The Armed Forces Institute of Pathology
Department of Veterinary Pathology

WEDNESDAY SLIDE CONFERENCE 2007-2008

Conference 1

5 September 2007

Moderator:

Dr. Michelle Fleetwood, DVM, Diplomate ACVP

CASE I – 07-15544 (AFIP 3066312).

Signalment: 13-year-old castrated male Quarter horse (*Equus caballus*).

History: There were multiple subcutaneous masses in the lateral aspect of both right and left proximal forearms. These lesions appeared within the past 6 months. Lesions are not apparently painful and there is no associated lameness or other clinical signs. The horse is heterozygous for the hyperkalemic periodic paralysis mutation. A portion of each lesion was excised and submitted for histopathology. No association with underlying skeletal muscle was detected at surgery.

Gross Pathology: Discrete firm pale tan nodular masses with normal overlying haired skin

Laboratory Results: *Blastomyces dermatitidis* was isolated from a lung swab prior to necropsy.

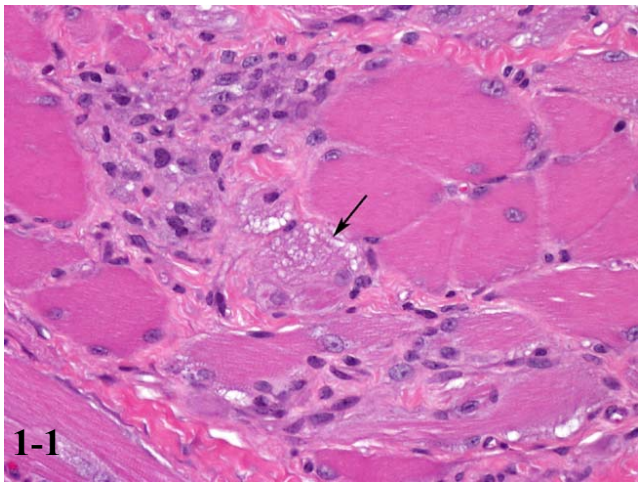
Histopathologic Description: Two wedge samples, one from the right foreleg and one from the left foreleg, were submitted and representative sections were submitted for histopathology. Both lesions are similar and are composed of haired skin with underlying cutaneous skeletal muscle (presumed cutaneous omobrachialis, although the site appears slightly more distal than anatomy texts describe for insertion of this muscle in the horse). Architecture of the skeletal muscle is markedly distorted to effaced, with expansion to form irregular nodular masses. Myofibers within the masses exhibit varying degrees of the following changes:

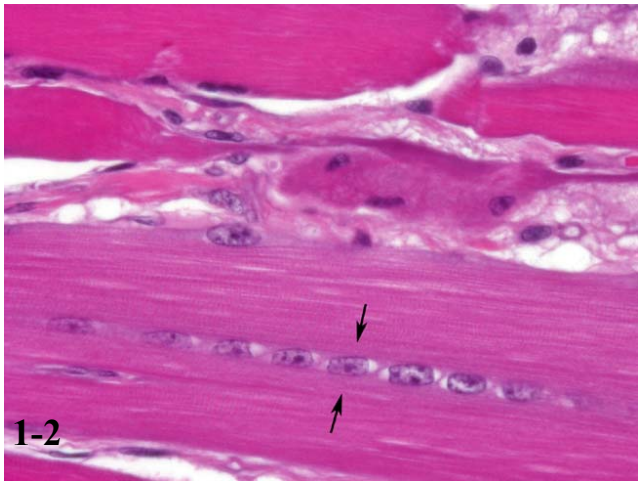
Disarray of orientation, with some fibers in transverse section, others in longitudinal section, and still others in oblique section

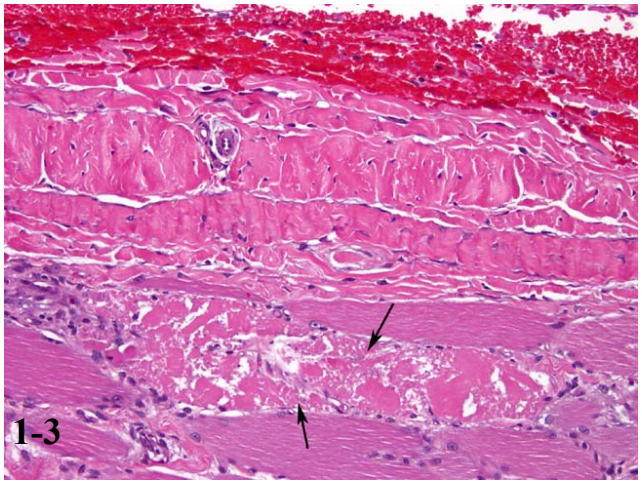
Severe chronic myopathic change, including marked variation in fiber size with fiber hypertrophy and also rounded to angular atrophy, endomysial and perimysial fibrosis, internal nuclei, fiber splitting, and subsarcolemmal pale zones containing pale pink to gray finely granular material (sarcoplasmic masses)

Degenerative (fig, 1-1) and **regenerative (fig. 1-2)** changes, including segmental coagulation **necrosis (fig. 1-3)** – often with macrophage infiltration – and vacuolar degeneration. Small diameter, slightly basophilic fiber segments with prominent euchromatic nuclei – often in clusters or short chains - are indicative of myofiber regeneration

Multifocal, typically mild to moderate, interstitial infiltrates of lymphocytes







Masson's trichrome stain confirms the presence of endomysial and perimysial fibrosis. Sarcoplasmic masses and vacuoles do not stain with either trichrome stain or Periodic acid-Schiff stain for glycogen, and no abnormal glycogen aggregates are present.

Contributor's Morphologic Diagnosis: Skeletal muscle, cutaneous omobrachialis: Pseudotumor consistent with focal myositis.

Contributor's Comment: The term muscle pseudotumor encompasses a group of benign non-neoplastic processes causing mass lesions within skeletal muscle.[1-5] The muscle pseudotumors recognized to date in animals are myositis ossificans, musculoaponeurotic fibromatosis ("desmoid tumor"), and fibrotic myopathy in horses, and myositis ossificans and a lesion simply termed muscle pseudotumor in dogs. The latter lesion is characterized by profound myopathic changes, interstitial connective tissue infiltration, mild to moderate myofiber necrosis and regeneration, and a variable degree of inflammation, most often lymphocytic.[2] These features are also typical of the muscle pseudotumor reported as focal myositis in people.[1,3-5] Diagnosis of any muscle pseudotumor relies on a clinical history of a nodular mass within skeletal muscle, with no other neuromuscular or systemic disease signs, as in the absence of this history a diagnosis of muscular dystrophy, chronic denervation atrophy, or chronic myositis is possible.

Muscle pseudotumors in people occur most often in limb muscle, although other sites are possible. Patients describe these lesions as either non-painful or as being associated with mild discomfort or dull pain.[1,3-5] Although trauma has been proposed as a cause, careful case studies of affected people have not detected a history of prior trauma to the area.[1,3-5] Subclinical muscle tearing has been speculated to be a possible cause.[3] Evidence of peripheral nerve damage has been detected within some muscle pseudotumors in people, but is not common and is thought to be a secondary event rather than a primary cause.[4] There is no apparent age or gender predisposition in people.[1,3-5]

In people, muscle pseudotumors must be differentiated from localized initial forms of polymyositis.[5] No such

1-1 Skeletal muscle, Quarter horse. Myofiber degeneration, characterized by swollen, pale, vacuolated sarcoplasm (arrows). (H&E 400X)

1-2 Skeletal muscle, Quarter horse. Myofiber regeneration, characterized by basophilic sarcoplasm with large frequently rowed, internalized nuclei (arrows). (H&E 600X)

1-3 Skeletal muscle, Quarter horse. Myofiber necrosis, characterized by hypereosinophilic sarcoplasm with loss of cross striations, fragmentation and pyknotic, karyolytic or karyorrhectic nuclei (arrows). (H&E 200X)

association has been identified in animals. This horse was otherwise clinically normal, and the history of being heterozygous for hyperkalemic periodic paralysis was not considered to be related to the development of these lesions. It is curious that this case occurred bilaterally, in what appears to be the distal cutaneous omobrachialis muscle, in a lateral location that is less likely to be traumatized than cranial areas. Similar to case studies of focal myositis in people, there was no history of trauma to this area.

Muscle pseudotumors in animals have not been described as being associated with pain. Locations include within limb muscle,[2] as in this case, but these lesions have also been seen in scapular[2] and laryngeal muscle (unpublished observations). In pseudotumors of dogs and horses that this contributor has studied, lymphocytic inflammation is extremely variable and often not prominent. A similar situation is described in people with focal myositis.[1,3] An additional characteristic histopathologic finding in focal myositis-like muscle pseudotumors in animals, apparently not described in human cases, is prominent disarray of myofiber arrangement, with the finding of transverse, longitudinal, and obliquely arranged myofibers within the same section.[2]

Surgical excision of these lesions is curative in people and also in animals. Progression beyond the initial growth phase, which can be rapid, is not described.[1,3-5] In this current case only portions of the lesions had been excised at the time of this submission. Follow up is planned in order to determine future behavior.

AFIP Diagnosis: Haired skin and skeletal muscle, cutaneous omobrachialis (per contributor): Myocyte degeneration, necrosis and loss, hypertrophy, and regeneration, focally extensive, moderate, with myofiber disarray, fibrosis, and mild chronic-active myositis

Conference Comment: The contributor provides a thorough review of muscle pseudotumors in dogs and horses. Not much is known about this idiopathic condition, and without knowledge of clinical history, or gross images, it is a difficult diagnosis to make. It is thought that focal myositis, myositis ossificans, and musculoaponeurotic fibromatosis (desmoid tumor) arise from an abnormal response to muscle trauma, while fibrotic myopathy results from a denervation injury. There was a small amount of variability in the amount of fibrosis and inflammation among slides. Several slides contained areas with a high mitotic rate, which were interpreted as areas of intense regeneration. No infectious organisms were seen on special stains performed at AFIP [Brown & Brenn (B&B), Brown & Hopps (B&H), Gomori's methenamine silver (GMS), Periodic acid-Schiff (PAS), Ziehl-Neelsen (ZN)].

This case presents great examples of the histologic changes in skeletal muscle response to injury. Degenerating muscle is swollen with pale vacuolated sarcoplasm. Necrotic muscle fibers are shrunken and hypereosinophilic, with a loss of cross-striations, and may be fragmented. Regenerative muscle has basophilic sarcoplasm with multiple centralized and linearly-arranged nuclei (nuclear rowing). They are often surrounded by an increased number of satellite cells. Other common changes include atrophy, hypertrophy and fibrosis. The myofiber disarray is a characteristic lesion of focal myositis/muscle pseudotumor in horses and dogs, and along with the clinical history, helps distinguish it from other causes of skeletal muscle degeneration and necrosis.

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CASE II - 07-533 (AFIP 3067221).

Signalment: 12-yr-old male, castrated, West Highland White Terrier (*Canis familiaris*), dog

History: Starting in November 2006, the patient developed periodic episodes of coughing fits (dry, hacking, non-productive). Coughing episodes increased over several weeks. In January 2007, the owners noticed the dog had increased respiratory rate and effort. The dog was

started on Clavamox® but the respiratory problems continued with no improvement. Two days prior to admission (1/9/2007), the owner reported that the dog had respiratory distress with an abdominal component, and lethargy.

On presentation, the patient's mucus membranes were cyanotic, pulse = 162, respiratory rate = 60 – 80, and crackles were auscultated bilaterally. No murmur was heard, but heart sounds were difficult to hear over the crackles. The dog was placed in an oxygen cage and heart rate decreased to 120 and mucous membranes were pink. Jugular pulses were increased. Cough could not be elicited on tracheal palpation. Respiratory rate and effort remained increased while in the oxygen cage.

Only one lateral thoracic radiograph was able to be obtained before the dog became very distressed and was placed back in the oxygen cage. The radiograph showed mild to moderate right sided cardiomegaly and diffuse interstitial to alveolar lung pattern, more pronounced dorsocaudally.

A brief echocardiogram, with the dog standing in the oxygen cage, revealed extremely enlarged right ventricle with thickened free wall.

Physical exam, radiographic and echocardiographic studies were all consistent with pulmonary fibrosis and pulmonary hypertension.

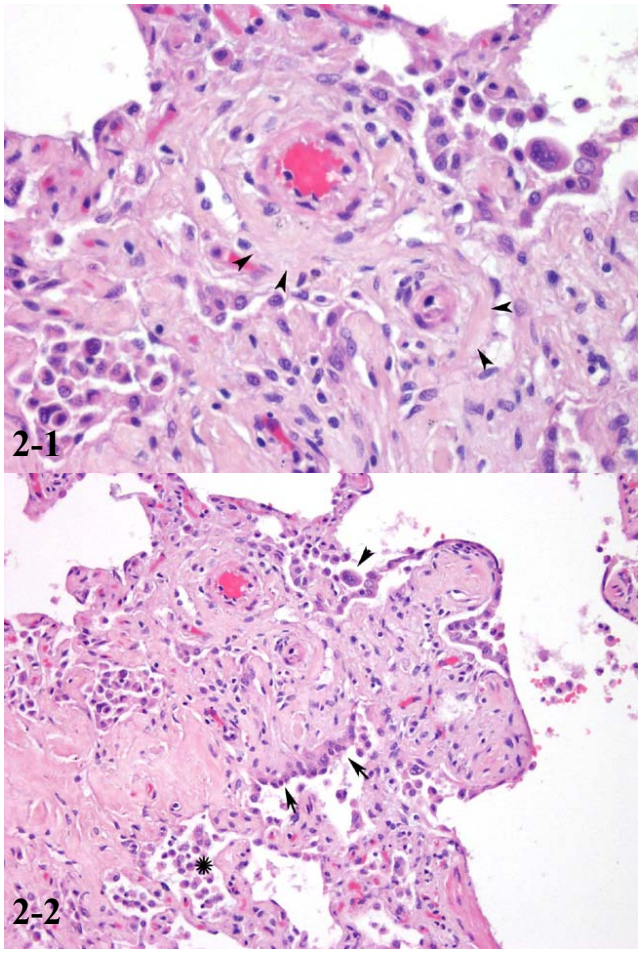
Laboratory Results: Complete blood count and chemistry profile were fairly unremarkable with the following abnormalities:

Leukocytosis (23.5000 x103/ul; reference range 4.900 – 16.900 x103/ul) with mature neutrophilia (19.270 x103/ul; reference range 2.800 – 11.500 x103/ul). No abnormalities were noted on the differential. Alkaline Phosphatase was markedly increased (1484 U/L; reference range 12 – 121 U/L)

Gross Pathology: The lungs did not collapse when negative pressure was released. All lung lobes were diffusely dark pink, firm, and were meaty and dark red on cut section. The capsular surfaces of both kidneys were pitted and irregular with a tightly adhered capsule and multifocal <1mm diameter cortical cysts. There were bilateral mature cataracts.

Histopathologic Description: Lungs – There is diffuse thickening of the alveolar septae with fibroblasts and homogenous eosinophilic fibrillar material (collagen). Occasionally, septae are **dramatically thickened (fig. 2-1)** up to 5 times. Partially or completely filling the alveolae are numerous **macrophages (fig. 2-2)** with light pink vacuolated cytoplasm with occasional **multinucleate cells (fig. 2-2)**. There is marked **type II pneumocyte hyperplasia (fig. 2-2)**. Occasionally there is light purple mineralized material with in the alveoli. Some sections contain a thick trabecula of dense collagen lined by hypertrophied type II pneumocytes.

Masson's trichrome stains shows moderate diffuse staining of the alveolar septae. There is multifocal to diffuse staining of cells within the alveolar septae for smooth muscle actin (myofibroblasts). There is negative staining for Collagen type I. (Reliable immunostains for collagen



2-1 Lung, West Highland White Terrier dog. Diffuse pulmonary interstitial fibrosis (arrowheads). (H&E 400X)
2-2 Lung, West Highland White Terrier dog. Pulmonary interstitial fibrosis with type 2 pneumocyte hyperplasia (arrows), numerous alveolar macrophages (star) and occasional multinucleated giant cells (arrowhead). (H&E 200X)

III, and IV were unavailable). Many intraalveolar cells stain positive for cytokeratin (pneumocytes).

Contributor's Morphologic Diagnosis: Lung – Marked, diffuse, chronic, interstitial fibrosis with type II pneumocyte hyperplasia.

Contributor's Comment: Idiopathic interstitial lung disease is a complicated and poorly understood disease process that, in the dog, has been described mostly in the terrier breeds with the West Highland White terrier having the highest incidence.[1] The clinical signs consist of coughing, dyspnea, exercise intolerance, and cyanosis. The signs develop slowly, and affected dogs deteriorate progressively over months.[2] Inspiratory crackles are a common physical exam finding and the main radiographic changes consist of mild to severe increased interstitial pattern and right sided cardiomegally. Bronchoscopic findings are often normal or show mild airway mucoid reaction.[2] Usually there are no hematologic or serum biochemical abnormalities.

Histopathologic findings consistently show generalized thickening of the interstitium by variable amounts of eosinophilic extracellular matrix. The process can range from diffuse to multifocal or regional. The most severe cases have multifocal areas of type II pneumocyte hyperplasia. There are often variable amounts of inflammatory cells (lymphocytes, plasma cells, macrophages.) Masson's trichrome stains the extracellular matrix expanding the alveolar septae as collagen.[1] Immunohistochemistry reveals that there can be a mixture of type I and type III collagen depending on the severity and chronicity of the disease.[1] Ultrastructurally, the extracellular matrix consists of numerous bundles of electron dense fibrils aligned parallel to one another. Individual fibrils have even spaced band periodicities (collagen).[1]

Differentials for idiopathic interstitial lung disease include, chronic bronchiolitis, neoplasia, and infectious diseases.[5] Idiopathic interstitial lung disease is of unknown etiology. Infectious processes, drug reactions, exposure to toxins or dust, and connective tissue disorders have been hypothesized as potential etiologies. Diagnosis, treatment, and determining an underlying etiology is difficult because by the time clinical signs are seen, there is usually irreversible loss of pulmonary function (fibrosis), and the inciting cause may no longer be present.

In human medicine there are a group of idiopathic pneumonias with similar features of shortness of breath, radiographic evidence of diffuse pulmonary infiltrates and varying degrees of inflammation, and fibrosis. The terminology in human medicine for these diseases has changed. Previously, many form of idiopathic interstitial pneumonia were termed "idiopathic pulmonary fibrosis", which is now reserved for a specific type also known as "usual interstitial pneumonia" or "cryptogenic pulmonary fibrosis".[3] This disease in humans has some similarities as the disease seen in West highland White terriers but technically the same. Other types of idiopathic interstitial pneumonias besides usual interstitial pneumonia, include, acute interstitial pneumonia, non-specific interstitial pneumonia, cryptogenic organizing pneumonia, and desquamative interstitial pneumonia-respiratory bronchiolitis interstitial lung disease.[3]

AFIP Diagnosis: Lung: Fibrosis, interstitial, diffuse, marked, with type II pneumocyte hyperplasia, and intraalveolar macrophages and multinucleated giant cells

Conference Comment: The contributor provides an excellent review of interstitial lung disease of the West Highland White Terrier. Idiopathic Pulmonary Fibrosis also occurs in middle-age to older cats. Adult horses develop nodules of interstitial pulmonary fibrosis (Equine multinodular pulmonary fibrosis).

Additional causes of pulmonary fibrosis were discussed. Anything that damages type I pneumocytes or alveolar endothelium may lead to pulmonary fibrosis. Causes of alveolar damage include irradiation, septicemia, thermal injury, vomit aspiration, toxic gases (e.g., oxygen toxicity) and toxins (e.g., paraquat).

Other conditions with an increased prevalence in West Highland White Terriers include craniomandibular osteopathy, polycystic liver and kidney disease, hyperplastic dermatosis, and chronic hepatitis and cirrhosis.

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CASE III – 05-4349 (AFIP 3064906).

Signalment: Female weaner pig

History: This pig is from a group of weanling pigs purchased by an FFA group. All had loose stools and fair body condition. Swine dysentery was suspected.

Gross Pathology: On gross necropsy, the submitting veterinarian noted swollen mesenteric lymph nodes and liquid gut contents; small and large intestines were purple.

Laboratory Results: Dark field examination of colonic scrapings were negative for spirochetes. Moderate numbers of *Campylobacter coli* were isolated from the intestines. PCR for *Lawsonia intracellularis* was not performed in this case.

Histopathologic Description: In a section of ileum there is a diffuse, proliferative and necrotizing inflammatory lesion. Intestinal glands are long and lined by tall, amphophilic cells with a high mitotic rate. Goblet cells are decreased in number. Peyer's patch lymphoid follicles are necrotic and proliferative glands are herniated into those spaces. Histiocytes replace follicular centers and surround necrotic foci. Glands in these and other areas are often dilated and filled with necrotic debris. The lamina propria is mildly expanded by lymphocytes and plasma cells.

Steiner's silver technique shows numerous short, curved rods within the apical portions of glandular epithelial cells.

Contributor's Morphologic Diagnosis: Proliferative ileitis (porcine proliferative enteropathy)

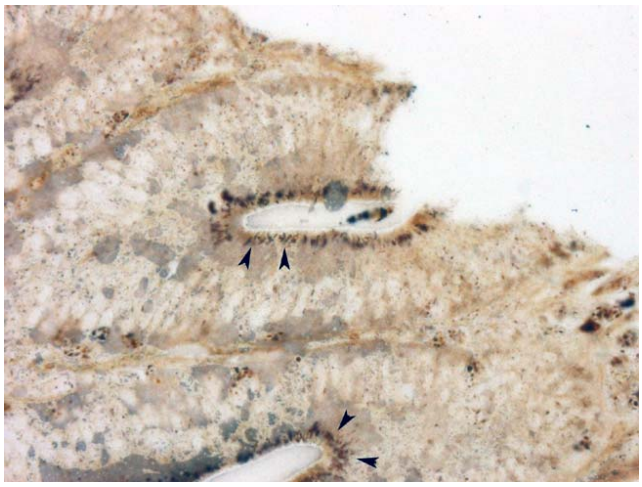
Contributor's Comment: Porcine proliferative enteropathy (PE) is a collection of syndromes all caused by infection by the obligate intracellular organism *Lawsonia intracellularis*.[1] The organism is prevalent in swine worldwide and is shed by infected pigs for weeks. Clinical disease is seen most commonly in feeder pigs. Signs vary from mild, subclinical disease with decreased weight gain and unthriftiness to severe diarrhea, cachexia and death or to death from acute intestinal hemorrhage. Morbidity and mortality vary with the different syndromes.

As an obligate, intracellular pathogen, pathogenesis of *L intracellularis* related disease requires active uptake by intestinal epithelial cells. Localization of lesions to the ileum may be related to uptake of organisms by epithelium associated with Peyer's patches. Organism are initially taken up in membrane-bound vesicles and later released into the cytoplasm where they multiply. Cell division is required for bacterial proliferation. The mechanism by which *L intracellularis* stimulates proliferation and dedifferentiation of ileal epithelial cells are poorly understood. Studies have shown, however, that the organism suppresses the inflammatory response by decreasing both B cell and T cell numbers, while macrophage numbers increase.[4]

Gross lesions are characteristic of the various forms of the disease. **Proliferative ileitis**, also called intestinal adenomatosis, is characterized by ridge-like thickening of terminal portion of the ileum, occasionally extending cranially or caudally to involve the cecum and proximal spiral colon. The marked thickening can be observed from the serosal surface as accentuation of the normal reticular pattern of the ileum. **Necrotic enteritis** is characterized by coagulative necrosis of the adenomatous mucosa, likely the result of an aerobic bacterial proliferation. Chronic infection, ulceration and stricture may result in a lesion called **regional ileitis**, characterized by severe hypertrophy of the muscular layers of the ileum. **Proliferative hemorrhagic enteropathy** may occur when extensive necrosis and ulceration causes massive hemorrhage into the lumen of the ileum. Grossly, the typical adenomatosis lesion is overlain by clotted blood and fibrin. Animals affected by this form of the disease may die acutely from exanquination.

In all forms of the disease, the histologic features are similar. The characteristic morphology is that of marked hyperplasia of intestinal crypt epithelium with loss of goblet cells and minimal inflammation. Mitotic activity is high and glands become crowded, branched and dilated by accumulation of necrotic debris. Hyperplastic glands may protrude into the lymphoid follicles of the submucosa (a prominent feature in this case).

Differential diagnoses for diarrhea and weight loss in feeder pigs include swine dysentery and salmonellosis, both of which have distinct gross and histologic lesions



3-1 Ileum, pig. Multifocally, obscuring the apical surface of enterocytes are myriad argyrophilic, short curved bacteria (arrowheads). (Warthin-Starry 600X)

centered mainly on the cecum and colon. Porcine circovirus-2, the agent of postweaning multisystemic wasting disease PMWR), reportedly can cause similar histologic lesions in the absence of co-infection with *L intracellularis*.[2] That intestinal lesion is characterized by a necrotic, proliferative enteritis with marked replacement of Peyer's patches by histiocytes and multinucleate giant cells, which can also be a feature of PE. However, characteristic botryoid cytoplasmic inclusions of PCV-2 infection should help differentiate the 2 diseases. No PCV-2 inclusions were seen in this case.

Although primarily a disease of pigs, *L intracellularis* can infect many species, most notably young horses, causing a similar proliferative enteropathy. The organism has also been investigated as an agent of inflammatory bowel disease in human beings.[6]

AFIP Diagnosis: Ileum: Ileitis, proliferative, diffuse, marked, with villar atrophy and fusion, lymphoid necrosis, crypt herniation and crypt abscesses

Conference Comment: *Lawsonia intracellularis* has been identified as the causative agent of a proliferative enteropathy in a number of species. It primarily affects the ileum in horses, sheep, ostriches, guinea pigs, pigs, rabbits and hamsters; the cloaca in emus; and the colon in ferrets, foxes and rats. The numerous **short curved rods (fig. 3-1)** can be visualized with a silver stain (e.g. Warthin-Starry) and are located in the apical portion of the intestinal epithelial cells.

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CASE IV - NADC WCS 02 (AFIP 2841700).

Signalment: 45-day-old, female, crossbred, Caesarian-derived, colostrum-deprived (CDCD) domestic swine (*Sus scrofa domestica*)

History: This pig was experimentally inoculated with 10^3 $TCID_{50}$ porcine circovirus type 2 (PCV 2) at 21 days of age. The pig was anorexic and icteric days 20-24 post inoculation. The pig was also febrile (rectal temperature > 40.0° C) for seven days prior to euthanasia and necropsy on day 24 post inoculation.

Gross Pathology: There was marked, generalized lymphadenopathy. Icterus was observed in the skin, sclera, subcutaneous tissue, pericardium, urine, and periosteal

tissues. The liver was markedly enlarged and had a mottled yellow, tan, and red color pattern. There were multifocal white foci throughout the parenchyma of the kidney.

Laboratory Results: PCR on fresh tissues for PCV2 was positive from multiple tissues; PCR on fresh tissues for porcine parvovirus was negative.
Virus isolation for PCV2 was positive from multiple tissues; virus isolation for PRRS virus was negative. In situ hybridization for PCV was positive from multiple tissues including the liver.

Contributor's Morphologic Diagnosis: Liver: hepatitis, diffuse, subacute, lymphohistiocytic, necrotizing, severe, with occasional intracytoplasmic botryoid inclusion bodies.

Contributor's Comment: These slides contain sections of liver in which there is diffuse alteration of the normal hepatic architecture. There is marked separation of hepatic cords due to distension of the sinusoids by clear space, erythrocytes, and low to moderate numbers of inflammatory cells. Hepatocytomegaly is a pronounced feature, and binucleated hepatocytes are commonly observed. Single-cell necrosis characterized by pyknosis, karyorrhectic debris, and Councilman bodies are a common feature. Foci of lymphocytes and macrophages can be seen haphazardly arranged throughout the sections. Neutrophils can occasionally be observed within the sinusoids. Intrahepatocellular bile pigment can frequently be observed. Some sections contain hepatocytes with intracytoplasmic, amphophilic to basophilic inclusion bodies. Multiple, variably sized inclusion bodies arranged in clusters (botryoid) can often be seen within a single cell. Less frequently basophilic intranuclear inclusion bodies are present.

Porcine circoviruses are members of the family *Circoviridae* which contain the smallest viruses known to infect animals. *Circoviridae* contain the genera circovirus (porcine circoviruses, pigeon circovirus, and psittacine beak and feather disease virus) and gyrovirus (chicken anemia virus). The human transfusion-transmitted virus (TTV) has been proposed to be grouped within the family *Circoviridae*.

Porcine circoviruses are icosahedral, nonenveloped, and contain a single-stranded, circular DNA genome of approximately 1,760 bases, and measure 17-20 nm in diameter. Porcine circoviruses have been sub-grouped into two types based on genomic differences. Porcine circovirus type 1 was first recognized as a contaminant of the PK-15 cell culture line and has not been proven to cause clinical disease in swine. Porcine circovirus type 2 has been associated with outbreaks of postweaning multisystemic wasting syndrome (PMWS) and porcine dermatitis and nephropathy syndrome (PDNS). PCV1 and PCV2 are antigenically similar but can be segregated by serologic tests.

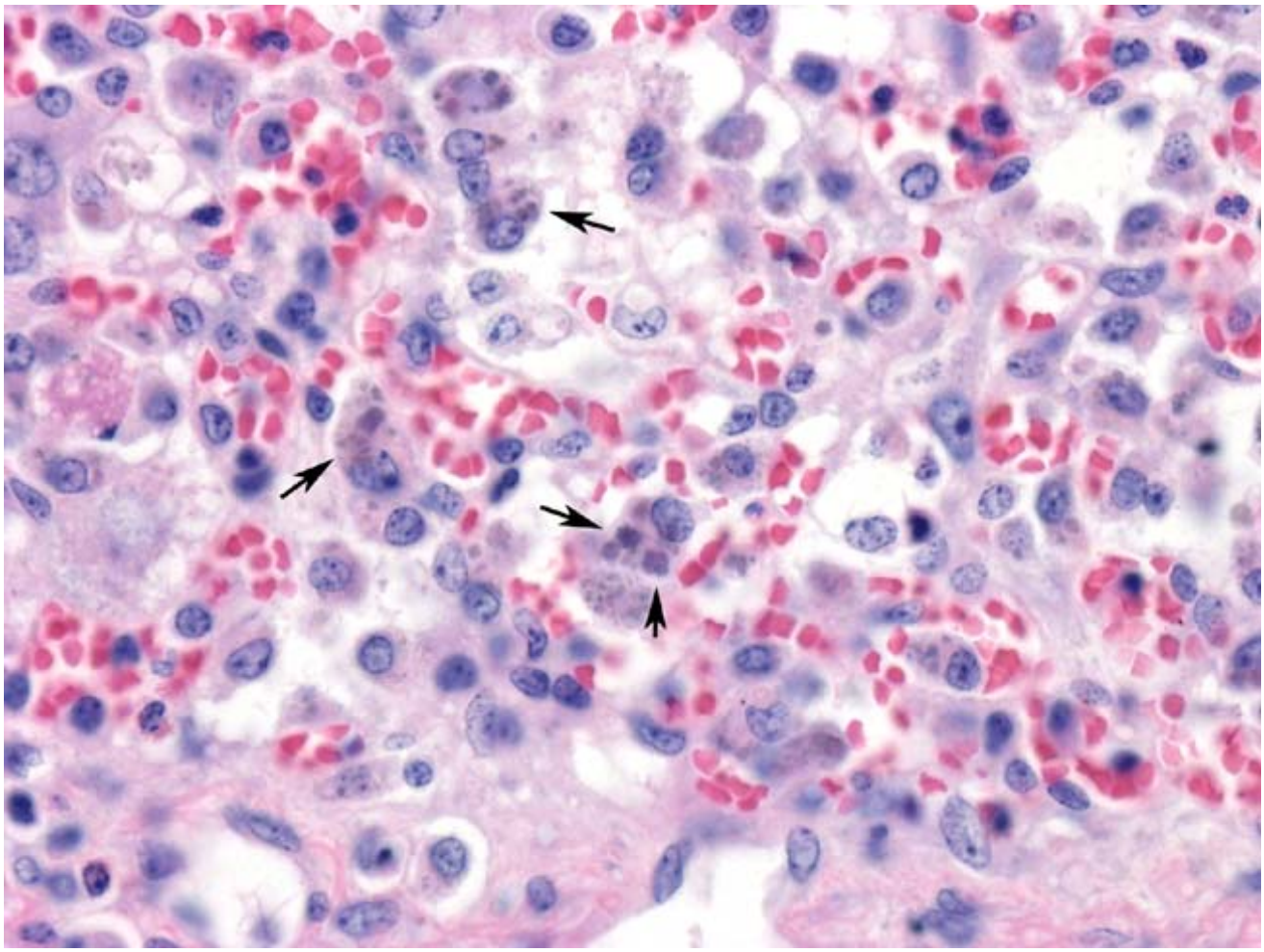
PMWS was first recognized in high-health status swine herds in western Canada in 1991 and has since been reported world-wide. PMWS is a low morbidity syndrome characterized by weight loss, failure to grow, diarrhea, dyspnea, and jaundice. Common gross lesions include generalized lymphadenopathy, hepatomegaly, gastric ulceration, nephritis, and interstitial pneumonia. Microscopically, there is disseminated depletion of lymphoid follicles, lymphohistiocytic inflammation in multiple tissues, interstitial nephritis, hepatitis, and bronchointerstitial pneumonia. The pathognomonic intracytoplasmic botryoid clusters of amphophilic to basophilic, variably sized inclusion bodies can be found within numerous cell types, particularly macrophages, depending on the stage of infection.

The lesions of PMWS have been reproduced with PCV2 alone and in combination with other viral agents, including porcine parvovirus and PRRS virus. This sample comes from experimental reproduction of PMWS in CDCD pigs with PCV2 alone.

AFIP Diagnosis: 1. Liver: Hepatitis, necrotizing and lymphohistiocytic, diffuse, severe, with karyomegaly and few basophilic botryoid intracytoplasmic inclusions
2. Gallbladder: Cholecystitis, neutrophilic, diffuse, mild, with pericholecystic edema.

Conference Comment: PMWS develops most often in pigs 5-12 weeks old and has a morbidity rate of approximately 5-10%. Although PCV2 alone can induce PMWS, PCV2 will result in more severe disease during a co-infection with either porcine parvovirus (PPV) or porcine reproductive and respiratory syndrome virus (PRRSV). Activation of the immune response increases replication of PCV2. The role of PCV2 in other diseases of swine is controversial because PCV2 can be isolated from healthy pigs. The isolation of PCV2 alone does not result in a diagnosis of PMWS; the diagnosis also requires the consistent gross and clinical signs.

The primary gross lesion of PMWS is generalized lymphadenopathy. Other gross findings may include hepatomegaly, gastric ulceration, nephritis and interstitial pneumonia. The histologic lesions of PMWS include lymphohistiocytic inflammation in multiple organs with **basophilic intracytoplasmic botryoid inclusions (fig. 4-**



4-1 Liver, pig. Multifocally, expanding hepatocyte cytoplasm there are basophilic to amphophilic botryoid inclusions (arrows). (H&E 600X)

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1), lymphoid depletion, and granulomatous interstitial pneumonia. Porcine dermatopathy and nephropathy syndrome (PDNS) is primarily associated with PCV2, but has also been associated with PRRSV, *Pasteurella multocida,* and *Streptococcus* sp. Gross lesions of PDNS include red papules over the hindquarters, perineum and ears, and enlarged edematous kidneys with petechiae. Histological lesions include vasculitis, hemorrhage, necrosis, and acute exudative glomerulonephritis.

Conference attendees discussed the differentiating PRRS from PMWS. Lymphocytes are the predominant inflammatory cell in cases of PRRS, whereas macrophages dominate in PMWS. The intracytoplasmic basophilic inclusion bodies are specific to a diagnosis of PCV2 infection.

PCV2 is a nonenveloped, icosohedral, DNA virus that forms paracrystalline arrays. Conference participants discussed other viruses that form paracrystalline arrays on EM. A useful mnemonic device used by AFIP residents at the AFIP is 'PICA' for Polyomavirus, Picornavirus, Iridovirus, Circovirus, and Adenovirus.

Not all sections contained gallbladder.

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