CASE 1 – 05-7666 (AFIP 3026263).

Signalment: 3.5-year-old cow

History: Animal with a suppurative osteomyelitis of the right mandible

Gross Pathology: In the right mandible, there was a hard mass 12 cm in diameter with ulceration of the adjacent gum. The mass was composed of many confluent fibrous nodules and several suppurative tracts. In the fibrous nodules, there were several cavities 1 mm to 1 cm in diameter containing variable amounts of yellowish pus with many sulfur granules.

Histopathologic Description: Most of the mandibular bone is replaced by a granulation tissue infiltrated by macrophages and plasma cells. The granulation tissue is surrounding many small abscesses with granules composed of large bacterial colonies (Gram-positive rod or coccoid-shaped and branching filamentous organisms) surrounded by radiating eosinophilic clumps (Splendore-Hoeppli material) (Fig. 1-1). There is a zone of neutrophils around the granules, surrounded by many large macrophages and plasma cells.

Contributor’s Morphologic Diagnosis: Chronic pyogranulomatous mandibular osteomyelitis, with large colonies of Gram-positive filamentous organisms.

Contributor’s Comment: This pyogranulomatous mandibular osteomyelitis with the presence of colonies of Gram-positive branching filamentous organisms forming sulfur granules is a good example of mandibular actinomycosis in cattle caused by *Actinomyces Bovis*.1,2 The osteomyelitis would result from an extension of the infection of the gums or periodontium by the bacteria, following injury by foreign bodies or as a complication of periodontitis.1 The excessive periosteal proliferation and the granulation tissue induced by the chronic inflammatory process, can cause a marked enlargement of the affected mandible (lumpy jaw).

AFIP Diagnosis: Bone; skeletal muscle; fibrous connective tissue, right mandible (per contributor): Pyogranulomas, multifocal to coalescing, with Splendore-Hoeppli material and colonies of Gram-positive filamentous bacteria, cow (*Bos taurus*), bovine.

Conference Comment: Actinomycetes are Gram-positive, non-acid-fast, branching filamentous rods. They are facultative anaerobes and normal inhabitants of the oral mucous membranes, tooth surfaces, and gastrointestinal tract.1,2 Actinomycosis, or lumpy jaw, is primarily a disease of cattle, although it has been reported in...
horses, pigs, deer, sheep and dogs. Infections usually are restricted to the bone of the mandible resulting in a chronic suppurative and fibrosing osteomyelitis, although infections have been reported to involve the maxilla, regional lymph nodes or tongue.

Infection usually occurs secondary to trauma with subsequent extension into the periosteum. The normal architecture of the mandible is progressively destroyed inciting a non-extensive proliferative periosteal reaction. The purulent exudate may contain necrotic trabecular bone (bone sand), or soft yellow granules containing mats of tangled, filamentous bacteria and Splendore-Hoeppli material (sulfur granules).

Residents at AFIP utilize the mnemonic “YACS” to develop a differential diagnosis when large colonies of bacteria are present in hematoxylin and eosin stained sections.

YACS stands for:
Y Yersinia sp.
A Actinomyces sp., Actinobacillus sp., Arcanobacter sp.
C Corynebacterium sp.
S Staphylococcus sp., Streptococcus sp.

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Contributor’s Morphologic Diagnosis: Glomerular and interstitial fibrosis, tubular necrosis with (dystrophic) mineralisation, oxalate crystal formation, mixed cellular interstitial nephritis; diffuse, moderate (end-stage renal disease); with intracellular sporogenic and gametogenic stages of apicomplexan coccidian parasites, consistent with *Klossiella equi* (*sporozoa, apicomplexa, coccidia*) infection, kidney, horse, *E. caballus*.

Contributor’s Comment: The parasitic genus *Klossiella* belongs to the subphylum *sporozoa* which is characterised by intracellular life-cycle and a apical complex at some point during its development. The trophozoites have no cilia or flagella. The reproduction...
involves both asexual (schizogony) and sexual (gametogony) phases. Following gametogony a zygote is formed, which divides to produce spores (sporogony). Klossiellidae can be found in the kidneys of equids, mice, guinea pigs, bats, opossums, and snakes. Renal infections with K. equi are often clinically apparent. Mild infections, usually self-limiting, are followed by a predetermined cycle of development, with the production of infective stages that are shed in the host urine, and are thought to be ingested by another host. There are few reports on K. equi-related nephritis in severely infected equids. Both sporogenic and gametogenic stages of Klossiella equi were identified in the kidneys. All stages developed in individual tubular epithelia cells. Schizonts were seen mostly in the proximal convoluted tubules, but also free within the lumen of a tubule. Macrogametocytes and microgametocytes were present in syzygy in the loop of Henle and collecting ducts. Sporonts with radiating sporoblasts and mature sporocyst containing sporoblasts were also seen in the loop of Henle's thick limb. Infection is thought to be an incidental finding, although it has been associated with nephrosis and nephritis in immune-compromised individuals. We agree with the contributor that it cannot be determined if the interstitial nephritis and crystals are the result of the K. equi infection.

AFIP Diagnosis: 1. Kidney, tubules: Degeneration and necrosis, multifocal, moderate, with cellular casts and protozoa (Fig. 2-3), etiology consistent with Klossiella equi, pony (Equus caballus), equine.


Conference Comment: The contributor gives an excellent description of Klossiella equi. Klossiella equi is the only known coccidian parasite of the equine urinary tract, with various stages of development located in the kidney. The life cycle is not currently known, although infection is presumed to occur via ingestion of infective sporocysts that were shed in the urine. It is also believed that one schizont generation develops in the glomerular endothelium and another in the proximal tubular epithelium, with sporogony occurring in the epithelium of the thick limb of Henle's loop. Infection is thought to be an incidental finding, although it has been associated with nephrosis and nephritis in immune-compromised individuals. We agree with the contributor that it cannot be determined if the interstitial nephritis and crystals are the result of the K. equi infection.

Ultrastructurally, developing sporoblasts are encased by a bilaminated cell membrane composed of an outer vermil granular layer, and an underlying dense inner layer.

We thank Dr. C. H. Gardiner, Ph.D., veterinary parasitology consultant to the AFIP, for his review of this case.

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References:
CASE III – R06-120 (AFIP 3027084).

Signalment: Two-month-old, Duroc-Hampshire cross, barrow, hog (Sus scrofa domesticus)

History: The animal presented and culled for necropsy was from a farrow to finish swine herd in central Taiwan. Piglets were born healthy and began developing skin lesions and weight loss 6-7 days prior to necropsy. Four piglets from a batch of 60 piglets in the nursery pen were affected. Two piglets were found dead. Recent management changes included new farrowing and nursery houses and pens for batch production.

Gross Pathology: The piglet was in fair body condition. The integument of the piglet had multiple 1 to 3 cm diameter, slightly raised, crusted skin lesions affecting all parts of the body. Lesions had dark-brown friable surfaces. There were multiple, black, raised, smooth, shiny nodules disseminated throughout the thoracic viscera, affecting the lungs and myocardium. Some dark, melanin like lesions were noted on the liver. All other organs were normal.

Laboratory Results: Specimens of skin, lung and liver were submitted for aerobic bacterial culture. No bacterial organism was cultured from these organs.

Histopathologic Description: Microscopically, the skin mass is well demarcated and nonencapsulated. The intact epidermis of the skin in section exhibits milil d epidermal hyperkeratosis while a large coalescing zone of superficial epidermal necrosis with inflammatory infiltration of neutrophils and histiocytes is observed in the affected skin. The skin mass is focally expanding the subcutaneous fat, compressing the underlying subcutaneous tissue and elevating the overlying dermis. The mass is composed of cl osely packed large, polygonal to sp indle-shaped cells arran ged in sh eets and short bundles contained with in a scant intervening fibrous stroma. Most tumor cells contain one or rarely two large and rounded nuclei. Cells along the superficial margins of the dermis abut on a nd occasionally surround the bulbs of hair follicles. The morphology of the tumor cells (melanocytes) is applicable to the metastatic focus in myocardium. Some myocardial tissue is destroyed and replaced by the growing metastases.

Contributor’s Morphologic Diagnoses:
Skin: Melanoma and moderate subacute necrotizing dermatitis, Duroc-Hampshire cross, swine.
Myocardium: Melanoma, metastatic.

Contributor’s Comment: Melanomas have been reported in a variety of domestic and wild animals.4,7,8 It is a devastating disease frequently encountered with both veterinary and human medicine. The Sinclair miniature and Duroc breeds have a genetic predisposition for melanomas; in addition, the Sinclair miniature pig has served as a model for spontaneous cutaneous melanoma in humans. Melano mas occur as congenital lesions and sporadically in all ages of Duroc-Jersey, Hormel, Sinclair and Duroc pig breeds, whereas these tumors are rare in other swine breeds. Regression of such tumors is common and in some breeds may occur in utero and at various times after birth.1,8 Other tumors arising from the skin may look clinically similar to melanoma. The se include melanocytoma, dermal hemangioma and hemangiosarcoma as well as pigmented lesions of the epidermis and adnexa.2,4

Specific immunohistochemistry (IHC) t o i dentify melanocytic tumors of swine is not used. In a recent study, normal and neoplastic porcine melanocytes were vimentin positive, cytokeratin negative, S-100 positive and al pha-1-antitrypsin (AAAT) negative, si milar to th e immunophenotype reported for human normal and ne o-
plastic melanocytes.6

AFIP Diagnosis: 1. Haired skin and subcutis: Melanoma, Duroc-Hamphshire crossbred (Sus scrofa domestica), swine.
2. Heart: Melanoma, metastatic.

Conference Comment: The contributor provides a complete, concise description of melanomas in pigs. In dogs, 56% of melanomas develop in the oral cavity.7 It is also the second most common subungual neoplasm.3,7 Known as the "great imitator", melanoma may appear with or without melanin granules; in an interwoven, whorled, or nested pattern; with round, polygonal, and/or spindled cells; or any combination of these types.3,7 Malignancy is determined by number of mitoses (>3/10 HPF).3,7 Melanocytic neoplasms involving the oral cavity, subungual region, and mucocutaneous junctions are almost always malignant.7 In feline cutaneous melanocytic neoplasms, extensive nuclear atypia, high mitotic activity, and an extensive mitotic rate, an H&E stained slide pre-treated with bleach can aid in evaluation. In this Wednesday Slide Conference case, the neoplasm has a mitotic rate of 1 per HPF, with some fields containing up to 3 mitotic figures.

Melanocytes are dendritic cells that are derived from neuroectodermal melanoblasts, and are normally found within the basal layer of the epidermis.7 Neoplastic transformations have been linked to various molecular changes such as mutation in the INK4a and INK4b and Waf-1 genes resulting in malfunction of tumor suppressor proteins (retinoblastoma protein and p53), proto-oncogene mutation and osteoid formation of deeply invasive melanomas.7,5 Extensive nuclear atypia, high mitotic activity, and an increased expression of Type I collagen to the angiogenic switch that facilitates the progression of microinvasive to deeply invasive tumors in a porcine cutaneous melanoma model.9

Melanomas are common in gray or white horses.7 More than 90% of these tumors are benign at initial presentation, but approximately two-thirds are thought to progress to malignancy.7 German Shepherd Dogs and Boxers are more prone to develop oral melanoma.7 Sin clair miniature and Duroc breeds of swine have a genetic predisposition to developing melanomas.7 Melanomas have also been reported in cats, cattle, sheep, and alpaca.7

References:
CASE IV - 04-0843 (AFIP 2985667).

Signalment: Adult, 55 lb. male pygmy goat, Capra hircus

History: The pygmy goat presented with ulcerated, oozing, pustular lesions on the face and muzzle prior to euthanasia.

Gross Pathologic Findings: Numerous confluent ulcerative, scab bby, ve rucous and proliferative oozing lesions are present on the muzzle, commissures of the lips, surrounding the eyes, left lateral tongue and the dental pad. A circular ulcer is also present on the left cheek below the left eye. Creamy white exudate drains from some of the larger lesions. The thorax contains creamy tan pus and the pleural surfaces are lined with thick exudate forming adhesions to the thoracic wall and diaphragm. The lungs are consolidated ventrally with multifocal variably sized abscesses containing thick tan pus.

Laboratory Results:
Aerobic bacterial cultures of the muzzle yielded heavy growths of Arcanobacterium pyogenes and m oderate growths of Pseudomonas aeruginosa and Staphylococcus intermedius.

Electron microscopy: Tissue from the muzzle and lips yielded Parapoxvirus (179 X 300nm)

Histopathologic Description: The lesion consists of locally extensive papillary projections of acanthotic, hyperkeratotic epidermis and extensive dermal (or submucosal) inflammatory infiltrate of neutrophils, histiocytes, and lymphocytes with occasional eosinophilic dermal pustules and microabscesses. Numerous small capillaries course throughout the dermis. Occasional ballooning vacuolation of keratinocytes with rare eosinophilic intracytoplasmic inclusions are seen. The epidermis is covered with thick serocellular crusts containing degenerating cells and small clusters of bacteria. Deep anastomosing rete pegs extend into the dermis (or submucosa).

Contributor’s Morphologic Diagnosis:
Muzzle: Lymphocytic, neutrophilic, histiocytic, pustular and proliferative dermatitis and stromatosis with papillomatous epidermal hyperplasia, acanthosis, hyperkeratosis and occasional eosinophilic intracytoplasmic inclusions in keratinocytes

Lungs: Severe fibrinosuppurative bacterial bronchopneumonia (not included)

Etiologic Diagnosis: Parapoxvirus

Contributor’s Comment: Contagious pustular dermatitis (contagious ecthyma, sore mouth, orf) is an infectious dermatitis of sheep and goats with worldwide distribution, caused by Parapoxvirus. The genus Parapoxvirus is a member of the Poxviridae family, and includes orf virus, bovine papular stomatitis virus, and pseudocowpox virus. It is an ovoid, enveloped, double stranded, DNA virus. Transmission is into skin abrasions through aerosols, direct contact, or through mucous membranes of the eyes, nose, and mouth. Lambs and kids are at greatest risk because they are immunologically naïve, and the colostrum from a previously infected animal does not provide protection. Due to its tropism for epithelial cells, Parapoxvirus will cause epidermal hyperplasia, producing papular lesions usually within 7 days. Papular lesions progress to vesicles, pustules, and then crusty scabs. In a 2002 study of 16 persistently infected goats, lesions regressed if infected goats were treated with antibiotics. Mortality rates in lambs is reported to be 15%. Transmission between sheep and goats can occur, but is uncommon. Parapoxviruses may also be transmitted to humans causing similar pustular lesions, commonly on the forearm, hand and neck.

Diagnosis of Parapoxvirus is based on the recognition of characteristic lesions and lesion distribution. Microscopically, eosinophilic intracytoplasmic inclusion bodies are visible, along with vacuolation and swelling of keratinocytes. The virus particles can be photographed with an electron microscope. The virus can survive in the environment for months in affected animals. Virulent, live virus vaccines do exist but are only recommended for use in persistently infected animals.
infected herds. Contagious pustular dermatitis is of economic significance because lambs and kids become reluctant to eat or suckle, causing weight loss and reduced growth rates. Differential diagnosis for contagious pustular dermatitis should include Foot and Mouth disease, Rinderpest, and Bluetongue.

**AFIP Diagnosis:**
1. Muco cutaneous junction, lip: Cheilitis, proliferative and necrotizing, focally extensive, severe, with intracytoplasmic eosinophilic inclusion bodies, pygmy goat (*Capra hircus*), caprine.
2. Haired skin, lip: Abscess, focal, with foreign material and fungal hyphae.

**Conference Comment:** Members of the parapoxvirus genus include orf virus, papular stomatitis virus, pseudocowpoxvirus, parapoxvirus of red deer in New Zealand, and squirrel parapoxvirus. Other species that have been tentatively in cluded include a uzdak disease virus, chamois contagious ect hyma virus, seal parapoxvirus. Seal parapoxvirus is the preferred term rather than 'sealpox virus' to distinguish it from the orthopoxviruses that cause similar clinical diseases.

Characteristic ultrastructural features of parapoxvirus include 250nm X150nm particles, with an oval- to dumbbell-shaped core surrounded by a membrane, lateral bodies, and a surface membrane.

Histopathologic lesions of contagious ecthyma are typical of other poxviral lesions except they usually have a very brief vesicle stage, a prominent ulcer and crust stage, and inclusion bodies present for only a brief period of time during the vesicular stage.

There is variation in sections. Some sections have a focal ulcer with bacterial colonies and neutrophilic mural folliculitis with fungal arthrospores, both likely secondary to the ulcerative lesions induced by the orf virus.

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**References:**