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CASE I – AFIP 2005-#2 (AFIP 2985000)

Signalment: An approximately one-year-old, fighting rooster, *Gallus domesticus*

History: This animal was part of a confiscation of 14 adult chickens and 20 chicks from an illegal fighting rooster premise. Adults ranged in age from 1-3 years, up to 4 years of age. This animal was in poor body condition with multiple lacerations. Euthanasia was performed.

Gross Pathology: The bird was in poor body condition with a prominent keel and marked atrophy of pectoral musculature. The skin of the head was irregularly thickened and both eyes were closed. There were multiple, firm, 1-2cm diameter, raised, pale yellow nodules and focal hemorrhages in the skin of the head and comb, with scab formation and small amounts of moist seropurulent exudate, and loss of feathers. Multiple lacerations were present in the skin on the head, legs and pectoral region. There were small amounts of yellow caseous material focally in the subcutis overlying the keel. On internal examination, there were small amounts of caseous yellow material in the pericardial sac. No gross lesions were identified in other visceral organs.

Laboratory Results: Microbiology: Skin, keel: *Staphylococcus aureus*
Parasitology fecal floatation: *Eimeria* sp. oocysts, *Capillaria* sp. eggs

Histopathologic Description: Multifocally, there is marked hyperplasia, ballooning degeneration and necrosis of epidermal and follicular epithelial cells. The lumina of feather follicles contain variable amounts of necrotic cellular debris, sloughed epithelium, clusters of coccoid bacteria and smaller numbers of rod-shaped bacteria. Throughout the affected foci, epithelial cells contain intracytoplasmic

eosinophilic A-type inclusion bodies (Bollinger bodies), and there is loss of nuclei in some infected epithelial cells. There are few foci of epidermal ulceration, focal necrosis of the superficial dermis and congestion of dermal vessels. Fibrin, necrotic cellular debris, extravasated red cells, degenerate heterophils, necrotic epithelium and large clusters of coccoid bacteria are found in superficial epidermal layers and lining the ulcerated areas. Large perivascular and interstitial infiltrates of lymphocytes and histiocytes, smaller numbers of heterophils and scattered focal hemorrhages are present throughout the superficial dermis and around feather follicles. There is separation of the epidermal layers and of the epidermis from the dermis (cleft formation) in multiple foci.

Other significant findings in this case were focally extensive bronchopneumonia.

Contributor's Morphologic Diagnoses: Skin, head: Epithelial hyperplasia, ballooning degeneration and necrosis, focally extensive, severe, chronic with intracytoplasmic eosinophilic A-type inclusions, etiology consistent with avipox virus

Dermatitis and folliculitis, lymphohistiocytic and heterophilic, focally extensive, severe, chronic with serocellular crusts, intraepidermal vesicles and epidermal ulceration

Contributor's Comment: Avian poxviruses (APVs) are members of the genus Avipoxvirus within the subfamily Chordopoxvirinae in the family Poxviridae (1). They are large linear dsDNA viruses that are found worldwide in all species of poultry and in more than 200 species of birds (2). Detection and differentiation of APV strains have been carried out by the use of polymerase chain reaction combined with restriction enzyme and nucleotide sequence analyses. Currently 10 defined species in the Avipoxvirus genus are described (1).

Avian poxviruses are immunogenically and antigenically distinguishable from each other, but varying degrees of cross relationships do exist (3). There is a substantial degree of host specificity in some avian poxviruses, especially those that infect wild birds (3). Fowlpoxvirus (FPV) is the type species of the genus (1). Unlike most DNA viruses, FPV matures and multiplies in the host cell cytoplasm of replicating cells and has an affinity for epithelial cells. FPV contains homologues of the poxvirus A-type inclusion (ATI) proteins. These inclusions protect mature virions from environmental insults, thus prolonging survival of the virus in nature (3).
Infection occurs through mechanical transmission of the virus to the injured or lacerated skin, through aerosol transmission by feathers and dried scabs containing poxvirus particles and by insect bites (3). Replication of viral DNA in epidermal epithelium at 12-24 hours post-infection is followed by appearance of infectious

virus and epithelial hyperplasia 36-48 hours post-infection (3). One of the characteristic features of avian poxvirus infection is cellular hyperplasia of affected tissue. The virus produces a hormone analogous to epidermal growth factor which induces cell division and results in proliferative lesions (3).

The disease may occur in one of two forms, cutaneous or diphtheritic, or both (3). In the diphtheritic form, slightly elevated, white opaque nodules or yellowish patches develop on the mucous membranes of the mouth, esophagus, tongue, or upper trachea (3). Histopathologic changes of tracheal mucosa include hypertrophy and hyperplasia of mucus producing cells, with subsequent enlargement of epithelial cells that contain eosinophilic intracytoplasmic inclusions (3). The severity of the pox lesions vary depending on the susceptibility of the host, virulence of the virus, and distribution of the lesions among other factors (3).
A differential diagnosis in this case would be Marek's disease (alphaherpesvirus). The inflammatory lesions in skin sections in Marek's disease are perivascular and localized around infected feather follicles (3). No gross or histopathologic lesions consistent with Marek's disease were identified in the sciatic nerve, brain or visceral organs.

AFIP Diagnoses: 1. Skin: Epidermal and follicular hyperplasia, ballooning degeneration and necrosis, focally extensive, marked, with eosinophilic intracytoplasmic inclusion bodies, chicken (*Gallus domesticus*), avian, etiology consistent with avipoxvirus.
2. Skin: Dermatitis and folliculitis, lymphohistiocytic and heterophilic, chronic, focally extensive, severe, with serocellular crust, multifocal ulcers and colonies of cocci.

Conference Comment: The contributor provides a thorough review of avian poxvirus infection. Attendees noted the perifollicular and perivascular distribution of inflammation and discussed these as similar features of Marek's disease (Gallid Herpesvirus-2); however, the microscopic lesions of cutaneous Marek's disease are predominantly lymphoproliferative inflammation surrounding feather follicles and inclusion bodies, when present, are intranuclear.

This case has all the classic, light microscopic features of poxviral infection: marked epithelial hyperplasia; ballooning (hydropic) degeneration and pathognomonic eosinophilic intracytoplasmic inclusion bodies (Bollinger bodies) located within epithelial cells.

Attendees developed a differential diagnoses for gross findings associated with the cutaneous (dry pox) and diphtheritic (wet pox) forms of disease:
Dry pox: Proliferative, hyperkeratotic and ulcerative cutaneous lesion

- *Trichophyton megninii* and *T. simii*: dermatophytic fungi.
- *Knemidokoptes gallinae*: mite in the basal shafts of feathers on the epidermis.

Wet pox: Caseous inflammation (yellow/white) in the pharynx/esophagus/crop:

- Vitamin A deficiency: Pustules on the mucosa of the mouth, pharynx, esophagus and crop in young birds, inflamed eyelids; squamous metaplasia of the nasal mucosa; keratinization of intestinal enterocytes, decreased goblet cells and blunting of villi (severe deficiency).
- Infectious laryngotracheitis: Alphaherpesvirinae (Gallid herpesvirus 1); mucohemorrhagic or caseous exudates of the trachea; intranuclear inclusion bodies in epithelial cells.
- *Trichomonas gallinae*: Raised caseous lesions in the mouth, pharynx, esophagus and crop.
- *Capillaria annulata* or *Capillaria contorta*: Thickened inflamed mucosa progressing to a sloughing mucosa.
- *Candida albicans*: White-grey pseudomembranous patches on the mouth, pharynx, esophagus and crop; pseudohyphae and budding yeast.
- Aspergillosis: Yellow-grey nodules in trachea, lungs and air sacs

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CASE II – 00-20410 (AFIP 2790169)

Signalment: 4 year old female Persian cat, (*Felis catus*)

History: Had single mass removed 2 months ago - now 3 masses about 1 cm in diameter in chain over shoulder area.

Contributor's Morphologic Diagnosis: Focal pyogranulomatous dermatitis and cellulitis with intralesional fungal hyphae and spores (dermatophyte pseudomycetoma)

Contributor's Comment: Dermatophytosis is a superficial infection of the keratinized layers of the skin, hair and nails by fungi of the genera *Microsporum*, *Trichophyton*, and *Epidermophyton*. The production of keratinases enables the fungi to utilize the usually chemically-resistant keratin proteins as a nutrient source. The fungi grow only within the non-viable keratinized tissues and appear unable to invade the living tissues of a healthy host. Accidental penetration of the dermis, usually from spontaneous or traumatic rupture of an infected hair follicle, results in an intense inflammatory reaction and disappearance of the fungal elements. On rare occasions, the dermatophytes persist in living tissue, inciting a chronic granulomatous or suppurative inflammatory reaction that is distinctive only because of the contained fungi. Even more rarely the fungi persist in well-structured discrete granulomas resembling mycetomas.

All reported cases of dermatophyte pseudomycetomas in cats have been caused by *M. canis*, and all affected cats have been Persians. This suggests that an underlying genetic defect related to the immune system may predispose Persian cats to this disease, but the precise defect has not been determined. Dermatophyte pseudomycetomas appear as firm, raised nodular areas that may ulcerate and drain. Lesions usually involve the dorsum of the trunk or base of the tail. Pseudomycetomas have developed in asymptomatic carrier cats, in cats with known superficial dermatophyte infection, and in cats with no previous history of dermatophytosis. Fungal elements are not often found in hair shafts or on skin overlaying pseudomycetomas. Cats with dermatophyte pseudomycetoma have a much poorer prognosis for cure than do cats with strict superficial infection. Surgical excision alone is not curative; lesions tend to recur at the surgical site.

Microsporum canis is the most common dermatophyte of the cat, and the cat is considered the natural host for this organism. Granulomas caused by traumatic implantation of non-dermatophytic fungi in the dermis or subcutis are designated as eumycotic mycetomas.

AFIP Diagnoses: 1. Haired skin and subcutis: Panniculitis and dermatitis, pyogranulomatous, nodular, focally extensive, marked, with multiple aggregates of fungal hyphae, Persian, feline.
2. Skin: Folliculitis and perifolliculitis, chronic-active, with intrafollicular arthrospores and fungal hyphae.

Conference Comment: The contributor provides a brief review of dermatophytosis in cats and, more specifically, pseudomycetoma development in Persian cats. There is some slight variation among slides with hair follicles containing arthrospores and fungal hyphae not present in all sections. Conference attendees also noted variation in the degree of folliculitis and perifolliculitis in the adjacent epidermis and dermis. The hyphae present within nodules are strongly PAS-positive and argentophilic with Grocott's methenamine silver.

Pseudomycetomas may originate by dermal invasion from infected hair follicles or subsequent to traumatic implantation of infected hairs. Within the deep dermis and subcutis of affected Persian cats, the hyphae are irregular in shape and size and have bulbous dilations. In this case, normal appearing dermatophyte hyphae, and sometimes arthrospores, are present in hair shafts above or adjacent to the pseudomycetoma.

Dermatophytes more commonly cause “ringworm”, an infection of the hair follicle and hair with keratinophilic fungi. Dermatophytosis can cause folliculitis or furunculosis and the presence of dermatophytes within hair shafts of furunculosis lesions, as seen in kerion, should not be confused with pseudomycetomas.

Attendees discussed the differences between eumycotic mycetomas and pseudomycetomas. Some authors have referred to this lesion as a mycetoma while others prefer pseudomycetoma. According to Ajello, Kaplan and Chandler, there are fundamental differences between the granules of the eumycotic mycetomas and the deep mycelial aggregates formed by dermatophytes. Included are the following:

"1. General absence of a developmental sequence of granule formation in eumycotic mycetomas in contrast to a sequential development ranging from individual mycelial filaments to small clusters of filaments and, finally, to large aggregates of mycelium in pseudogranules produced by the dermatophytes.
2. Striking and abundant Splendore-Hoeppli reaction material which surrounds pseudogranules in all stages of their development in contrast to varying amounts or absence of such precipitate around eumycotic granules.
3. Mycelium of the pseudogranules is less abundant and not as intricately interwoven and compact as in the eumycotic granules.
4. Cement is not present in pseudogranules; it may or may not, depending on the etiologic agent, be present in the granules of eumycotic mycetomas.
5. The pseudogranules of the dermatophytes appear to have an endogenous origin with mycelial elements entering the dermis through a break in the follicular epithelium."

Gross, Ihrke, Walder and Affolter provide a similar description:

"Eumycotic mycetomas are opportunistic fungal infections that form variably pigmented tissue grains or granules composed of dense aggregates of organisms plus host-derived material. Similar to the tissue grains seen with actinomycosis, and dermatophytic and bacterial pseudomycetomas, these tissue grains are composed of fungal aggregates imbedded in amorphous eosinophilic material presumed to be antigen-antibody complexes formed as a result of the Splendore-Hoeppli reaction."

Attendees noted that dermatophyte hyphae and arthrospores were identified within and surrounding hair shafts but never hair bulbs. The conference moderator pointed out that each hair has a keratogenous zone located above the hair bulb where keratinization occurs. The zone is conical and is known as Adamson's fringe. Below this fringe the cells of the hair root are nucleated and non-keratinized; above this fringe the cells become keratinized. It is now accepted that dermatophytes can infect hair only to the level of Adamson's fringe, but not below it, because these fungi are able to live only in cells that have cornified completely, such as the stratum corneum and nail plate (6).

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CASE III – S05-300 (AFIP 2991414)

Signalment: Dog, Rottweiler, female, 10 years

History: A mass on the subcutis of the thorax was submitted by a referring veterinarian.

Gross Pathology: The submitted sample was formalin fixed, white, soft skin tissue, with clear mucoid fluid.

Laboratory Results: The neoplastic cells were stained strongly positive for vimentin and moderately but variably positive for Alcian blue.

Histopathologic Description: The submitted tissue is unencapsulated, composed of spindle cells in varying cellularity. Cells have a round to ovoid, hyperchromatic nucleus with vesicular chromatin and visible nucleoli, and varying amounts of cytoplasm with indistinct cell borders. Aggregation of cells in islets and whirl structures, with proliferated vascular tissue at the centers is noted. Extracellular myxoid substance accumulation is also noted, especially in loose, low cellularity areas. Adipose tissue is involved by tumor cell infiltration. Mitotic figures are rare.

Contributor's Morphologic Diagnosis: Myxosarcoma, haired skin, canine.

Contributor's Comment: Myxosarcoma of fibroblast origin is rare, occurring mostly in middle-aged or older dogs and cats, distinguished by its abundant myxoid matrix rich in mucopolysaccharides (1). Cases in the eye, brain, and atrium of dogs have been reported (2). Histopathologically, this case is an unencapsulated proliferation of stellate to spindle shaped fibroblastic cells, loosely arranged in an abundant myxoid matrix. Varying cellularity is noted in different areas of the submitted tissue, and mitoses are rare. Nuclei of tumor cells tend to be small and hyperchromatic.

AFIP Diagnosis: Skin: Peripheral nerve sheath tumor of the skin and subcutis of dogs (hemangiopericytoma), myxoid type, Rottweiler, canine.

Conference Comment: The contributor provides a good case for discussing the controversy which surrounds naming subcutaneous spindle cell neoplasms with similar morphology.

In this case, we prefer the diagnosis of peripheral nerve sheath tumor of the skin and subcutis of dogs (PNST), myxoid type, as the tumor is composed of wavy spindle cells arranged in bundles, palisades and perivascular whorls. The cell of origin for these neoplasms remains controversial. Some pathologists prefer to

restrict the term peripheral nerve sheath tumor to those neoplasms that arise and spread within peripheral nerves. Others contend that there is a subset of PNSTs that arise in the skin and subcutis, presumably from small peripheral nerves.(3)

The WHO classification of peripheral nerve sheath tumor of the skin and subcutis of dogs, formerly canine cutaneous spindle cell sarcoma, is a general term that includes neoplasms split into two categories:

- Benign PNST of the skin and subcutis:
    - Neurofibroma - composed of Schwann cells and perineural cells
    - Schwannoma - solely of Schwann cell origin

- Malignant PNST of the skin and subcutis
    - Neurofibrosarcoma
    - Malignant Schwannoma

- Canine hemangiopericytoma is also included with PNSTs due to similar histomorphologic features.

Gross et al. address the controversy and state, "Recent studies indicate that hemangiopericytomas have been overdiagnosed in both humans and dogs and that 'hemangiopericytoma' is often used to denote the histologic pattern created by a variety of spindle cell tumors with a whorling pattern, rather than a specific tumor of pericytes." Additionally, "differential diagnoses for true hemangiopericytoma include other spindle cell tumors with whorling pattern, such as PNSTs… and that differentiation of hemangiopericytoma from PNSTs can be difficult, as cytologic features may be strikingly similar."(4)

Regardless of the cell of origin, the biological behavior of PNSTs is well known. They can be locally aggressive, are often difficult to completely excise and are prone to local recurrence; however, metastasis is rare and generally follows multiple recurrences.

Light microscopic characteristics are of a well-circumscribed dermal or subcutaneous tumor composed of spindle to ovoid cells with small amounts of eosinophilic cytoplasm. Typically there are areas of densely packed neoplastic spindle cells in short interlacing streams and bundles (Antoni A-like); intermixed with areas of fewer, more loosely and haphazardly arranged neoplastic cells (Antoni B-like). Nuclear regimentation (Verocay bodies) is common and neoplastic spindle cells often whorl (fingerprint pattern) around capillaries and or collagen. Additionally, clefts and lipid-laden macrophages are often present within and surrounding the neoplasm.

Gross et al. have added a further subclassification to benign PNSTs: Myxoid peripheral nerve sheath tumors, which are similar to PNSTs but have an abundant background of mucin. "Myxosarcoma may need to be distinguished from myxoid liposarcoma and myxoid peripheral nerve sheath tumors…In contrast to myxosarcoma, myxoid peripheral nerve sheath tumors are composed of spindle cells arranged in concentric whorls or palisades; and the tumor cells have a basement membrane demonstrable by electron microscopy." Additionally, "In contrast to benign peripheral nerve sheath tumors, formation of a lobular pattern and large, concentric whorls of the tumor cells are not seen with myxomas and low-grade myxosarcomas."(4)

Unfortunately, immunohistochemistry of benign peripheral nerve sheath tumors in dogs and cats is unreliable. Although canine and feline benign PNSTs consistently express vimentin, they vary significantly in their expression of glial fibrillary acidic protein (GFAP) and S100 protein. Likewise, immunohistochemistry is not useful in the definitive diagnosis of hemangiopericytoma, as specific markers for pericytes do not exist.(4)

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CASE IV – PN1/05 (AFIP 2983579)

Signalment: 2 years old, female, spayed, Shar Pei, dog.

History: The dog developed idiopathic mucinosis at 1.5 years of age (as did its two siblings). Steroids were not administered. The dog had also a history of

recurrent fever treated with several antibiotic compounds (not specified by the referring veterinarian). The dog was brought to a private practitioner a week after vaccination for an acute onset of severe depression, fever, vomiting, diarrhea, dyspnea and skin lesions. The dog had severe bilateral inguinal cutaneous edema, cyanosis, erosions and hemorrhagic bullae. Lesions extended to both hind limbs. Despite intravenous antibiotics (enrofloxacin) and steroid therapy, the dog underwent cardiorespiratory arrest two hours after admission.

Gross Pathology: The dog had severe facial deformity (Fig. 3). Vesicles and bullae (Fig. 4) were present on all limbs and lateral trunk. These lesions contained abundant clear viscous material (Fig. 5). Cutaneous lesions described by the referring veterinarian were confirmed at necropsy (Fig. 6). Severe hind limb swelling extended to both hocks. On cut sections, the dermis, panniculus and skeletal muscles were diffusely hemorrhagic and necrotic (Fig. 7). Inflammation, hemorrhage and necrosis extended to the retroperitoneal area. Multiple splenic infarcts and diffuse hepatic discoloration were observed.

Laboratory Results:
Cytology: Cytologic specimens obtained from the inflammatory exudate of the muscles of hind limbs were characterized by a prevalence of degenerated neutrophils (karyolysis) with elevated numbers of intracytoplasmic large, round, 1-2 micron bacteria (cocci).
Bacteriology: *Staphylococcus aureus* was isolated in pure culture from the muscular lesions and from the exudate. The antibiogram revealed partial resistance to penicillin, ampicillin, amoxicillin, enrofloxacin, erythromycin and complete resistance to chloramphenicol, doxycycline, tetracycline and sulphonamides.
Special Stains: Alcian-PAS stain at pH2.5 was performed on tissue sections of the Shar Pei in areas of mucinotic skin not involved by the inflammatory process and compared with a normal mongrel dog and a "normal" Shar Pei (Fig. 1). Severe diffuse accumulation of mucin (non-sulfated mucopolysaccharides) extending to the deep dermis, panniculus and dissecting muscles was observed in the dog. The accumulated material was PAS negative. In some areas diffuse erosions of the skin were covered by elevated numbers of Gram positive bacteria (Fig. 2).

Histopathologic Description: Haired Skin: Diffuse epidermal necrosis is present and associated with multifocal (varies among biopsies) dermo-epidermal separation (vesicles/bullae). The dermis is characterized by abundant deposition of mucin, severe, diffuse edema and multifocal areas of haemorrhage. Perivascular accumulation of degenerated neutrophils (karyorrhexis) and lesser numbers of macrophages and mast cells is present. Vessels are characterized by hyperaemia, vascular wall necrosis, intraluminal fibrin thrombi in small veins of upper dermis, and fibrinocellular thrombi in the deep vessel (not always present).

Contributor's Morphologic Diagnoses:

Haired skin:

1) Severe, acute, perivascular to interstitial, hemorrhagic and neutrophilic dermatitis with acute necrotizing vasculitis and intravascular thrombi with epidermal necrosis and dermo-epidermal vesicles.
2) Severe, diffuse, cutaneous mucinosis, Shar Pei, dog.

Contributor's Comment: Additional microscopic findings were: severe, diffuse purulent and necrotizing myositis; multiple splenic infarcts with areas of diffuse fibrosis; and moderate diffuse, hepatic amyloidosis with hepatic cord atrophy. Intravascular thrombi containing elevated numbers of bacteria were observed in lungs, meninges and lesional skin. These findings were consistent with septic DIC.

Lesions in this dog appeared to derive from the association of idiopathic mucinosis and a type II necrotizing fasciitis.

Mucinosis refers in general to abnormal accumulation of glycosaminoglycans in the dermis (11). The accumulated mucin consists of non-sulfated mucopolysaccharides, with prevalence of hyaluronic acid, that are metachromatic and stain with Alcian blue at a pH greater than 1.0 (11). Cutaneous mucinosis can be localized or generalized both in dogs and humans (7, 8). In humans, generalized forms have been associated with hypothyroidism, diabetes, acromegaly or discoid lupus erythematosus (4). Localized forms are classified as primary (cutaneous focal mucinosis, lip focal mucinosis, myxoid cysts, follicular mucinosis) and secondary forms such as pretibial myxedema of hyperthyroidism, *granuloma anulare*, and cutaneous neoplasms (4). In dogs, most forms of localized or diffuse mucinosis are idiopathic or associated with hypothyroidism and systemic lupus (7, 8). Idiopathic generalized mucinosis is a genodermatosis that has been described prevalently in Shar Peis (3). Cutaneous wrinkles typical of this breed derive from the variable accumulation of dermal mucins, which is maximal in puppies and juvenile dogs and decreases with age (3). Idiopathic generalized mucinosis represents the pathologic condition caused in Shar Peis by an excessive and uncontrolled production of dermal glycosaminoglycans that has not been associated with abnormal thyroid function. Idiopathic mucinosis develops more frequently in Shar Peis under two years of age and generally responds to corticosteroid treatment (3). In severe cases, the accumulation of dermal mucins may lead to severe facial deformity and formation of grossly visible mucinotic bullae with ulceration and secondary bacterial infections (3, 7, 8). Microscopically, the main lesion of idiopathic mucinosis of Shar Peis is a variably severe dermal thickening with disruption of normal dermal architecture with collagen bundles separated by abundant pale blue material (3). In the more severe cases subepidermal vesicles are visible. Confirmation of the mucinous nature of the infiltration is based on positivity to Alcian blue at pH2.5 and PAS negativity (3). An involvement of mast cells in the pathogenesis of cutaneous mucinosis has been hypothesized (7) and cases of idiopathic mucinosis

associated with cutaneous mastocytosis/mast cell tumors have been described in Shar Peis (3, 5).

The lesions observed in the skin, muscles and deep fascia of the inguinal region and hind limbs were consistent with a necrotizing fasciitis leading to toxic shock that closely resembled type II fasciitis of humans. Fasciitis is an acute to hyperacute, rapidly progressing inflammation of soft tissues and muscular fascia (9). In humans, fasciitis is classified into three types. Type I fasciitis is causes by a mixed bacterial population composed by variable combinations of *Bacteroides spp., Clostridium spp., Proteus spp., Streptococcus spp and Staphylococcus spp.* (9). Type II fasciitis is a monomicrobic infection caused more commonly by group A Streptococci or by *S. aureus* (9). Type III fasciitis is the fulminant form of the disease caused by marine organisms such as *Vibrio vulnificans* and *V. parahaemolyticus* (9). Predisposing factors in man are related to trauma, surgery, diabetes, immune depression and odontogenic chronic infections (1). Necrotizing fasciitis presents as a rapidly advancing, painful erythema, edema progressing to necrosis, blistering and ulceration. In humans the abdominal wall, perineum and extremities are commonly involved. Histopathology is characterized by infiltration of skin, soft tissues and fascia with neutrophils, areas of necrosis, hemorrhage and thrombosis (9). Differential diagnoses may include any type of panniculitis; however, the rapid and aggressive clinical behavior is characteristic and leads to toxic shock syndrome if the adequate antibiotic therapy is not instituted (9).

In this dog, the findings of the monomicrobic infection with *S. aureus*, the gross and microscopic lesions, and the rapidly progressive clinical course were consistent with a type II fasciitis. This dog presented a severe hereditary form of mucinosis that affected other two siblings with similar severity and may have concurred to the secondary bacterial infection leading to dermatitis and fasciitis. Antibiotic resistance may have arisen from the cyclical antibiotic therapy administered during the recurrent febrile episodes and may have lead to toxic shock syndrome. A secondary infection with *Staphylococcus spp.* and *Enterococcus sp.* in a Shar Pei with idiopathic mucinosis has been described, partially supporting this hypothesis (5).

The febrile episodes and the hepatic amyloidosis could have also contributed to immune depression facilitating the entrance and diffusion of bacteria from the skin. Recurrent fever in association with hepatic amyloidosis was consistent with the condition named "Familial Shar Pei Fever" that has been described as an inherited autosomal recessive disease (10) and in some reports referred to as familial renal amyloidosis (2). This syndrome is characterized by episodic self limiting fever lasting 12-36 hours and commonly associated with swelling of the tibiotarsal joints ("Swollen Hock Syndrome"). Dogs generally develop renal (not present in this dog) and hepatic amyloidosis (present in this case). Approximately 26% of dogs will develop renal failure (2, 10). Other causes of death associated with this syndrome have been multiorgan thromboembolism, pulmonary embolism, DIC, and

streptococcal toxic shock syndrome (10). Increased systemic levels of IL-6 have been recognized as the trigger of the production of acute phase reactant proteins by the liver (10).

AFIP Diagnoses: 1. Skin and subcutis: Vasculitis, necrotizing, with dermal and epidermal necrosis, hemorrhage, dermal-epidermal separation, and acute inflammation, Shar Pei, canine.
2. Skin, dermis: Mucinosis, diffuse, severe.

Conference Comment: The contributor provides an interesting case and a wonderful review of cutaneous mucinosis in Shar-Peis complicated by concurrent necrotizing vasculitis. As stated by the contributor, *Staphylococcus aureus* was isolated from the muscle and exudate and grown in pure culture. *S. aureus* is a Gram-positive cocci which frequently grows in grapelike clusters and is a normal inhabitant of the skin and mucous membranes. *S. aureus* is also a very common cause of numerous suppurative diseases, the most common cause of food poisoning in humans and, due to superantigen production, results in diseases such as Toxic Shock Syndrome (TSS).

Below is a list of the more common virulence factors produced by *S. aureus* and how they contribute to disease:

- Alpha toxin: the most potent membrane-damaging toxin produced by *S. aureus*; creates a pore in the cell membrane through which cellular contents leak; not produced by all strains; systemic release causes septic shock
- Beta toxin: type C sphingomyelinase, damages membranes rich in lipid
- Leukocidin: forms a pore in affected cell membranes; also hemolytic
- Exotoxins
    - Superantigens; stimulate T-cells non-specifically without normal antigenic recognition
        - Enterotoxins; six types, responsible for food borne illness
        - Toxic shock syndrome toxin (TSST)
    - Exfoliatin toxins (ETA, ETB); associated with scalded skin syndrome in neonates (12)

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