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Armed Forces Institute of Pathology
Washington, DC 20306

CASE I – H05-0631 (AFIP 2987675)

Signalment: Ara (*Ara chloroptera*), male, 5 years old

History: The ara showed an irregular, soft mass on his right leg, measuring 7 to 10cm in diameter. Radiographs revealed lytic areas within this mass. The animal was euthanatized.

Gross Pathology: Necropsy revealed a slightly enlarged liver. The mass on the right leg consisted of several nodes with yellowish caseous centres and numerous miliary nodules.

Laboratory Results: Bacterial cultures of heart and liver were negative. Impression smears of liver and intestine were negative in the Ziehl-Neelsen stain, but few acid fast bacteria were detected in smears of the mass on the leg.

Histopathologic Description: Subcutaneous tissue of the right leg: Fibrous connective tissue diffusely infiltrated with macrophages, lymphocytes, heterophils and plasma cells. Scattered groups of epitheloid and multinucleated giant cells. Multiple foci are present with central caseous necrotic material consisting of degranulating heterophils, surrounded by epitheloid and multinucleated giant cells.

Contributor's Morphologic Diagnosis: Subcutaneous tissue of the right leg: Panniculitis, granulomatous, diffuse, severe, with intralesional acid fast bacteria.

Contributor's Comment: This ara was presented at the departement of zoo and wildlife medicine because of a mass on his leg. Radiographs revealed a lytic pattern and tuberculosis was suspected. The owner admitted that he himself had

suffered from pulmonary tuberculosis two years previously. He first refused to have the bird euthanatized but later agreed for the sake of his other birds (a 55 year old Amazon and several budgerigars).

At necropsy, typical subcutaneous caseous lesions were found on the right leg. Furthermore, the liver was enlarged. Impression smears of liver and intestine revealed no acid fast bacteria whereas smears of the leg mass showed a small number of acid fast bacteria. Histopathology revealed typical lesions consisting of tuberculous nodules with central necrosis, surrounded by epitheloid macrophages and multinucleated giant cells. For cultivation, parts of the mass on the right leg were sent to the national reference center for mycobacteria where *Mycobacterium tuberculosis* was identified.

This case is one of few rare reports describing an infection with *M. tuberculosis* in a bird living in a household with a person who also had active tuberculosis previously. It is likely that the ara contracted the disease from his owner. Moreover, the bird may have acted as a source of infection for other birds. So far, it is not clear whether humans can acquire the infection from birds; environmental sources are considered the principal origin of mycobacteriosis in humans (1, 2).

Avian mycobacteriosis has a worldwide distribution and the most common mycobacteria species that infect birds are Mycobacterium avium, of the serotypes 1,2,3 and 8 as well as Mycobacterium genavense. Since Mycobacterium avium and M. intracellulare show nearly equal growth characteristics and species-specific antigens, they are grouped together and termed the M. avium-intracellulare (MAI) complex. Some investigations on the etiological agents of mycobacteriosis in pet birds have been carried out recently. Mycobacterium genavense was found to be the main causative agent followed by M. avium intracellulare complex and to a much lesser extent, M. tuberculosis. Isolates like M. fortuitum, M. gordonae, M. nonchromogenicum were found in one or two species (2,3,4,5).

The route of infection depends on the organism. M. tuberculosis seems to be contracted directly from people by inhalation of aerosolized bacteria, whereas M. avium and M. genavense are contracted by ingestion of the organism. The latter two appear to be ubiquitous in the environment. The genetic susceptibility, the immune response and possible stressors like malnutrition, overcrowding or other diseases and the number of organisms to which the bird is exposed determine whether it will get infected by Mycobacteria or not. (2,5).

The clinical findings in birds infected with mycobacteria can vary extremely. Often, it seems to be a chronic wasting disease which may result in death. Some infected birds are found dead without previous abnormal appearance or behaviour. At clinical examination, an enlarged liver or a thickened intestine may be noticed. M.

avium and M. genavense typically cause a widely disseminated disease. Mycobacteria spread from the intestine which is first colonized following ingestion and any organ system may be affected. The liver, spleen, lung, air sac, skin and bone marrow are most often involved. Less common are cutaneous, subcutaneous or ocular granulomatous lesions (2,3,4,5).

An antemortem diagnosis is only successful in biopsies of skin lesions or those taken during laparascopy. Post mortem impression smears stained according to Ziehl-Neelsen are a fast procedure with a clear diagnosis in positive cases (2,3,4,5). Cultivation of mycobacteria requires much time and experience. Histological lesions can also vary and according to some reports are divided into three groups. In the first group, only a proliferation of epitheloid cells laden with mycobacteria and associated inflammatory cells such as heterophils and round cells are noted. In the second group, single epitheloid cells can be seen and in the third group, large expanses of epitheloid cells laden with mycobacteria, without accompanying inflammatory infiltrates, are found. There seems to be a variation of these findings depending on the host species. However, there is no diversity in the histology of lesions between the different species of mycobacteria (2,3,4).

AFIP Diagnosis: Subcutis, right leg (per contributor): Panniculitis, granulomatous, diffuse, severe, green-winged macaw (*Ara chloroptera*), avian.

Conference Comment: The contributor provides an excellent review of mycobacterial infections. Although *Mycobacterium avium* may be much more common in birds**,** especially under crowded conditions, this case demonstrates the susceptibility of psittacines to *M. tuberculosis*.

Following inhalation, mycobacteria are endocytosed by macrophages via mannose receptors which bind a cell wall glycolipid called lipoarabinomannan. Cord factor (trehalose dimycolate) is a glycolipid that inhibits or decreases PMN chemotaxis, phagosome-lysosome fusion, TNF secretion and microsomal enzyme function. By inhibiting phagosome-lysosome fusion the mycobacteria are able to survive and replicate within the phagosome. There are a number of virulence factors which contribute to infection by *M. tuberculosis* including Wax D and mycolic acids within the mycobacterial cell wall. Muramyl dipeptide and various glycolipids attract antigen–processing cells for antigen presentation to naïve T-cells.

Antigen presenting cells such as alveolar macrophages present mycobacterial antigen and MHC class II proteins, to naïve T-cells. Binding of the T-cell receptor with mycobacterial antigen and exposure to the cytokine interleukin-12 (IL-12), released by the antigen presenting cell, drives the differentiation from naïve CD4+

T-cell to T-helper 1 lymphocyte which, in-turn, secretes interferon gamma (IFN-∂). IFN-∂ "activates the macrophages" which promotes phagosome-lysosome fusion, exposing mycobacteria to a destructive acidic environment. Activation also results in increased production of inducible nitrous oxide synthase (iNOS) which generates free radicals capable of destroying mycobacteria. Activated macrophages also release tumor necrosis factor (TNF) which is chemotactic for monocytes and induces them to differentiate into epithelioid macrophages or histiocytes. These epithelioid macrophages are characteristic of the delayed type hypersensitivity response and, through the secretion of several mediators of inflammation such as TNF, IL-1 and additional IL-12, continue to amplify the T helper 1 lymphocyte response. Additionally, they also secrete platelet-derived growth factor (PDGF) which stimulates fibroblast proliferation and collagen synthesis. The end result is continued inflammation, lymphocyte activation, and fibrosis resulting in the formation of a granuloma.

The hallmark of disease caused by *M. tuberculosis* is the development of tubercles. Tubercles form when granulomas develop and coalesce. The center of a tubercle may contain caseous necrotic debris bound by epithelioid macrophages, multinucleated giant cells, fibroblasts, collagen, lymphocytes and plasma cells. Although rare in birds, but not other species, tubercles may become calcified.

Tuberculosis in man has been recognized since the age of the ancient Egyptians. Currently, it is the second leading cause of death due to infectious disease, behind the Human Immunodeficiency Virus (HIV), and there are approximately 8-10 million new cases each year.

The presence of classical granulomas should promote the investigator to consider mycobacteriosis as a cause. Mycobacteria are long, thin, non-motile and non-spore forming bacilli. The acid-fast reaction can help identify acid retention in the walls of the mycobacteria which makes them appear as tiny, red threads within macrophages and cellular debris, most commonly found at the edge of a lesion. Delayed type hypersensitivity, the tuberculin response and granuloma formation develop through a classic sequence of events involving multiple inflammatory cells, mediators of inflammation and growth factors and must be a process familiar to every student of pathology (6).

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CASE II – 8005-1011 (AFIP 2985455)

Signalment: 15 week old, intact male, Labrador Retriever, *Canis familiaris*.

History: A two cm diameter mass on the right maxilla was removed by the referring veterinarian and submitted for histopathology. The mass recurred over the next two weeks. The patient was referred to Mississippi State University College of Veterinary Medicine, and a CT scan demonstrated that the mass invaded from the maxilla to the zygomatic arch and cribriform plate. The animal was euthanized March 9, 2005.

Gross Pathology: A four cm by two cm, firm mass expands the right maxilla, just cranial to the zygomatic arch. The surface of the mass is ulcerated and hemorrhagic. On cut surface, the mass is firm and fibromatous and bordered by thin cortical bone. The submandibular lymph nodes are enlarged. The other abnormalities noted on necropsy are mild pulmonary edema and endoparasitism (*Dipylidium* sp.).

Histopathologic Description: Maxillary mass: A poorly circumscribed neoplasm is composed of irregular cords of odontogenic epithelium in a pale, basophilic mesenchyme (suggestive of dental pulp) and small amounts of collagenous, fibrovascular supporting tissue. The morphology of the neoplastic epithelial cells varies widely. Well-differentiated cuboidal to columnar epithelial cells palisade along eosinophilic material with fine, tubular cavities (dentin) or hyaline material (enamel). The features of these cells include vacuolated, basophilic cytoplasm, round to oval apical nuclei, finely stippled chromatin, and small nucleoli. Poorly

differentiated epithelial cells are pseudostratified and blend into the surrounding stellate stroma. The stroma is composed of spindle, stellate, and fewer polygonal cells with variably distinct margins and moderate, amphophilic to basophilic cytoplasm. The nuclei are round to oval and contain finely stippled chromatin and inconspicuous to small nucleoli. In one section, the mass compresses trabecular bone, and reactive bone formation is present. The gingival surface is ulcerated and covered by a moderate amount of beaded, eosinophilic, fibrillar material (fibrin) and a moderate number of degenerating neutrophils and macrophages and fewer lymphocytes and plasma cells. Immunohistochemistry demonstrates that the epithelial cells have positive cytoplasmic staining for cytokeratin; the mesenchyme stains positively for vimentin.

Contributor's Morphologic Diagnosis: Ameloblastic fibro-odontoma

Contributor's Comment: Odontogenic tumors are rare in animal species. Multiple classification schemes exist for these tumors. One scheme divides odontogenic tumors based on the inductive effects of the odontogenic epithelium on the surrounding epithelial tissues. In addition, tumors may be classified as epithelial, mesenchymal, or mixed odontogenic tumors. The World Health Organization divides tumors based on benign or malignant characteristics (1).

Ameloblastomas are locally invasive, slow growing odontogenic epithelial tumors that typically do not metastasize (1). These tumors occur more frequently in dogs and cattle than other species and may arise at any age. Ameloblastomas occur more commonly in the mandible (2). Those tumors that occur within bone are central, whereas, gingival tumors are peripheral. The prominent features of ameloblastic basal cells are as follows: palisading epithelial cells, apical nucleus, cytoplasmic clearing, and intercellular bridging (3). Odontogenic epithelial cells may occur in follicular or plexiform patterns. The tumor cells originate from the dental lamina, outer enamel epithelium, dental follicles of unerupted teeth, oral epithelium, or odontogenic epithelium (2). Keratinizing ameloblastomas are a type of ameloblastoma with pronounced keratinization of the epithelial cells (3). Acanthomatous ameloblastoma, previously named acanthomatous epulis, also arises from odontogenic epithelium, with prominent acanthocytes. These tumors are common in dogs, and may be bilateral. The tumors contain sheets of odontogenic epithelium with central acanthocyte formation (3). Amyloid-producing odontogenic tumors arise from odontogenic epithelium, and have features similar to ameloblastomas. However, amyloid matrix is interspersed among the epithelial cells (3).

Ameloblastic fibromas are typically slowly expanding, well-circumscribed, non-invasive odontogenic tumors (1), which occur more commonly in cats (2) and cattle (3). These tumors consist of epithelium similar to but less well developed than that of ameloblastomas. The connective tissue found throughout the tumor is composed of cellular fibroblastic tissue similar to dental papilla (1).

Ameloblastic fibro-odontomas occur in dogs, horses, and cows. These tumors resemble ameloblastic fibromas, but contain dentin and enamel and a more differentiated enamel epithelium (2). Gardner argues that these only occur in animals with mature dentition; in immature individuals, the tumor may be a developing stage of an odontoma (1). A malignant ameloblastic fibro-odontoma with metastasis was recently described in a dog (4).

Odontomas, often classified as hamartomas, contain well-differentiated dental tissues, including enamel, dentin, cementum, and dental pulp or its precursor, dental papilla. Those tumors with organized tooth structures, or denticles, are compound odontomas. Tumors with disorganized tooth components are complex odontomas (1). Odontomas are more common in cattle and horses; they usually occur in the mandibular or maxillary arch, distorting the bone and nearby teeth (2).

Odontoameloblastomas are very rare tumors that contain ameloblastic epithelium and distinct areas of compound or complex odontoma (2). Their biological behavior resembles that of ameloblastomas (1).

This tumor demonstrates many features of an ameloblastic fibro-odontoma, but may be a developing compound odontoma because of the age of the animal and the presence of denticles in the mass initially presented for histopathology. Ameloblastic fibro-odontomas are described as encapsulated, well-circumscribed neoplasms. The tumor in this case appears on CT scan to be invading the adjacent bone and histologically is poorly circumscribed. These features of malignancy are accompanied by cellular atypia; however, metastasis was not noted.

AFIP Diagnosis: Maxilla, right (per contributor): Odontogenic tumor, favor Ameloblastic fibro-odontoma, Labrador Retriever, canine.

Conference Comment: The Department of Oral Pathology reviewed this case and agreed that the neoplasm is consistent with an ameloblastic fibro-odontoma.

Teeth develop from two embryonic tissues: buccal cavity squamous epithelium and embryonic mesenchyme. During early tooth development, a portion of buccal cavity squamous epithelium invaginates into the subjacent embryonic mesenchyme and forms the dental lamina which ultimately forms the enamel organ and ameloblastic cell layer. All other parts of the tooth including dentin, cementum, and pulp, derive from embryonic mesenchyme.
Dental epithelial and mesenchymal cells have an inductive influence on each other. The ameloblastic epithelium induces differentiation of the dental papilla mesenchyme into odontoblasts, which form dentin. The presence of dentin induces the ameloblasts to form enamel. After odontogenesis, ameloblasts

disintegrate; thus, damaged enamel cannot be repaired. Odontoblasts remain viable for the life of the tooth.

The World Health Organization currently divides odontogenic tumors into four major groups (5):

1) Tumors of odontogenic epithelium **without** odontogenic mesenchyme
    a. Ameloblastoma
    b. Amyloid producing odontogenic tumor
    c. Canine acanthomatous ameloblastoma (formerly know as acanthomatous epulis)

2) Tumors of odontogenic epithelium **with** odontogenic mesenchyme
    a. Ameloblastic fibroma
        1. Ameloblastic fibro-odontoma
    b. Feline inductive odontogenic tumor
    c. Complex odontoma
    d. Compound odontoma

3) Tumors composed primarily of odontogenic ectomesenchyme
    a. Cementoma
    b. Cementifying fibroma

4) Tumors derived from the tissues of the periodontal ligament
    a. Fibromatous epulis of periodontal ligament origin

Since the submitted neoplasm has both epithelial and mesenchymal components exhibiting ameloblastic and odontoblastic differentiation, conference attendees agreed that it belonged with the **tumors of odontogenic epithelium with odontogenic mesenchyme** group. There was debate; however, as to which of the four neoplasms from that group best resembled this neoplasm. There is both ameloblastic epithelium present and odontoblasts forming dentinal tubules as well as internalized epithelial cells reminiscent of stellate reticulum. Additionally, there are multiple abnormally shaped, tooth like structures or denticles within the mass separated by dense collagenous connective tissue. Most agreed the neoplasm was most consistent with either ameloblastic fibro-odontoma or a developing compound odontoma.

Although dental neoplasms may be locally destructive, as in this case, a good prognosis is warranted if excision is complete; metastasis is unreported.

Categorizing odontogenic neoplasms can be a challenge which requires a basic understanding of odontogenesis, dental anatomy, a categorizing scheme and

experience. The moderator stressed the importance of practicing how to describe odontogenic neoplasms using the appropriate terminology (i.e. don't let Ames be the first place you've had to write and describe dentinal tubules and stellate reticulum) and the need for each resident to develop and add a standard odontogenic neoplasm description to their repertoire.

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CASE III – ND1 (AFIP 2983853)

Signalment: Three bighorn (*Ovis canadensis canadensis*) rams

History: These rams were hunter harvested in the fall of 2004. All animals were considered clinically normal. Lung tissue was collected by a referring veterinarian and forwarded to the diagnostic laboratory.

Gross Pathology: Fixed tissue only was submitted. There were well-defined, multifocal areas of pallor, primarily subpleural, in the pulmonary parenchyma.

Histopathologic Description: Microscopic examination revealed multiple, unencapsulated, well-demarcated foci characterized by inflammation, fibrosis and numerous intralesional nematodes. Representative foci showed moderate to marked interstitial lymphocytic to plasmacytic inflammation in both alveolar septa

and affected locations subjacent to the pleura. Alveoli contained various amounts of proteinic material, lymphocytes, macrophages, and numerous nematode eggs, nematode larvae and cross sections of adult nematodes. Granulocytes were randomly present in small numbers but were not a significant component of the exudate. Adults and larvae were present in terminal bronchioles and some bronchi as well. Larva demonstrated the pointed tail characteristic of protostrongylids. There was atelectasis of unaffected adjacent parenchyma. Proximate bronchioles and bronchi were accentuated by smooth muscle hypertrophy, increased amounts of peribronchiolar and peribronchial connective tissue, scattered lymphoplasmacytic inflammation and moderate epithelial hyperplasia.

Contributor's Morphologic Diagnosis: Marked, multifocal lymphoplasmacytic and histiocytic pneumonia with interstitial fibrosis and numerous intralesional nematode ova, larva and adults consistent with *Protostrongylus stilesi*.

Contributor's Comment: Lungworm infections are well-reported in bighorn sheep. *Protostrongylus stilesi* and *P. rushi* are the two species most commonly associated with the condition. *Muellerius capillaris* has been reported, but this appears to be uncommon. In many areas the nematode is considered ubiquitous within resident sheep populations. The parasite is recognized as an important part of the pneumonia complex reported in bighorns and various techniques have been attempted to reduce the worm load in susceptible groups.

Protostrongylids belong to the order Strongyloidea, superfamily Metastrongyloidea, and family Protostrongylus. Adult worms reside in alveoli, bronchioles and bronchi of sheep. Adult males are thread-like brown nematodes measuring 16 to 28 mm in length while females measure 25 to 35 mm. Larva and eggs can be found in lung tissue as well. Following the hatching of embryonated eggs, L1 larva pass up the trachea either through the mechanism of coughing or the action of the mucociliary apparatus. Once in the mouth, L1 larva are swallowed and pass in the fecal pellets. The L1 larva are very resistant to the environment, apparently being able to overwinter in fecal material. This may be in part due to the fact that L1 larva are found in higher concentrations in the core of a fecal pellet rather than the edges. When conditions are favorable, L1 larva leave the fecal pellet and penetrate the foot tissue of the intermediate host, a terrestrial gastropod. Studies have indicated that moisture is an important predisposing factor in the movement of L1 larva in that the intermediate host is more available in wet conditions. Several different species of gastropod have been identified as suitable intermediate hosts. Larval development continues within the gastropod to the L3 or infective stage; this may take anywhere from two to six weeks. At this point the larva containing gastropod is ingested by a sheep and infection occurs. The larvae subsequently molt to an L4 stage, penetrate the intestinal wall, enter lacteals, undergo a final molt in draining lymph nodes, enter the lymphatics and reach the heart and lungs. Finally, the larva migrate from alveolar capillaries into alveoli, bronchioles and

bronchi where they develop into adults. The prepatent period is five to six weeks and patency is long, reported to exceed two years. The life cycle is complicated by the ability of the nematode to move via the uterine artery into the fetal circulation in pregnant ewes. L3 larva have been found in the liver and lungs of fetal lambs.

AFIP Diagnosis: Lung: Pneumonia, lymphoplasmacytic, histiocytic and eosinophilic, chronic, multifocal, moderate, with bronchiolar smooth muscle hypertrophy, and myriad metastrongyle eggs, larvae, and few adults, etiology consistent with *Protostrongylus* sp., bighorn sheep (*Ovis canadensis canadensis*), ovine.

Conference Comment: The contributor provides an excellent review of lungworm infestations in bighorn sheep, with reference to domestic sheep as well.

In general, there are three well known and common parasitic pneumonias of sheep and goats. All three are caused by metastrongyles which can be differentiated from the true strongyles and trichostrongyles by having coelomyarian instead of platymyarian musculature. Although difficult to recognize, another distinguishing feature of adult metastrongyles are accessory hypodermal chords. Metastrongyle larvae can often be identified by a characteristic finger-like projection at the tip of their tail (6).

Dictyocaulus filaria commonly affects lambs and goat kids and causes partial obstruction of small bronchi, atelectasis, eosinophilic bronchitis, lymphoid and type II pneumocyte hyperplasia and an alveolar exudate. *Muellerius capillaris* also known as the "nodular lungworm" affects both sheep and goats and forms numerous subpleural nodules, especially in the dorsal part of the caudal lung lobes. Nodules are the result of an eosinophilic and granulomatous response to subpleural adults, eggs and larvae. *Protostrongylus rufescens* usually affects lambs and goat kids and can cause mucopurulent nasal discharge, anorexia, diarrhea and weight loss (7).

Multiple species are affected by lungworms. Below is a list of the more common lungworms in domestic animals and phocid pinnipeds. This list is intended to be used as a training aid and is by no means all inclusive.

Lungworms of domestic animals:

- *Aelurostrongylus abstrusus* – cats; catarrhal bronchiolitis, submucosal gland hyperplasia, granulomatous alveolitis, alveolar fibrosis
- *Capillaria aerophila* – dogs, cats, foxes; dogs and cats very mild infection
- *Crenosoma vulpis* – foxes, occasionally dogs; eosinophilic catarrhal bronchitis

and bronchiolitis
- *Filaroides hirthi*, *F. milksi* – dogs, mink; pyogranulomatous, eosinophilic pneumonia
- *Angiostrongylus vasorum* – dogs, foxes; inhabits pulmonary artery and right ventricle
- *Dictyocaulus filaria* – sheep and goats; catarrhal and eosinophilic bronchitis and bronchiolitis
- *Dictyocaulus viviparous* – cattle; pneumonia, bronchitis, pulmonary edema and emphysema
- *Dictyocaulus arnfieldi* – horses, donkeys; obstructive or eosinophilic bronchitis, edema, atelectasis
- *Muellerius capillaris* – sheep and goats; small nodular lesions on the lung surface
- *Protostrongylus rufescens* – sheep and goats; lambs and kids; lives in bronchioles, causes pulmonary nodules.
- *Metastrongylus apri* – pigs; growth retardation, bronchitis, catarrhal inflammation

Lungworms of phocid pinnipeds:
- *Otostrongylus circumlitis* - the only other lungworm of phocid pinnipeds (seals: harbor, ringed, spotted, ribbon, Baikal, grey, bearded, northern elephant)
    - Large roundworm found in large bronchi and bronchioles; causes
    - vasculitis
- *Parafilaroides* spp. – spp. based on host and geographic range
    - *P. gymnurus* – final host: phocid seals (harbor, ringed, harp, spotted, grey, bearded, Baikal); range: coastal waters of Canada, Europe, and Russia
    - *P. hydrurgae* – final host: leopard seal; range: Southern Ocean
    - *P. decorus*- final host: California sea lion, Stellar sea lion, northern fur seal; range: Pacific waters of the United States

P. hispidus – final host: phocid seals (ringed and grey); range: coastal
    - waters of Canada
    - *P. caspicus* – final host: Caspian seal; range: Caspian Sea

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CASE IV – B7968-03 (AFIP 2984962)

Signalment: 5 years, male, Petit Basset Griffon Vendéen, *Canis familiaris*, dog

History: Nausea, vomiting and marked salivation for less than 2 weeks at presentation to the clinician. Clinically, mandibular glands were bilaterally tender and enlarged, and the dog had a low-grade fever (39.1°C). Both glands were removed and antibiotic treatment was instituted. The condition was markedly improved after a few days but the case was lost for long term follow-up.

Laboratory Results: Leukocytosis ($17.2x10^9$WBC/l, 85% neutrophils, no left shift). Hematocrit 36% (N 43-52).

Histopathologic Description: A piece of one mandibular salivary gland for examination. There is a sharply delineated area of parenchymal coagulative necrosis with preserved lobular architecture. Fibroblast-rich immature granulation tissue, inflammatory edema and hemorrhage occur in the necrotic area and multifocally in adjacent lobules. Mild to moderate infiltrates of polymorphonuclear leukocytes appear multifocally, even within neighboring glandular acini. Several epithelial ducts with squamous metaplasia and pleomorphic irregular epithelial hyperplasia occur in the lesions and sometimes show prominent mitotic activity and

mild nuclear atypia. Necrotic acinar cells occur multifocally intimately associated with metaplasia and hyperplasia, indicating metaplasia of glandular cells. Only in some sections, focal necrotizing arteritis with fibrinoid necrosis and even thrombosis, is evident in the interstitial tissue bordering the necrotic parenchyma.

Contributor's Morphologic Diagnosis: Necrotizing sialometaplasia.

Contributor's Comment: Necrotizing sialometaplasia in humans is a self-limiting benign inflammatory disorder, mainly of the minor salivary glands, and affecting major glands only rarely (1). It is also termed salivary gland infarction. Major morphologic features include squamous metaplasia of ducts and acini, lobular coagulation necrosis with preservation of lobular architecture, granulation tissue, and, in minor salivary glands, overlying pseudoepitheliomatous mucosal hyperplasia (1). The cause is not established but the necrosis is of ischemic type and underlying blood vessel injury is often proposed. Several factors have been proposed to explain vascular changes (1). This morphologic entity also occurs in dogs and cats, but involvement of mandibular glands is characteristic in these species (2,3,4,5) and the disease has much more severe clinical signs than the human analogy (5). In one large series of salivary gland specimens submitted to a diagnostic laboratory, the diagnosis was established in 9/160 dogs and 11/85 cats (2). In those cases, though an ischemic basis was considered likely, arterial thrombosis was only found in one specimen, whereas three canine cases described by others (3,5) had vascular thrombi. The metaplastic and hyperplastic epithelial changes are considered as a reparative response (1,2). Since they, as in the present case, often show pseudocarcinomatous features, the diagnosis may not be straightforward but can be confused with salivary gland malignancies in both humans and animal species (1,4,5).

AFIP Diagnosis: Salivary gland, mandibular: Coagulative necrosis (infarct), multifocal, with ductular hyperplasia and squamous metaplasia, Petit Basset Griffon Vendéen, canine.

Conference Comment: The contributor provides an excellent and concise review of necrotizing sialometaplasia. In humans, four criteria must be met for a diagnosis of necrotizing sialometaplasia:

1) lobular necrosis of salivary tissue
2) squamous metaplasia conforming to duct outlines, acinar outlines, or both
3) maintenance of salivary lobular morphology
4) time-variable prominence of granulation tissue and acute and chronic inflammation (5).

Necrotizing sialometaplasia most commonly affects terriers, is extremely painful and often causes nausea, inappetence and vomiting. Most importantly, in chronic cases, squamous metaplasia and cellular atypia of salivary ducts can appear very similar to salivary gland neoplasia, especially if occluded ducts are surrounded by abundant fibrous tissue making them resemble islands of neoplastic cells.

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