Joint Pathology Center
Veterinary Pathology Services

WEDNESDAY SLIDE CONFERENCE 2025-2026

Conference #3 — 03 September 2025

CASE I:

Signalment:
5.5-year-old, male castrated, domestic short-hair cat (*Felis catus*)

History:
The cat was presented to the emergency service for a two-day history of lethargy and anorexia and a one-day history of labored breathing. The cat was reportedly indoor-only with no other animals in the house, had no history of illness, and had not been given any medications or preventatives. Thoracic auscultation revealed muffled heart sounds, decreased ventral lung sounds, and harsh dorsal lung sounds. The cat's pulses were strong and synchronous, and no murmur or arrhythmias were appreciated. A brief thoracic ultrasound revealed a large amount of pleural effusion. Following a discussion about differentials and prognosis, the owner elected humane euthanasia with necropsy.

Gross Pathology:
The thoracic cavity contained 180 mL of malodorous, tan to dark yellow to pale green, opaque effusion with free-floating aggregates of yellow to pale green friable material admixed. The same material covered the pericardium and multifocally covered the parietal and visceral pleura throughout the thoracic cavity, with the right side more severely affected than the left. The lung lobes were diffusely mildly

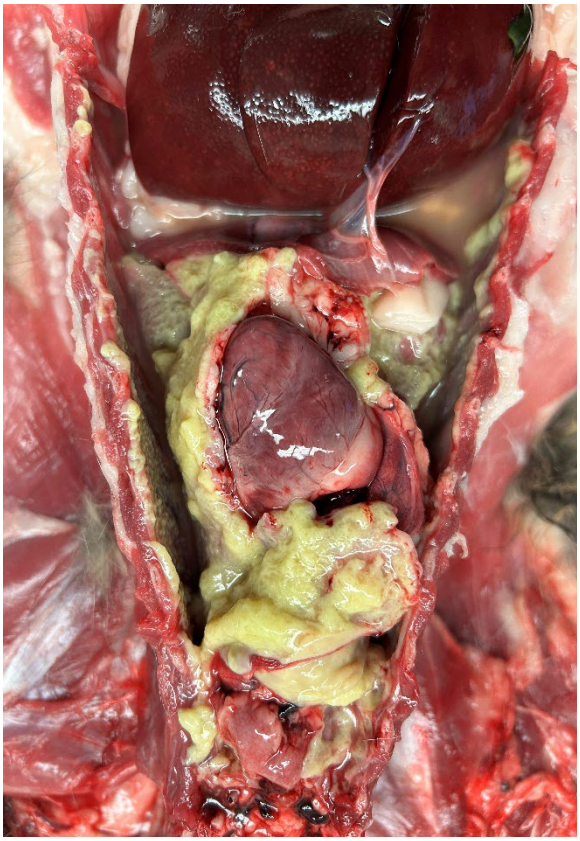

Figure 1-1 The pleura and pericardium are covered by aggregates of yellow to pale green friable material. (Photo courtesy of: UPenn School of Veterinary Medicine, Dept. of Pathobiology, https://www.vet.upenn.edu/).

rubbery and collapsed. The cranial aspect of the right caudal lung lobe was expanded by multiple, coalescing, approximately 0.3 cm diameter, tan to yellow nodules that oozed opaque, mucoid, yellow to gray exudate on cut section. Sections of the cranial portion of the

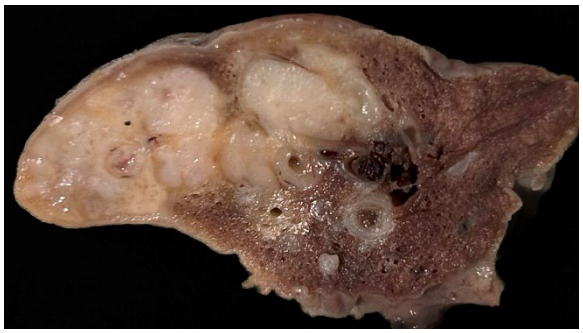

Figure 1-2: Lung, cat. There is marked consolidation of an apical section of formalin-fixed lung. (Photo courtesy of: UPenn School of Veterinary Medicine, Dept. of Pathobiology, https://www.vet.upenn.edu/).

right caudal lung lobe hovered below the surface in 10% formalin, while sections from the other lung lobes floated in 10% formalin.

There was no evidence of thoracic trauma or migrating foreign material on gross postmortem examination.

Laboratory Results:
Aerobic culture of the pleural fluid isolated *Escherichia coli*, *Actinomyces* sp. (suspect *Canibacter oris*), and *Staphylococcus aureus*. Aerobic culture of fresh lung tissue isolated *Escherichia coli*. Anaerobic culture of both the pleural fluid and lung tissue had no growth.

Microscopic Description:
One section each of the right caudal lung lobe and pericardium are examined. The parenchyma of the right caudal lung lobe is severely expanded by coalescing aggregates of viable and nonviable neutrophils amidst abundant fibrin and cellular debris, admixed with fewer epithelioid macrophages and occasional multinucleated giant cells. These aggregates are further encircled by a ring of maturing fibrous connective tissue with few admixed lymphocytes and plasma cells. These foci of inflammation are centered on large airways and rarely contain fragments of bronchiolar walls that have been effaced. Less affected bronchi and bronchioles occasionally have eroded to ulcerated epithelium with intraluminal coagula of fibrin, neutrophils, foamy macrophages, erythrocytes, and proteinaceous fluid. The visceral pleura is covered by a mat of viable and nonviable neutrophils with fewer epithelioid macrophages enmeshed in abundant fibrin, cellular debris, and mixed bacteria comprising cocci and short to filamentous bacilli. The underlying pleural connective tissue is diffusely thickened by granulation tissue with infiltrating epithelioid macrophages, lymphocytes, and plasma cells. The pericardial pleura is similarly affected.

Gram-stained sections of the right caudal lung lobe and pericardium demonstrate myriad gram-positive and gram-negative filamentous and short bacilli bacteria, both extracellular and within the cytoplasm of macrophages associated with the parietal pericardium, pulmonary visceral pleura, and pulmonary parenchymal lesions. An acid-fast-stained section (Ziehl-Neelsen) of the pericardium demonstrates that the filamentous and bacilli bacteria are uniformly acid-fast negative.

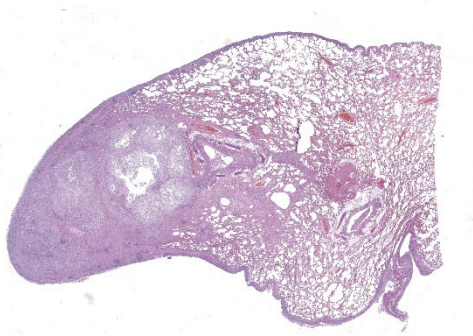

Figure 1-3. Lung, cat. At subgross magnification, the apex of the lung and a thin rim immediately beneath the pleura is consolidated. At the tip of the section, airways are filled and effaced with abundant inflammatory infiltrate which extends into the surrounding parenchyma. (HE, 10X).

Contributor's Morphologic Diagnoses:
Cat, right caudal lung lobe: severe regionally extensive chronic fibrinosuppurative and pyogranulomatous bronchopneumonia and pleuritis with bronchiectasis, granulation tissue, fibrosis, and bacilli and filamentous bacteria.

Cat, pericardium: severe diffuse chronic fibrinosuppurative and pyogranulomatous pericarditis with granulation tissue and bacilli and filamentous bacteria.

Contributor's Comment:
Pyothorax, or thoracic empyema, is characterized by accumulation of suppurative exudate within the pleural space.[1] Cats between 4-6 years old are predominantly affected, and no sex or breed predispositions have been identified.[2–4] More than 80% of feline pyothoraces are associated with a mix of obligate anaerobes (e.g., *Clostridium*, *Fusobacterium*, and *Bacteroides* sp.) and facultative aerobic bacteria (e.g., *Pasteurella* and *Actinomyces* sp.) which are reported constituents of the normal feline oropharyngeal flora, though non-oropharyngeal bacteria (including *Staphylococcus aureus* and *Escherichia coli*) have been isolated in a smaller percentage of cases.[4-9] It follows that pyothorax has frequently been associated with bite trauma which, by direct penetration of the thorax or by local extension of a subcutaneous abscess, can inoculate the pleural space with oropharyngeal bacteria.[2,3,10] Other reported routes of infection in cases of pyothorax include esophageal rupture, inhaled or migrating foreign bodies, larval migrans, therapeutic thoracic interventions (e.g., thoracocentesis or thoracic surgery), and spread of inflammation from a distant site.[3] While chest bite trauma remains an important risk factor for pyothorax, current evidence suggests that aspiration of oropharyngeal bacteria, leading to colonization of the lower respiratory tract and subsequent parapneumonic spread, is a more likely source of pleural infection in cats.[3,4,11] This mechanism of infection is also the most common mechanism of infection in human anaerobic pyothorax and equine pleuropneumonia.[4,12,13]

In this case, the distribution of lung lesions, i.e. a focal parenchymal lesion in the right caudal lobe as well as pleural lesions throughout all lobes, in context with the absence of chest trauma, is most suggestive of parapneumonic spread from bronchopneumonia arising from aspirated oropharyngeal bacteria. The bacterial isolates from the lung and pleural effusion are consistent with the findings in the gram- and acid-fast-stained sections of tissue and correspond to organisms reported in the feline pyothorax literature.

Contributing Institution:
University of Pennsylvania School of Veterinary Medicine
Department of Pathobiology
https://www.vet.upenn.edu/

JPC Diagnoses:
Lung: Bronchopneumonia, necrotizing and pyogranulomatous, chronic-active, focally extensive, severe, with pleural granulation tissue, bronchiectasis, and mixed bacteria.

JPC Comment:
COL (Retired) Jeremy Bearrs, former director of the Joint Pathology Center, spearheaded today's conference with a case that ended up as a staff favorite! This case's discussion started off with some clarifying definitions of pneumonia-related terms that are used ubiquitously by the pathologist that have specific meanings and should be used accurately. These included: "bronchopneumonia", referring to an exudative pulmonary lesion originating at the

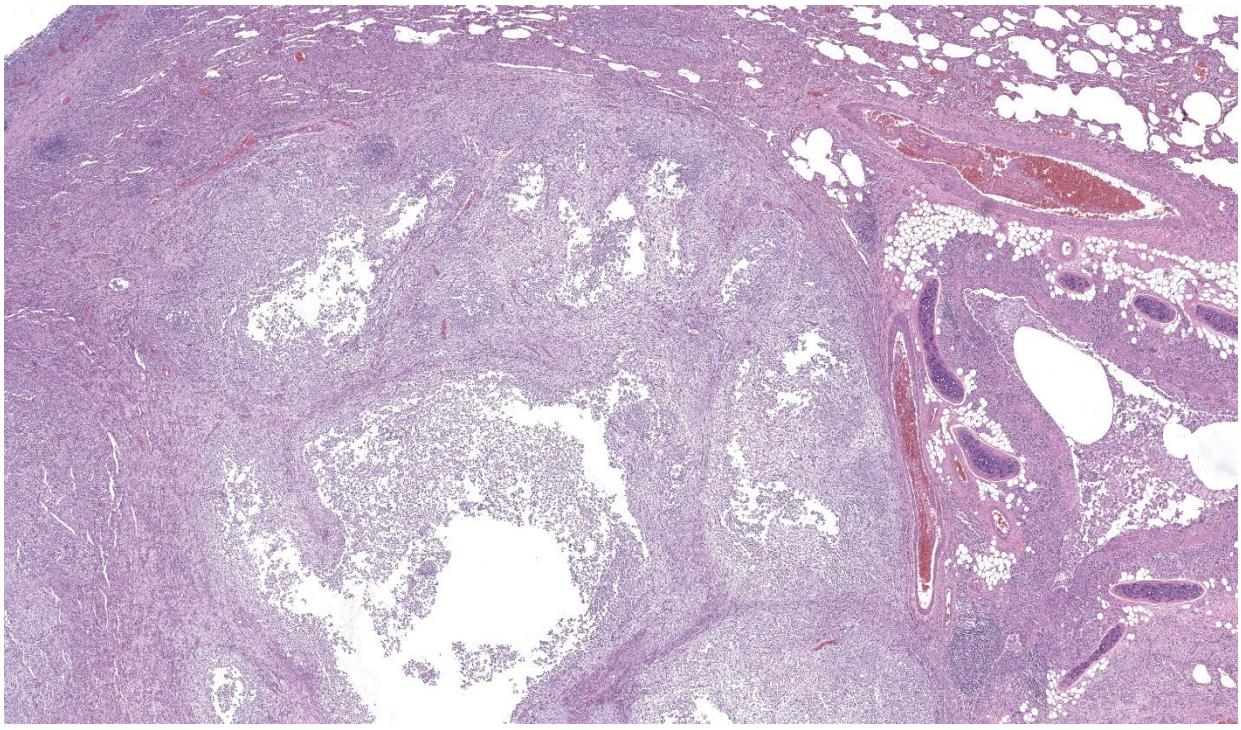

Figure 1-4: Lung, cat. A bronchiole is filled with an exudate of innumerable neutrophils and foamy macrophages which efface the wall and extends into the submucosa and fills the adjacent alveolar parenchyma. (HE, 33X).

bronchiolar-alveolar junction; bronchopneumonias usually start via airborne entry to the respiratory tract, are most often seen in the cranioventral lung lobes grossly, and often have an inflammatory exudate filling airways; "interstitial pneumonia", referring to generally diffuse destruction and inflammation centered upon the three components of the alveolar wall, frequently undergoing exudative, proliferative, and fibrosing phases, and typically enters the lung via bloodborne route of entry (think "viral") or secondary to toxins; "bronchointerstitial pneumonia", defined as the destruction of both bronchiolar and alveolar epithelium, typically via an airborne route of entry; "bronchitis", defined as a type of pulmonary inflammation that affects the bronchi specifically (note that "bronchopneumonia" does NOT, by definition, include the bronchi); and "bronchiectasis/bronchiolectasis", meaning a bronchus or bronchiole, respectively, is irreversibly expanded by inflammation and/or inspissated material as a sequela to loss of elastin and increased fibrosis from a chronic inflammatory response. These terms laid the groundwork for more descriptive accuracy and conversation by the conference participants. Among other notable points of discussion was a challenge to participants to name the major large colony-forming bacteria, which was prompted by the presence of sizeable bacterial colonies in the case slide. These bacteria include *Yersinia, Actinomyces, Actinobacillus, Campylobacter, Corynebacterium, Staphylococcus, Streptococcus, Nocardia,* and *Trueperella* (YAACCSS-NT). On a final note, Dr. Bearrs made an important point to mention knowing which bacteria are excep-

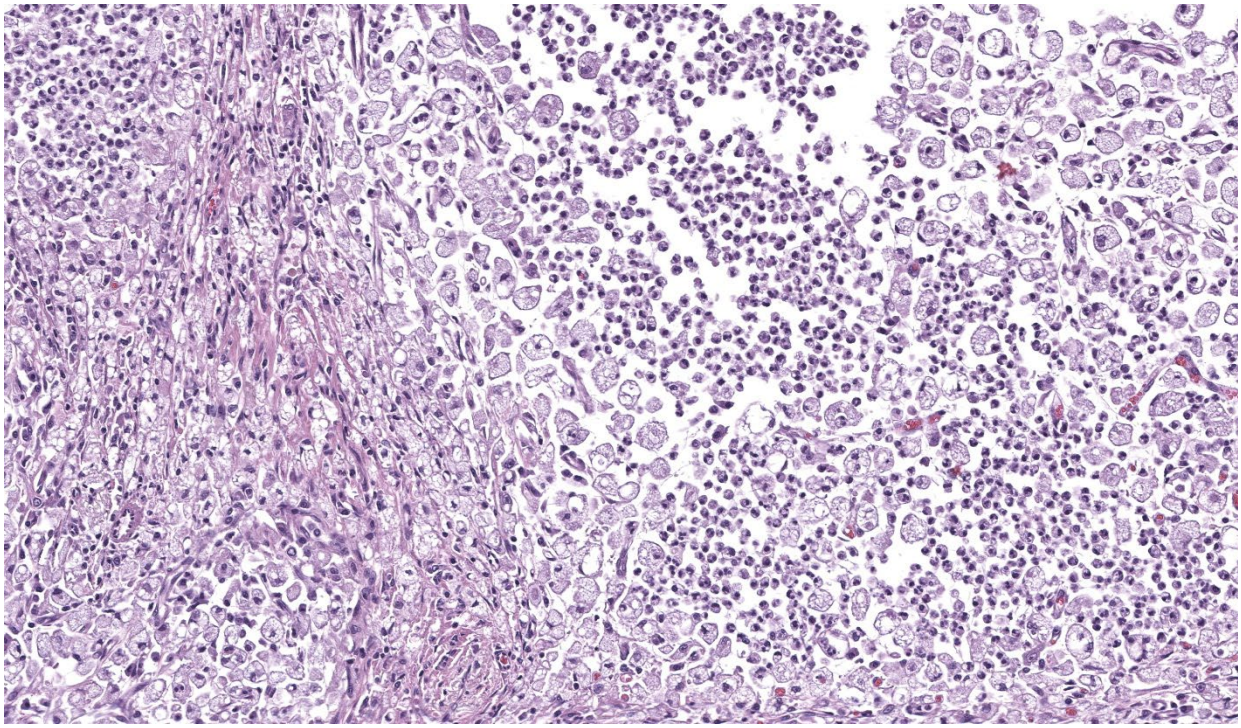

Figure 1-5: Lung, cat. Higher magnification of the inflammatory exudate. (HE, 363X)

tions to general rules, such as *Clostridium piliforme*, which is one of very few Clostridial species that are gram-negative.

Feline infectious peritonitis (FIP), congestive heart failure (CHF), pyothorax, and neoplasia represent the overwhelming majority of cases of pleural effusion in cats.[4] In an elegantly succinct manner, the contributor wrote a terrific comment about routine causes of pyothorax in cats. The possibility of aspiration from a regurgitation that the owners may not have been aware of (because, you know, cats) is certainly worth considering given the presence of E. coli. While the pathogenesis of an aspiration pneumonia with pleural spread might be considered reasonably straightforward, understanding how any form of pulmonary inoculation, including aspiration, leads to pneumonia and parapneumonic disease is worth reviewing.

Normal bacterial flora can be symbiotic with their host when they stay where they're supposed to be, but can become dangerous pathogens when they go where they aren't. Considering the bacteria cultured from this case (*E. coli, S. aureus*, and *Actinomyces* spp), *E. coli* will be used as an example. There are a variety of non-pathogenic *E. coli* strains that reside in the GI tract of cats (and most mammals) that are generally considered beneficial. However, they can also be opportunistic when they end up in, say, the lungs because some kid thought it was funny to make their cat gag at the sound of tape being ripped and it threw up its breakfast. Any event of vomiting or regurgitation can result in an aspiration, though this is most commonly seen during sedation or anesthesia.

Those beneficial gut bacteria, having been forcibly ejected from their home and sucked into the respiratory tract along with other bacteria from the oropharynx, find themselves in a strange and foreign place full of opportunity, far beyond the normal protective mechanisms of the coughing reflex and the mucociliary apparatus. Thus, the party begins. The presence of bacteria in the airways causes inflammation and it's not long before the "cops" show up to try and handle the wayward bacteria. Alveolar macrophages, being the resident neighborhood watch, show up first, having been summoned to the scene by pro-inflammatory cytokines such as IL-1, IL-6, IL-8, and TNFα. However, these cells can only do much, so they start calling in additional support in the form of neutrophils. With all these inflammatory cells and their myeloperoxidases showing up, there is rapid accumulation of pus full of bacteria, dead cells, fibrin, fluid, and damaged tissue. That's the short version of how a suppurative aspiration pneumonia is born.

As the bacteria continue to grow and translocate throughout the lungs, they eventually reach the pleural surface. From there, it's just a hop, skip, and a jump into the pleural cavity. This is usually a potential space with just a minute amount of fluid within it to allow for lubrication during respiration, but the inflammation from the raging pneumonia can result in additional fluid accumulation and edema around the lungs.[4] Bacteria can move out into that fluid and, where they go, neutrophils will follow and do what they do…kill things and make pus. In cats (and dogs), the mediastinum is fenestrated, so there is frequently bilateral accumulation of fluid.[4] That suppurative pneumonia has now graduated to a pyothorax.

Pyothoraces can be notoriously challenging to treat and most require aggressive medical management +/- surgery. In cats, survival rates from pyothorax are reported to be only 62%, with a 58% complication rate with thoracotomy tube placement.[11] Post-treatment complications are common and include pleural adhesions, pulmonary fibrosis, abscesses, sepsis, cardiac disease, recurrent infections, bronchopleural fistulas, and even death. However, parapneumonic disease in indoor cats from single-cat households is rare. The moral of the story? Keep your "murder mittens" in the house and, aside from the good that it would do for songbird populations, reduce their risk of pyothorax!

References:

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CASE II:

Signalment:
2-month-old, female, Yorkshire swine *(Sus scrofa domesticus*).

History:
This animal was found dead after exhibiting coughing and poor appetite for an unknown duration. It came from a group of 30 pigs, many of which had pruritus and black "greasy" exudate of the extremities. These animals had been purchased from multiple sources and introduced to the property within the last six weeks. This pig, and several others had areas of pruritic skin with black, "greasy" exudate, most severely on the distal extremities. Previous bacterial culture of these lesions had identified *Staphylococcus hyicus*.

Gross Pathology:
Distal extremities: The dorsal aspects of the pasterns of all four limbs are carpeted with dark brown, crusty, raised plaques. The lesions are most severe on the forelimbs (Fig 1).
Thorax: Multifocal strands of tan to yellow friable material (fibrin) are loosely adhered between the pleural surfaces of the lungs and the

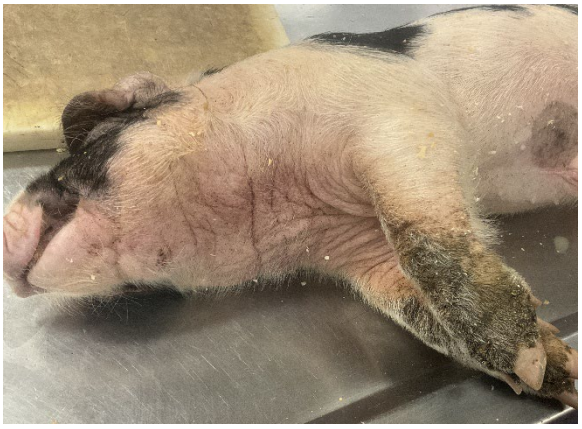

Figure 2-1: Haired skin, pig. The dorsal aspects of the pasterns of all four limbs are covered with dark brown, crusty, raised plaques. The lesions are most severe on the forelimbs. (Photo courtesy of: University of Missouri Veterinary Medical Diagnostic Laboratory https://vmdl.missouri.edu/).

body wall. The lungs are diffusely wet, heavy, soft, pink and exude dark red fluid on cut section. All examined sections float in formalin. The pericardium contains ~5 mL of pink, clear, watery fluid. The hilar lymph nodes are mildly enlarged to 1.5 - 2x normal size.
Abdomen: The abdomen contains approximately 50 mL of dark red, clear, watery peritoneal fluid. There are multifocal strands fibrin adhered between visceral organs. The stomach contains bright yellow to green semiliquid ingesta. The descending colon contains formed feces. There is mild congestion in the liver, and black, round, flat spots on the left lateral lobe of the liver. The remainder of the gross examination is unremarkable.

Laboratory Results:
Bacteriology: *Staphylococcus hyicus* was cultured from the liver.

Microscopic Description:
Skin: In the dermis, there is marked parakeratotic hyperkeratosis, with numerous colonies of extracellular cocci, and intracorneal arthropod mites. The mites are up to 300-400 µm in diameter, have a chitinous exoskeleton with dorsal spines, short jointed appendages, striated skeletal muscles, and internal gastrointestinal and reproductive tracts. The mites often contain birefringent internal crystalline material, suspected to be scybala. The epidermis is hyperplastic with prominent rete pegs, and the superficial dermis is infiltrated by marked numbers of lymphocytes, plasma cells, macrophages, and fewer eosinophils.

Contributor's Morphologic Diagnoses:
Haired skin: Severe, locally extensive, chronic, lymphoplasmacytic and histiocytic hyperplastic dermatitis with hyperkeratosis, intralesional arthropods (*Sarcoptes scabiei* presumed), and numerous colonies of extracellular cocci.

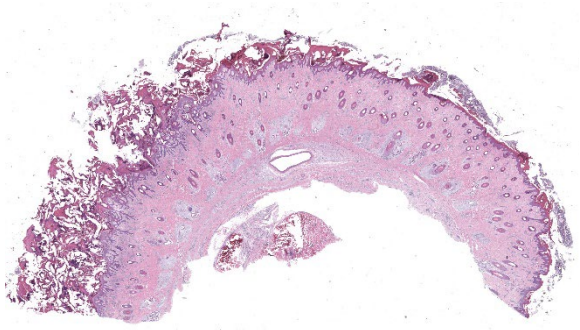

Figure 2-2: Haired skin, pig. At subgross magnification, there is severe hyperkeratosis overlying a hyperplastic epidermis. There is moderate inflammation of the underlying dermis. (HE, 10X)

Contributor's Comment:
Microscopic evaluation revealed two concurrent pathogenic processes within the exudative skin lesions observed grossly: exudative epidermitis (greasy pig disease) caused by *Staphylococcus hyicus*, and sarcoptic mange, caused by *Sarcoptes scabiei*.

Staphylococcus hyicus is a Gram-positive, coagulase-variable, facultatively anaerobic bacterium which typically causes disease in piglets between 5 and 60 days old. The most common clinical finding is greasy, often crusting exudate widely dispersed over the body, but most severely affecting the feet. It is typically transmitted from animal to animal, or is sometimes acquired from the environment, and enters the skin through penetrating wounds.[3] Strains of *S. hyicus* that have the potential to cause clinical disease do so by producing exfoliative toxins. These toxins, including ExhA, ExhB, ExhC, ExhD, SHETA, and SHETB, are thought to cause exfoliation of the epidermis through the cleavage of porcine desmoglein 1, an integral component of the epidermal desmosomes.[9] Infections are often introduced into herds by new animals, and morbidity and mortality rates can be high in

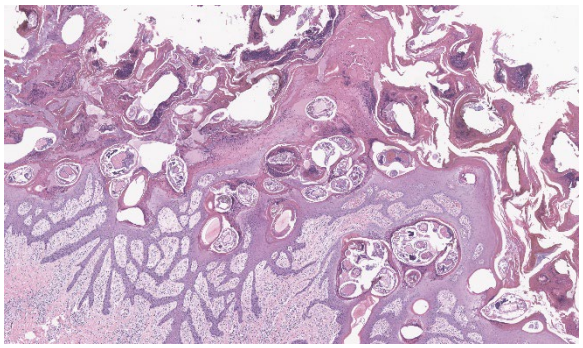

Figure 2-3: Haired skin, pig. There are numerous cross- and tangential sections of adult and nymphal mites within the lamellar keratin and rarely in the underlying epidermis. There are numerous pustules within the hyperkeratotic plaque. (HE, 65X)

younger piglets.[3] In addition to abrasions and wounds from rough surfaces and fighting, additional predisposing factors for infection are infestation with ectoparasites such as mites.[4,7,8] The isolation of *Staphylococcus hyicus* from the liver in this case suggests the animal developed bacteremia.

Sarcoptes scabiei var *suis* is a specific variety of *Sarcoptes scabiei* mite which is globally endemic in swine and is the causative agent of Sarcoptic mange. It is typically transmitted by direct contact, but it may also be spread by fomites and can be easily introduced into a naïve herd by a single infected animal or contaminated equipment. This disease is most prevalent in younger animals, and typically manifests as papules which progress to scaling, oozing, crusts, and alopecia, and often progresses to lichenification in chronic cases. Affected areas are afflicted with severe pruritus. The mechanism of injury to the skin is a combination of mechanical trauma caused by the mite's feeding and burrowing behavior, chemical irritation from ectoparasite saliva and feces, and a hypersensitivity reaction to Sarcoptes antigens.[1]

Contributing Institution:

University of Missouri Veterinary
Medical Diagnostic Laboratory
https://vmdl.missouri.edu/

JPC Diagnoses:

1. Haired skin: Epidermal hyperplasia and hyperkeratosis, diffuse, severe, with mild lymphoplasmacytic dermatitis, intracorneal adult and nymphal mites and eggs.

2. Haired skin: Epidermitis, pustular, subacute, regionally extensive, moderate with extracellular cocci.

JPC Comment:

"Greasy pig disease" has been covered several times in the Wednesday Slide Conference, including as recently as last year (Case 1, Conference 4, 2024-2025, Case 1, Conference 9, 2008-2009, and Case 3, Conference 8, 2009-2010). It always provides a solid descriptive opportunity for conference participants and is truly a classic entity. This year's case, though, had additional guests on the slide in the form of *Sarcoptes scabiei* var *suis*, making this a great "two-fer" case. The slides provided by the contributor were simply beautiful; you

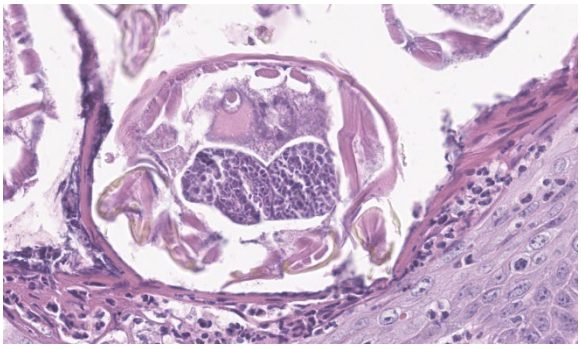

Figure 2-4: Haired skin, pig. Cross sections of adult arthropods demonstrate a brown, spiked chitinous exoskeleton, jointed appendages with skeletal muscle, a hemocoel, and a densely cellular nervous system. (HE, 900X)

could almost draw a line right down the middle of the tissue to demarcate the more routine lesions from *Staphylococcus hyicus* on the right side compared to the far more severe lesions on the left from both the mites and the bacteria together. Many thanks to the contributor for an excellent submission of these two infectious dermatologic entities.

Conference discussion focused on the virulence factors of *S. hyicus* that enable it to cause the exudative epidermitis it is famous for. This bacterium has a variety of exfoliative toxins, such as ExhA, ExhB, ExhC, ExhD, *S. hyicus* exfoliative toxin A (SHETA), and SHETB. These toxins selectively digest desmoglein-1 in porcine skin.[4] Desmoglein-1 is a tight junctional adhesion molecule that is primarily expressed in the superficial epithelium of the skin, playing a critical role in maintaining cell–to-cell adhesion and tissue integrity. When broken down, the cells stop "holding hands" and separate from one another. Coupled with sebaceous hyperplasia within the dermis as a sequela of inflammation, these broken cell junctions enable leakage of sebaceous material onto the surface of the skin, thus the name "greasy pig disease." Conference participants were also quizzed about other commonly encountered desmogleins, including desmoglein-2 (found in desmosomes in skin, cardiomyocytes, and intestines), desmoglein-3 (found between basilar epithelial cells and their basement membranes in the skin; also the known target of pemphigus vulgaris), and desmoglein-4 (found in desmosomes between epithelial cells both in the epithelium of the skin and in hair follicles, and helps to anchor the hair follicle into the dermis).

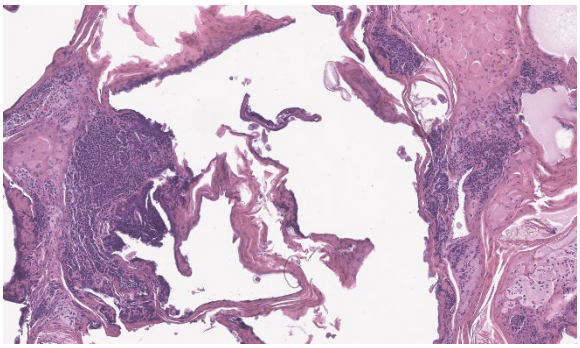

Figure 2-5: Haired skin, pig. There are numerous pustules within the hyperkeratotic crust. (HE, 311X)

Shifting now to the maddeningly itchy *Sarcoptes scabiei* mite, "scabies" or "sarcoptic mange" is caused by *Sarcoptes scabiei,* a burrowing mite, of which there are numerous subspecies that are host specific. Female mites invade the stratum corneum of their selected host and create cozy homes for themselves in the form of tunnels, where they live, move, feed, defecate, and lay eggs.[7] Upon locating a host, the mite secretes saliva that lyses the epithelium of the stratum corneum. As the mite works its way deeper with its cutting mouthparts, it uses its two anterior-most pairs of legs to "swim" forward and create a tunnel. The mite intakes water and nutrients from the host's extracellular fluid and lymph that leaks into the space around the mite's mouthparts while they dig.[7] The females, once mated, will lay their eggs in a burrow that offshoots from their tunnel. The eggs hatch into larvae, which channel their way out of their nursery burrow within the stratum corneum and grow into two subsequent nymphal stages: protonymphs and tritonymphs.[7] The tritonymphs mature into adults on the skin and males will roam about looking for unmated females to repeat the life cycle with.

Scabies is most common in tropical countries, but is ubiquitous and can be seen anywhere,

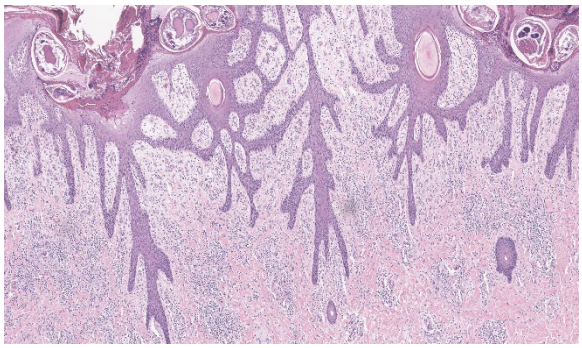

Figure 2-6: Haired skin, pig. The epidermis is markedly hyperplastic, forming deep rete ridges into the underlying moderately inflamed dermis. (HE, 105X)

including cold regions where people (and animals) will huddle together for warmth, as prolonged physical contact is the main mode of mite transmission between hosts.[7] Transmission can occur indirectly on contaminated fomites, but environmental temperature plays a strong role in mite survivability while off-host. Mites don't survive long in warmer climates, regardless of humidity, due to being unable to maintain water balance, but have increased survivability in cooler temperatures with high humidity.[7]

So, which came first, the chicken or the egg? It is the opinion of conference participants that, in the case of this particular young pig, the *Sarcoptes scabiei suis* mites likely set up shop first, causing superficial trauma to the skin of the pig and inducing severe itch, which would have resulted in additional self-trauma from scratching. As a result, the *Staphylococcus hyicus*, seeing as how they are opportunistic commensals, would have had an easy time infecting the skin further and causing additional dermatologic insult. Talk about an itchy one-two punch.

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CASE III:

Signalment:
5-year-old, male castrated, Rottweiler, canine.

History:
The dog was presented to the Auburn University Bailey small animal teaching hospital with one week history of a wet productive cough. Thoracic radiographs showed pneumonia and CBC revealed eosinophilia. On thoracic CT, there was severe bronchiectasis within the accessory lung lobe and mild focal bronchiectasis within the left caudal lung lobe. Bacterial and fungal culture were negative on bronchoalveolar lavage fluid. The patient was sent home on marbofloxacin and prednisone. The owners have noted the cough has approved with treatment but still not ideal. Three months later, the dog returned to the teaching hospital and the right caudal, right accessory, and left caudal lung lobes were removed and submitted for histopathological examination.

Gross Pathology:
Right caudal, right accessory, and left caudal lung lobes had multiple, markedly dilated bronchi or bronchioles filled with light pink to brown inspissated material. The walls of several bronchi was markedly thickened and the intervening lung parenchyma was multifocally collapsed.

Laboratory Results:
Bronchoalveolar lavage fluid submitted for bacterial and fungal cultures was negative.

Microscopic Description:
Diffusely, bronchioles and bronchi are markedly ectatic and filled with large amount of inspissated material composed of larger numbers of eosinophils, degenerate neutrophils, admixed with macrophages, mucin, serum, sloughed epithelial cells and eosinophilic cellular and basophilic nuclear debris. Large

Figure 3-1: Lung, dog. The bronchi and bronchioles are markedly dilated, have a thickened wall and are filled with a pale tan, firm, dry exudate. In some sections, the adjacent pulmonary parenchyma is consolidated and pale tan. (Photo courtesy of: Auburn University http://www.vetmed.auburn.edu/academic-departments/dept-of-pathobiology/).

numbers of similar inflammatory cells also infiltrate the bronchial wall. The lining mucosal epithelium is diffusely moderately hyperplastic or occasionally eroded or ulcerated. Multifocally, bronchi and bronchioles are also surrounded by moderate numbers of eosinophils, neutrophils and macrophages. There is moderate hyperplasia of bronchus-associated lymphoid tissue. Inflammatory exudate multifocally extends into the adjacent alveolar lumina. The adjacent normal alveoli contain moderate numbers of neutrophils, eosinophils and intraalveolar macrophages. The lung parenchyma surrounding the markedly expanded bronchi is multifocally collapsed with closely apposed alveolar septa. Multifocally, there is mild pleural fibrosis. Occasionally, there is mild smooth muscle hypertrophy of bronchioles and tunica media of small caliber blood vessels. Bacterial and fungal organisms are not observed by Gram and GMS stains, respectively.

Contributor's Morphologic Diagnoses:
Lung; right caudal lung lobe, right accessory and left caudal lung lobes: Severe, chronic, multifocal bronchiectasis and bronchiolectasis

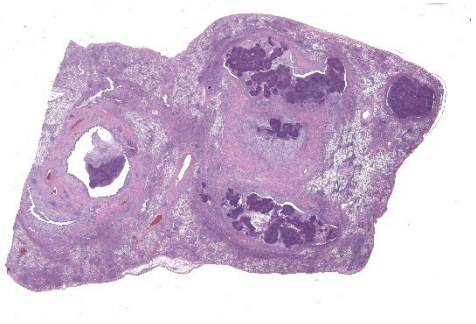

Figure 3-2: Lung, dog. Approximately 66% of the lung is consolidated by inflammation. Airways are ectatic and filled with a densely cellular luminal exudate which extends into the adjacent parenchyma . (HE, 10X).

with marked eosinophilic, suppurative bronchitis and bronchiolitis.

Contributor's Comment:

Eosinophilic bronchopneumopathy (EBP) is an uncommon, chronic, usually steroid-responsive condition of young adult dogs. EBP has been described in several breeds of dogs with Siberian huskies and Alaskan malamutes being overrepresented.[5] The presentation varies from mild to severe, intermittent to chronic, and self-limiting to sometimes fatal. The most common clinical sign is persistent cough, followed by gagging and retching. Other common clinical symptoms include dyspnea, exercise intolerance and nasal discharge that is usually yellow-green to mucopurulent. Radiographic findings include diffuse bronchointerstitial pattern, peribronchial cuffing with or without bronchiectasis.[5] Approximately 50% of the dogs have peripheral eosinophilia[2]. The disease is characterized by eosinophilic infiltration of the lung and bronchial mucosa with epithelial hyperplasia, ulceration or squamous metaplasia. The destruction of the walls of the airways leading to bronchiectasis has also been reported.[5]

The cause of EBP is unknown, however it is thought to be due to hypersensitization to aeroallergens. Immunological and immunohistochemical studies show that bronchoalveolar (BAL) fluid contains decreased numbers of CD8+ T cells, while CD4+ T cell number is increased in the bronchial mucosa and pulmonary interstitium. The predominance of CD4+ T cells supports the role of a dominant Th2 immune response in the affected dogs.[4] The dog in the current case was presented with characteristic clinical signs and blood eosinophilia. Based on the imaging findings of bronchiectasis with negative bacterial and fungal culture, EBP was the primary differential. In most cases, the cytological evaluation of BAL fluid usually reveals marked eosinophilia, which along with imaging findings is sufficient to confirm the diagnosis of EBP. The macroscopic lesions vary from no discharge to the presence of abundant yellow-green mucopurulent material within bronchi or bronchioles, thickening of bronchial and bronchiolar walls, bronchiectasis and consolidation of adjacent parenchyma. Typical histologic findings include eosinophilic infiltrate beneath or within the mucosal epithelium and varying degrees of

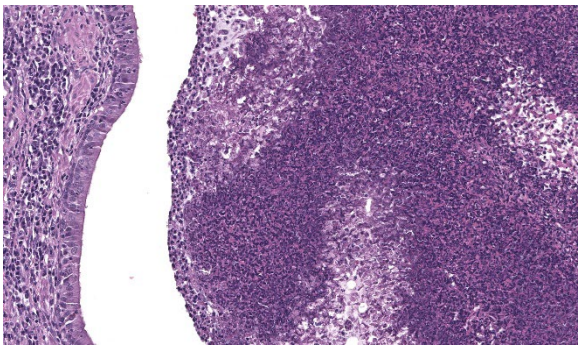

Figure 3-3: Lung, dog. The exudate in the airway lumina is predominantly composed of degenerating eosinophils admixed with fewer macrophages and neutrophils. (HE, 370X).

mucosal thickening, infiltration by other inflammatory cell types, collagenolysis, and fibrosis. In cases of extensive involvement of lung parenchyma, there is diffuse eosinophilic and granulomatous infiltrate, with focal eosinophilic granulomas centered on necrotic tissues can be present.[3] The diagnosis of EBP was confirmed only after ruling out other causes of eosinophilic infiltrate in the lung and negative bacterial and fungal culture. The tracheobronchial parasites *Crenosoma vulpis*, *Eucoleus aerophilus, Oslerus osleri*; the lungworm *Angiostrongylus vasorum* and *Filaroides hirthi*; occult *Dirofillaria immitis* infection are the main differential diagnosis.[2] There was no evidence of parasite eggs, larvae or adults in the examined sections. The lesions were primarily centered on bronchioles and bronchi, with mild to moderate involvement of the pulmonary parenchyma. A rare condition called eosinophilic pulmonary granulomatosis is also characterized by similar clinical signs including blood eosinophilia should be included in the differential diagnoses list, but in this condition, there are nodular necrotizing lesions formed by eosinophils, epithelioid macrophages, type II pneumocyte proliferation, which were absent in this case.[3] Other causes of eosinophilic infiltrate in the lung parenchyma include lymphomatoid granulomatosis, carcinomas and lymphomas. The mainstay of treatment for EBP is the long-term administration of corticosteroids such as prednisolone.[1] In summary, the clinical diagnosis relies on a typical history of chronic respiratory distress, demonstration of bronchopulmonary eosinophilia by cytology or histopathologic examination, and exclusion of known causes of lower airway eosinophilia.

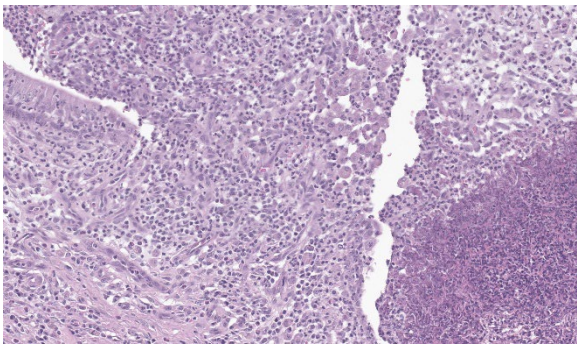

Figure 3-4: Lung, dog. There is multifocal necrosis of airway epithelium with infiltration of the airway wall and adjacent parenchyma by inflammatory cells. (HE, 381X).

Contributing Institution:
Auburn University http://www.vetmed.auburn.edu/academic-departments/dept-of-pathobiology/

JPC Diagnoses:
Lung: Bronchiolitis, eosinophilic and granulomatous, chronic, multifocal to coalescing, severe, with bronchiolectasis, necrotizing alveolitis, and Type II pneumocyte hyperplasia.

JPC Comment:
Today's third case took conference participants on another "Magic School Bus"-esque trip into the lungs in the form of a disease that has more names than it knows what to do with: eosinophilic bronchopneumonopathy. Conference discussion started off with a brief nod to the Rottweiler breed and its storied history as descendants from Roman dogs that moved with their humans across the Alps and ultimately into Rottweil, Germany. The dogs ultimately became known as "Rottweiler metzgerhunds", and were common companions of butchers, where these stocky canines would be seen pulling carts of meat for sale through the streets of Rottweil. Despite this case of eosinophilic bronchopneumonopathy being in a Rottweiler, however, they are not considered

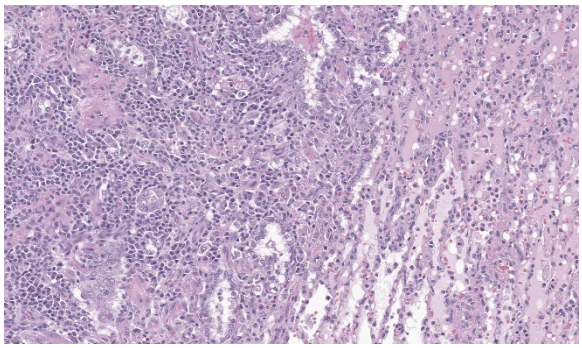

Figure 3-5: Lung, dog. Alveolar parenchyma adjacent to affected airways demonstrates one or more of the following: filling of alveoli and expansion of alveolar septa by eosinophils, macrophages and neutrophils, lymphocytes, and plasma cells admixed with edema and cellular debris, septal fibrosis, and type II pneumocyte hyperplasia. (HE, 381X).

a predisposed breed. Alaskan Malamutes and Siberian Huskies, however, are.

This case provided a fantastic example of true bronchiectasis with abundant inflammation and debris filling the larger airways in section. Eosinophilic bronchopneumopathy is one of the most common diseases associated with bronchiectasis in dogs, with over a quarter There was some discussion about the brightly eosinophilic material admixed with the eosinophils filling these airways, which was interpreted as likely to be a combination of necrotic eosinophils and major basic protein. A more substantial review of eosinophils was covered in last week's conference (Conf 2, Case 3), so that topic won't be belabored further today.

This condition is considered to be both "eosinophilic" and "granulomatous" due to the profound presence of both eosinophils and macrophages. In the course of this disease, there is an upregulated Th2 response, favoring CD4+ T-helper cells over those that are CD8+. The Th2 response is important for fighting extracellular parasites and allergens via production of cytokines like IL-4, IL-5 (chemotactic for eosinophils), and IL-13.[6] These cytokines trigger IgE antibody production, recruit and activate cells such as eosinophils and mast cells, increase mucus production, and promote tissue healing. While protective against parasites and involved in wound healing, an overactive Th2 response can cause chronic inflammatory conditions.[6] Despite being a common condition in dogs, the exact cause of eosinophilic bronchopneumonopathy in dogs is not known. There are conflicting papers that argue for or against an association with heartworm disease, although there isn't much argument that heartworm disease is not the *only* cause of this condition, and it is ultimately suspected that EBP is due to a hypersensitivity reaction of some kind.[3,4,5]

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CASE IV:

Signalment:
5 year old, neutered male, Shetland sheepdog, dog (*Canis familiaris*).

History:
This 5-year-old Shetland sheepdog had a history of anorexia, diarrhea, vomiting and anuria of 4 days duration. Blood chemistry values were consistent with renal failure (exact values not reported). The dog was treated with intravenous fluids and diuretics, with no improvement in its condition. Due to the progression of the clinical signs and poor prognosis (without treatment), the owner elected for euthanasia. The dog was sent to our diagnostic laboratory, and a complete necropsy was performed.

Gross Pathology:
The dog was in good body condition. There were 10 and 20 ml of serous yellowish fluid in the pericardial sac and peritoneal cavity, respectively. Both kidneys showed a slightly irregular/pitted and mottled surface; on cut section, the cortex appeared slightly granular, and the medulla pale and firm. The stomach was empty, with a few shallow ulcers of varying size in the fundus.

Laboratory Results:
N/A

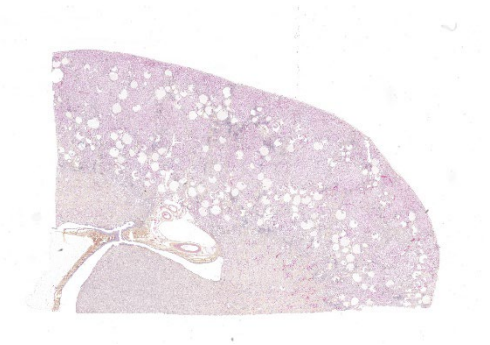

Figure 4-1: Kidney, dog. At subgross magnification, Bowman's spaces are diffusely dilated up 500um. (HE, 10X)

Microscopic Description:
Both kidneys presented similar lesions. Almost all glomerular chambers (Bowman's spaces) are variably dilated, often markedly (cystic dilation, up to about 500 µm), with a thickened/sclerotic, undulating and often mineralized Bowman's capsule (basement membrane) Most glomerular tufts are either absent or shrunken and sclerotic with occasional synechiae. In the cortex, there is a moderate multifocal chronic tubulointerstitial nephritis with tubular atrophy and loss, peritubular sclerosis (thickened basement membrane) and occasional luminal crystals; tubular dilation is present but mild and multifocal. Several tubular basement membranes are diffusely mineralized. In the medulla there is a mild to moderate fibrosis with scant inflammation; rarely, dilated tubular structures lined by a simple columnar eosinophilic or stratified cubic/columnar amphophilic epithelium are present.

Other significant changes in other organs (not submitted) included gastric mucosal mineralization and submucosal vasculopathy ("*uremic gastritis*"), and changes suggestive of bilateral parathyroid chief cell hyperplasia, consistent with renal secondary hyperparathyroidism.

Contributor's Morphologic Diagnoses:
1) Kidney: Glomerular chamber (Bowman's space) dilation, diffuse, moderate to marked

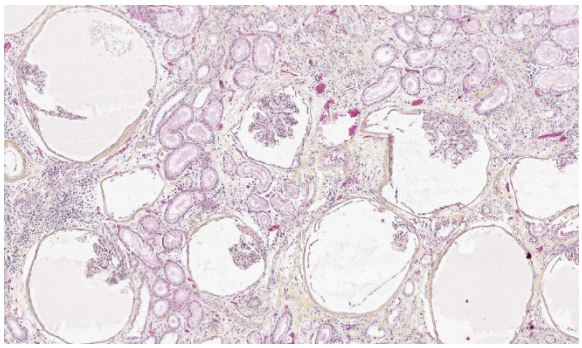

Figure 4-2: Kidney, dog. Within dilated Bowman's spaces, glomerular tufts are small and often adherent to the inner aspect of Bowman's capsule. At this (HE, 140X)

(cystic glomeruli), with moderate multifocal tubulointerstitial nephritis, consistent with glomerulocystic kidney disease

2) Multifocal glomerular and tubular basement membrane (metastatic) mineralization

Contributor's Comment:

Glomerulocystic kidney disease (GCKD) is a rare disease reported mostly in humans, and also in 3 dogs and a single stillborn foal; it is part of the polycystic kidney disease (PKD) complex.[1-7] In dogs, the disease has been described in a Shiba, a Belgian Malinois, and a Blue merle collie.[3,6-7] In humans, GCKD is mostly observed in infants and young children, but adults may be affected.[2,6] The canine cases involved adult animals, with ages ranging from 11 months to 5 years, as in our case. Diseases of the PKD complex are well described in humans and, to a lesser degree, in animals.[1,4] They are part of the larger group of renal cystic diseases that include multiple hereditary, nonhereditary and acquired conditions.[1,4] In diseases of the PKD complex, there is a progressive dilation of different portions of the nephron or collecting duct with the eventual formation of cysts.[4,6] In GCKD, it is the glomerular chambers (Bowman's spaces) that are cystic; in humans, the adjacent portion of the proximal convoluted tubules is also dilated.[1] A glomerular cyst has been defined as a glomerulus with a 2- to 3-fold dilatation of its Bowman's space.[2]

Although periglomerular fibrosis and proximal tubular obstruction due to ischemic changes have been suggested as a possible mechanisms,[4,7] the pathogenesis remains largely unknown in animals. In humans, the pathogenesis is still unclear, but there have been some advances in the understanding of the pathophysiology. For instance, it has been proposed that a ciliopathy may be involved, similarly to other renal cystic diseases; several genes involved in renal development are also under investigation (GCKD can develop due to changes in Wnt or hedgehog signaling).[2] In humans, GCKD is often associated with other lesions or diseases, including autosomal dominant polycystic kidney disease (ADPKD) and the tuberous sclerosis complex.[1,2] Three clinical variants have been originally described: malformation syndrome-associated GCKD, renal dysplasia-associated GCKD, and primary GCKD (heritable and sporadic).[2,6] A more recent classification of GCKD has been published in 2007: 1) familial nonsyndromic (e.g. ADPKD in infants), 2) associated with inheritable malformation syndromes (e.g. tuberous sclerosis complex), 3) syndromic, non-Mendelian (e.g. trisomy 9, 13 or 18), 4) sporadic (new mutations), and 5) acquired and dysplastic kidneys (e.g. hemolytic uremic syndrome and obstructive uropathy).[2] There are mouse models of GCKD that are relevant to the human disease.[2]

As with other chronic glomerular diseases, secondary chronic tubulointerstitial nephritis will develop in time.[3] Glomerulocystic disease

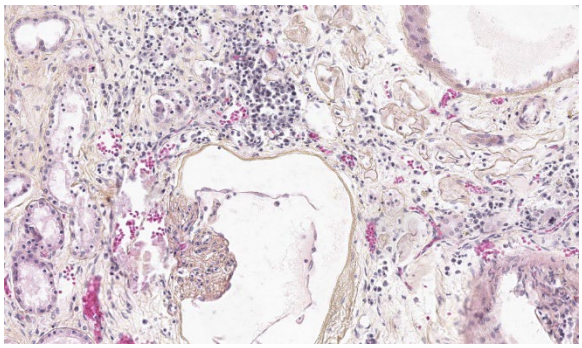

Figure 4-3: Kidney, dog. Occasional glomeruli are sclerotic, with marked fibrosis of the glomerular tufts. There is also diffuse interstitial fibrosis with marked atrophy of entrapped tubules and scattered aggregates of lymphocytes and plasma cells. (HE, 380X)

(GCKD) must be differentiated from "glomerulocystic change", in which cystic glomeruli are secondary to renal scarring from different renal pathologies.[3] In the present case, the chronic tubulointerstitial nephritis is considered to be secondary to the glomerular pathology.

Contributing Institution:
Faculty of veterinary medicine, Université de Montréal, St-Hyacinthe, Quebec, Canada:
http://www.medvet.umontreal.ca

JPC Diagnoses:
Kidney: Glomerulocystic atrophy, chronic, diffuse, severe, with tubular degeneration and necrosis, basement membrane mineralization, and multifocal lymphocytic interstitial nephritis and fibrosis.

JPC Comment:
The last case for today's conference represented a condition so uncommonly encountered that there was prolonged discussion about differential diagnoses and why this condition was not those things. Differentials included Lyme disease, which would have tubular degeneration, lymphoplasmacytic interstitial nephritis, and glomerulonephritis; Renal dysplasia, which has a trifecta of findings including fetal glomeruli, primitive tubules, and fetal mesenchyme; and urolithiasis leading to hydronephrosis, which would have dilation/ectasia of tubules at all levels, renal pelvic dilation, and would likely have protein casts within tubules. The defining features of glomerulocystic disease that separate it from these other conditions are dilation of the glomerular tuft with cystic expansion of Bowman's space and glomerular atrophy with no concurrent glomerulonephritis. Additionally, the proximal convoluted tubules (PCTs) closest to the glomeruli are the most affected and may also demonstrate a degree of dilation due to stenosis between the glomeruli and the PCTs. There may also be a lymphoplasmacytic interstitial nephritis, which was seen in this case.

An interesting feature of this condition is that the basement membranes of multiple tubules and glomeruli were mineralizing, even in the absence of obvious degeneration. Hmm! A review of clinical pathology data from a pair of 2008 case reports in dogs with glomerulocystic disease was conducted during conference and revealed that dogs affected with this condition can have an abnormal Calcium/Phosphorus ratio secondary to their renal disease, so much so that metastatic mineralization can occur.[5]

Additionally, the dogs in the case report had low hematocrit, low hemoglobin, and low reticulocyte count.[5] All three of these can be explained by the loss of the renal juxtaglomerular apparatus in this disease that is responsible for sensing feedback on erythrocyte concentrations within the blood and subsequently

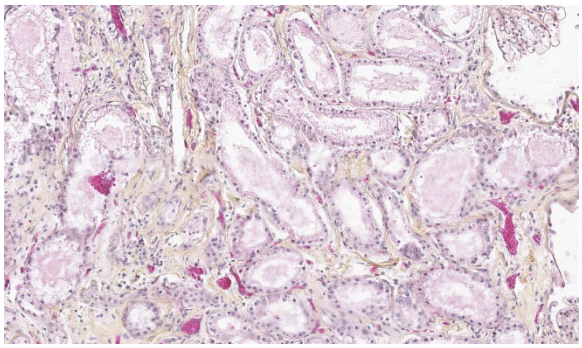

Figure 4-4: Kidney. Tubules demonstrate a range of changes within the fibrotic interstitium: cell swelling and vacuolation, necrosis and sloughing, and accumulation of protein within the lumen. (HE, 400X).

stimulating erythropoietin production when needed. If there's no stimulus to make more red blood cells, of course your HCT, Hbg, and reticulocytes are going to be lacking and an anemia will result.

Lastly worth nothing is that the dogs in the case report were also azotemic and acidotic.[5] The metabolic acidosis in these cases is due to a combination of the azotemia and anemia. Fewer red blood cells to transport oxygen leads to tissue hypoxia and an increase in anaerobic glycolysis, which produces lactic acid. Azotemia causes acidosis due to the kidneys being unable to properly excrete waste products that generate acid, such as phosphates and sulfates, and they lose the ability to regenerate and resorb bicarbonate, which is a vital buffer of acids in the bloodstream. Understanding how these clinical findings translate to the lesions pathologists see is critical to being able to logically follow a disease pathogenesis, to know where to look for lesions in particular diseases, and to understand how to make sense of pathophysiology. As such, the clin path review during this conference case was well-received by all participants and much appreciated.

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