjacent to several islands of normal perianal glands. The mass is composed of round cells arranged in cords, nests and sheets on a fibrous stroma. Neoplastic cells often separate and surround pre-existing perianal glands. Neoplastic cells are round, with a centrally placed round to oval nucleus, indistinct nucleoli, and a small amount of eosinophilic to clear cytoplasm. Histochemical staining with periodic acid-Schiff (PAS) and silver impregnation stain demonstrates that neoplastic cells are often surrounded by a prominent basement membrane that resembles “chicken-wire.”

Immunohistochemically, neoplastic cells are diffusely, strongly positive for vimentin, multifocally, weakly positive for desmin, and negative for alpha-smooth muscle actin, calponin, cytokeratins (AE1/AE3, 7, 14, CAM5.2 and CK-MNF), chromogranin A, synaptophysin, PGP9.5, NSE, CD31, Factor VIII, melan-A, PNL2, S-100, MHC Class II, Iba-1 and CD18. The cytoplasmic border of each neoplastic cell is strongly positive for type IV collagen.

Contributor’s Morphologic Diagnosis: Perianal region; glomus tumor.

Contributor’s Comment: Glomus tumors are rare, benign neoplasms in humans and animals, which originate from the glomus cells that compose the glomus body, an arteriovenous anastomosis. Glomus tumors typically occur in areas that reflect the normal anatomic location of the glomus body; most tumors occur in the subungual region of the fingers. In humans, these tumors are occasionally reported in various other locations, including the precoccygeal area, head, neck, bone, nerve, stomach, colon, nasal cavity and trachea. Human glomus tumors are classified, based on the proportion of glomus cells, vascular structures and smooth-muscle components, into three subtypes: the classical glomus tumor (solid type), glomangioma (angiomatous type), and glomangiomyoma (myxoid type). The classical (solid) is the most common and accounts for approximately 75 percent human glomus tumors.

Glomus tumors are rare in animals, though there are a few case reports in dogs and cats. Similarly to humans, most tumors in dogs and cats arise on the lower extremities and the digit.4-1, 4-2
Although glomangioma has been reported in a cow and a dog, most glomus tumors in animals are most consistent with the classical glomus tumor (solid type) in humans. Histopathologically, glomus tumors are composed of small round cells with round nucleus and eosinophilic cytoplasm, arranged in sheets, nests, cords, ribbons or duct like structures. Nests and individual tumor cells are surrounded by a basement membrane. Variably sized vascular structures are present within the neoplasm, and tumor cells often palisade along vessel walls. Immunohistochemically, nearly all glomus tumors express vimentin and alpha-smooth muscle actin. Desmin is variably expressed. The basement membranes surrounding neoplastic cells typically express type IV collagen and laminin.

All glomus tumors reported in dogs and cats demonstrate palisading of tumor cells along vessel walls, as well as positive immunoreactivity for vimentin and alpha-smooth muscle actin. Although the present case does not display all of these features, the morphological and immunohistochemical characteristics are most consistent with a glomus tumor. In particular, the basement membrane around each tumor cell is strongly suggestive of a glomus tumor. Glomus tumors in humans and animals must be distinguished from epithelial tumors (such as trichoblastoma), canine hemangiopericytoma, synovial sarcoma and epithelial leiomyoma. In this case, all of these tumors were ruled out based on the histopathological and immunohistochemical features of the neoplastic cells.

JPC Diagnosis: Haired skin, perianal region: Glomus tumor.

Conference Comment: The glomus is a convoluted segment of arteriovenous shunt, composed of an afferent arteriole and an efferent venule with multiple communications, enveloped by collagenous tissue. Blood flow in these shunts is controlled by the glomus body, which (in humans) is typically found in the dermis of the fingertips and is involved in regulating body temperature. Glomus tumors arise from modified smooth muscle cells of the glomus body. In veterinary medicine, glomus tumors are most frequently described in dogs, but have also been reported in cats, horses, non-human primates and a cow. This tumor typically arises on the distal extremities; however three of the four reported equine glomus tumors occurred on the head or neck. Nevertheless, more cases must be examined in order to determine whether there is a true predilection for this site in horses. Interestingly, the single bovine case report describes multiple glomus tumors of the urinary bladder, associated with bovine papillomavirus type 2 (BPV-2) infection. Malignant glomus tumors in humans are defined by being larger than 2 cm with a deep location (below the muscular fascia), having marked nuclear atypia, having more than five mitoses per 50 high-power fields, or having atypical mitotic figures. Due to the small number of identified cases in animals, there are no firmly established criteria of malignancy, although there are rare reports of aggressive, biological behavior.

This case is challenging, in that it demonstrates some, but not all of the classic histomorphologic and immunohistochemical features of a glomus tumor. After extensive debate within conference and consultation with pathologists from the Join Pathology Center soft tissue subspecialty, we are unable to definitively diagnose a glomus tumor; however we concur with the contributor’s conclusion that the microscopic and staining characteristics are most consistent with this entity.

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References: