

54th AAVLD Diagnostic Pathology Slide Session



**American Association of Veterinary Laboratory
Diagnosticians
Buffalo, New York
Saturday, October 1, 2011
3:30-6:00 PM**

54th AAVLD Diagnostic Pathology Slide Session October 1, 2011 Buffalo, New York

| Case # | Slide label | Presenter | Species |
|---------------|---|---------------------|----------------|
| 1 | AAVLD 2011 Case # 1 | Alison Tucker | Dog |
| 2 | AAVLD 2011 # 2 | Scott D. Fitzgerald | Dog |
| 3 | AAVLD 2011 Case # 3 | Pritpal S. Malhi | Dog |
| 4 | AAVLD 2011 Case # 4 MSPCA-Angell | Pamela J. Mouser | Cat |
| 5 | AAVLD 2011 Case # 5 U. of GA. Vet Coll. | Moges Woldemeskel | Dog |
| 6 | AAVLD 2011 Case # 6 | Brian G. Caserto | Dog |
| 7 | AAVLD 2011 Case # 7 | Francisco A. Uzal | Pig |
| 8 | AAVLD 2011 Case # 8 University of Tennessee Veterinary Pathology | Amanda J. Crews | Dog |
| 9 | MSU DCPAH AAVLD 2011 Case # 9 | Dodd Sledge | Steer |
| 10 | AAVLD 2011 Case # 10 University of Tennessee Veterinary Pathology | Julia Lankton | Frog |
| 11 | ADDL Purdue University AAVLD 2011 Case # 11 | Duane Murphy | Mare |
| 12 | AAVLD 2011 Case # 12 | Alfonso De la Mora | Foal |
| 13 | AAVLD 2011 Case #13 | Sandra Scholes | Heifer |
| 14 | AAVLD 2011 Case #14 | Peter Moisan | Boer doe |
| 15 | AAVLD 2011 Case #15 NMDA-VDS | John M. Ragsdale | Dog |
| 16 | AAVLD 2011 Case #16 | J. Lamoureux | Horse |
| 17 | AAVLD 2011 Case #17 | Melanie Ammersbach | Dog |
| 18 | AAVLD 2011 Case # 18 | Jeff Hayes | Deer |

54th AAVLD Diagnostic Pathology Slide Session
October 1, 2011 Buffalo, New York

| Case # | Page | Presenter | Species | Organ | Diagnosis |
|--------|-------|---------------------|----------|------------------------|--|
| 1 | 4 | Alison Tucker | Dog | Kidney | Collagenofibrotic glomerulonephropathy |
| 2 | 5 | Scott D. Fitzgerald | Dog | Pericardium | Mesothelioma |
| 3 | 6 | Pritpal S. Malhi | Dog | Liver | Xylitol toxicosis |
| 4 | 7 | Pamela J. Mouser | Cat | Skin | Fungal pododermatitis |
| 5 | 8 | Moges Woldemeskel | Dog | Salivary gland | Sialometaplasia |
| 6 | 9 | Brian G. Caserto | Dog | Liver | Polycystic liver disease |
| 7 | 10 | Francisco A. Uzal | Pig | Colon | <i>Clostridium difficile</i> colitis |
| 8 | 11 | Amanda J. Crews | Dog | Skin | Hepatocutaneous syndrome |
| 9 | 12 | Dodd Sledge | Steer | Rumen | Rumen acidosis, mycotic rumenitis |
| 10 | 13 | Julia Lankton | Frog | Liver, kidney | Systemic Ranavirus |
| 11 | 14 | Duane Murphy | Mare | Placenta | Actinomycete-associated placentitis |
| 12 | 15 | Alfonso De la Mora | Foal | Intestine | Necrotizing enterocolitis |
| 13 | 16 | Sandra Scholes | Heifer | Brain | Angiocentric leukoencephalopathy |
| 14 | 17 | Peter Moisan | Boer doe | Placenta | <i>Chlamydophila abortus</i> placentitis |
| 15 | 18 | John M. Ragsdale | Dog | Skin | Vogt-Koyanagi-Harada-like syndrome |
| 16 | 19 | J. Lamoureux | Horse | Thyroid gland | Thyroid carcinosarcoma |
| 17 | 20-22 | Melanie Ammersbach | Dog | Bone marrow | Myelomonocytic leukemia |
| 18 | 23 | Jeff Hayes | Deer | Liver, lung, kidney | Malignant catarrhal fever |

NOTE: Case 17 is a cytology case; four photomicrographs are included on pages 21 and 22 of the proceedings in place of a glass slide.

Collagenofibrotic Glomerulonephropathy in a Mixed-Breed Dog

Alison Tucker¹, Reginald Ridenhour¹, Rachel Cianciolo², George Lees², Fred Clubb, Jr²

¹North Carolina Veterinary Diagnostic Laboratory System

²Texas Veterinary Renal Pathology Service

Signalment: 5 month old, intact male, 4.5 kg, mixed breed dog

Clinical History: According to the history provided, this dog was acquired as a stray and had been unremarkable for 1 month, after which there was progressive poor growth and antisocial behavior for 1 month. There was a 2 day course of vomiting, diarrhea, and seizure-like activity. Examination by the referring veterinarian identified depression, convulsions and vertical nystagmus. The pup was euthanized and submitted for necropsy. Clinical chemistry results were not provided. Gross findings at necropsy were confined to poor body condition and bilaterally small, slightly firm kidneys with irregular cortical surfaces.

A 3 μ , hematoxylin and eosin stained section of kidney is included in the slide set.

Microscopic Description: In the cortex there is generalized expansion of glomerular mesangium by eosinophilic material, increased mesangial cellularity (up to 20 nuclei per section) and compression of capillary lumina. Endothelial cell proliferation causes endocapillary hypercellularity. Parietal and visceral epithelial cells are enlarged. Synechia are focally present and are associated with circumferential periglomerular fibrosis and rare crescent formation. There is tubule loss with parenchymal collapse and interstitial fibrosis, distension of many remaining tubules with homogeneous eosinophilic (proteinaceous) material, and occasional acute degeneration and necrosis as well as regeneration of tubule epithelial cells. The mesangial extracellular material is not congophilic. With Masson Trichrome staining the mesangial extracellular material is light blue. The mesangial extracellular material is light pink with Periodic Acid Schiff staining and basement membranes are dark magenta.

The mesangial extracellular material is immunoreactive for collagen type III.

Electron microscopy: The mesangium contains nonbranching fibrils, 29 – 58 nm diameter, with faint periodicity. No electron-dense deposits are detected in mesangium or filtration membrane.

Diagnosis: Kidney: Collagenofibrotic Glomerulonephropathy

Comment: Collagenofibrotic Glomerulonephropathy is a recently described disorder in humans that has been reported in dogs, a cat, pigs and a cynomolgus macaque. The human syndrome is divided into juvenile onset and adult onset; both have proteinuria and hypertension with progression to renal failure. There is deposition of type III collagen within the glomerular mesangium but not in other tissues, with the exception of one human case on maintained on dialysis for 7 years. While some veterinary cases may also have immune complex deposition in the GBM, this is not a consistent finding and may be a secondary change. Increased circulating procollagen III peptide levels have been documented in human cases but the pathogenesis of this syndrome is not completely described.

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- Kamiie, J, et al, Collagenofibrotic glomerulonephropathy with fibronectin deposition in a dog, *Vet Pathol*, 2009, 46 (4), 688-692.
- Koeman, JP, et al, Proteinuria associated with glomerulosclerosis and glomerular collagen formation in three Newfoundland dog littermates. *Vet Pathol*, 1994, 31(2), 188-193.
- Nakamura, S, et al. Renal glomerular fibrosis in a cat. *Vet Pathol*, 1996, 33(6), 696-699.
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An Unusual Case of Pericardial Mesothelioma in a Dog

Scott D. Fitzgerald, Benjamin Adu-Addai

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A 9.5 year-old male castrated mixed breed dog had a history of ascites, lethargy and surgical removal of 16 l of serosanguinous fluid from its abdomen one week earlier. The dog was euthanized and submitted to the Diagnostic Center for Population and Animal Health for necropsy. The principal gross finding was a mass attached to the heart base and major vessels within the pericardial sac. The mass measured 10 x 6 x 3 cm, with an irregular pale and friable cauliflower-like surface, and was attached to the right auricle. There was minimal fluid present within the pericardial sac, and the rest of the heart was grossly normal.

Histologically, the mass consisted of sheets cords, and papillary projections of large round to polygonal cells, with plentiful eosinophilic to clear cytoplasm, medium sized round nuclei, a low mitotic index, and small amounts of fibrovascular stroma. There was no histologic evidence of distant metastasis. The initial histologic diagnosis was pericardial mesothelioma, and immunohistochemical staining to confirm the diagnosis was performed. Staining for pancytokeratin (AE1/AE3) was strongly immunopositive in the cytoplasm of most neoplastic cells. Staining for vimentin was also strongly immunopositive in the cytoplasm of many neoplastic cells. These stains confirmed this neoplasm had markers of both epithelial and mesenchymal cells, consistent with mesothelioma. Other common heart base tumors including neuroendocrine tumors (thyroid, parathyroid, chemodectoma) and hemangiosarcoma were ruled out based on histology and immunohistochemical staining.

Canine pericardial mesotheliomas have been previously described and reviewed. This neoplasm was somewhat unusual in that it was restricted to the heart base as a single mass, while previous reports usually describe a neoplasm diffusely spread over the inner surface of the pericardial sac, or as multiple sessile or pedunculated masses over the epicardial surface. Two histologic types of pericardial mesothelioma have been reported, fibrous and epithelial; this tumor was epithelial in histologic appearance. The literature reports that pericardial mesotheliomas may spontaneously arise secondary to pericardial effusion, although a more likely pathogenesis may be that the occult neoplasms are giving rise to pericardial effusion. This case was unusual in that little or no pericardial effusion was present at necropsy, although massive peritoneal effusion associated with a necrotic and granulomatous mesenteric mass was present. We were unable to identify any sites of mesothelioma within the abdominal viscera; however, prior surgery and marked necrosis of the mesenteric mass may have obscured small metastatic foci of mesotheliomas.

References:

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Xylitol Toxicosis in a Dog

Pritpal S. Malhi, Bhupinder Bawa and Brad DeBey

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Signalment: A 6 year old male, neutered Golden Retriever/Standard Poodle mix

History: The dog was presented to the referring veterinarian with a history of ingesting an unknown amount of xylitol sweetener and an acute onset of vomiting and diarrhea of 48 h duration. The dog did not respond to therapy, and died approximately 45 minutes after presentation. A necropsy was conducted by the referring veterinarian. There were dermal hemorrhages on the ventral trunk. Hemorrhages were also noticed multifocally on the intestinal serosal surface, cranial lung lobes, and on the cranial pole of the right kidney. There was free blood in the abdominal cavity. The stomach contained thick, slimy, dark-brown substance. The liver was very dark and intestines were dark purple. A blood sample was submitted for CBC and serum chemistry. Tissues from the liver, heart, lung, pancreas, spleen, lymph node, kidney, urinary bladder, stomach, small intestine and the large intestine were submitted for histopathology.

Laboratory findings: The dog had elevated serum alanine aminotransferase (22862 IU/L; reference range 12-118 IU/L), elevated alkaline phosphatase (364 IU/L; reference range 5-131 IU/L), elevated total bilirubin (2.3 mg/dL; reference range 0.1-0.3 mg/dL), elevated hematocrit (64%; reference range 36-60%), elevated BUN (43 mg/dL; reference range 6-31 mg/dL), slightly elevated creatinine (2.1 mg/dL; reference range 0.5-1.6 mg/dL), elevated phosphorous (9.3 mg/dL; reference range 2.5 to 6.0 mg/dL), and decreased glucose (31 mg/dL; reference range 70-138 mg/dL) concentrations.

Histopathology findings: The hepatic parenchyma had diffuse, massive hepatocellular necrosis and loss. The necrotic hepatocytes were characterized by homogenous, vacuolated, eosinophilic cytoplasm with lack of nuclei or presence of karyorrhectic debris. The hepatic lobules were diffusely filled with erythrocytes. There were occasional viable hepatocytes remaining around portal areas. The lungs had moderate, multifocal to coalescing areas of alveolar hemorrhage. The heart had mild, multifocal, subepicardial and interstitial hemorrhages. In the colon, there was diffuse submucosal hemorrhage, extending multifocally to the serosa. Scattered mucosal hemorrhage was also present. The small intestine also had hemorrhage diffusely in tunica submucosa, scattered in the tunica muscularis and in the mesenteric adipose tissue. The capsule of the spleen was wrinkled (splenic contraction).

Final Diagnosis: A diagnosis of massive hepatocellular necrosis secondary to xylitol toxicity was made based on history, clinical pathology and histopathology findings. Multifocal hemorrhages (alveolar and intestinal) were secondary to liver failure and therefore lack of clotting factors.

Comments: Xylitol, a pentose sugar alcohol is widely used as a sugar substitute by humans. In dogs, xylitol is a potent stimulator of the insulin secretion (2), and therefore causes hypoglycemia (1,2). Xylitol induced hepatotoxicity in dogs has been reported (1). Xylitol is metabolized in the liver, and a proposed mechanism is hepatocellular necrosis secondary to ATP depletion (1,2).

References:

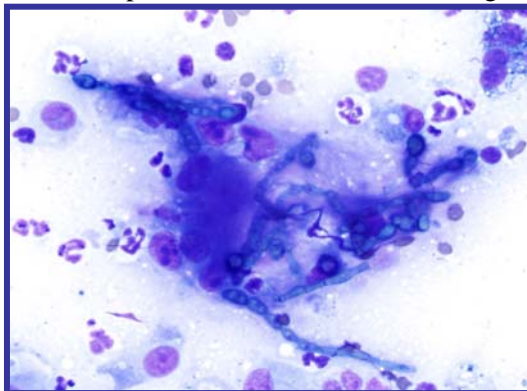
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2. Xia, Z. He, Y. Yu, J. (2009). Experimental acute toxicity of xylitol in dogs. *J Vet Pharmacol Ther* 32(5): 465-69.

Pyogranulomatous pododermatitis with dematiaceous fungal hyphae (phaeohyphomycosis) in a cat

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A 10-year-old domestic longhair cat was presented to Angell Animal Medical Center Surgery Service with a chronic (~1 year duration) nonhealing wound on the left hind paw. Previous treatment with Clavamox reportedly yielded a partial response followed by lesion recurrence. At presentation, the fifth digit of the left hind paw had three puncture wounds, associated swelling to level of the metatarsal area, and drainage of purulent material. Soft tissue swelling around the first phalanx of the affected fifth digit was confirmed radiographically, without significant bony changes. Cytology of a fine needle aspirate consisted of nondegenerate neutrophils, macrophages (including multinucleated types), fewer lymphocytes, plasma cells, and rare eosinophils. Several 3-5 micron wide, bulbous, septate, pale green-blue, branching fungal hyphae were present in the background and partially phagocytized by macrophages (see image). The fourth and fifth digits were subsequently amputated at the level of the proximal metatarsal diaphysis, and samples were submitted for histopathology and bacterial & fungal culture.



Grossly, the ~2 cm raised mass on the dorsum of the lateral (fifth) digit was mottled brown to dark brown on cut section. Histologically, epithelioid macrophages with fewer multinucleated giant cells, neutrophils, lymphocytes, and plasma cells infiltrated the dermis and subcutis in vague coalescing granulomas. Numerous intra- and extracellular brown-pigmented fungi were present, including round to bulbous forms up to 15-20 microns in diameter and elongate hyphae 3-7 micron in width with distinct septa and non-parallel walls. No bony invasion was identified; inflammation and fungal organisms extended to the proximal surgical margin. Treatment with oral itraconazole was initiated pending fungal culture/sensitivity results. *Phialophora verrucosa* was isolated. The owner stopped treatment prematurely due to difficulty medicating the cat. Five months after digit amputation, a bleeding ulcer was noted on the left tarsus. Clinicopathologic evidence of renal disease was also detected at this time. The left hindlimb was amputated; recurrent fungal infection was confirmed histologically in the tarsal soft tissue, underlying bone, and left popliteal lymph node. The patient was euthanized within a month following hindlimb amputation due to poor quality of life associated with chronic renal failure.

Phaeohyphomycosis is an opportunistic infection caused by dematiaceous, or dark-pigmented, fungi. Cutaneous, subcutaneous, visceral, cerebral, and disseminated disease can occur. Phaeohyphomycosis is uncommon in cats, with most reports involving single cases. The agent isolated in this case, *Phialophora verrucosa*, has been described in three cats, in which affected sites included the pinna¹, right muzzle², and left front paw³. In all cases, including the present case, lesions recurred at or near the original site following surgical excision. In two cats^{1,3} and in the present case, lesions persisted or progressed despite antifungal treatment. This patient, as well as two of the reported cases,^{1,2} was euthanized due to clinical signs associated with renal disease; one of the two cats was also FIV-positive.¹

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Necrotizing sialometaplasia in a 4-month-old dog

Moges Woldemeskel

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A 4-month-old, male, German shepherd dog developed a swelling in the left sublingual area. A surgical biopsy specimen was examined to rule out a neoplasia. The mass contained a section of a submandibular salivary gland. In a sharply demarcated area, encompassing about 50% of the salivary gland, the salivary acini and ducts were necrotic, occasionally mineralized and exhibited squamous metaplasia. Moderately abundant reactive fibrosis separated the affected area from normal salivary tissue. Moderate diffuse lymphoplasmacytic inflammation was present in the stroma. The microscopic finding is consistent with necrotizing sialometaplasia, a rare, benign, non-neoplastic reactive condition often associated with ischemia due to vascular derangement or thrombus consequent to inflammation and/or trauma. Necrotizing sialometaplasia is an interesting lesion in that its gross presentation and microscopic findings resemble a malignancy and can be mistaken for a neoplasia. Proper diagnosis helps to avoid inappropriate treatment.

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Polycystic Liver Disease in a Boston terrier

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A 9-year old castrated male Boston terrier was referred to the Kansas State University Veterinary Medical Teaching Hospital for acute onset lethargy, icterus, vomiting, and diarrhea. Grossly there was diffuse icterus and severe liver disease. The liver was enlarged with rounded edges, and yellow tinged, with a generalized multifocal pattern of cysts ranging from 3mm to 10 mm.

Histologic lesions in the liver included 1-10 mm diameter cysts lined by simple cuboidal epithelium, separated by small amounts of fibrous connective tissue and clear fluid. Adjacent to some cysts were random areas of coagulative and lytic hepatocellular necrosis. Hepatocytes contained large amounts of lipofuscin and small amounts of copper, and there was mild to moderate canalicular bile stasis. There was multifocal renal tubular necrosis, and many tubules contained granular red-orange casts (hemoglobin), and proteinaceous fluid. Cholestasis due to the presence of biliary cysts was considered the most likely explanation of the icterus and vomiting. Biliary cysts were considered congenital, and may be a result of dysregulation of biliary proliferation and secretion, and abnormal matrix interactions.

The presence of increased numbers of slowly progressive biliary cysts in the liver without severe fibrosis and portal hypertension most closely resembles autosomal dominant polycystic liver disease (ADPLD) of humans. This disease only manifests clinically in the 5th or 6th decade, as abdominal distension, early satiety, pain, abdominal hemorrhage, and infection of the biliary cysts. Severe cases may warrant surgery or liver transplant if obstructive cholestasis, liver failure, or compression of the caudal vena cava is present. It is caused by a mutation in the beta subunit of glucosidase II (hepatocystin) or a mutation in *SEC63* (involved in protein translocation and folding) in 25% of cases. Cysts are thought to progressively enlarge from microhamartomas (Von Meyenburg complexes) as a result of a ductal plate malformation. Other ductal plate malformations generally have severe fibrosis and portal hypertension that are not seen in ADPLD (Caroli's disease and congenital hepatic fibrosis). Other conditions which may have liver cysts include autosomal dominant polycystic kidney disease (ADPKD; mutations in polycystin; *PKD1 and 2*), which is dominated by renal cysts, and has liver cysts in 1/3 of cases; and the autosomal recessive polycystic kidney (ARPKD; mutation in fibrocystin/polyductin; *PKHD1*), which almost always has liver cysts in addition to renal cysts, and affects infants and young individuals. Mutations affecting glycosylation (congenital disorders of glycosylation) may also cause polycystic liver disease in humans, but the exact pathogenesis is not yet known.

References:

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***Clostridium difficile* colitis in a piglet**

Francisco A. Uzal

California Animal Health and Food Safety laboratory, San Bernardino Branch, UC Davis

A 1 week old Kunekune piglet with a history of respiratory difficulty that started at birth, was submitted for post-mortem examination and diagnostic work up. Grossly, there was severe mesocolonic edema, pasty-to-watery yellowish contents in the colon and the colonic mucosa was covered with a thin pseudomembrane. Histologically there was neutrophilic infiltration of the lamina propria, with multifocal erosion and ulceration of the colonic mucosal epithelium and exudation of neutrophils into the lumen (volcano lesions). The mucosa was covered by a pseudomembrane composed of neutrophils, fibrin, bacilli and cell debris. There was also colonic serosal and mesenteric edema. *C. difficile* was isolated from colonic content. Toxins A/B of this microorganism were also detected in colonic content by ELISA. FAT for Transmissible gastroenteritis virus (TGEV) performed on frozen colonic sections was positive. No other pathogens were detected in the colon of this piglet. ELISA for alpha, beta and epsilon toxins of *C. perfringens* type C was negative. Pathogenesis of *C. difficile* infection in domestic animals is likely mediated by toxins A (TcdA, an enterotoxin) and/or B (TcdB, a cytotoxin). TGEV is considered a predisposing factor for *C. perfringens* type C infection in piglets and it is possible that in this case it also acted as a predisposing factor for the *C. difficile* infection. Isolation of *C. difficile* from piglets with suppurative colitis provides a strong presumptive diagnosis of infection by this microorganism, but definitive diagnosis should be based on detection of its toxins. In this case, the suppurative lesions in the colon, coupled with positive *C. difficile* culture and toxin detection confirm a diagnosis of *C. difficile* infection.

Hepatocutaneous Syndrome in a Dog

Amanda Jane Crews, Danielle Reel, Kim Newkirk

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History & gross lesions: A 12 year old male neutered red long haired Chihuahua presented to the referring veterinarian (rDVM) with ascites. Surgical exploration revealed a small, multinodular liver and liver biopsies were taken. Following biopsy submission and review, some additional history from the rDVM revealed flaking and crusting of all four feet. This affected all footpads on all four limbs, multifocally. Three weeks later the ascites returned; due to the poor prognosis this animal was euthanized and submitted for necropsy. At necropsy, footpads from all four limbs are covered in brown crusts, which were either firmly adhered or easily peel away. Similar crusts are on the forelimbs, left cubital region, nose, prepuce and both hocks. The liver is diffusely small with disseminated brown to red nodules separated by depressed tan areas (parenchymal collapse).

Microscopic diagnosis: Haired skin: Moderate to marked regionally extensive epidermal hyperplasia with intracellular edema and parakeratotic compact hyperkeratosis

Liver: Severe chronic regionally extensive to coalescing hepatic lipidosis and loss with nodular hyperplasia

Comments: Gross and histologic changes in the liver and skin are consistent with hepatocutaneous syndrome. Clinically, hepatocutaneous syndrome is recognized by skin lesions (superficial necrolytic dermatitis) which are characterized by erythema, crusts, erosions and ulcers with a bilaterally symmetrical distribution over the footpads, face, distal extremities, ventrum, external genitalia, and pressure points. Skin lesions are consistently reported on the foot pads. Grossly, the liver has the appearance of macronodular regeneration with a foremost firm, collapsed parenchyma. Histologically, pathognomonic skin lesions are called “red, white and blue” for the parakeratosis, intraepidermal edema and basilar hyperplasia, respectively. Histologically, the liver contains foci of regenerative nodular hyperplasia separated by areas of parenchymal collapse containing heavily vacuolated hepatocytes. Hepatic changes are considered idiopathic, but have been suggested to be due to an underlying metabolic, hormonal, or toxic etiology. The pathogenesis of the associated skin lesions is unknown, but hepatic dysfunction with derangement of glucose and amino acid metabolism has been suggested. Liver disease is the primary cause of the skin lesions in most cases. Skin lesions have also been rarely reportedly to be due to glucagon-secreting pancreatic tumors, diabetes mellitus and pancreatic carcinoma (cat). In humans, skin lesions are primarily caused by glucagon secreting pancreatic islet cell tumors causing hyperglucagonemia.

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A Sudden Mortality Event in Feedlot Steers in Southern Michigan

Dodd Sledge, Daniel Grooms, Wilson Rumbelha, Thomas Herdt, Thomas Mullaney,
Rebecca Smedley

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(Sledge, Rumbelha, Mullaney, Smedley); Department of Large Animal Clinical Sciences,
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In July of 2008, a feedlot in southern Michigan experienced a sudden mortality event. Of 85 1200lbs Holstein steers that had been on feed for 200 days, 50 died in a 2-day period. On the first day of the event, 34 animals were found dead. Living animals had varying degrees of clinical signs. Severely affected animals were recumbent, had muscle tremors, and appeared blind. Less affected animals were anorexic, ataxic, and had diarrhea. No animals had obvious bloating. Despite supportive treatment, another 16 animals died by the following day and several animals remained recumbent or ataxic. Diarrhea and ataxia in those animals that survived the first two days resolved over the subsequent 2-7 days. A steer that was found recumbent on the initial day of the mortality event and that lived for 5 days, but remained recumbent was euthanized and submitted to the Diagnostic Center for Population and Animal Health.

At necropsy, the mucosa of the rumen was dark black, did not peel easily from the underlying submucosa, and was multifocally ulcerated. Rumen papillae of the ventral sac were often thickened, blunted, and/or fused. There were also three diamond-shaped, focally extensive dark black to red areas of necrosis of the wall of the ventral rumen sac. The rumen contents had a pH of 5.40 and consisted of large amounts of whole kernel corn and lesser fibrous ingesta.

Histologically, there was **moderate to marked epidermal hyperplasia with laminated ortho-to parakeratotic hyperkeratosis throughout the fore stomachs** with the rumen and reticulum being most severely affected. There were also **focally extensive infarctions of the rumen wall associated with fungal invasion and thrombosis of submucosal arteries**. Based on the gross and histologic findings a diagnosis of subacute rumen acidosis with fungal rumenitis was made.

While no peracutely-affected animals were examined, **the necropsy findings from the examined animal and the history suggest that the cause of this mortality event was grain overload**. The syndrome of grain overload (lactic acidosis) is typically associated with a sudden change in feed to large amounts of easily fermentable carbohydrates. Two days before the first animals were found dead at this feedlot, the rancher ran out of corn silage and began feeding whole kernel corn ad libitum with supplemental protein pellets.

In the pathogenesis of grain overload, an initial decrease in rumen pH is associated with a shift in rumen microbiota. The growth of *Streptococcus bovis* and subsequently *Lactobacillus* spp are promoted at pH of 5.5 and 5.2, respectively. Both of these organisms produce lactic acid, which further lowers rumen pH and increases intraluminal osmotic pressure. Shifting of fluid into the rumen lumen can result in hypovolemic shock and death. Animals that live beyond the initial insult can develop rumenitis as was observed in the necropsied steer.

While grain overload is highly suspected, other causes of sudden mortality cannot be definitively ruled out in this case given that only one chronically affected animal was examined. The rancher was particularly concerned about a potential toxicant; however, gas chromatography-mass spectrometry (GCMS) and trace and heavy metal screens identified no toxins and nutritional analysis found suitable levels of crude protein and urea in the feed.

Ranaviral infection in a wood frog (*Lithobates sylvaticus*) tadpole

Julia Lankton, Debra Miller, and Matthew Gray

College of Veterinary Medicine, University of Tennessee, Knoxville, Tennessee (Lankton, Miller)

Center for Wildlife Health, University of Tennessee, Knoxville, Tennessee (Miller, Gray)

Signalment and history: 30 day old wood frog (*Lithobates sylvaticus*) tadpole challenged with an endemic *Ranavirus* isolate (*Frog virus 3*)

Clinical signs: Tadpoles exhibited lethargy and buoyancy difficulty and began to die one week after exposure, with 100% mortality in 2.5 weeks.

Gross lesions: Cutaneous ecchymoses

Histopathology: There is moderate to marked multifocal acute hepatocellular and renal tubular degeneration and necrosis and multifocal to focally extensive splenic necrosis. There is necrosis of the hematopoietic tissue within the mesonephros. Degenerate and viable hepatocytes and renal tubular epithelial cells occasionally contain one to two 4µm diameter eosinophilic cytoplasmic inclusion bodies.

Discussion: In North America, ranaviruses have caused more amphibian die-offs than any other pathogen, yet little is known about the pathogenesis of ranaviral disease. This tadpole was part of a series of studies evaluating virulence and microscopic lesions in different species of amphibians exposed to different ranavirus isolates. Wood frog tadpoles are often involved in naturally occurring ranavirus-associated mortality events. Experimental challenges have shown them to be highly susceptible to multiple isolates of ranaviruses, such that they are theorized to serve an epidemiological role of superspreader of ranaviruses during die-offs. Death often occurs within days with few to no clinical signs of disease, although hemorrhage, lethargy and buoyancy difficulty can be seen in terminal stages with more chronic morbidity. Histological examination is often unrewarding in animals that die shortly after exposure; however, organ necrosis (e.g., within the liver, spleen and mesonephros) and occasional cytoplasmic inclusions have been seen. Non-specific hepatocellular and renal tubular degeneration and rare inclusion bodies have been seen with less virulent isolates and longer survival times. In other species (e.g., southern leopard frogs (*Lithobates sphenoccephalus*)), morbidity and mortality occur quickly with one ranavirus isolate but more slowly with another. In suspected reservoir species (e.g., American bullfrogs (*Rana catesbeiana*)), there appears to be resistance to the virus and rare mortality. Understanding variations in susceptibility and pathology will facilitate development of conservation strategies that reduce the likelihood of an outbreak in wild or captive amphibian populations. Future investigation will target virus location within the body at various time intervals post-viral exposure.

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Actinomycete-Associated Placentitis in a Mare

Duane Murphy

Heeke Animal Disease Diagnostic Laboratory, Purdue University

Signalment and History: This fetus and placenta were reportedly aborted 5 weeks premature. The mare had “bagged up” or developed an udder 1-2 weeks before the abortion occurred. Otherwise, the mare appeared to be healthy and apparently had a good appetite on the day following abortion.

Gross findings: The submitted fetus was still enclosed within the intact placenta. It weighed 23 kg, and crown-to-rump length was 89 cm. No gross lesions were found in the fetus. The placenta had 25-cm mucosal lesion located at the distal body of the uterus, near the point where the two uterine horns bifurcate. The mucosa in this lesion was thin and pale except at the margins, where it was thick, gray, friable, and surrounded by a reddened line of hyperemia.

Microscopic description: The placenta had extensive areas of epithelial necrosis which were heavily infiltrated with neutrophils, and covered with a thick layer of necrotic debris. Embedded within the debris were scattered star burst-shaped granules suggestive of sulfur granules. Warthin-Starry and acid-fast stains revealed the presence of small branching filamentous bacilli within these granules. These bacilli were not acid fast, and did not stain with Brown & Brenn gram stain. No remarkable histologic lesions were present in the fetal tissues.

Morphologic diagnosis: Placenta; Necrotizing and suppurative placentitis with intralesional filamentous bacilli

Comments: No bacteria were isolated from the fetal tissues. A mix of bacteria were isolated from the placental mucosa, including an “actinomycete-like organism” (not further identified). The lesions in this case are similar to those described by Hong, et al (1993) for nocardioform actinomycete-associated placentitis. A number of actinomycete-like organisms have been associated with this lesion including *Crossiella equi*, *Amycolatopsis* spp., *Nocardia* spp., and *Rhodococcus rubropertinctus*. I had never seen this lesion until this spring, when I saw three different cases within a 2-week period. Apparently, a large number of cases of nocardioform placentitis were also seen in Kentucky this spring. The reason for this increased incidence is not known.

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Necrotizing enterocolitis in a two day old foal

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A foal developed acute diarrhea twenty hours after birth, followed by dehydration and weakness. Euthanasia was elected due to the severity of the clinical signs. Gross examination revealed liquid, dark red content with fibrin strands and tan fragments of necrotic tissue in the jejunum, ileum, cecum and colon. Histology of small intestine showed multifocal, superficial to deep mucosal necrosis covered by a diphtheritic pseudomembrane composed of fibrin, cell debris, neutrophils and large numbers of rods. Within the lamina propria and submucosa there was necrotizing vasculitis in numerous blood vessels, with intraluminal colonies of coccobacilli. Coccobacilli thromboembolism was also observed in lung and liver. *Actinobacillus equuli subsp. haemolyticus* and *Streptococcus equi ssp. zooepidemicus* in large numbers were isolated from lung, liver and small intestine. Large numbers of *Clostridium difficile* and *Clostridium perfringens* (not typed) were also cultured from the small intestine. The *C. perfringens* toxins ELISA test performed on small intestinal content was positive for alpha toxin, but negative for beta and epsilon toxins, while the ELISA for *C. difficile* A and B toxins was negative.

Actinobacillus equuli is an important cause of neonatal infections in foals that may be acquired in utero, during parturition, or postnatally, producing septicemia, nephritis, polyarthritis, pneumonia, hemorrhagic enteritis, meningitis and omphalophlebitis. The route of infection in most cases is thought to be the umbilicus with distribution by blood. *C. difficile* is a cause of necrotizing and/or hemorrhagic enteritis in foals, and necrohemorrhagic typhlocolitis in adult horses. In this case, the necrotizing enteritis described was considered to be produced by co-infection with *A. equuli* and *C. difficile*.

Angiocentric encephalopathy in a heifer

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Clinical history

A previously healthy 2 years old in-calf heifer, one of a group of nine at grass developed ataxia, low head carriage, sweating with peeling of skin around its muzzle, progressing to recumbency and death within 2 days. Further history was obtained following the histological examinations, indicating that this heifer developed clinical signs 4 days after the group was treated with a combined closantel/ivermectin anthelmintic and died on day 5 after treatment.

Post mortem and laboratory results

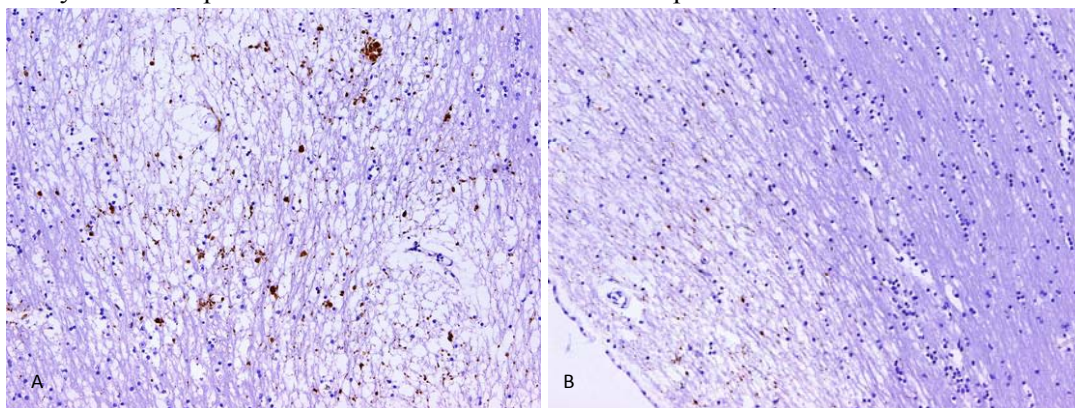
Numerous haemorrhages were present in the subcutis, epicardium and thymus. There was no significant bacterial isolate from the liver, OvHV-2 DNA was not detected and lead concentrations were within background limits.

Histopathology and immunohistochemistry

Marked rarefaction of the neuroparenchyma, particularly involving perivascular and subependymal white matter, was present in HE sections, particularly in cerebrum and brainstem, accompanied by sparse minor swelling of neurites. Beta amyloid precursor protein (β APP) immunohistochemistry labelled numerous small neural processes in areas of rarefied perivascular (fig A) and sub-ependymal (fig B) neuroparenchyma.

Comment

Although a convincing gliovascular response was not detected in areas of rarefaction in the HE sections, the results of β APP IHC indicated the presence of extensive axonal injury in association with areas of rarefaction. Immunohistochemical labelling for β APP is a sensitive means of detecting axonal injury in a range of traumatic, toxic and metabolic/hypoxic CNS disorders^{1,2,3}. The character of the white matter lesions is very similar to those of closantel toxicity in small ruminants⁴ albeit with a slightly different distribution. The information supplied by the farmer suggested that the animal was unlikely to have been over-dosed, however halogenated salicylanide compounds such as closantel have low therapeutic indices.



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***Chlamydophila abortus* in a Small Flock of Boer Goats**

Peter Moisan, Kimberly Hagans

North Carolina Department of Agriculture

Presented to the Monroe Laboratory of the NCDA was a pair of late term aborted Boer goat fetuses with placenta from one. The history indicated that the herd of 21 goats was assembled in December 2010 and began aborting (8 fetuses from 3 does) in February 2011. Abortions were between 120 and 140 days gestational age. Gross findings included moderate autolytic change and generalized edema in the tissues of each fetus. Pathological features were not identified grossly in the placenta.

Histological findings were limited to the placenta, liver, and spleen. Necrotizing placentitis with necrotizing stromal vasculitis was the main change in the placenta. Clumps of necrotic debris and neutrophils were admixed with intact and detached trophoblasts, which often had undergone karyorrhexis. Occasional trophoblasts contained finely granular intracytoplasmic elementary bodies, consistent with chlamydial organisms. Necrosis of small arteries in the placental stroma was striking. Degenerate neutrophils and nuclear debris were located within the muscular layers of several arteries. The placental stroma was moderately edematous as well. Multifocal necrosuppurative inflammation of splenic and hepatic tissue was also apparent. Autolytic changes in these tissues precluded further characterization of the extent of the lesions.

ELISA testing of placenta confirmed the presence of chlamydial agents.

This case was considered unusual inasmuch as the disease was diagnosed in goats, though it is classically regarded as a sheep disease primarily. *Chlamydophila abortus* is one of the main causes of abortion in small ruminants in North America (the others being *Coxiella burnetii*, *Toxoplasma gondii*, and *Campylobacter* species). These are all enzootic diseases and zoonotic agents, thereby increasing the significance when diagnosed.

The most significant gross feature of the chlamydial abortion is the red brown exudate over the cotyledons and intercotyledonary space. Pinpoint foci of necrosis in liver and spleen are often described. These features were not apparent in the tissues from this case. The microscopic appearance of the chlamydial lesion strongly suggests *C. abortus*. The necrotic trophoblasts contain a dusting (moderate numbers) of the elementary bodies within the cytoplasm. Lesions in the liver and spleen are necrotizing to necrosuppurative and often accompanied by autolysis, as with our case. ELISA is the most rapid and reliable means of testing at our laboratory.

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Vogt-Koyanagi-Harada-like Syndrome in a Dog

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Four skin biopsies taken from the right upper lip margin, right side of the nose, right side of the muzzle, and right axilla of a 2 year old, male, Labrador Retriever-cross dog were examined. The dog had a history of severe bilateral glaucoma with enucleation three months prior to the submission of the skin biopsies. A month after the enucleation, the skin lesions started to develop. At the time the biopsies were taken, the dog had severe crusting, scaling, and depigmentation adjacent to the nose, on the muzzle, in the area of both eyes, in the axilla, and on the ventrum.

Microscopically, all four biopsies of haired skin are characterized by a lichenoid infiltrate of numerous large macrophages mixed with variable numbers of neutrophils, lymphocytes and plasma cells in the superficial dermis. Small numbers of macrophages contain melanin granules. The large macrophages rarely extend into the basal layer of the epidermis obscuring the dermal-epidermal junction with rare apoptotic cells in the basal layer of the epidermis. The epidermis is thick and hyperplastic with multifocal epidermal ulceration in three of the biopsies. In three of the biopsies, the stratum corneum is thickened by multiple coalescing subcorneal pustules and crusts. The subcorneal pustules and crusts contain serum, numerous intact and degenerate neutrophils and occasionally cocci. Based on the microscopic lesions, the diagnosis of Vogt-Koyanagi-Harada-like (VKH-like) syndrome with secondary bacterial overgrowth, crusting, and pustulation was made.

Canine VKH-like syndrome (canine uveodermatologic syndrome) is a rare ocular and skin disease that occurs most frequently in Akitas, Alaskan Malamutes, Chow Chows, Samoyeds, Siberians Huskies, and their crosses, but it has been reported in multiple breeds of dogs. VKH-like syndrome occurs most commonly in dogs 6 months to 6 years of age. A sex predilection has not been reported. The disease in dogs is similar to VKH in humans and is believed to be an immune-mediated disease directed against melanocytes.

The skin disease in dogs most commonly occurs as bilateral depigmenting facial dermatitis involving the muzzle, eyelids, nasal planum, and lips. The pawpads, perianal skin, pinnae, scrotum, vulva, and occasionally the hard palate may also be involved. The microscopic lesions in the skin consist of a lichenoid infiltrate of large macrophages in the superficial dermis. The histiocytic infiltrate extends up to the dermal-epidermal junction, but only occasionally extends into the basal layer of the epidermis. The macrophages often contain fine granules of melanin. There are rare apoptotic cells within the epidermal basal layer. The epidermis is hyperplastic with secondary crusts and pustules with variable ulceration. There can also be nodular aggregates of macrophages around hair follicles.

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Thyroid Carcinosarcoma in a Horse

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A 28-year old Arabian gelding was euthanized after a three-day history of respiratory distress and hemothorax. At necropsy, several liters of serosanguineous fluid were present within the pleural and peritoneal cavities. A 15-cm x 20-cm x 20-cm irregular, dark red, and friable mass was present cranial to the heart, adjacent to the right ventricle and adhered to the pericardial sac and the pleural surface of the cranial right lung lobe. A portion of the mass extended approximately 13-cm cranially along the right carotid artery. On cut section, the mass was dark red, cavitated, and necrotic. An additional large mass was present at the level of the thoracic inlet. Multiple nodules ranging in size from 2-5-cm in diameter were noted adhered to and occasionally surrounding the carotid arteries, bilaterally. On cut section, these masses were mottled white to yellow and dark red, with occasional mineralization and cystic spaces containing yellow viscous fluid. At the cranial aspect of the right lateral neck, slightly caudal to the larynx, a similar appearing, 10-cm x 11-cm x 11-cm mass was also present.

Histologically, the neck mass was identified as thyroid and presented as a poorly demarcated, multilobulated neoplasm composed of pleomorphic epithelial cells that replaced and compressed thyroid gland parenchyma. The neoplastic cells were cuboidal to columnar to polygonal, contained a moderate amount of pale eosinophilic cytoplasm, and occasionally formed follicular structures. Nuclei were round to oval with finely stippled chromatin, exhibited mild anisokaryosis, and frequently contained one prominent nucleolus. Mitoses were 0-1 per ten high power fields. In addition, large portions of the mass were occupied by proliferating neoplastic spindle cells arranged in streaming bundles, with scant eosinophilic cytoplasm and oval nuclei. Mitoses were rare in these cells. All other grossly described masses including the mineralized masses, as well as sections of lymph node, were characterized by similar neoplastic cell populations. The areas of grossly observed mineralization corresponded to large areas of well differentiated cartilage and mineralized metaplastic bone.

Immunohistochemistry strongly labeled neoplastic spindle cells with vimentin. Focally, the neoplastic epithelial cells were positive for MNF116 (pancytokeratin), thyroid transcription factor-1 and thyroglobulin. The neoplastic cells did not react with antibodies to calcitonin, synaptophysin, or muscle specific actin.

Based on these findings, the neoplasm was diagnosed as a metastasizing thyroid carcinosarcoma. To our knowledge, there are no published reports of thyroid carcinosarcomas in horses. In humans, thyroid carcinosarcomas (now commonly classified as pleomorphic carcinomas) are highly malignant tumors in which extrathyroid extension precludes initial diagnosis. These neoplasms are locally aggressive, often resulting in extension into the soft tissues of the neck, surrounding and invading large blood vessels and nerves, with spread into the larynx, trachea, and esophagus.

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Juvenile myelomonocytic leukemia in a dog

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A 13 month-old spayed female Golden Retriever-Poodle cross was referred to the University of Guelph with a 5 day history of lethargy, anorexia, pyrexia and non-regenerative anemia, thrombocytopenia and leukocytosis. The leukocytosis consisted primarily of neutrophils. The dog was given prednisone for 48 hours and referred. At the University of Guelph, a complete blood count confirmed anemia (hematocrit 0.31, reference interval 0.39-0.56), and revealed severe thrombocytopenia ($23 \times 10^9/L$; RI 117-418 $\times 10^9/L$) and leukocytosis ($64.7 \times 10^9/L$; RI 4.9-15.4 $\times 10^9/L$). The leukocytosis was comprised of a marked neutrophilia ($45.3 \times 10^9/L$; RI 2.9-10.6 $\times 10^9/L$) with a left shift ($9.71 \times 10^9/L$; RI $<0.3 \times 10^9/L$), a lymphocytosis ($7.12 \times 10^9/L$; RR: 0.8-5.1 $\times 10^9/L$) and monocytosis ($2.59 \times 10^9/L$; RR: 0.0-1.1 $\times 10^9/L$). Serum iron concentration was increased; total iron binding capacity, vitamin B12 and folate concentration were unremarkable.

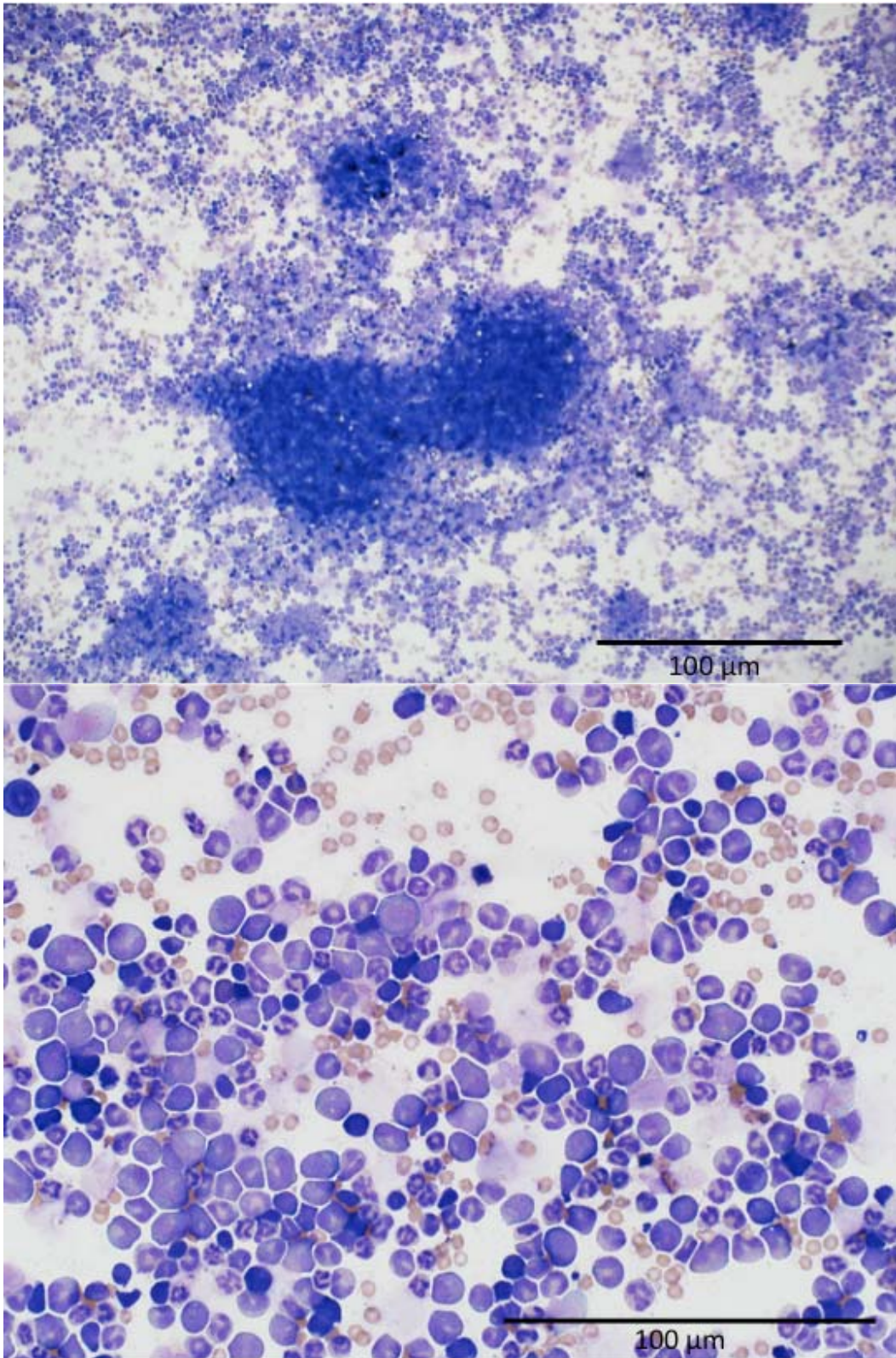
A sternal bone marrow aspirate was extremely cellular, granules lacked fat tissue, and the granulocytic to erythrocytic cell ratio was $> 30:1$. There was marked granulocytic hyperplasia comprised of mature and immature granulocytes with a most pronounced increase in myelocytes and metamyelocytes. Megakaryocytes were nearly absent, and rubricytes were severely decreased. Among rubricytes early maturational stages predominated. Approximately 10-15% of all cells were blast cells.

The interpretation from this bone marrow aspirate was leukemia, most consistent with the human condition juvenile onset myelomonocytic leukemia. Differential diagnoses included leukemoid response to an inflammatory stimulus, chronic granulocytic leukemia, or myelodysplastic syndrome.

The dog was treated with chemotherapy consisting of doxorubicin, thioguanine and prednisone for 13 days, however, anorexia and lethargy worsened, the hematocrit decreased to 0.11, and the dog was euthanized 10 days after diagnosis. The only gross lesion identified at post mortem examination was diffusely reddened bone marrow. Histologically, there were increased neutrophils in the splenic red pulp and lymph node, and a hypocellular bone marrow.

Juvenile myelomonocytic leukemia (JMML) is a rare and aggressive hematologic malignancy of children. A range of genetic lesions affecting the Ras/mitogen-activated protein (MAP) kinase pathway and imparting high sensitivity to granulocyte-macrophage colony-stimulating factor (GM-CSF) has been identified in affected patients. Dyserythropoiesis, increased fetal hemoglobin, decreased serum iron and vitamin B12 occur in a subset of patients, and are associated with additional lesions in myeloid precursor cells.

This case was unusual as the age of the dog was rather young for non-lymphoid leukemia, the degree of leukocytosis comprised of morphologically relative normal cells was marked, and there was concurrent cytopenia of both other cell lines. Therefore, this was neither a typical presentation of acute leukemia nor of chronic myeloproliferative neoplasia. Molecular features of most leukemias in animals have not been determined, but the clinical features of this leukemia were most similar to JMML of humans.



Figures 1-4: Bone marrow cytology, modified Wright's stain. Fig 1 (400X) demonstrates a highly cellular bone marrow granule (approximated 100% cellularity) devoid of fat, with abundant coarse iron.

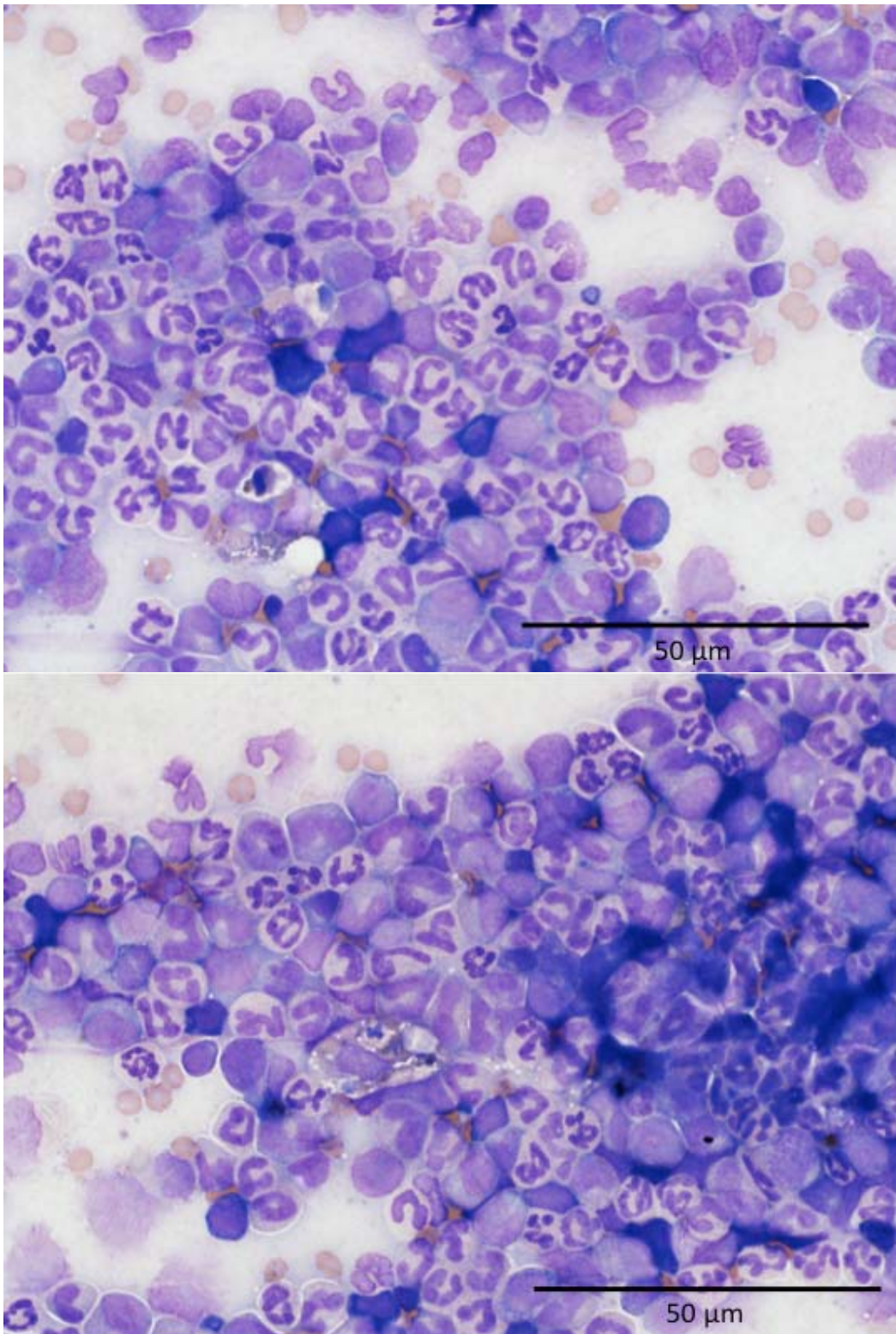


Fig 2 (600x), 3 and 4 (1000X) show an increased granulocytic to erythrocytic cell ratio (> 30:1), with marked granulocytic hyperplasia comprised of mature and immature granulocytes. Megakaryocytes are nearly absent, and rubricytes are severely decreased. Among rubricytes early maturational stages predominated. Approximately 10-15% of all cells are blast cells.

Malignant catarrhal fever in a white-tailed deer associated with WTD-MCFV

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Signalment: 6-month-old male white tailed deer (*Odocoileus virginianus*)

Clinical History: The body of the dead deer was presented to the ADDL for necropsy on 11/30/10. The animal died spontaneously on 11/29/10 after a two day course of illness that included laying down more than usual on 11/27/10, and the next day exhibited weakness, ataxia, walking in a circle, disorientation, and reportedly held its neck in a “crooked” manner. Earlier on the day the deer died, it showed lethargy and reluctance to rise. It had been on the property for approximately 2 months prior to onset of clinical signs.

Gross lesions: There was a 2.5 x 1.5 cm full thickness triangular shaped ulcer in the cranial aspect of the rumen wall, with a 0.2-1.0 cm rim of hemorrhage surrounding this defect. Ingesta was noted in the omentum, which adhered focally to the ileum and cecum (localized septic peritonitis). There was a second 1x1 cm erosion in the rumen mucosa. The abomasal mucosa was markedly and diffusely congested, and there were multiple ecchymotic hemorrhages on the tips of mucosal folds. Hepatic and retropharyngeal lymph nodes were estimated to be twice normal size.

Ancillary test results: Brain tissue was determined to be negative for rabies (Ohio Department of Health). PCR assay of spleen and lymph node was negative for nucleic acid of EHD and BVD viruses (Ohio ADDL). Multiplex PCR of spleen and lymph node was positive for nucleic acid of WTD-MCFV, negative for nucleic acid of OvHV-2, CpHV-2, AIHV-1, AIHV-2, Ibex-MCFV (USDA-ARS, Washington State University).

Histopathology: Portal triads throughout the liver are expanded by large numbers of lymphocytes, which are also present in moderate numbers in subcapsular regions. There is cuffing of multiple medium sized arteries and veins by moderate numbers of lymphocytes throughout the lung section. Multiple predominantly lymphocytic foci are present in the cortical interstitium of the kidney, and there is a similar but minimal inflammatory infiltrate present in the medulla.

Morphologic Diagnoses:

Liver: Marked, diffuse, subacute lymphocytic portal hepatitis

Lung: Moderate, multifocal, subacute, lymphocytic perivascular interstitial pneumonia

Kidney: Mild to moderate, multifocal, subacute lymphohistiocytic interstitial nephritis

Discussion: Microscopic lesions were strongly suggestive of a systemic viral infection. Multiplex PCR assay¹ confirmed the presence of nucleic acid of WTD-MCFV, a gammaherpesvirus reported to cause malignant catarrhal fever in white-tailed deer, but for which the reservoir host is unknown^{2,3}. White-tailed deer are also susceptible to MCFV associated with gammaherpesviruses of sheep, goats and wildebeest^{4,5,6,7}.

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