The Armed Forces Institute of Pathology
Department of Veterinary Pathology
WEDNESDAY SLIDE CONFERENCE
2005-2006

CONFERENCE 21
5 April 2006

Conference Moderator: Dr. Thomas Lipscomb, DVM, Diplomate ACVP
Senior Consulting Pathologist
Department of Veterinary Pathology
Armed Forces Institute of Pathology
Washington, DC

CASE I – CPHU (AFIP 2988198)

Signalment: The presented sample is the lung of adult female rat (*Bandicota indica*) captured in the village at southern coast of Sri Lanka.

History: After the Sumatran earthquake on Dec. 26, 2004, the World Health Organization warned against a prevalence of zoonoses in tsumami-striken areas around the Indian Ocean. The Japanese government sent research teams of medical and veterinary scientists to these areas for the investigation of zoonotic diseases in humans and animals.

Gross Pathology: The lungs were diffusely consolidated. A cyst, 7 mm in diameter, containing larvae of *Taenia taeniaeformis* (*Cysticercus fasciolaris*) was found on the left lobe of the liver. Except for these visceral lesions, the rat appeared normal.

Histopathologic Description: Many eggs containing larvae are lodged in the thickened alveolar walls. Most of them seem to be located within alveolar capillaries and a few eggs within the arterioles. A few hatched larvae are phagocytized by multinucleated giant cells in the alveolar lumina. Many macrophages, epithelioid cells, multinucleated giant cells, eosinophils, lymphocytes and plasma cells infiltrate the alveolar walls and interstitium, and they frequently form granulomas around the eggs. Four sections of adult worms are in the small arteries showing severe proliferative endarteritis. Bronchiolar mucosa is thickened, and shows goblet cell hyperplasia and infiltrations of eosinophils.

In the cerebrum, not presented, mild meningitis was observed.

Contributor's Morphologic Diagnosis: Eosinophilic and granulomatous bronchopneumonia due to Angiostrongylus infestation (Pulmonary angiostrongyliasis of rodents)

Contributor's Comment: *Angiostrongylus (A.) cantonensis* lives in the pulmonary arteries and right ventricles of rodents. Copulation occurs in the pulmonary artery and females produce eggs which develop into first stage larvae. They penetrate the alveoli, migrate through the respiratory tract into the alimentary tract and pass out of the definitive host in the feces. They then infect a molluscan intermediate host, usually terrestrial snails such as *Achatina fulica* or aquatic snails such as *Pila* spp. Third-stage larvae emerge a little over 2 weeks later and infect the rodent definitive host, usually when it eats an infected mollusk. At least 24 species of rodents can act as definitive hosts for *A. cantonensis*, including *Rattus norvegicus* and *Rattus rattus*. A wide range of animals may act as paratenic hosts.[1] From the rat intestine, the third-stage larvae embark upon an obligatory migration through the CNS, to which they are carried by the bloodstream. In the brain or spinal cord, third-stage larvae leave the capillaries, wander through tissues apparently at random, moulting twice en route to the subarachnoid space. On reaching the brain or spinal cord surface, fifth-stage larvae attempt to re-enter the central circulation by penetrating veins, and are then carried to their ultimate destination, the pulmonary artery.[2]

A. cantonensis is found in Southeast Asia, the Pacific and Australia, including Polynesia, Indonesia and Papua New Guinea. Because of its lack of host specificity and the mobility of rats, *A. cantonensis* has become established throughout much of the tropical and sub-tropical parts of the world, such as Madagascar, Japan, Egypt, the Ivory Coast of Africa, India, Samoa and Fiji, Cuba, Puerto Rico and southeastern USA. Infection is transmitted to humans and animals by eating raw molluscs (slugs, snails and so on) or raw food that has been contaminated by them.

A. mackerrasae and *A. malaysiensis* are close relatives of *A. cantonensis* and they share virtually the same life cycle, but only *A. cantonensis* has been confirmed to be a human pathogen. We collected the adult worms from the lungs of rats and sent them to the parasitology department. Although the parasites presented here are most probably *A. cantonensis,* a final diagnosis of the subspecies has not been made yet.

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AFIP Diagnosis: Lung: Pneumonia, granulomatous and eosinophilic, diffuse, severe, with numerous morulated and larvated eggs and intra-arterial adult metastrongyle nematodes, proliferative histiocytic and eosinophilic endarteritis, bronchiolar epithelial hyperplasia, and mild eosinophilic bronchiolitis, etiology

consistent with *Angiostrongylus* sp., greater Bandicoot rat (*Bandicota indica*), rodent.

Conference Comment: The contributor provided an excellent review of *Angiostrongylus cantonensis* infection. Angiostrongylids belong to the Family Metastrongyloidea within the Order Strongylida. Unlike the other strongyle families i.e. the true strongyles and trichostrongyles, metastrongyles have coelomyarian musculature and accessory hypodermal chords. (3)

Within the pulmonary artery, adults measure 125-135 μm in diameter with a 3-5 μm thick smooth, eosinophilic, hyalinized, anisotropic cuticle, coelomyarian musculature that lines a pseudocoelom, accessory hypodermal chords, an intestine composed of a few, large multinucleated cells (known colloquially as a "strongyle gut") and paired uteri with developing eggs.

Angiostrongylus cantonensis is the most common cause of human eosinophilic meningitis. Most cases of eosinophilic meningitis have been reported from Southeast Asia and the Pacific Basin, although the infection has spread to many other areas of the world, including Africa and the Caribbean. Humans can acquire the infection by eating raw or undercooked snails or slugs infected with the parasite or by eating raw produce that contains a small snail or slug, or part of one. There is some question whether or not larvae can exit the infected mollusks in slime (which may be infective to humans if ingested, for example, on produce). The disease can also be acquired by ingestion of contaminated or infected paratenic animals (crabs, freshwater shrimp). In humans, juvenile worms migrate to the brain, or rarely the lungs, where they eventually die. Clinical symptoms of eosinophilic meningitis are caused by the presence of larvae in the brain and the local host reaction. Symptoms include severe headaches, nausea, vomiting, stiff neck, seizures, and neurologic abnormalities. Occasionally, ocular invasion occurs. Eosinophilia is present in most cases. Most patients recover fully. (4)

Another angiostrongylid of veterinary importance is *Angiostrongylus vasorum*, a parasite of the right ventricle and pulmonary artery of dogs and foxes. The adult worms cause proliferative endarteritis; however, the most severe damage is caused by the eggs and larvae. Eggs lodge in arterioles and capillaries where emerging larvae erupt into alveolar spaces inciting marked fibrosis. Clinical disease is not usually noted until the chronic stage, which can occur months to years after the initial infection. Fibrosis in the lung can lead to right-sided cardiac failure. It is rare for acute disease to result in death of the dog. (5)

This case was reviewed by Dr. C.H. Gardiner, parasitology consultant for the Department of Veterinary Pathology, AFIP.

Contributor: Laboratory of Comparative Pathology, Department of Veterinary Clinical Sciences, Graduate School of Veterinary Medicine, Hokkaido University http://www.hokudai.ac.jp/veteri/

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CASE II – 51307 (AFIP 2985121)

Signalment: Captive-born 8 day old male bottlenose dolphin (*Tursiops truncatus*)

History: Calf was born after prolonged labor and did not nurse until 11.5 hours of age. Animal did well nursing for next seven days. On the eighth day, animal did not nurse well and was repeatedly "disciplined" by dam. Briefly nursed only two more times before dying. Animal was submitted for necropsy examination.

Gross Pathology: Animal was presented in good post-mortem condition. Muscling was good, but subcutaneous and visceral fat stores were reduced. There were numerous recent and remote skin lacerations and abrasions, consistent with "disciplining" behavior. No teeth had yet erupted. The lungs were slightly rubbery and edematous, and there was a small amount of mucopurulent discharge in the trachea. The heart was grossly normal with a patent ductus arteriosus. The surface of the brain was grossly normal.

Laboratory Results: Cultures taken at necropsy produced heavy growths of *Streptococcus zooepidemicus* and *Escherichia coli*.

Histopathologic Description: Included are sections of cerebellum with or without brainstem. Prominence of the external granular layer of the cerebellum is consistent with animal's age. Expanding the meninges and Virchow-Robin spaces

are large numbers of macrophages and viable and degenerate neutrophils, with frequent plasma cells and lymphocytes. There are large numbers of intra-lesional large bacterial cocci, appearing within the cytoplasm of macrophages as well as extra-cellularly in pairs and large colonies. Tissue Gram stains reveal large Gram positive cocci. Occasional vessels are thrombosed with fibrin and enmeshed erythrocytes and leukocytes. Inflammation was also present in the choroid plexus and the optic nerve meninges (not submitted).

Septic thrombi were present in the lungs, and bacteria were additionally observed in the adrenals, heart, several lymph nodes, and associated with inflammation in the soft tissue of the umbilicus. Aspirated squamous cells were observed in the lungs, consistent with fetal stress. There was extra-medullary hematopoiesis in the liver and spleen, and lipidosis in the liver and kidneys.

Contributor's Morphologic Diagnosis: Brain: Meningitis, suppurative, diffuse, acute, severe, with myriad intra-cytoplasmic and extra-cellular Gram positive bacterial cocci, consistent with *Streptococcus zooepidemicus*.

Contributor's Comment: Like cattle and horses, bottlenose dolphins have epitheliochorial placentation (http://medicine.ucsd.edu/cpa/index.html), although it is diffuse rather than cotyledonary or microcotyledonary. As such, there is no transfer of maternal antibodies in the dolphin fetus, and neonates are dependent on colostrum for passive transfer of pre-formed antibodies. In primates, rodents, and other animals with hemochorial placentation, there is accumulation of maternal IgG but not other classes of antibody in the fetus to levels approaching those of the dam[1]. In cats and dogs, where there is endotheliochorial placentation, transfer of IgG is less efficient, and antibody concentrations may only be 5-10% of those of the dam.

Colostrum contains primarily IgG (65-90%), with lesser amounts of IgA and some IgM and IgE. Unlike milk, the IgG in colostrum is derived predominately from serum, rather than local production by resident plasma cells in the mammary gland. Colostrum additionally contains trypsin inhibitors which, in combination with the immaturity of the digestive enzymes in the neonate, allow much of the antibody to bypass degradation. Specialized FcRn receptors, MHC class Ib heterodimers, on the apical surface of the enterocytes bind immunoglobulin, and it is taken into the cell by pinocytosis, later to enter lacteals or capillaries. In general, permeability is highest immediately after birth, and declines after about six hours to very low levels by 24 hours. Gut closure is generally considered complete by 48 hours.

This particular dolphin had clinical and pathological evidence of intra-uterine stress, and did not nurse for nearly twelve hours post-partum. Because the ability to passively absorb pre-formed antibodies declines rapidly from birth, the delay in

nursing likely contributed to at least partial failure of passive transfer (FPT). In domestic animals, septicemia as a sequela of FPT commonly occurs within the first 5-8 days post-partum, and may be manifest as polyarthritis, pneumonia, or meningitis [2]. The umbilicus is often the source for such infections. The bacteria cultured in these infections are often derived from the local environment or are commensals.

Strep. *zooepidemicus* (*Strep*. *equi subspecies zooepidemicus*, Lancefield group C) has been isolated from septicemic foals[2], and has been identified as a cause of mortality in captive *Tursiops* species[3]. In horses, *Strep*. *zooepidemicus* is a mucosal commensal and opportunistic pathogen, causing suppurative infections in joints, lymph nodes, nasal cavities and lungs in animals stressed by viral infection, heat or injury[4]. Additionally, *Strep*. *zooepidemicus* has been associated with meningitis in humans as a suspected zoonosis[5].

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AFIP Diagnoses: Brainstem; cerebellum: Leptomeningitis, histiocytic and neutrophilic, acute, diffuse, severe, with myriad short bacilli, bottlenose dolphin (*Tursiops truncatus*), cetacean.

Conference Comment: The similarity of this case of apparent partial failure of passive transfer in a dolphin calf to cases in bovine calves is interesting in light of the close phylogenetic relationship between dolphins (and other cetaceans) and artiodactyls such as cattle.

Gram-stained sections examined at the conference demonstrated that the bacteria are short gram-negative bacilli compatible with *Escherichia coli,* which was cultured. No gram-positive bacteria were found. The case was further studied in consultation with AFIP's Department of Infectious and Parasitic Diseases. They found only gram-negative bacilli. The bacteria were compared to a case of known cultured *E. coli* in a human kidney and were found to be very similar. Their conclusion was that the bacteria are consistent with *E. coli.* They noted that the apparent absence of the cultured *Streptococcus* might be a result of rarity or sampling. *E. coli* is a common cause of neonatal septicemia in domestic animals and humans and is one of the first potentially pathogenic bacteria to which neonates are exposed following parturition.

The contributor noted an excellent web-page on comparative placentation provided by Dr. Kurt Benirschke and the University of California at San Diego. The web address is http://medicine.ucsd.edu/cpa/authorfs.html

Contributor: Johns Hopkins University School of Medicine, Department of Comparative Medicine, Broadway Research Building, Rm. 863, 733 North Broadway, Baltimore Maryland, 21205

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CASE III – 399-04 (AFIP 3003942)

Signalment: 4 weeks old, female, Ayshire, bovine

History: The calf was reared in a calf-rearing farm where there had been problems with acute tympany. Calves were brought to this farm at around two weeks of age. A week after arrival several calves were anorexic, lethargic and bloated. The calf was found dead a few days later. The calves were fed milk replacer *ad libitum*. The milk replacer was mixed with 35 – 40°C water and added to large containers in which it gradually cooled down to environmental temperature.

Gross Pathology: The calf was in good nutritional condition but severely dehydrated. The abomasum was markedly dilated and contained gas and a moderate amount of blood stained liquid. The abomasal wall was edematous with multifocal hemorrhages and mucosal erosions. On the serosal surfaces, especially on the abomasum, there was fibrinous exudate. The rumen contained partly digested roughage and a large amount of oil. The small intestine was congested. No other specific lesions were observed.

Laboratory Results: Bacteriology and PCR: *Clostridium perfringens* was isolated from the abomasum and small intestine and PCR was used to specify it as type A.

Histopathologic Description: Abomasum: Within the mucosa there is marked diffuse congestion and moderate inflammatory infiltrate consisting mainly of neutrophils and lesser number of lymphocytes that multifocally expand and extend to the submucosa and through the muscle layer to the serosa. There is nearly diffuse superficial necrosis of the mucosa with multifocal hemorrhages that extend randomly deeper into the abomasal wall with disruption of the serosa and adhered fibrinous exudate admixed with neutrophils. Closely attached to the mucosal epithelium and within the intraluminal inflammatory exudate there are numerous rod-shaped bacteria (8-10 μm long).

Contributor's Morphologic Diagnosis: Abomasum: Abomasitis, hemorrhagic and suppurative, acute, diffuse, severe with necrosis and numerous rod-shaped bacteria.

Contributor's Comment: Abomasal tympany with inflammation is an emerging disease in calves. In Finland it is most prevalent in calves fed *ad libitum* milk replacer. Severe acute bloat and high mortality are typical for the disease. Typically *C. perfringens* type A or *Sarcina*-like bacteria alone or together are found in these cases. Many infectious agents are capable of causing abomasal lesions, however, only infection with *C. septicum-, C. perfringens* type A- and *Sarcina*- like bacteria are associated with moderate to severe tympany with necrotizing abomasitis in calves. Braxy, which is caused by *C. septicum,* is associated with frozen feed (1,2).

Clostridial organisms are part of the normal bacterial microflora of the gastrointestinal tract of ruminants and they are widely found in the environment. *C. perfringens* type A is the most common one of the five types of *C. perfringens* and the only one that is found both in the intestinal tract of ruminants and soil. The significance of this bacterium as a pathogenic organism in bovine enteric diseases is still not clear although it has been reported as the cause of enterotoxemia syndrome in Belgian Blue calves and clinical disease has been produced by intraruminal inoculation (3,4,5). *C. perfringens* strains are divided into five types on the basis of their production of four major exotoxins. All these five *C. perfringens* types can also produce enterotoxin during sporulation. This enterotoxin is the major factor in food poisonings in humans caused by *C. perfringens* type A containing the *cpe-* gene and it has also been isolated from foals and pigs with diarrhea. α-toxin is the major exotoxin produced by type A strains but some of these strains can also produce β2- toxin. This novel β2- toxigenic *C. perfringens* has been isolated from piglets and horses with enteric disease. In cattle it is still controversial how big a role these toxins have in the pathogenesis of abomasitis (3,6,7). *Sarcina*-like bacteria are part of the normal bacterial flora in the stomachs of monogastric animals and they are also very likely normal inhabitants of the rumen of cattle. In healthy lambs *Sarcina*-like bacteria have not been isolated

from the abomasum. In lambs with abomasitis *Sarcina sp.* have been isolated with *C. fallax* and *C. sordellii.* (8,9,10).

Since a small amount of *C. perfringens* type A and *Sarcina*-like bacteria reside normally in the gastrointestinal tract of cattle, a change towards their excessive growth has to happen for them to cause clinical disease. Because bacterial growth in the rumen often precedes abomasitis, it is critical to prevent the milk replacer from entering the forestomachs during the first weeks of life. This can occur if there is insufficient closure of the reticular groove while feeding or if too much milk replacer is fed at a single time. Management factors are crucial in preventing the growth of other bacteria, for example *Lactobacillus-* or *Clostridium spp.* in the rumen and/or abomasum, that can contribute to the growth of *C. perfringens* type A and *Sarcina*-like bacteria in the gastrointestinal tract. The problems seem to be associated with poor hygiene, high storage temperature and inadequate cooling of the milk replacer, sudden change of feed and feeding of low quality milk replacer based on plant proteins (1,10,9,11).

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AFIP Diagnosis: Abomasum: Abomasitis, necrotizing, fibrinosuppurative and hemorrhagic, acute, transmural, severe, with numerous mucosa-adherent bacilli, Ayshire, bovine.

Conference Comment: Of the five toxigenic types of *Clostridium perfringens*, designated types A-E based on their production of the four major exotoxins, *C. perfringens* type A is the most common. Enteric proliferation of this type is recognized as a cause of hemorrhagic enteritis in several species including black-footed ferrets, chickens, horses, pigs, lambs, goats, calves, and humans. Clinical signs and histologic lesions are caused by a lecithinase known as alpha toxin, the major toxin produced by *C. perfringens* type A. Alpha toxin is both hemolytic and cytotoxic by virtue of its effects on cell membranes. Enterotoxin, the principal toxin involved in foodborne illness, is released upon lysis of sporulating cells. (1,11,12)

Within the last few years another *Clostridia perfringens* toxin identified as ß2 has been described. The biologic activity of the ß2-toxin is similar to that of the ß1-toxin. The gene that codes for ß2-toxin is referred to as cpb2. All cpb2 positive strains of *C. perfringens* do not, however, produce ß2 toxin *in vitro*. Cpb2 positive *C. perfringens* has been found in various animal species with and without enteric disease. Some hypothesize that predisposing factors such as dietary change and antibiotic therapy can result in selection of ß2-toxigenic *C. perfringens* which may lead to enteritis or enterotoxemia. (13)

Below is a simple chart of the five types of *C. perfringens*, the toxins they produce and diseases they cause.

Clostridium perfringens - Types, toxins and diseases					
Type	Toxin				Diseases
	Alpha	Beta	Epsilon	Iota	
A	+ +	-	-	-	Gas gangrene Food Borne Illness humans Necrotic enteritis - Chickens Gastroenteritis - Ferrets Yellow lamb disease - enterotoxemia, western US Colitis X in horses - unproven association
B	+	+ +	+	-	Lamb dysentery Hemorrhagic enteritis - calves, foals, guinea pigs - UK, S. Africa, Middle East
C	+	+ +	-	-	Enterotoxic hemorrhagic enteritis - neonatal lambs, goats, cattle, pigs Struck - Adult sheep, UK
D	+	-	+ +	-	Overeating disease/ pulpy kidney - Sheep, cattle, goats Focal symmetric encephalomalacia - Sheep
E	+	-	-	+ +	Enterotoxemia - calves, lambs. guinea pigs, rabbits
Table adapted from Barker et al, 1993 p.237 & Jones et al, 1997 p. 421					

Braxy, caused by *Clostridium septicum*, is another disease of lambs and calves resulting in abdominal distention, abomasitis, and high mortality. The factors that initiate bacterial invasion are unknown but are thought to be secondary to injury by frozen, spiny or coarse ingesta. Microscopic findings characteristic of braxy include abomasal edema and emphysema, areas of coagulative necrosis bordered by neutrophils (occurring primarily in the submucosa but can be transmural),vasculitis, thrombosis, hemorrhage and the presence of Gram-positive bacilli.

Contributor: National Veterinary and Food Research Institute (EELA), Helsinki, Finland
http://www.eela.fi/fi/index.html

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CASE IV – Ex50c (AFIP 2987649)

Signalment: A 10 year-old male Pinscher, canine

History: A 10 year-old male Pinscher presented with a 4-month history of intermittent pain of the left forelimb. The dog occasionally lifted the affected limb and avoided using it, but was not consistently lame. No abnormalities were found on palpation, radiography and computerized tomography and a diagnosis was not made at the initial examination. The dog was re-examined a month later at which point a small mass was palpated in the region of the brachial plexus. Exploratory surgery revealed a localized fusiform swelling in the C7 spinal nerve at the level of the brachial plexus. The swelling was 6 cm long and 1.5 cm diameter at its widest point. Adjacent nerves adhered to the surface of the mass. The forelimb was amputated. At the time of case submission, 3 months following the operation, the dog is in good health.

Gross Pathology: On cut section the mass was pale and hard.

Histopathologic Description: Multiple sections of a mass surrounded by a fibrous capsule. Multifocally neoplastic cells extend through the capsule and form small nodules either in direct continuity with or adjacent to the main mass. Within the tumor, the cellularity and pattern of arrangement is variable. The most widespread element consists of oval to spindle cells in moderately to densely cellular sheets and fascicles with a small to moderate amount of collagenous stroma. Neoplastic cells have eosinophilic cytoplasm with indistinct margins and oval vesicular nuclei with one or more nucleoli. A trend to whorl formation is observed in a region of neoplastic proliferation immediately adjacent to an area with relative preservation of nerve fibers. Here, neoplastic cells multifocally form a few concentric laminae around a central axonal core. Small foci where the neoplastic cells assume an epithelioid appearance or are separated by large amounts of mucinous extracellular matrix are present.

There are several areas with smooth homogenous and eosinophilic stroma, suggestive of neoplastic osteoid with entrapped oval to polygonal neoplastic cells, either singly or in groups. Neoplastic cells in this area are spindled, irregular and polygonal with large vesicular nuclei and one or more prominent nucleoli. There is anisokaryosis and the morphology is reminiscent of osteosarcoma.

An anaplastic epithelial element is present and consists of groups of disorganized glandular and cystic structures lined by cuboidal, columnar, squamous, or attenuated cells with moderate to abundant occasionally vacuolated cytoplasm and large round to oval vesicular to finely granular nuclei with one or more nucleoli. A few small clusters of squamous epithelial cells with localized keratinization in

continuity with the neoplastic glandular structures are found (not present in all sections). Throughout the mass mitotic figures are uncommon and single necrotic cells are found in low number. There is multifocal mild lymphocytic and lesser plasmacytic infiltration of the tumor and the surrounding connective tissue.

Contributor's Morphologic Diagnosis: Malignant peripheral nerve sheath tumor with divergent differentiation

Contributor's Comment: Tumors of the peripheral nervous system (PNS) are uncommon in domestic animals, with the exception of multicentric schwannoma / neurofibroma, in cattle which is usually incidental (1, 2). Most cases are encountered in dogs, where the most common sites of origin are the nerve roots of the brachial plexus, often C6-C8. A typical history in these cases is of slowly progressive lameness, pain and muscle atrophy in the affected limb. Compression of the cranial thoracic spinal cord may lead to Horner's syndrome with mild upper motor neuron and general proprioceptive signs in the ipsilateral pelvic limb. Tumors of thoracic and lumbar spinal nerves tend to present with signs of acute spinal cord compression. The trigeminal nerve is the most commonly affected cranial nerve and a mass at this location may manifest as unilateral atrophy of the muscles of mastication and loss of facial sensation. If the tumor impinges on the CNS, brain stem signs may ensue (1).

The typical gross appearance of tumors arising in peripheral nerves is grayish fusiform thickening of several nerve trunks, sometimes with fusion into a common tumor mass (1, 2). Many PNS tumors in the dog are anaplastic and malignant as evaluated by histologic criteria and biologic behavior. Poorly differentiated PNS tumors are best designated malignant peripheral nerve sheath tumor (MPNST). Determination of the cell of origin – schwannian, perineurial, fibroblastic or other is often impossible in routine sections (1). Schwannoma may be used to describe well-differentiated variants (2). Both benign and malignant tumors may show divergent differentiation (2). In human MPNST, cytologic and histologic pattern variation is the rule. Distinctive features found in some cases include melanin pigmentation and divergent mesenchymal or epithelial differentiation (3). The most common secondary elements are cartilage and bone (4). In the dog differentiation to primitive cartilage, bone, skeletal muscle, keratinizing squamous epithelium, glandular epithelium and melanin production have been observed (1, 4).

The MPNST in this case has mesenchymal and epithelial components, both of which are morphologically malignant - osteosarcoma and adenocarcinoma respectively. A MPNST arising in LI and L2 with similar histologic features was reported in a dog (2). Immunohistochemical staining of that tumor showed that the mesenchymal cells stained diffusely for vimentin, S-100 and NSE while the epithelial cells were positive for pancytokeratin only (4). In general,

immunohistochemistry is not considered reliable for the diagnosis of peripheral nerve sheath tumors (2).

The theory behind the divergent differentiation in MPNST is that migratory stem cells of the neural crest differentiate to neuroectodermal structures (which give rise to melanocytes, ganglion cells, Schwann cells etc.) and multipotential ectomesenchymal cells (which give rise to leptomeninges, bone, cartilage, and muscles of the head and neck). Studies have suggested that the epithelial component is not heterotopic but could arise from Schwann cells or mesoectodermal cells intrinsic to peripheral nerves. In humans, the presence of divergent differentiation warrants a poor prognosis (4).

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AFIP Diagnosis: Malignant peripheral nerve sheath tumor with adenocarcinomatous divergent differentiation, Doberman Pincher, canine.

Conference Comment: The contributor has provided a rare case and a thorough review of malignant peripheral nerve sheath tumors with divergent differentiation. Attendees recognized the spindle shape and characteristic whorling pattern of a peripheral nerve sheath tumor but were surprised by the presence of the epithelial component. No unequivocal osteoid was identified in the sections examined at the conference.

Readers are encouraged to review conference 17, case 3, 2005-2006 for a case of a peripheral nerve sheath tumor of the skin and subcutis of dogs.

Contributor: Weizmann Institute of Science, Department of Veterinary Resources, Rehovot, Israel 76100

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Carl I. Shaia, DVM
Major, Veterinary Corps, U.S. Army
Wednesday Slide Conference Coordinator
Department of Veterinary Pathology
Armed Forces Institute of Pathology
Registry of Veterinary Pathology*