37th Annual Meeting of the Midwest Association of Veterinary Pathologists

August 2nd - 3rd, 2018
Grange Insurance Audubon Center, Columbus, Ohio

Guest speakers:
Rachel Cianciolo, VMD, PhD, DACVP (Anatomic)
Jessica Hokamp, DVM, PhD, DACVP (Clinical)

The Ohio State University and the International Veterinary Renal Pathology Service

THE OHIO STATE UNIVERSITY
### Presentation Schedule

#### Thursday, 8/02/18

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker number</th>
<th>Presenter</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00-9:00 AM</td>
<td>Registration</td>
<td>Registration and</td>
<td>Continental Breakfast</td>
</tr>
<tr>
<td></td>
<td>number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9:00-9:10 AM</td>
<td>Welcome</td>
<td>Welcome and opening</td>
<td>remarks</td>
</tr>
<tr>
<td></td>
<td>number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9:15-10:30 AM</td>
<td>Rachel</td>
<td>Rachel Cianciolo</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td></td>
<td>Cianciolo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:30-10:45 AM</td>
<td>BREAK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10:45-12:00 AM</td>
<td>Jessica</td>
<td>Jessica Hokamp</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td></td>
<td>Hokamp</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12:00-1:00 PM</td>
<td>LUNCH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1:00</td>
<td>1</td>
<td>Mark Hoenerhoff</td>
<td>University of Michigan</td>
</tr>
<tr>
<td>1:11</td>
<td>2</td>
<td>Allison Watson</td>
<td>University of Tennessee</td>
</tr>
<tr>
<td>1:22</td>
<td>3</td>
<td>George Sandusky</td>
<td>Indiana University School of Medicine</td>
</tr>
<tr>
<td>1:33</td>
<td>4</td>
<td>Ethan Biswell</td>
<td>Purdue University</td>
</tr>
<tr>
<td>1:44</td>
<td>5</td>
<td>Erica Corda</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>1:55</td>
<td>6</td>
<td>Keith Nelson</td>
<td>MPI Research</td>
</tr>
<tr>
<td>2:06</td>
<td>7</td>
<td>Andrea Pohly</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>2:17</td>
<td>8</td>
<td>Denae LoBato</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>2:28</td>
<td>9</td>
<td>Rachel Neto</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>2:39</td>
<td>10</td>
<td>Natalie Kirk</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>2:50-3:05</td>
<td>BREAK</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3:05</td>
<td>11</td>
<td>Larissa Kipa</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>3:16</td>
<td>12</td>
<td>Lauren Himmel</td>
<td>Vanderbilt University</td>
</tr>
<tr>
<td>3:27</td>
<td>13</td>
<td>Craig Sarver</td>
<td>Ohio Department of Agriculture</td>
</tr>
<tr>
<td>3:38</td>
<td>14</td>
<td>Rebecca Kohnken</td>
<td>AbbVie</td>
</tr>
<tr>
<td>3:49</td>
<td>15</td>
<td>Michelle Magagna</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>4:00</td>
<td>16</td>
<td>James P. Cronin</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>4:11</td>
<td>17</td>
<td>Laura Lee</td>
<td>University of Wisconsin-Madison</td>
</tr>
<tr>
<td>4:22</td>
<td>18</td>
<td>Dane Rahoi</td>
<td>University of Tennessee</td>
</tr>
<tr>
<td>4:33</td>
<td>19</td>
<td>Agnes Wong</td>
<td>Purdue University</td>
</tr>
<tr>
<td>4:44</td>
<td>20</td>
<td>Gillian C. Shaw</td>
<td>University of Wisconsin-Madison</td>
</tr>
<tr>
<td>4:55</td>
<td>21</td>
<td>Jessica Hanlon</td>
<td>Purdue University</td>
</tr>
<tr>
<td>5:06</td>
<td>SOCIAL HOUR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6:00-7:30</td>
<td>DINNER</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Presentation Schedule

**Friday, 8/03/18**

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker number</th>
<th>Presenter</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00-8:00</td>
<td></td>
<td><strong>CONTINENTAL BREAKFAST</strong></td>
<td></td>
</tr>
<tr>
<td>8:00</td>
<td>22</td>
<td>Gordon Ehrensing</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>8:11</td>
<td>23</td>
<td>Alexandra Harvey</td>
<td>University of Wisconsin</td>
</tr>
<tr>
<td>8:22</td>
<td>24</td>
<td>Eileen Henderson</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>8:33</td>
<td>25</td>
<td>Annie Zimmerman</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>8:44</td>
<td>26</td>
<td>Leah Stein</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>8:55</td>
<td>27</td>
<td>Dodd Sledge</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>9:06</td>
<td>28</td>
<td>Sarah Coe</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>9:17</td>
<td>29</td>
<td>Wallaya Manatchaiworakul</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>9:28</td>
<td>30</td>
<td>Margaret Martinez</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>9:39</td>
<td>31</td>
<td>Erica Noland</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>9:50</td>
<td>32</td>
<td>Grant Burcham</td>
<td>Purdue University</td>
</tr>
<tr>
<td>10:01-10:20</td>
<td></td>
<td><strong>BREAK</strong></td>
<td></td>
</tr>
<tr>
<td>10:20-10:40</td>
<td></td>
<td><strong>BUSINESS MEETING</strong></td>
<td></td>
</tr>
<tr>
<td>10:40</td>
<td>33</td>
<td>Josh Lorbach</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>10:51</td>
<td>34</td>
<td>Mallory DiVincenzo</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>11:02</td>
<td>35</td>
<td>Tuddow Thaiwong</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>11:13</td>
<td>36</td>
<td>Raisa Glabman</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>11:24</td>
<td>37</td>
<td>Frank J. Simutis</td>
<td>Bristol-Myers Squibb Company</td>
</tr>
<tr>
<td>11:35</td>
<td>38</td>
<td>Pankaj Kumar</td>
<td>Charles River Laboratories</td>
</tr>
<tr>
<td>11:46</td>
<td>39</td>
<td>Marie Pinkerton</td>
<td>University of Wisconsin</td>
</tr>
<tr>
<td>11:57</td>
<td>40</td>
<td>Shelley Newman</td>
<td>Long Island University</td>
</tr>
<tr>
<td>12:08</td>
<td>41</td>
<td>Ryan Jennings</td>
<td>The Ohio State University</td>
</tr>
</tbody>
</table>

**CONCLUDING REMARKS**

**LUNCH (MEETING ENDS)**
<table>
<thead>
<tr>
<th>Case #</th>
<th>Presenter</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>MH-2018</td>
<td>Mark J. Hoenerhoff</td>
<td>University of Michigan</td>
</tr>
<tr>
<td>SP17-3734</td>
<td>Allison Watson</td>
<td>University of Tennessee</td>
</tr>
<tr>
<td>ML16-089</td>
<td>George Sandusky</td>
<td>Indiana University School of Medicine</td>
</tr>
<tr>
<td>A17-12524</td>
<td>Ethan Biswell</td>
<td>Purdue University</td>
</tr>
<tr>
<td>SP-18-360</td>
<td>Erica Corda</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>1235813-009</td>
<td>Keith Nelson</td>
<td>MPI Research</td>
</tr>
<tr>
<td>18-H41878-17</td>
<td>Andrea Pohly</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>18-35563-2A</td>
<td>Denae LoBato</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>1736520-4</td>
<td>Rachel Neto</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>17-H51053-2A</td>
<td>Natalie Kirk</td>
<td>University of Illinois</td>
</tr>
<tr>
<td>SP-17-14737</td>
<td>Larissa Kipa</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>518100</td>
<td>Lauren Himmel</td>
<td>Vanderbilt University Medical Center</td>
</tr>
<tr>
<td>ODA-ADDL CS</td>
<td>Craig Sarver</td>
<td>Ohio Department of Agriculture ADDL</td>
</tr>
<tr>
<td>Abbvie 18-067</td>
<td>Rebecca Kohnken</td>
<td>AbbVie</td>
</tr>
<tr>
<td>SP-18-3760</td>
<td>Michelle Magagna</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>18-1062</td>
<td>James P. Cronin</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>17B840</td>
<td>Laura Lee</td>
<td>University of Wisconsin-Madison</td>
</tr>
<tr>
<td>10-434</td>
<td>Dane Rahoi</td>
<td>University of Tennessee</td>
</tr>
<tr>
<td>A18-3553</td>
<td>Agnes Wong</td>
<td>Purdue University</td>
</tr>
<tr>
<td>18RD0840</td>
<td>Gillian C. Shaw</td>
<td>University of Wisconsin-Madison</td>
</tr>
<tr>
<td>ID</td>
<td>Name</td>
<td>Institution</td>
</tr>
<tr>
<td>--------</td>
<td>-----------------------</td>
<td>--------------------------------</td>
</tr>
<tr>
<td>A18-8135</td>
<td>Jessica Hanlon</td>
<td>Purdue University</td>
</tr>
<tr>
<td>A18-8136</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17RD3607</td>
<td>Alexandra Harvey</td>
<td>University of Wisconsin-Madison</td>
</tr>
<tr>
<td>NC-18-471</td>
<td>Gordon Ehrensing</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>RE-17-95</td>
<td>Eileen Henderson</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>SP-18-0005249</td>
<td>Annie Zimmerman</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>NO-18-406</td>
<td>Leah Stein</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>SP-18-0005543</td>
<td>Dodd Sledge</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>SP-17-0011830</td>
<td>Sarah Coe</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>SP-18-0006936</td>
<td>Wallaya Manatchaiworakul</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>14-1959</td>
<td>Margaret Martinez</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>SP-17-0006465</td>
<td>Erica Noland</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>Purdue-1</td>
<td>Grant N. Burcham</td>
<td>Purdue University</td>
</tr>
<tr>
<td>18-189</td>
<td>Josh Lorbach</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>17-338-1</td>
<td>Mallory DiVincenzo</td>
<td>The Ohio State University</td>
</tr>
<tr>
<td>MSU-VDL-17-6426</td>
<td>Tuddow Thaiwong</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>SP17-0006285</td>
<td>Raisa Glabman</td>
<td>Michigan State University</td>
</tr>
<tr>
<td>XN16005</td>
<td>Frank J. Simutis</td>
<td>Bristol-Myers Squibb Company</td>
</tr>
<tr>
<td>50</td>
<td>Pankaj Kumar</td>
<td>Charles River Laboratories</td>
</tr>
<tr>
<td>18NX35</td>
<td>Marie Pinkerton</td>
<td>University of Wisconsin</td>
</tr>
<tr>
<td>18-330</td>
<td>Shelley Newman</td>
<td>Long Island University</td>
</tr>
<tr>
<td>18-1124</td>
<td>Ryan Jennings</td>
<td>The Ohio State University</td>
</tr>
</tbody>
</table>
Digital slides for the 2018 Meeting of the MAVP may be accessed at:
https://histology.vet.ohio-state.edu/mavp-2018
Case History:

Case #: MH-2018

Presenter: Mark J. Hoenerhoff, DVM, PhD, DACVP

Corresponding Institution: University of Michigan In Vivo Animal Core

Signalment: Male Suffolk lamb (<1yr) (Ovis aries)

History:
This sheep had a week-long history of intermittent fever, inappetence, and mild anemia following shipment and arrival at our facility. The sheep failed to respond to supportive care, developed dark brown urine, became recumbent, and was euthanized.

Gross findings:
Both kidneys were diffusely enlarged 1.5-2 times normal size, and mottled dark brown to tan along the capsular surface. They were wet on cut surface, with radiating linear red streaking from the cortex to the medulla, and multifocal irregular 0.5cm dark brown foci, petechiae, and ecchymoses within the medulla. There was mild pallor of the semimembranosus muscles bilaterally within the region of administered intramuscular injections.
**Case Synopsis:**

**Case #:** MH-2018  
**Presenter:** Mark J. Hoenerhoff, DVM, PhD, DACVP  
**Corresponding Institution:** University of Michigan In Vivo Animal Core

**Signalment:** Male Suffolk lamb (<1yr) (*Ovis aries*)

**Histopathology:**

Within sections of kidney, there was multifocal tubular dilation, loss of tubular epithelium, and tubular necrosis. There were numerous eosinophilic granular and hyaline casts within tubular lumens. The lesions extended throughout the cortex and medulla, into the collecting ducts. Throughout the glomeruli, Bowman’s space was expanded by eosinophilic, proteinaceous material. Bilaterally within sections of semimembranosus skeletal muscle, there were well-delineated zones of hypereosinophilic, fragmented, and shrunken myofibers with absence of nuclei, surrounded by reactive fibroplasia, macrophages containing hemosiderin pigment, and occasional multi-nucleated giant cells (injection site). The adjacent surrounding musculature was histologically normal.

**Morphologic diagnosis:**

1. Kidney: Tubular degeneration and necrosis, multifocal, severe, with intralesional granular and hyaline casts.  
2. Skeletal muscle: Myonecrosis, with granulating fibrosis, focal, bilateral, severe.

**Additional diagnostic tests:**

Multiple CBC, serum chemistry, and urinalysis assessments were performed, and nutritional/mineral analysis on liver was pursued. CBC showed progressive anemia over three days (RBC 13M/ul → 8.8M/ul; Hct = 47 → 25.2) and decreased Hb (12g/dl → 6.9g/dl). Serum chemistry showed hemolyzed serum with increasing CPK (2386U/L → 5753U/L), creatinine (6mg/dl → 9.4mg/dl), and BUN (125mg/dl → 196mg/dl). AST was minimally elevated (284U/L), and there was mild hyponatremia (121mmol/L) and hypochloridemia (79mmol/L). Urine collected by cystocentesis was dark brown in color, which persisted following centrifugation. Urine specific gravity was 1.015, with numerous granular casts noted on sediment exam. Free blood was not observed. Hepatic Vitamin E levels were marginal.

Okajima histochemical stain on sections of kidney was positive for hemoglobin as observed as bright orange coloration of granular casts. Immunohistochemistry for myoglobin was negative.

**Comments:**

Pigmentary nephrosis occurs in general as a result of systemic release of large amounts of hemoglobin or myoglobin from the body’s cells. Hemoglobinuric nephrosis occurs secondary to a severe systemic hemolytic event, in which large amounts of hemoglobin are released from lysed blood cells. If the capacity for reabsorption is exceeded, hemoglobinemia results in spillover of hemoglobin in the urine (hemoglobinuria). Hemoglobin is not directly toxic to the kidney, but can contribute to renal ischemia secondary to hemolytic anemia by affecting glomerular filtration rate{Newman, 2012 #4497}. Causes of hemoglobinuric nephrosis include chronic copper toxicity in sheep, leptospirosis in cattle, red maple (*Acer rubrum*) toxicity in horses, autoimmune hemolytic anemia in dogs, and babesiosis in dogs and cattle9. While
chronic copper toxicity is the most common cause of hemoglobinemia and hemoglobinuric nephrosis in sheep\(^3\), other causes include Leptospira interrogans and Clostridium perfringens type A (yellow lamb disease\(^5\), hemotropic mycoplasma (*M. ovis*)\(^7\), selenium or copper deficiency\(^13\), and Brassica consumption and onion toxicity\(^1\).

In contrast, myoglobinuric nephrosis results from extensive muscle necrosis and secondary release of the muscle protein, myoglobin, into the systemic circulation. As myoglobin passes into the kidney, it collects in renal tubules in the form of granular casts. Excessive amounts of myoglobin contribute to renal ischemia similar to the mechanism involved in hemoglobinuric nephrosis, by affecting glomerular filtration and tubular blockage from cast formation, and can exacerbate ischemic tubular necrosis in an already compromised kidney. Myoglobinuric nephrosis has been reported in various wildlife species as a consequence of acute rhabdomyolysis following capture or restraint (capture myopathy), including ungulates and birds\(^6\), white-tailed deer\(^4\). The condition has been observed in nonhuman primates and humans\(^12\), racing dogs\(^15\), and horses\(^11\) secondary to exertional rhabdomyolysis, and in quarterhorses, warmbloods or draft horses with equine polysaccharide storage myopathy (EPSSM), thought to be an inherited condition leading to abnormal accumulation of polysaccharides within muscle fibers\(^14\). In pigs, it is associated with porcine stress syndrome, secondary to malignant hyperthermia induced by halothane anesthesia or stress during shipping or handling in animals with an autosomal recessive defect in the ryanodine receptor or mutation in the dystrophin gene\(^10\). In stranded cetaceans, a similar syndrome of capture myopathy characterized by muscle necrosis and secondary myoglobinuric nephrosis leading to kidney failure has been reported\(^6\).

Differentiating myoglobinuric and hemoglobinuric nephrosis is impossible based on routine H&E evaluation of the kidney, as the lesions are indistinguishable. Details of the clinical history, bloodwork, and other ancillary diagnostics are needed to confirm the cause of pigmentary nephrosis histologically. In this case, neither gross evidence of significant muscle injury supporting myoglobinemia nor a severe hemolytic event supporting hemoglobinemia was observed. The pallor of the semimembranosus and semitendinosus muscles was attributed to the associated intramuscular injections of vitamin B12, doxycycline, and vitamin E during supportive care. It is uncertain as to how much the focal muscle necrosis due to intramuscular injection impacted the levels of creatinine kinase, but ruminants can show very high levels of CK in the serum secondary to relatively mild muscle injury, so multiple intramuscular injections and effects of prolonged recumbency could have produced CK levels observed in this animal. In addition, excessive hemoglobin in the serum can cause falsely elevated levels of creatinine kinase in animals with hemoglobinemia\(^2\). While the appearance of the urine can be similar in both conditions, hemoglobin will precipitate in urine following addition of ammonium sulfate and centrifugation. Additionally, one distinguishing characteristic clinically can be the appearance of serum following centrifugation of a blood sample. While animals with hemoglobinemia have reddish discoloration of the serum due to hemolysis, the serum of animals with myoglobinemia should be clear following centrifugation. Ultimately, Okajima histochemical staining of kidney confirmed the presence of hemoglobin in tubular casts, and myoglobin immunohistochemistry was negative on sections of kidney. A definitive cause for the hemoglobinuric nephrosis observed in this animal remains unknown, although *Mycoplasma ovis* has been reported in this flock previously.
References:


Case History:

Case #: SP17-3734

Presenter: Allison Watson, DVM (Linden Craig, DVM, PhD, DACVP)

Corresponding Institution: University of Tennessee

Signalment: 1-year-old male Quarter horse

History: This horse was euthanized after a 2-week history of severe progressive muscle atrophy, persistent tachycardia, pyrexia, and dribbling urine following treatment for rhabdomyolysis. The colt did not respond to aggressive treatment with intravenous fluids, antibiotics, and anti-inflammatory drugs.

Gross findings: There was severe, bilaterally symmetric atrophy of the epaxial and gluteal musculature. The cranoventral lung lobes were diffusely firm, tan to white, and sank in formalin.
Case Synopsis:

Case #: SP17-3734

Presenter: Allison Watson, DVM (Linden Craig, DVM, PhD, DACVP)

Corresponding Institution: University of Tennessee

Signalment: 1-year-old male Quarter horse

Histopathology: Gluteal muscle: There is multifocal, segmental necrosis with abundant mineralization. Areas of necrosis and mineral are surrounded by macrophages, fibroblasts, and scattered multinucleated giant cells. There is multifocal variably severe myocyte atrophy. Adjacent myocytes are hypereosinophilic and swollen with loss of striations.

Lung: The alveolar septa are diffusely markedly mineralized and the septa and alveoli are expanded by loose fibrous connective tissue and stellate to plump fibroblasts. Alveoli rarely contain eosinophilic homogenous material (fibrin), scattered alveolar macrophages, or hemorrhage. Blood vessel walls are multifocally mineralized.

Morphologic diagnoses:
Severe chronic-active polyphasic segmental myocyte degeneration, necrosis, and mineralization
Severe chronic pulmonary alveolar septal mineralization with fibroplasia

Additional diagnostic tests: Heterozygous for E321G MYH1 mutation

Final Diagnosis: Equine Systemic Calcinosis

Comments: Systemic calcinosis is an uncommon, fatal, mineralizing degenerative myopathy that typically affects young Quarter horse and Paint breeds. This disease is characterized by atrophy of the epaxial and gluteal muscles, malaise, and polyphasic muscular necrosis and mineralization. Soft tissue mineralization of the lungs, kidneys, and heart has been reported and was present in this horse; however, this degree of pulmonary mineralization and fibroplasia has not been described. Hyperfibrinogenemia, hyperphosphatemia, and an elevated calcium phosphorus product are common serum biochemical findings. The cause of the elevated calcium and phosphorous product is not known, but it is thought to be related to underlying systemic disease leading to inflammatory osteolysis and hyperphosphatemia. A recent study identified a MYH1 mutation in Quarter horses with immune mediated myositis. This mutation has also been associated with non-exertional rhabdomyolysis in Quarter horses (Stephanie Valberg, personal communication). This horse was heterozygous for the MYH1 mutation, and rhabdomyolysis may have contributed to development of systemic calcinosis.

References:
Case History

Case #: ML16-089

Clinical History and Current Terminal Event:

Decedent was a 45 year old male participating in a competitive swim event in central Indiana when he became unresponsive towards the end of the 2 mile US open water race and was pulled from the water.

According to his wife, the patient was physically active and only had clinical history of coughing and bloody sputum 1.5 years prior to death where a bronchoscopy and CT scan were performed and the decedent was prescribed antibiotics.

After a similar episode a year later, same treatment and decedent was given an inhaler and a 30-day follow-up appointment. Decedent has family history of cardiac events. Father passed away from heart attack (forties).

Gross Autopsy Findings: Marion County Morgue

Several enlarged organs included cardiomegaly, hepatomegaly, and splenomegaly. Left ventricle hypertrophy (LVH) was found with some occlusion of the left descending coronary artery. In addition, moderate aortic atherosclerosis was present.

The lungs were edematous. Small 1.3 cm mass found in lower lobe of right lung with multiple bilateral scars.

Toxicology screen was performed: Pseudoephedrine blood concentration 867 ng/mL. Slightly above normal level for the lab (850 ng/mL.)

Marion County Coroner called Dr. Sandusky to help the widow with the case.
Case Results: ML16-089
Histology performed by Dr. Sandusky
*Note: Only lung tissue was released from Coroner’s office

Histopathologic Description of Lung Findings
- Diffuse pulmonary congestion seen in all 10 sections
- 8: focal areas of pleural thickening
- 7: focal areas of pulmonary edema
- 5: focal pulmonary hemorrhage and hemosiderin laden alveolar macrophages
- 6: Multiple areas of small bone formation
- 1: bone marrow formation
- 2: significant foci of fibrocartilage beginning to form bone
- 1: Plant Fiber in lung

Morphologic Dx: Diffuse pulmonary congestion, edema and mineralization in lungs, diffuse pulmonary ossification

Cause of Death: Drowning, LVH, Mild CAD, diffuse pulmonary ossification

Discussion

Cause of Sudden Death:

- Coronary artery atherosclerosis: The most common on the list.
  - NOTE: Usually 75% concentric stenosis of all 3 coronaries, often more severe stenosis
- Cocaine heart:
  - Vasospasm, fiber necrosis, rhythm disturbances
- Coronary malformations
  - Having only one Cor Artery: (Pete Maravich had no left main, (J. For. Sci. 35: 981, 1990), or having one come off the pulmonary artery.
- Outflow problems
  - Hypertrophic cardiomyopathy, Aortic valve stenosis from most any cause
- Cor pulmonale
  - Pulmonary embolus, maybe 50,000 extra "sudden death" cases among previously-healthy people in the U.S. per year
- Conduction system problems / rhythm woes
  - Recreational inhalant use (i.e., glue sniffing, etc.) sensitizes the heart to rhythm disturbances
- Myocarditis (even a little patch can cause rhythm problems and even death: "Hank Gathers's disease"); even a little patch can cause rhythm problems and even death
- Channelopathies
  - The LONG QT INTERVAL DISEASES, -- there are now ten different loci and over a hundred alleles; full-genome search Nat. Genet. 41: 388,
2009). Several different channelopathies including some sodium channel mutations (Circulation 101: 1698, 2000; Circulation 102: 584 & 921, 2000) and a common potassium channel mutation (Circulation 100: 1264, 1999). This is known to be a common cause of sudden death with no anatomic findings at autopsy; this includes SIDS cases.

- Swimming seems to trigger sudden death when the mutation is in the potassium channel KCNQ1 (Mayo Clin. Proc. 74: 1088, 1999)

- Hypertensive Heart Disease
  - In systemic hypertension, the left ventricle undergoes hypertrophy and, later, dilatation.
  - The hypertrophy is mostly the result of pushing against the greatly increased load (more blood, more vascular resistance). Some hypertensive do have abnormally high cardiac outputs.
  - There are rumors that some hypertensive suffer from chronic excess of catecholamine’s which can exacerbate the hypertrophy.
  - Ultimately, the hypertensive left ventricle will probably fail. To make the diagnosis, the heart must weigh more than 350 gm, and the left ventricle be more than 1.5 cm thick, with no other reason

Marion County Cardiovascular Deaths 2000 to 2012.

Comparing Types of Heart Deaths

References:


Case History:

Case #: A17-12524

Presenter: Ethan Biswell and Abigail Durkes

Corresponding Institution: Purdue University

Signalment: 7 day old bay Quarter horse filly

History: Presented acutely laterally recumbent, hypoglycemic, with possible hepatomegaly (via ultrasound).

Gross findings: The mucous membranes, conjunctiva, and adipose tissue are mildly icteric. The pericardial sac contains ~20-25 ml of amber colored fluid. The liver is markedly enlarged with rounded edges, weighing 2.85 kg (5.97% bw with normal being 1-2% bw). The parenchyma is diffusely firm and contains multifocal random areas of pallor of variable size and shape. The hepatic lymph nodes are enlarged, 3x normal size, and edematous. The spleen is mildly enlarged and engorged with blood. All sections of the gastrointestinal tract have variable amounts of petechiae, and ecchymoses found within all layers (most severe on the mucosal and serosal layers) and are occasionally transmural. Segmentally the jejunal lumen contains mild to moderate amounts of blood. The rest of the small intestines and large intestines contain normal to slightly soft green to brown digesta/feces. Variable amounts of petechiae and ecchymoses are noted within the epicardium, lungs, skeletal muscle, and few joints (right stifle, right hind fetlock, and right carpus).
Case Synopsis:

Case #: A17-12524

Presenter: Ethan Biswell and Abigail Durkes

Corresponding Institution: Purdue University

Signalment: 7 day old bay Quarter horse filly

Histopathology: Multiple sections of liver are given. The hepatic parenchyma contains variably sized, randomly distributed, multifocal to coalescing necrotic foci characterized by hepatocyte loss and replacement with hemorrhage, degenerate leukocytes (mainly neutrophils, macrophages, and lymphocytes), and karyorrhectic debris. At the edges of the necrosis are hepatocytes with pyknotic, karyolytic, or karyorrhectic nuclei and either hypereosinophilic or absent cytoplasm. Intact hepatocytes at the edge of the necrosis contain outlines of stacks of bacilli within the cytoplasm.

Morphologic diagnosis: Multifocal necrotizing hepatitis

Additional diagnostic tests:

Bacterial cultures of the lungs, liver, and small intestine are negative for growth of pathogens. Bacterial cultures of the large intestines are positive for Clostridium perfringens; however this is considered post-mortem growth due to lack of correlated lesions.

Warthin Starry stain is positive for multiple large bacilli within the cytoplasm of hepatocytes near the edges of necrotic lesions. This is highly indicative of Clostridium piliforme.

Comments:

Tyzzer’s disease is a rapidly progressive and typically fatal disease caused by the bacterium Clostridium piliforme. Clostridium piliforme is a Gram-negative, pleomorphic, motile, endospore-bearing, rod-shaped and flagellated obligate intracellular bacterium. This disease causes an enterohepatic syndrome that has been described in many animal species (equine, rodents, rabbits, muskrats, dogs, ect.)<sup>2</sup>, though probably most thoroughly in foals. Clinical findings of lethargy, fever, anorexia, and icterus are reported regularly, and typically the animals rapidly decline into developing seizures, coma, and death.<sup>4</sup> Typical laboratory findings include leukopenia, metabolic acidosis, hypoglycemia, and elevated hepatic enzymes.<sup>4</sup> Diagnosis of this organism is chiefly based on clinical signs, postmortem findings, and special stains (Warthin Starry), however a polymerase chain reaction (PCR) is now available.<sup>1,4</sup> This bacteria is common in the environment, but thus far it has been difficult to culture which has led to little being discovered about its epidemiology, pathogenesis, and immunity. Tyzzer’s has been shown to most frequently infect foals between 1-4 weeks of age that are born in spring, April to May foals are 7.2 times more likely to develop disease, and was associated with heavy spring rainfall and high protein/nitrogenous diets fed to nursing mares.<sup>2,4</sup> Foals born of mares younger than 6 years old are 2.9 times as likely to develop this disease.<sup>2</sup> Prevention is key and on farms with a history of Tyzzer’s disease careful foal and paddock management are essential. It is recommended that young foals should have access to well-grassed paddocks that are away from any potentially contaminated soil, and all manure should be removed frequently.<sup>3</sup>

References:


Case History:

Case #: SP-18-360

Presenter: Erica Corda

Corresponding Institution: Michigan State University

Signalment: 5-year-old castrated male Labrador retriever

History: This dog was referred to the Michigan State University Veterinary Medical Center (MSU VMC) for pyrexia and severe neutropenia (60/µL) that had been documented 1 week prior to admission to the MSU VMC. One month prior, the dog had been presented to the primary veterinarian for surgical excision of two subcutaneous thoracic lipomas. On that occasion, a preanesthetic CBC revealed mild leukocytosis with moderate eosinophilia and neutrophil concentrations within reference intervals. He tested negative for heartworm disease, ehrlichiosis, Lyme disease, and anaplasmosis (4Dx SNAP test, IDEXX Laboratories). Postoperative analgesia was achieved with gabapentin and carprofen administrated orally BID for 7 days, and prophylactic cefpodoxime was given SID for 10 days. A 3-day regimen of fenbendazole was prescribed for a possible parasitic infection. Since that time, the dog appeared weak.

Clinical and laboratory findings: On presentation to MSU, the dog was pyrexic (105.8 °F), and there was a firm, warm, subcutaneous swelling without discharge at a sternal surgical incision site. The left mandibular and prescapular lymph nodes were mildly enlarged. Blood was collected for CBC (Table 1), serum chemistry (Table 2) and blood gas analysis. Bone marrow aspirate and core biopsies were collected on day 2 of the MSU VMC visit.

Table 1. Selected hemogram results

<table>
<thead>
<tr>
<th>TEST</th>
<th>UNIT</th>
<th>DAY 0</th>
<th>DAY 2</th>
<th>REF. INT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hct, spun</td>
<td>%</td>
<td>42</td>
<td>32</td>
<td>40 – 55</td>
</tr>
<tr>
<td>Platelets</td>
<td>×10³/µL</td>
<td>147*</td>
<td>138*</td>
<td>160 – 401</td>
</tr>
<tr>
<td>WBCs</td>
<td>×10³/µL</td>
<td>2.4</td>
<td>5.1</td>
<td>6.1 – 12.0</td>
</tr>
<tr>
<td>Seg. neutrophils</td>
<td>×10³/µL</td>
<td>0.0</td>
<td>0.1</td>
<td>4.0 – 8.1</td>
</tr>
<tr>
<td>Band neutrophils</td>
<td>×10³/µL</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0 – 0.1</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>×10³/µL</td>
<td>1.8</td>
<td>2.9</td>
<td>1.1 – 3.1</td>
</tr>
<tr>
<td>Monocytes</td>
<td>×10³/µL</td>
<td>0.6</td>
<td>1.9</td>
<td>0.1 – 0.7</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>×10³/µL</td>
<td>0.0</td>
<td>0.2</td>
<td>0.1 – 1.9</td>
</tr>
<tr>
<td>nRBC</td>
<td>100/WBC</td>
<td>4</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>nRBC conc.</td>
<td>×10³/µL</td>
<td>0.1</td>
<td>0.6</td>
<td></td>
</tr>
</tbody>
</table>

* Few small platelet clumps present

Table 2. Selected serum clinical biochemistry results

<table>
<thead>
<tr>
<th>TEST</th>
<th>DAY 0</th>
<th>REF. INT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total protein</td>
<td>6.7 g/dL</td>
<td>5.4 – 6.7</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.4 g/dL</td>
<td>2.8 – 3.6</td>
</tr>
<tr>
<td>Globulins</td>
<td>4.3 g/dL</td>
<td>2.3 – 3.7</td>
</tr>
<tr>
<td>Iron</td>
<td>48 µg/dL</td>
<td>109 – 250</td>
</tr>
</tbody>
</table>
Case Synopsis:

Case #: SP-18-360

Presenter: Erica Corda

Corresponding Institution: Michigan State University

Signalment: 5-year-old castrated male Labrador retriever

Histopathology: Sections of 2 long cores of trabecular bone and marrow included approximately 2 cm of intact medullary tissue. Hematopoietic cellularity was moderate to high and varied from about 50% to 90% with the remaining space being filled primarily by adipocytes. Megakaryocytes were present in moderate number, and there was a moderate amount of hemosiderin. The myeloid to erythroid ratio was difficult to assess given the large number of blasts, but it appeared increased because the blasts were interpreted as myeloblasts. There were few myeloid cells beyond myelocytes; band and segmented neutrophils were nearly absent. However, the eosinophil lineage appeared orderly and complete. Erythroid precursors were present in moderate numbers and appropriately arranged in islands. Erythroid maturation appeared orderly. There were also a small to moderate number of plasma cells and an increase in macrophages containing degraded cellular material.

Morphologic diagnosis: Myeloid hyperplasia with early to mid-stage maturation arrest of the neutrophil lineage; although there are enough blasts to consider an acute myeloid leukemia, the normal bone marrow architecture, the preserved eosinophil lineage, the phagocytic activity, and the CBC findings are all most suggestive of precursor-targeted immune-mediated neutropenia.

Additional diagnostic tests: Cytologic evaluation of the bone marrow aspirate collected at the same time as the core confirmed a myeloid appearance of the blasts and revealed a mildly increased number of small lymphocytes. No atypical cell population was detected.

The mildly enlarged left mandibular lymph node was assessed cytologically, and the findings supported reactive lymphoid hyperplasia. Cytologic evaluation of smears obtained from the sternal incision swelling revealed mild macrophagic inflammation but no neutrophilic inflammatory component or sepsis.

Comments: The bone marrow core findings in this case suggested the possibility of acute myeloid leukemia given the large number of marrow blasts with evidence of some myeloid maturation, but that was considered much less likely for the reasons noted above. Cytologic evaluation of the marrow helped support a nonneoplastic process, but acute leukemia still could not be completely excluded. Neutropenia secondary to sepsis could also have been considered, but the persistence of severe neutropenia for over a week without typical clinical evidence of severe septicemia suggested otherwise, and the degree of hyperplasia was too great. Clinical progression supported a diagnosis of immune-mediated neutropenia as the neutrophil concentration had climbed to 14,000/µL on day 8 of therapy with prednisone (1 mg/kg SID).
Immune-mediated neutropenia is an uncommon hematologic disorder in dogs and can be primary (idiopathic) or potentially secondary to drugs, infection, or neoplasia. In most suspected cases, marrow myeloid hyperplasia progresses to segmented neutrophils, though band neutrophils often exceed segmented neutrophils. A marked left shift with early maturation arrest, as seen in this case, is reported but is less common.1,2 The mechanism for immune-mediated neutropenia in dogs is thought to be antibody-mediated destruction of neutrophils or their precursors. Anti-neutrophil antibodies have been assessed in some cases,3,4 but thorough analytical and diagnostic validation of assays has not been done, and testing is not routinely available. The diagnosis is usually based on bone marrow examination and clinical findings, including response to immunosuppressive therapy.

In the case presented here, drugs administered by the referring veterinarian (gabapentin, carprofen, a cephalosporin, and fenbendazole) may or may not have played an initiating role.5,6,7 Neutropenia has been associated with each of these drugs, though through various mechanisms including generalized marrow suppression and bone marrow necrosis which were not evident. The degree of hyperplasia in the face of severe neutropenia did not fit a recovery from generalized hypoplasia. These and other drugs may also induce an immune-mediated neutropenia, but rapid recovery is typically expected after drug withdrawal, and all of the drugs had been discontinued 2-3 weeks prior to presentation. Whatever the precipitating event, it is noteworthy in this case that eosinopoiesis appeared unimpaired, neutrophils being selectively affected as is consistent with a specific immune response to one cell lineage.

Secondary infections and fever are common in dogs with immune-mediated neutropenia, and they typically respond quickly to symptomatic therapy while neutropenia persists. This dog may have been septic and certainly had evidence of inflammation: pyrexia, reactive lymph node, warm swelling at previous surgical incision, hyperglobulinemia, hypoalbuminemia, and hypoferremia. Lack of neutrophils at the incision site in a severely neutropenic dog do not exclude infection with a pyogenic organism, but no organisms were seen and the swelling may have been sterile.

References:
Case History:

Case #: 1235813-009

Presenter: Keith Nelson

Corresponding Institution: MPI Research, a Charles River Company

Signalment: 5 ½ month old, male beagle canine.

History: The animal had arrived in the facility in mid-August, two weeks prior to presentation, and had not been used for study purposes. Animal was found with vomitus under the cage during routine room check along with blood coming from the mouth. The animal was laterally recumbent and pale. Breathing was labored and shallow, with increased heart rate. Animal was humanely euthanized after veterinary consultation.

Gross findings: Lungs were diffusely reddish black, heavy and wet. All other tissues were normal.
Case Synopsis:

Case #: 1235813-009

Presenter: Keith Nelson

Corresponding Institution: MPI Research, a Charles River Company

Signalment: 5 ½ month old, male beagle canine.

Histopathology: The lung had widespread suppurative and necrotizing pneumonia with interstitial and alveolar edema and hemorrhage. Multifocally expanding and effacing the lung parenchyma, including alveoli and small bronchioles, were abundant infiltrates of neutrophils admixed with necrotic cellular debris. Alveoli, alveolar walls, peribronchiolar and perivascular interstitium, and pleura were filled and expanded by abundant eosinophilic proteinaceous fluid (edema) and hemorrhage, admixed with neutrophils and cell debris. There were numerous aggregates of small rod-shaped bacteria throughout the affected areas. Multifocally, bronchioles had intraluminal accumulations of degenerate neutrophils admixed with necrotic debris.

Morphologic diagnosis: Lung: Necrosuppurative and hemorrhagic pneumonia, multifocal

Additional diagnostic tests:

Gram Stain – Gram +

Lung culture – *Escherichia coli* 3+.

PCR for virulence factors – Colony necrotizing factor-1 (cnf-1) positive.

Comments:

Hemorrhagic pneumonia in canines may have multiple potential causes. All of these may present with reddened, heavy, congested and edematous lungs on gross examination. Among these are coagulopathies, and primary viral and bacterial infections. Primary or toxic coagulopathies generally present as hemorrhage without significant associated inflammation. While necrosis may be present, it is more likely due to infarction than a cytotoxic effect. Canine Influenza virus presents with tracheitis, bronchitis, and bronchioloar acute inflammation and hemorrhage. While alveolar inflammation and hemorrhage may be present, it is a secondary or less common finding. Although secondary bacterial infections may occur, producing significant pulmonary inflammation, tracheitis and bronchitis are features of this disease. Bacterial causes include *Leptospira* sp. and *Streptococcus equi* ssp. *zooparvum* (*S. equi*), in addition to *Escherichia coli*. *Leptospira* causes a hemorrhagic pneumonia in dogs, presenting with alveolar hemorrhage and necrosis, coupled with fibrin thrombi, but without affecting major airways and with no leptospiral organisms present in the lung. *S. equi* infection reported in dogs presents as a fibrinosuppurative, necrotizing, and hemorrhagic pneumonia, with Gram+ intracellular cocci present in the lung. In this instance, animals presented with bronchointerstitial hemorrhage, necrosis, acute inflammation, edema, and infiltrates of short Gram+ bacterial rods within the lungs. This presentation is suggestive of an *E. coli* pneumonia and culture and virulence factor testing showed non-enteropathogenic *E. coli* were present, expressing colony necrotizing factor 1 (CNF-1).
CNF-1 positive non-enteropathogenic *E. coli* has been associated with urinary infections in humans, as well as animals, and is rarely reported as causing pneumonia in dogs, cats, horses, and a tiger cub, as well as in humans. In dogs, it has been primarily reported in young beagle research dogs, with one report in a pet cocker spaniel breed. None of the infected animals were reported to have immunodeficiencies or concurrent infections. The research animals affected generally presented soon after shipping from the supplier. This is a similar history to that seen in this case. Additionally, over the past 8 years at our facility, we have seen 8 other cases that were confirmed through culture and PCR, all *E. coli* that were CNF-1+. All of these were young dogs and presented soon after arrival from the supplier. Another 7 cases with similar lung findings did not have microbiology and/or PCR done or were not CNF-1+, but did have abundant *E. coli* cultured.

Colony necrotizing factor (CNF) is found in two variants; CNF-1, identified in humans and domestic animals, and CNF-2, which has only been identified in ruminants. Both the O4 and the O6 serotypes of *E. coli* have CNF, with CNF-1 consistently produced by necrotoxigenic *E. coli*. CNF-1 is associated in humans and animals with *E. coli* found in urinary tract infections, pyometra, and prostatitis. Additionally, as in this case, it may occasionally be isolated in other extra-intestinal infections, including pneumonias.

References:


Case History:

Case #: 18-H41878-17

Presenter: Andrea Pohly, DVM

Corresponding Institution: University of Illinois

Signalment: 15-year-11-month-old, male Cheetah (*Acinonyx jubatus*)

History: This zoo-housed animal presented for a history of weakness, lethargy, shaking/tremoring, polydipsia, and minimal interest in food. Bloodwork and urinalysis findings were consistent with renal failure with marked elevations in BUN and creatinine, isosthenuria, rare granular casts, and 2+ blood in the urine. The animal was anesthetized for a CT scan and died while under anesthesia.

Gross findings:

The animal was in adequate body condition as evidenced by slightly decreased subcutaneous and visceral adipose tissue stores. The right kidney was shrunken, irregular, and had a focal depression in the cortex that extended into cut surface. There were multifocal, red to tan nodules ranging from 0.2 to 2 cm in diameter throughout the spleen. Within the right lobe of the pancreas, there was a 2 cm in diameter, fluid-filled cystic structure. The liver contained multiple irregular, dark red, flat foci that ranged from 0.3 x 0.2 to 0.7 x 0.5 cm. Within the right frontal sinus, there was a 1 cm in diameter, red to tan, bony nodule that was surrounded by a coagulum of green to yellow, mucoid material. On the right postcruciate gyrus of the cerebral cortex, there was a 0.5 cm in diameter tan, soft, umbilicated focus that extended approximately 1 cm into the cut surface.
Case Synopsis:

Case #: 18-H41878-17

Presenter: Andrea Pohly, DVM

Corresponding Institution: University of Illinois

Signalment: 15-year-11-month-old, male Cheetah (Acinonyx jubatus)

Histopathology:

Cerebrum: Within the right postcruciate gyrus, there is a 12 mm in diameter focus of neuropil that is expanded, infiltrated, and effaced by a large nodule composed of innumerable extracellular and occasionally intrahistiocytic yeasts. These yeasts are pale basophilic, round, and 5-15 um diameter with a 1 um thin wall; they are surrounded by a 2-8 um thick, clear, colorless capsule. Occasional yeasts exhibit narrow-based budding. Within the center of the nodule, low numbers of macrophages, lymphocytes, and plasma cells multifocally surround the yeasts. Larger numbers of foamy macrophages (Gitter cells), lymphocytes, and plasma cells surround the periphery of the nodule. The surrounding neuropil is markedly compressed, and often contains variably sized clear spaces (vacuolar change). Within this area, there are numerous, markedly swollen, hypereosinophilic axons (spheroids), and occasional swollen, pale neurons with eccentric nuclei (chromatolysis). Multifocally, intralesional perivascular interstitium and overlying leptomeninges are infiltrated by sheets of macrophages, lymphocytes, and plasma cells with perivascular cuffing up to 8 cells thick.

Morphologic diagnosis:

1. Cerebrum (Right postcruciate gyrus): Focal, severe, chronic granulomatous and lymphoplasmacytic meningoencephalitis with abundant intralesional yeasts consistent with Cryptococcus spp.
2. Cerebrum (Right postcruciate gyrus): Focally extensive spongiosis and astrocytosis

Additional diagnostic tests:

Periodic acid-Schiff (PAS) staining: Fungal yeasts exhibit strong positive staining of the cell wall. The capsules do not stain.

Comments:

These findings are consistent with Cryptococcus spp. infection, which, in this case, affected the right frontal sinus and extended into the right postcruciate gyrus of the cerebral cortex.

Cryptococcus, a saprophytic fungus, is found worldwide with the vast majority of pathogenic infections caused by either C. neoformans or C. gattii (1). The exact pathogenesis of Cryptococcus has not been fully elucidated, but it is thought that initial infection occurs through inhalation of spores where it can then disseminate systemically from the nasal cavity or lungs to various organs including the skin, eyes, and central nervous system (2). While Cryptococcus is the most common fungal etiology in domestic cats and can cause disease in numerous domestic species, pathogenic infections have also been reported in a variety of nondomestic...
species including cheetahs, porpoises, and koalas (2,3,4). Various factors are thought to play a role in disease progression including initial site of infection, immunocompetence of the affected individual, and predisposing hereditary factors that remain poorly understood. Because cheetahs, as a species, have experienced a genetic bottleneck, it has been suggested that a lack of genetic diversity may predispose them to fatal Cryptococcus infections (2).

A unique feature and major virulence factor of Cryptococcus is its thick polysaccharide capsule that both protects the organisms and contributes to host immune evasion and downregulation of inflammatory cell stimulation (5). Microscopically, the capsule appears as a clear, colorless halo surrounding the cell wall of the yeast organisms. This characteristic is due to the highly hydrophilic nature of the capsule (5). During routine hematoxylin and eosin staining, the capsule is dehydrated, causing it to contract and give it its characteristic “soap bubble” or halo appearance. Special staining with mucicarmine can be used to positively stain the polysaccharide component of the capsule. Additionally, periodic acid-Schiff (PAS) staining can be used, as in this case, to highlight the glycogen present in the fungal cell wall.

References:


Case History:

Case #: 18-35563-2A

Presenter: Denae LoBato, DVM, DACVP

Corresponding Institution: University of Illinois

Signalment: 4 year old female Maltese mixed breed dog

History:

This dog presented to the referring vet for ovariohysterectomy. At the time of surgery, the animal appeared to be in heat. The surgeon noted a 2 cm soft mass in the middle of the left uterine horn that exuded opaque white to yellow fluid when incised. A sample from this area was submitted for biopsy.

Gross findings:

A partial uterine horn and both ovaries were received. One uterine horn contained an approximately 2cm in diameter, raised, soft tan to pink mucosal mass that projected from the mucosal surface into the lumen. There were multiple yellow nodules up to 4mm in diameter in both ovaries on cut section.
Case Synopsis:

Case #: 18-35563-2A

Presenter: Denae LoBato, DVM, DACVP

Corresponding Institution: University of Illinois

Signalment: 4 year old female Maltese mixed breed dog

Histopathology:

Uterus: In this segment, the endometrium is diffusely markedly thickened up to 40 times normal thickness by severely elongated, villous projections of cuboidal to columnar pseudostratified epithelium arranged in thin papillary fronds along a core of fibrovascular stroma surrounding large cysts filled with eosinophilic to mucinous material. There are occasional multinucleated syncytial cells within these spaces. This layer is separated from the underlying endometrial glands by a layer of fibrous connective tissue composed of spindle cells arranged in streams within loose collagenous stroma. The endometrial glands are moderately to markedly hyperplastic and ectatic, and contain brightly eosinophilic material. There is mild multifocal hemorrhage within the less affected hyperplastic endometrium.

Morphologic Diagnosis:

Uterus: Pseudo-placentational endometrial hyperplasia

Additional Diagnostic Tests: n/a

Comments:

Pseudo-placentational endometrial hyperplasia (PEH) is a relatively uncommon form of endometrial hyperplasia in the dog that— as its name suggests — mimics placentation. Unlike other forms of endometrial hyperplasia, this condition generally results in one to multiple discrete masses, and has been associated with infertility. While also known as a deciduoma, PEH is considered the more accurate term for this non-neoplastic process. Histologically, PEH is characterized by three layers: 1. long hyperplastic villi and cysts resembling normal placenta, 2. fibrous connective tissue, and 3. hyperplastic endometrial glands. Previous studies have suggested a correlation with high progesterone levels during the luteal phase. The presence of multiple ovarian corpora lutea in this dog supports progesterone stimulation in this case. PEH lesion must be differentiated from true placentation, which can be complicated by the presence of multinucleated trophoblasts in both conditions. However, dogs with PEH lack fetal membranes.

References:

Case History:
Case #: 1736520-4
Presenter: Rachel Neto

Corresponding Institution: University of Illinois at Urbana-Champaign

Signalment: 11-year-old, intact female, Goeldi’s marmoset (Callimico goeldii)

History: The zoo-housed animal presented for necropsy following signs of lethargy and anorexia for about 1 week prior to death. Significant weight loss was noted in the weeks before death.

Gross findings:
The animal was in poor body condition with decreased subcutaneous and visceral adipose tissue and musculature overlying the ribs and vertebral prominences. Diffusely, the skin and subcutis were moderately yellow (icterus).

The liver was moderately enlarged with rounded edges. The left medial liver lobe was markedly expanded by a 4.5 cm x 4 cm x 2 cm, nodular, poorly demarcated, light brown soft mass. On cut surface, the mass was solid, and partially brown with a central tan to yellow friable region. All hepatic lobes were multifocally rounded and expanded by ill-defined similar, smaller masses. Scattered throughout the remaining liver parenchyma there were numerous multifocal to coalescing, 1-3 mm in diameter, well demarcated, flat to slightly raised, friable, tan to yellow foci.
Case Synopsis:

Case #: 1736520-4

Presenter: Rachel Neto

Corresponding Institution: University of Illinois at Urbana-Champaign

Signalment: 11-year-old, intact female, Goeldi’s marmoset (Callimico goeldii)

Histopathology:

Liver: The hepatic parenchyma is markedly disrupted by two distinct processes. The first is characterized by multifocal to coalescing, well demarcated, variably sized foci composed of large numbers of intact and necrotic neutrophils mixed with abundant cellular debris and eosinophilic amorphous and heterogenous material (lytic necrosis) replacing hepatocellular cords. Frequently associated with the necrotic regions, there are small to medium colonies of coccobacilli. Moderate numbers of hepatocytes adjacent to the necrosis exhibit either a swollen and highly vacuolated cytoplasm (vacuolar degeneration) or a hypereosinophilic cytoplasm with karyolitic nucleus (coagulative necrosis). The second process is composed of multiple foci of a well demarcated, variably encapsulated, expansile and occasional infiltrative highly cellular proliferation of numerous well-differentiated adipocytes mixed with extensive hematopoietic tissue composed of variable amounts of maturing erythroid, granulocytic and megakaryocytic cells. Frequently, the center of larger masses is composed of groups of adipocytes with membrane hypereosinophilia and loss of cellular detail (necrosis), surrounded by moderate numbers of multinucleated giant cells and multiple islands of hematoidin pigment (fat necrosis and chronic hemorrhage).

Morphologic diagnosis:

1. Liver: Multifocal to coalescing, random, severe, acute, necrosuppurative hepatitis with intralesional colonies of coccobacilli
2. Liver: Multiple hepatic myelolipomas

Additional diagnostic tests:

Aerobic culture of liver samples returned pure and heavy growth of Yersinia enterocolitica. No strict anaerobes were isolated and PCR for Mycobacterium spp. was negative.

Comments:

Pathologic findings were conclusive for severe yersinial hepatitis and concurrent multiple hepatic myelolipomas in this case.

The most important Yersinia species in nonhuman primates are Y. enterocolitica and Y. pseudotuberculosis (1). These are gram negative, rod to coccoid bacteria that may be shed in feces of asymptomatic animals or other species in the environment, such as rodents and birds (2). Transmission occurs via the fecal-oral route. In the intestines, the bacteria invade the intestinal epithelium or ileal M cells, reaching submucosal lymphoid follicles and ultimately disseminating via lymphatics and the hepatic venous system (1,2). Virulent strains of Yersinia spp. are able to resist phagocytosis by neutrophils and intracellular killing by macrophages (1). Yersiniosis in nonhuman primates usually presents as a triad of lesions: necrotizing/suppurative hepatitis and splenitis, mesenteric lymphadenitis, and ulcerative enterocolitis (1).
Hepatic myelolipomas are infrequently reported in domestic animals; however, retrospective studies of populations of Goeldi’s monkeys revealed a relatively high prevalence of this benign tumor in this species (3,4), reaching a prevalence up to 17.2% (4). Interestingly, older female animals, as in this example, were at higher risk. The majority of the tumors were multifocal (4), as also noted in this case. It was previously thought that hepatic myelolipomas were merely incidental lesions (3); however a more recent retrospective review found that these tumors can be associated as causative lesions of hepatic necrosis, cholestasis, lobular collapse, hepatitis, and icterus in Goeldi’s marmosets (4).

References:
Case History:

Case #: 17-H51053-2A

Presenter: Natalie Kirk, DVM

Corresponding Institution: University of Illinois

Signalment: 1-year-old, male Great Horned Owl (*Bubo virginianus*)

History:

This owl presented to the wildlife medicine clinic with severe anemia, leukopenia, and hyperproteinemia and was later found dead in its cage and submitted for necropsy.

Gross findings:

The owl was in poor body condition as evidenced by decreased pectoral musculature, a prominent keel, and minimal subcutaneous and visceral adipose stores. The air sacs were mildly opaque. There was a focal, dark red area within the mucosa of the ventriculus that was covered with fur. Additionally, there were numerous thin, white nematodes in the ventriculus that extended to and partially occluded the duodenum.
Case Synopsis:

Case #: 17-H51053-2A

Presenter: Natalie Kirk, DVM

Corresponding Institution: University of Illinois

Signalment: 1-year-old, male Great Horned Owl (Bubo virginianus)

Histopathology:

Heart: Moderate numbers of lymphocytes, plasma cells, and macrophages multifocally and transmurally infiltrate all layers of the heart, separate and surround cardiomyocytes, and multifocally form perivascular, nodular aggregates. Adjacent cardiomyocytes are occasionally shrunken and hypereosinophilic with loss of cross striations and a karyolytic to absent nucleus (necrosis), or are lost with replacement by loose fibrous connective tissue.

Morphologic diagnosis:

Heart: Moderate, multifocal, lymphoplasmacytic and histiocytic pancarditis with multifocal myocyte necrosis and myocardial fibrosis

Additional diagnostic tests:

Immunohistochemistry for West Nile Virus: Scattered cardiomyocytes exhibit strong cytoplasmic immunoreactivity.

Comments:

West Nile virus (WNV) is an arthropod-borne virus in the genus Flavivirus that is most commonly transmitted by mosquitoes (6). Other modes of transmission have been reported, including through contaminated water, direct contact, or ingestion of infected prey (2). WNV is maintained in a sylvatic (rural) transmission cycle between wild birds and mosquitoes and causes outbreaks in humans and horses as dead end hosts in the urban transmission cycle. WNV causes disease in many avian species as well as mammals and reptiles (6, 2).

Among birds, WNV causes a wide range of pathologic changes, including subclinical disease, peracute death, and chronic illness. Corvids (including crows and jays) are highly susceptible and typically die rapidly after infection; clinical signs may be absent or include depression, anorexia, dehydration, ruffled feathers, abnormal head posture, ataxia, and sudden death (2). Gross changes are usually minimal and may include splenomegaly (5). Highly susceptible species have large amounts of virus detectable via IHC in blood and tissues; histologically, the most common findings are necrosis in the spleen, heart, and liver accompanied by minimal inflammation. CNS lesions are usually absent (1, 2, 5).

Conversely, owls and other raptors may experience a more prolonged course of disease. In addition to those clinical signs mentioned above, raptors may develop impaired vision, blindness, and long term sequelae including feather abnormalities and relapses of neurologic signs (2). Gross findings are more common in these animals and include dehydration, multiorgan hemorrhage, splenomegaly, hepatomegaly, myocardial pallor, and cerebral atrophy and malacia (2). Histologic lesions are found primarily in the CNS, heart, kidney, spleen, and liver and consist of lymphoplasmacytic and histiocytic inflammation and necrosis, as seen in this
case (2). Owls in particular tend to have lower amounts of antigen detectable via IHC in the brain, kidney, or heart compared to more susceptible species, such as crows (7).

Differences in lesions and WNV-related death have been noted between species of owls. Larger body size and northern native breeding range are both associated with increased WNV-related death (3). Larger birds may have an increased arthropod burden while the observed differences in susceptibility based on geographic distribution may be related to differences in immunocompetence. In a 2006 study by Gancz et al., northern species were found to have antigen detectable via IHC in the blood and all major organs. Birds of five other species (including great horned owls) did not have antigen in the blood, and antigen was sparsely localized in the kidney, CNS, heart, and pancreas. In this study, antigen was most reliably detected in the kidney, while in a previous study (1), antigen was most reliably detected in the heart.

References:


Case History:

Case #: SP-17-14737

Presenter: Larissa Kipa

Corresponding Institution: Michigan State University

Signalment: 4-year-old intact female beagle

History: This beagle was referred to the Michigan State University Emergency and Critical Care Medicine (MSU ECCM) unit for evaluation of anemia five weeks after delivering a litter of puppies. She was lethargic, had lost 8 pounds, and had become anorexic 2-3 days before presentation. The puppies in the litter had begun dying at 2 weeks of age, and only one was still alive at presentation.

The beagle was normoproteinemic with a hematocrit of 22%, and she was given a transfusion of packed red blood cells. Microscopic review of the blood smear revealed macrocytic ovalocytic erythrocytes with poorly regenerative anemia, suggesting precursor-targeted immune-mediated anemia (PIMA) with myelofibrosis, and this was supported by subsequent bone marrow aspirate and core biopsies. Urinalysis with culture also identified a urinary tract infection with *Escherichia coli*.

The beagle was started on Clavamox for the urinary tract infection, and an immunosuppressive dose of prednisone for treatment of PIMA, along with clopidogrel, an antiplatelet medication given to reduce the risk of thromboembolism. Her hematocrit remained stable in the mid-20s over the next month, though her activity level increased. After one month, she developed a mildly distended abdomen presumed to be ascites secondary to a thromboembolism in her liver, and she was started on aspirin in addition to her clopidogrel and prednisone. Two weeks later, she became lethargic again and continued to have a distended abdomen. Her hematocrit was 10%, and she received another blood transfusion and a splenectomy as therapy for refractory PIMA. The clopidogrel and aspirin were discontinued in preparation for surgery, and two days later the beagle underwent a complete key-hole splenectomy. The spleen was submitted for histologic examination.
Case Synopsis:

Case #: SP-17-14737

Presenter: Larissa Kipa

Corresponding Institution: Michigan State University

Signalment: 4-year-old intact female beagle

Histopathology:

The splenic red pulp was hypercellular with increased megakaryopoiesis and neutropoiesis and without a proportional increase in late-stage erythroid precursors, despite the anemia. However, there was a large population of cells consistent with early erythroid precursors and supportive of a marked left shift in the erythroid lineage. Within regions rich in these cells were low numbers of rubricytes but essentially no metarubricytes. Erythroid cells were intermixed with other hematopoietic cells, lymphoid cells, and macrophages, many of which contained small amounts of hemosiderin. The few rubricytes that were present were not in normal erythroid islands; instead, most were present individually or in clusters of 2 or 3, or they were within macrophages. The white pulp, including scattered lymphoid follicles with normal polarity, lacked overt abnormalities. Plasma cells were present in moderate number.

Morphologic diagnosis:

Spleen: Increased hematopoiesis with evidence of ineffective erythropoiesis, an early erythroid maturation arrest, and rubriphagocytosis; these findings support splenic manifestations of precursor-targeted immune-mediated anemia (PIMA).

Comments:

The pathogenesis of PIMA is unknown, but it is thought to be caused by immune-mediated destruction of erythroid precursors in the bone marrow and other organs that may be hematopoietically active. PIMA can present with varying patterns (hypo-, normo-, or hypercellular) depending on the stages of the precursors being phagocytized, and in our experience, the patterns in the spleen and bone marrow are not always the same. In this case, splenic maturation arrest at the rubricyte stage indicated a mid-stage PIMA pattern with predominant phagocytosis of rubricytes.

With early- or mid-stage PIMA patterns, a greatly increased number of early erythroid precursors may suggest a hemic cell neoplasm. However, careful inspection in this case revealed mixed cells with a degree of erythroid maturation and phagocytosis of intact erythroid precursors, best seen in macrophages with cytoplasmic hemosiderin surrounding the phagocytized intact cells. What may appear to be anisocytosis and anisokaryosis of a neoplastic population is actually a reflection of maturation, with the more mature erythroid precursors being smaller with smaller nuclei and more heterochromatin. Intermixing of other hemic cells, especially reactive macrophages, may also contribute to the appearance of pleomorphism, and megakaryocytes may be misidentified as atypical cells such as histiocytes with pleomorphic nuclei. This case demonstrates the importance of considering PIMA as a differential when similar findings are present in splenic tissues from anemic dogs.
Two weeks after splenectomy, the beagle’s anemia started to become regenerative and her activity level returned to normal. Her hematocrit steadily increased over the next six months, and was 37% at her latest recheck appointment. Her prednisone dose is being tapered, and aside from recurrence of her urinary tract infection and an episode of chocolate intoxication, she has been doing well.

References:

Case History

Case #: 518100

Presenter: Lauren Himmel, DVM, PhD, DACVP

Corresponding Institution: Vanderbilt University Medical Center

Signalment: Adult male Nppa knockout mouse

History: The mouse was submitted for euthanasia following palpation of a large, round, right-sided abdominal mass. It had been receiving an experimental compound for several months and 1 week prior had undergone an electrophysiology study wherein atrial fibrillation was induced. This mouse was also housed separately from his cagemate due to pugilism.

Gross findings: At necropsy, the mouse was in excellent post-mortem condition and had a body condition score of 3/5. The preputial glands were mildly cystic. There was marked right-sided hydronephrosis with left-sided renal hypertrophy. There were no other significant gross lesions. Only the kidneys, heart, lungs, liver, and spleen were examined histologically.
Case Synopsis

Case #: 518100

Presenter: Lauren Himmel, DVM, PhD, DACVP

Corresponding Institution: Vanderbilt University Medical Center

Signalment: Adult male Nppa knockout mouse

Histopathology: The renal pelvis is severely dilated and the parenchymal architecture of the kidney is severely atrophic, with only a thin crescent of tissue remaining beneath the renal capsule and near complete loss of nephronal constituents. The compressed tissue is markedly fibrotic with degenerate and atrophic tubules, few largely sclerotic glomeruli, frequently hyalinized arterioles, and numerous aggregates of lymphocytes, plasma cells, hemosiderophages, and neutrophils. The dilated pelvis contains a large coagulum of hemorrhage, proteinaceous material, intra- and extracellular brightly eosinophilic rhomboidal crystalline structures, and hemosiderophages. There is inversion of the renal pelvis and pelvic fat into the hydronephrotic space, wherein there is edema, fibromyxomatous tissue, and infiltrates of lymphocytes, plasma cells, Mott cells, and neutrophils. Also in the dilated pelvic space is a polypoid mass composed of hyperplastic urothelial fronds overlying a newly-formed fibrovascular core. Within this mass, the urothelium demonstrates multifocal cytoplasmic hyalinosis with marked eosinophilic and mild neutrophilic transmigration. The stromal core of the papilloma contains numerous eosinophils, neutrophils, plasma cells, Mott cells, lymphocytes, and histiocytes which frequently contain eosinophilic crystalline material. At the renal artery, there is focal, nodular adventitial expansion by fibromyxomatous proliferation and infiltrates of lymphocytes, plasma cells, neutrophils, and histiocytes. Perirenal vasculitis and steatitis is present multifocally. Periureteral, nodular aggregates of lymphocytes, plasma cells, and neutrophils are identified in some sections.

Morphologic diagnosis: Hydronephrosis with intrapelvic urothelial papilloma and urothelial cell hyalinosis

Additional diagnostic tests: None performed

Comments: Hydronephrosis and urothelial cell hyalinosis are common findings in inbred mice and, interestingly, occur concurrently with a growth disturbance of the renal pelvis in this case. The diagnosis of papilloma of the renal pelvis was chosen over the differential diagnosis of urothelial papillary hyperplasia based on the newly-formed and inflamed stromal stalk. Urothelial proliferative lesions in rodents occur as responses to bacterial infection, urinary tract toxins, calculi, renal papillary necrosis, and urinary tract obstruction. Squamous metaplasia is often associated with chronic inflammation in urothelial-lined surfaces in rodents. Urothelial cell papilloma is thought to represent an intermediate step in the development of carcinoma. Chemically-induced neoplasms tend to consist of solid nests of epithelial cells, while those that are spontaneously-occurring tend to appear as urothelium lining a fibrovascular core, as in this case. Per the submitting investigator, the test article being administered to this mouse was not expected to be tumorigenic.

Hyalinosis of epithelia is most prevalent in strains of B6, 129, and Swiss backgrounds. Cells of the respiratory tract, stomach, gallbladder, and pancreatic ducts have swollen, hyaline, eosinophilic cytoplasm, often with polygonal, crystalline accumulations of the material
extracellularly and within macrophages.\textsuperscript{2,3} In the lung it can be found in conjunction with acidophilic macrophage pneumonia.\textsuperscript{2} This substance has been shown to contain iron, alpha-1 antitrypsin, immunoglobulin, granulocyte breakdown products, and Ym1 (Chil3)/Ym2 (Chil4) chitinase-like lectins.\textsuperscript{2,4,5} It is often found in conjunction with another pathologic process (e.g. inflammation, tumor) of the organ system in which it is found. Immunohistochemical staining is readily performed to identify Ym1/Ym2 proteins.\textsuperscript{2,4} Uni- or bilateral hydronephrosis is found commonly in laboratory mice and is considered a finding of multifactorial etiology.\textsuperscript{2,6} Some strains have a documented higher incidence of congenital or hereditary hydronephrosis.\textsuperscript{7} It can also be associated with urinary tract obstruction (e.g. mouse urologic syndrome), abdominal neoplasia, and infection.\textsuperscript{2,7}

The \textit{Nppa} knockout mouse is deficient in atrial natriuretic peptide precursor A. It bears a targeted mutation leading to constitutive, systemic loss of \textit{Nppa}. As many transgenic mice, this mouse is on a mixed B6 and 129 background. It is available in cryopreserved status from commercial vendors (Taconic, JAX) and is included in the KOMP Repository.\textsuperscript{8} Homozygous mice have elevated blood pressure on low or high salt diets, while heterozygous mice develop the hypertensive phenotype only on high salt diets. As such, these mice are used in studies of cardiovascular disease and RAAS pathophysiology. GWAS studies have associated certain human \textit{NPPA} alleles with increased disease susceptibility for blood pressure and renal phenotypes,\textsuperscript{9,10} making this a potentially relevant mouse model.

References:

Case #: ODA-ADDL CS

Presenter: Craig Sarver

Corresponding Institution: Ohio Department of Agriculture ADDL

Signalment: 6 years old, female, Domestic Short Haired feline

History: The cat was presented to the ADDL on 5/31/2018 via the mail. The owner had 6 cats, 3 have died suddenly with signs of anemia, high fever, lethargy, kidney disease, and liver disease. All 3 have been covered in ticks.

Gross findings: The mucus membranes and subcutaneous tissues were pale yellow. The thoracic cavity contained approximately 15cc of clear yellow fluid. The lungs were 69 grams, wetter than normal and moderately congested. The heart was 18.3 grams (.4% of body weight). The stomach was empty. The small intestines had multiple, 1-2mm, mucosal hemorrhages. The colon had blackish green feces and the rectum had green formed feces. The fecal examination was negative. The spleen was 31.9 grams, 13.7x4.2x1.1cm, and markedly congested. The liver was 138.2 grams mottled tannish red. The kidneys were 18.6 (right) and 18.7 (left) grams. The urinary bladder had approximately 10cc of dark yellow urine (S.G.: 1.030, pH: 6, GlucoseL100mg/dL, Bilirubin: 4, Protein: 30mg/dL). The rest of viscera had no gross lesions. The brain was 25.4 grams.
Case Synopsis: *Cytauxzoon felis* in an Ohio Cat

**Case #:** ODA-ADDL CS

**Presenter:** Craig Sarver

**Corresponding Institution:** Ohio Department of Agriculture ADDL

**Signalment:** 6 years old, female, Domestic Short Haired feline

**Histopathology:**

Kidney: Within scattered glomerular tufts are low numbers of monocytes containing intracytoplasmic schizonts. The foamy macrophages are enlarged and contain cytoplasmic schizonts with numerous 1-2 micron in diameter, round to oval, basophilic organisms (merozoites). The glomeruli have slightly increased numbers of mesangial cells and mildly thickened capillaries. Scattered renal vessels contain schizont laden macrophages.

Lung: Multiple pulmonary vessels and septal capillaries have numerous schizont-laden macrophages like those described in the kidney. Scattered vessels are partially occluded with intrahistiocytic schizonts.

Liver: Approximately 30-50% of the hepatocytes have loss of differential staining, hypereosinophilia, pyknotic nuclei, and cellular debris (necrosis). The hepatic vessels have myriads of schizont-laden macrophages with smaller numbers in the sinusoids that are like those described in the kidney. Scattered hepatocytes have golden brown pigment (hemosiderin) and/or greenish yellow pigment (bile) within the cytoplasm. Occasional macrophages contain erythrocytes (erythrophagocytosis).

**Morphologic diagnosis:** Kidney, lung, and liver, blood vessels (veins, arteries and arterioles): Histiocytosis, multifocal, mild to marked with intrahistiocytic intracytoplasmic schizonts, morphology consistent with *Cytauxzoon felis*

Liver: Hepatic necrosis, multifocal, marked with hemosiderosis, bile stasis and erythrophagocytosis

**Additional diagnostic tests:** Cytauxzoon PCR - Positive

**Comments:** Comments: *Cytauxzoon felis* is a protozoan hemoparasite in the family of Theileriidae that causes severe clinical disease and high mortality in domestic and exotic cats in the south central and southeastern United States. The natural reservoir is the North American bobcat (*Lynx fufus*) where the Cytauxzoon infection is usually subclinical. The infection is transferred from wild bobcats to domesticated cats by tick vectors (*Dermacentor variabilis* and *Amblyomma americanum*) causing clinical signs of depression, anorexia, pyrexia, dehydration, pallor, icterus, dark urine and dyspnea.

The life cycle of *C. felis* requires a hard tick vector as a definitive host and a felid host as an intermediate host. Both *Dermacentor variabilis* and *Amblyomma americanum* are competent vectors. Since there is no transovarial transmission, only nymphs and adults are infective to felids. All felids are capable hosts, but no other mammals are. Bobcats and domestic cats are the most common hosts. After inoculation by a tick vector during a blood meal, sporozoites directly enter macrophages of a felid host, in which they undergo schizogony, resulting in formation of mature schizonts that rupture the infected macrophages and release copious
merozoites. Numerous enlarged schizont-laden macrophages occlude small blood vessels of various organs, which is responsible for acute cytauxzoonosis. Merozoites enter erythrocytes, undergo binary fission, and ultimately kill their host cells, resulting in release of merozoites. Merozoites enter other erythrocytes, and the asexual cycle continues. Some intraerythrocytic merozoites differentiate into gametocytes, which are infectious for a tick vector. In the tick host, the gametocytes develop into ray bodies that fuse to form a diploid zygote in the gut. Zygoters mature into motile haploid kinetes that enter the tick's salivary glands, where they undergo multiple fission to produce numerous sporozoites that are infectious for a felid host.

References:


Case History:

Case #: Abbvie 18-067

Presenter: Rebecca Kohnken

Corresponding Institution: AbbVie

Signalment: 1 year, 10 month old male Fischer-344 (wild type) rat

History: This animal was noted to have increased respiratory effort and a necrotic tail tip. The rat was euthanized due to poor respiratory condition.

Gross findings: On gross examination, the spleen was noted to be enlarged, and the liver was mottled with a rough texture.
Case Synopsis:

Case #: Abbvie 18-067
Presenter: Rebecca Kohnken
Corresponding Institution: AbbVie

Signalment: 1 year, 10 month old male Fischer-344 (wild type) rat

Histopathology:

Section of kidney. The outer cortical surface of the kidney is diffusely irregular. There are two concurrent processes occurring in this tissue- a neoplastic disease and a degenerative disease. Firstly, throughout the cortex and medulla, interstitial and peri-tubular arterioles are mildly dilated and contain a monomorphic population of neoplastic round cells. Cell are large with distinct cellular boundaries, abundant pale basophilic occasionally granular cytoplasm, central round to oval to irregularly shaped nuclei with open chromatin and occasionally prominent nucleoli. Anisocytosis and anisokaryosis are mild and there is minimal atypia. Mitoses are rare. Secondly, throughout the cortex, approximately 25% of glomeruli are affected by a spectrum of changes that includes mild thickening of the glomerular basement membrane, hypertrophy of mesangial cells, segmental increases in extracellular matrix (sclerosis), and focal adhesion of the glomerular tuft to Bowman’s capsule (synechiae). Proximal convoluted tubules are frequently characterized by basophilic cytoplasm, increased thickness of the tubular basement membrane, and peri-tubular to interstitial fibrosis. Tubular epithelial cytoplasm often contains variably sized globular eosinophilic droplets, as well as stippled to globular brown-golden pigment. Multifocally, cortical tubules are mildly dilated and characterized by simplified and attenuated epithelium. Often these degenerate tubules are associated with interstitial infiltrates of lymphocytes and plasma cells as well as interstitial fibrosis. Multifocally within the medulla, mildly dilated tubules contain eosinophilic proteinaceous fluid within the lumen.

Morphologic diagnosis:

Kidney:

1) Large granular lymphocytic leukemia

2) Chronic progressive nephropathy (characterized by segmental glomerulosclerosis, intratubular protein, tubular basophilia, interstitial fibrosis)

Additional diagnostic tests: None

Comments:

This animal is part of a Fischer 344 colony and was not subjected to any experimental manipulation, nor exposed to any pharmaceutical test article. This case presents two concurrent diseases, each of which is not uncommon in aged male Fischer 344 rats.

The first is large lymphocytic granular (LGL) leukemia, a round cell neoplasm with a natural killer cell-like histogenesis. This neoplasm occurs in up to 59% of male Fischer 344 rats and is a major cause of death in aged animals. There are loose associations of increased incidence of LGL with oral gavage with oils and certain chemical exposures, as well as a lower incidence
with dietary restriction. Clinically, animals present with rapid and significant weight loss, and are often icteric. Other clinical signs may occur based on the organ involvement of the disease, as with the respiratory distress in this case resulting from pulmonary LGL. Clinical pathology can be useful in antemortem diagnosis of LGL. A typical hemogram would reveal the classical features of a hemolytic anemia with spherocytes, polychromasia (reticulocytosis), neutrophilia with a left shift, and thrombocytopenia. There may be variable numbers of the atypical neoplastic cells in circulation. These cells may feature erythrophagocytosis- which is also often observed in the spleen- and it is this activity of the neoplastic cells that results in spherocytic anemia and clinical icterus. Clinical chemistry often reveals hyperbilirubinemia and increased liver enzymes, which is due to hepatocellular degeneration that is often a feature of LGL. This may be due to hypoxia within the liver from sludging of blood through sinusoids clogged with neoplastic cells. Urinalysis, then, may reveal hemoglobinuria and bilirubinuria. Clotting abnormalities are also common, up to and including disseminated intravascular coagulation. A Coomb’s test can also be performed, which would demonstrate the presence of anti-erythrocyte immunoglobulin.

Typical gross findings include severe slenomegaly. LGL originates in the spleen, leading to diffuse expansion of the red pulp with neoplastic cells featuring erythrophagocytosis. The disease can variably disseminate to other organs. Note that the disease is referred to as leukemia, however it’s origination in the spleen and dissemination in the blood might warrant a designation of stage 5 lymphoma. Other gross findings would be dependent on the tissue involvement of the tumor. Histology is that of an intra-vascular round cell tumor. Cellular features, such as granulation of the cytoplasm, which lend this tumor its name, may be better appreciated in cytologic preparations.

The second disease process occurring in this case is that of chronic progressive nephropathy (CPN), a common age-related finding in rats. In fact, depending on the strain, CPN may occur in up to 75% of aged individuals. In addition to age (greater than 12 months), predisposing factors for development of CPN include sex (males more often affected than females), strain (high incidences observed in Sprague-Dawley and Fischer 344), diet (those higher in protein), immunologic factors (deposition of IgM within the mesangium may suggest an complement-mediated/immune component to disease pathogenesis, however immune complexes are not present), and endocrine factors (prolactin levels have been correlated to incidence). Clinically, affected rats lose weight. Diagnostic tests often reveal proteinuria, and advanced cases may be further characterized by azotemia. Proteinuria is due to loss of protein in the glomerular filtrate. In advanced disease, renal insufficiency and renal failure may occur, leading to the well-described sequelae of kidney disease in any species, including secondary hyperparathyroidism.

Though this case does not represent a toxic response to a test article, the findings present are relevant for toxicologic pathologists. So-called background findings are those that naturally occur in a species, such as LGL leukemia and CPN, that may obscure or confound a finding associated with toxicity. The pathologist must be familiar with the features of these spontaneous diseases so as to distinguish them from possible toxic effects.

References:


Percy, D.H. and S.W. Barthold, Pathology of Laboratory Rodents and Rabbits, 3rd Ed. 2012
Case History: Intrapulmonary sequestrum in a dog

Case #: SP-18-3760

Presenter: Michelle Magagna, DVM and Kurt Williams, DVM, PhD

Corresponding Institution: Michigan State University Veterinary Diagnostic Laboratory

Signalment: 1-year-old male neutered Wirehaired Pointing Griffon dog

History:
A 1-year-old neutered male Wirehaired Pointing Griffon presented with a 2-3 day history of lethargy, dyspnea, pyrexia, and coughing. Bloodwork revealed a leukocytosis. A thoracic CT scan was performed, and findings were suggestive of right middle lung lobe torsion with subsequent necrosis. The hilar bronchus supplying this lobe was noted to be focally narrowed, and a large vessel was identified adjacent to this bronchus. The dog was taken to surgery and a right middle lung lobectomy was performed. The right middle lung lobe was noted to be enlarged and “emphysematous.” The dog recovered uneventfully, and the lung was submitted to the Michigan State University Veterinary Diagnostic Laboratory for histopathologic examination.

Gross findings:
On gross examination of the formalin-fixed right middle lung lobe, a fairly well-demarcated region of pulmonary parenchyma within the distal aspect of the lobe was replaced by variably-sized cystic spaces ranging from 0.2-1.5 cm in diameter. Few cysts were lined by bright yellow-orange material. The hilar bronchus at the proximal surgical margin of the lobe appeared abnormally small. This bronchus was opened and traced distally, and few gelatinous tan accumulations of mucus and inflammatory debris were located within the lumen of the distal airways. A definitive area of bronchial compression or obstruction was not identified. A large blood vessel located adjacent to the hilar bronchus was noted extending down the pleural surface, branching over the cystic region in the distal portion of the lung lobe.
Case Synopsis: Intrapulmonary sequestrum in a dog

Case #: SP-18-3760

Presenter: Michelle Magagna, DVM and Kurt Williams, DVM, PhD

Corresponding Institution: Michigan State University Veterinary Diagnostic Laboratory

Signalment: 1-year-old male neutered Wirehaired Pointing Griffon dog

Histopathology:

Normal pulmonary architecture within the distal aspect of the lung lobe was diffusely replaced by variably enlarged airspaces interspersed with bands of dense fibrosis and granulation tissue. Airspaces and bronchiole lumens multifocally contained accumulations of neutrophils or foamy vacuolated histiocytes admixed with occasional multinucleated giant cells. Many histiocytes were laden with granular brown hemosiderin pigment. Few locally extensive areas of hemorrhage, fibrin deposition, and necrosis were scattered throughout the sections. Alveolar septae were expanded by moderate infiltrates of neutrophils and contained scattered foci of dystrophic mineralization. There were multiple profiles of markedly thick-walled arteries extending along the pleural surface and adjacent to bronchovesicular bundles in the region of the hilus. Verhoeff van-gieson staining highlighted an internal and external elastic lamina for many of these enlarged vascular profiles, consistent with a systemic arterial origin. Vessels throughout the pulmonary parenchyma frequently contained increased numbers of circulating leukocytes and intraluminal fibrin aggregates. Pulmonary architecture was largely intact in the proximal portion of the lung lobe. Alveolar septa in this region were multifocally expanded by neutrophils, and alveoli contained scattered neutrophils and histiocytes.

Morphologic diagnosis: Lung: Suspected intralobar pulmonary sequestrum

Additional diagnostic tests: N/A

Comments:

Pulmonary sequestration is a rarely reported condition in human medicine and has not yet been described in veterinary species. This condition is classified within the spectrum of congenital lung malformations, and is defined as an abnormal mass of pulmonary parenchyma that is disconnected from the proximal tracheobronchial tree and supplied by an aberrant systemic artery rather than the normal pulmonary circulation. Pulmonary sequestra are further characterized as either extralobar or intralobar. Extralobar sequestra are distinct masses that are separate from the normal lung lobes and encased in their own layer of pleura. Intralobar sequestra occur within the pulmonary parenchyma (usually within the distal aspect of a lobe) and are contained within the normal visceral pleura. In both forms, the affected pulmonary parenchyma undergoes marked cystic change secondary to air-trapping and frequently develops localized pockets of secondary necrosis and inflammation. Diagnosis of pulmonary sequestration depends on identification of the aberrant systemic feeding vessel. In most cases, this vessel arises directly from the thoracic aorta or one of its branches and often is found running down the pleural surface of the lobe, unassociated with the normal bronchovascular bundles. Histologically, these feeding vessels should have an internal and an external elastic lamina, identifying them as being of systemic origin.
The underlying developmental defects resulting in pulmonary sequestration have not been definitively characterized, but some degree of bronchial atresia or obstruction is identified in most cases. Bronchial atresia is not unique to pulmonary sequestration, and is central to the pathogenesis of many other cystic congenital lung malformations. The defining feature of pulmonary sequestration that allows it to be differentiated from other congenital cystic conditions is the presence of an aberrant systemic feeding artery.

Despite the congenital nature of pulmonary sequestration, these lesions in humans often are asymptomatic and will go unnoticed until later in life when the patient presents with secondary infection or intrapulmonary hemorrhage. Surgical removal is the recommended treatment and is considered curative. In this case, the dog recovered uneventfully after surgical removal of the affected lung lobe and has remained apparently healthy since.

References:

Case History:

Case #: 18-1062

Presenter: James P Cronin

Corresponding Institution: The Ohio State University

Signalment: 5 year old spayed female mixed breed dog

History: Polyuric over last 48 hours. Intractable vomiting over last 24 hours. Abdomen painful on palpation. Severe azotemia (BUN too high to read, Creatinine 13.6). Urine specific gravity 1.014. Abdominal radiographs revealed intragastric foreign material. Euthanasia elected.

Gross findings:
The kidneys were pale tan, soft to firm, and contained an irregularly depressed cortical surface.

The stomach was filled with dark red, gelatinous exudate (hemorrhage), and the gastric mucosa contained dozens of well-demarcated, irregularly shaped, dark red foci that ranged from pinpoint to 1.5 cm in diameter.

There was a 1.0 x 0.5 cm, firm to hard, slightly raised, roughened, dark red focus on the intimal surface of the main pulmonary artery.
Case Synopsis:

Case #: 18-1062

Presenter: James P Cronin

Corresponding Institution: The Ohio State University

Signalment: 5 year old spayed female mixed breed dog

Histopathology: 2 slides submitted.

Slide 1: Stomach and main pulmonary artery

Slide 2: Kidney (2 sections)

Morphologic diagnosis:

Stomach: Multifocal, marked mineralization of tunicae mucosa, submucosa (most prominently affecting arteriolar tunica intima), and muscularis that is frequently associated with coagulative necrosis, associated neutrophilic inflammation, and hemorrhage.

Main pulmonary artery: Focally extensive, marked fibrinoid vascular necrosis of vasa vasorum with necrosis and mineralization of underlying tunica media and hemorrhage. Focally extensive, marked intimal mineralization with necrosis.

Kidney (2 sections): Diffuse, marked, acute tubular necrosis with mineralization superimposed on diffuse, marked, chronic sclerosing and proliferative glomerulonephropathy with tubular degeneration and atrophy, interstitial fibrosis, and lymphoplasmacytic interstitial nephritis.

Additional diagnostic tests: Special stains: Von Kossa on slide 1. Masson’s Trichrome, Jones’ Silver, and PAS on slide 2. Results will be revealed in Powerpoint presentation.

Comments:

This case provides an excellent example of glomerulopathy-induced renal failure and nonrenal lesions of uremia in a dog. Our primary differential diagnosis for this lesion is membranoproliferative glomerulonephritis (MPGN), which is caused by immune-complex deposition on the luminal (subendothelial) surfaces of capillary walls and the resultant inflammatory response. TEM and IF are needed to definitively identify the presence of immune-complex deposits and differentiate MPGN from other membranoproliferative patterns of glomerular injury. Other causes of a membranoproliferative pattern of glomerular injury include thrombotic microangiopathy and C3 glomerular nephritis. In this case, the resultant tubulointerstitial effects of chronic glomerular disease are evident (interstitial fibrosis, tubular degeneration and atrophy, and lymphoplasmacytic interstitial nephritis).

In uremic gastropathy, large areas of gastric mucosa are often swollen, suffused with red-black blood, and may be mineralized or ulcerated. Mucosal infarction occurs secondary to arteriolar necrosis and/or thrombosis. Mineralization of the middle and deep zones of the gastric mucosa is common. Necrosis and mineralization of the muscular tunics are sometimes present (as in this case).

The left atrium is a common site of mineralization and necrosis in uremic dogs. In this case, the main pulmonary artery was affected.
References:


Case History:

Case #: 17B840

Presenter: Laura Lee, DVM

Corresponding Institution: University of Wisconsin-Madison

Signalment: 8-year-old neutered male longhaired Dachshund dog

History:

The dog presented with a six-month history of episodic rectal prolapse, tenesmus, hematochezia, and diarrhea. Three biopsies had previously been performed over a fourth month period. One was from manually exfoliated tissue and two were from endoscopically collected tissue. The manually exfoliated tissue was diagnosed as “inflammatory polyp with ulceration,” and the endoscopic biopsies were diagnosed as “mild to moderate chronic lymphoplasmacytic gastroenterocolitis” and “colorectal polypoid hyperplasia with severe ulcerative, suppurative, and lymphoplasmacytic colitis (inflammatory polyp)”, respectively. There was no evidence of invasion below the mucosa in any sample. After concern for neoplastic transformation, the dog presented for CT scan and excisional biopsy. CT revealed several soft tissue attenuating and heterogeneously enhancing concentric rectal luminal nodules and masses. Surgery revealed numerous polyps and multifocal areas of necrotic tissue in his distal colon.

Gross findings:

A 6.0 cm long section of colonic and rectal tissue is received. The mucosa exhibits a diffuse irregular and proliferative appearance; it is approximately 1.5 cm thick and on cut section, some of the proliferative areas are dark brown.
Case Synopsis:

Case #: 17B840

Presenter: Laura Lee, DVM

Corresponding Institution: University of Wisconsin-Madison

Signalment: 8-year-old neutered male longhaired Dachshund dog

Histopathology:

Examined are full thickness sections of large intestinal mucosa in which multifocally expanding the mucosa are moderately demarcated polypoid structures lined by a segmentally attenuated, eroded and ulcerated epithelium. The masses are predominately composed of large lakes of a wispy pale amphophilic to basophilic material (mucus), numerous plump fibroblasts (reactive), and small vascular profiles lined by plump endothelial cells (vascular proliferation). Often fibroblasts are arranged perpendicularly to these vessels (granulation tissue). There are a few small superficial tortuous glandular structures lined by dysplastic epithelium characterized by mild cellular crowding, and loss of cellular polarity, though these foci are seen in the areas where are numerous neutrophils, lymphocytes, and plasma cells. Some of this glands are dilated and contain mucus. There are also multiple areas of bone (osseous metaplasia). The adjacent mucosa exhibits mild glandular ectasia and increased numbers of goblet cells; a few of the dilated glands contain eosinophilic cellular and karyorrhectic debris (crypt abscesses). Within the submucosa there are a few foci of glandular herniation in the region of a lymphoid aggregate; these glands do not exhibit cellular atypia. A few scattered inflammatory cells extend to the submucosa including neutrophils, lymphocytes, and plasma cells. There are multifocal areas of acute hemorrhages along the muscular layers (most likely surgical).

Morphologic diagnosis:

Marked multifocal to locally extensive colorectal polypoid hyperplasia with cystic mucous glands, multifocal mucosal ulceration, osseous metaplasia, and neutrophilic and lymphoplasmacytic colitis (colorectal inflammatory polyp)

Additional diagnostic tests: N/A

Comments:

Histopathological findings including mild to severe leukocyte infiltration, interstitial accumulation of mucus, proliferation of granulation tissue, and osteoid formation are consistent with colorectal inflammatory polyps of Miniature Dachshunds. In Japan, there is a marked breed predilection for colorectal inflammatory polyps in Miniature Dachshunds. Inflammatory polyps in Miniature Dachshunds (IPMD) have been proposed as a novel form of inflammatory bowel disease. The clinical presentation is characterized by periodic intermittent large bowel diarrhea, hematochezia, and/or tenesmus. The polyps are located in the descending colon and rectum and endoscopically appear as single or multiple irregularly thickened, protruding mucosal outgrowths. Histologically, lesions are characterized by thickened mucosa with goblet cell hyperplasia and increased mucus production, dilated crypts with abundant mucinous material as well as interstitial accumulation of mucus or cystic spaces filled with mucinous material, mild to severe leukocyte infiltration, proliferation of granulation tissue, and osteoid formation. IPMD are classified into 3 stages based on epithelial and inflammatory components. Stage 1 polyps have
more epithelial tissue and a predominantly lymphocytic inflammatory infiltrate compared to stages 2 and 3, which have less epithelial tissue, more granulation tissue, and more severe, predominantly neutrophilic and histiocytic inflammatory infiltrate.7,8

Researchers have implemented immunohistochemistry to better characterize IPMD and distinguish them from neoplastic cells of adenomas and adenocarcinomas. Non-dysplastic epithelial cells in IPMD exhibit positive staining for CK20 and negative staining for beta catenin, whereas adenomas and adenocarcinomas are negative for CK20 and positive for beta catenin. Further, inflammatory polyps exhibit greater COX-2 and FGF-2 staining than adenomas and adenocarcinomas. Dysplastic cells seen in stage 3 IPMD exhibit negative CK20 and positive beta catenin staining and could represent neoplastic transformation.7

This case describes colorectal inflammatory polyps in a Dachshund living in Madison, Wisconsin. Although colorectal inflammatory polyps in Miniature Dachshunds have been well-characterized in Japan, they have not previously been described in the United States. Further, the Dachshund in this case is not miniature based on client reported size or recorded patient weight ("miniature" is defined as 11 pounds and under at 12 months of age and over by the American Kennel Association). This case suggests that all sizes of Dachshund may have a predilection for colorectal inflammatory polyps.

References:

Case History:

Case #: 10-434
Presenter: Dane Rahoi, DVM
Corresponding Institution:
The University of Tennessee College of Veterinary Medicine
Signalment: Tennessee walking horse, 13 year-old, female

History:
This horse was presented to the University of Tennessee College Of Veterinary Medicine for acute onset lethargy and decreased appetite. The owner reported that horse had been previously normal and began acting depressed after a recent storm had blown down several tree limbs within the horse’s pasture. Upon presentation the gums and conjunctiva were pale yellow (icterus). Packed cell volume (PCV) was 20% and total protein (TP) was 7.8 g/dL at presentation. During hospitalization the horse began passing dark brown urine and PCV continued to decrease, reaching 15%. The horse became markedly azotemic and the owners elected euthanasia on the third day of hospitalization.

Gross findings:
A 379kg 13 year-old Tennessee walking horse mare presents for necropsy in good body condition (body condition score 3/5) and fair postmortem condition. Bilaterally within the renal cortex and medulla are multifocal very thin linear, up to approximately 20mm long x 1mm wide, black streaks.
Case Synopsis: Hemoglobinuric nephrosis (Red Maple Toxicity) in a Tennessee Walker Horse

Case #: 10-434

Presenter: Dane Rahoi, DVM

Corresponding Institution:
The University of Tennessee College of Veterinary Medicine

Signalment: Tennessee walking horse, 13 year-old, female

Histopathology:
Throughout the cortex, tubules often contain variable accumulations of bright red-to-orange granular material (hemoglobin). The material is multifocally admixed with neutrophils, sloughed epithelial cells, and karyorrhectic debris. The affected tubular epithelium is variably attenuated and epithelial cells occasionally contain pale to hyper eosinophilic cytoplasm with pyknotic and karyorrhectic nuclei (degeneration and necrosis). There are multifocal interstitial aggregates of perivascular neutrophils and lymphocytes throughout the cortex. Medullary tubules also contain rare accumulations of bright red-to-orange granular material. Throughout the cortex tubules also less frequently contain round pale yellow to amphophilic birefringent crystals (calcium carbonate).

Morphologic diagnosis: Marked acute multifocal tubular degeneration and necrosis with intratubular hemoglobin (hemoglobinuric nephrosis)

Comments: Marked acute tubular necrosis with intratubular hemoglobin is consistent with hemoglobinuric nephrosis secondary to acute hemolytic anemia. The signalment and history combined with the clinical, gross, and histologic findings in this case are highly suggestive of red maple (Acer rubrum) toxicity. Ingestion of red maple leaves can cause potentially fatal hemolytic anemia, methemoglobinemia, pigmentary nephrosis, and ischemic tubular necrosis in horses. This occurs due to oxidative damage to equine erythrocytes, although the specific toxic principles are only recently being understood. It has been previously implicated that gallic acid and tannins, which are present in red maple leaves, were the primary oxidants in red maple toxicity (1). However it has been shown that oxidative damage is also brought about through the metabolism of these compounds by bacterial flora of the ileum to produce a more potent oxidizing agent, pyrogallol (2). It is through the oxidative actions of pyrogallol that hemolysis is thought to primarily occur in red maple toxicity.

References:


Case History:

Case #: A18-3553

Presenter: Agnes Wong

Corresponding Institution: Purdue University

Signalment: 6-month-old, intact male, Sprague Dawley rat

History: This rat presented to the Animal Disease Diagnostic Laboratory with a history of progressive weight loss. The animal was reported to have lost 17% of its body weight over a one week period.

Gross findings:

Multiple, linear, white to pale-tan, firm, chalky streaks are along the left epicardium and extend into the left ventricular endocardium and interventricular myocardium.

Diffusely, multiple irregular depressions are along the capsular surface of both kidneys and extend roughly 1-2 mm into the parenchyma. The cortices of both kidneys are mottled pale-tan to dark red with multiple cysts ranging from pinpoint to 1.5 cm in diameter.
**Case Synopsis:**

**Case #:** A18-3553  
**Presenter:** Agnes Wong  
**Corresponding Institution:** Purdue University  
**Signalment:** 6-month-old, intact male, Sprague Dawley rat

**Histopathology:**

Heart: In approximately 90% of the sections examined, the myofibers of the endocardium, myocardium, and epicardium are necrotic or degenerate. Degenerate cardiomyocytes are swollen and have cytoplasmic vacuolation. Necrotic cardiac myocytes are hypereosinophilic, shrunken and fragmented with pyknotic or karyolytic nuclei. Separating, surrounding, and replacing degenerate and necrotic cardiac myofibers, are abundant basophilic granular material (mineral) and increased immature and mature collagen (fibrosis). Inflammatory cells composed of macrophages, lymphocytes and plasma cells, infiltrate necrotic and mineralized tissue. Similar inflammation is moderate in non-mineralized necrotic regions of the heart.

**Morphologic diagnosis:**

Heart: Myocardiocyte mineralization, degeneration, necrosis and fibrosis with lymphohistiocytic myocarditis

**Comments:**

This rat had concurrent renal lesions (tubular ectasia with protein casts, interstitial fibrosis, and interstitial nephritis) consistent with chronic progressive nephropathy. The extensive myocardiocyte mineralization was likely caused by mineral imbalance secondary to renal failure and dysfunction. There are two forms of pathologic tissue mineralization/calcification: dystrophic and metastatic calcification. Dystrophic mineralization of dead tissue is a result of biochemical processes leading to increased intracellular calcium during necrosis. Metastatic calcification of vessels is due to the imbalance in calcium and phosphate concentrations in the blood secondary to renal disease, primary hyperparathyroidism, or vitamin D toxicosis.

Metastatic calcification can occur on the intima and media of vessels and was once considered to be a passive process of mineral deposition as calcium and phosphate concentrations increased. Research on vascular calcification secondary to chronic kidney disease (CKD) in the past decade have demonstrated that metastatic calcification is an active process involving changes in osteochondrogenic regulatory proteins. An imbalance of calcification promotors and inhibitors and a switch in vascular smooth muscle cell (VSMC) phenotype are few of the cellular changes involved in vascular calcification. Inhibitors of osteochondrogenic mineralization including matrix γ-carboxyglutamic acid protein, osteoprotegerin, and osteopontin, are decreased in patients with CKD. VSMCs have an increased expression of osteochondrogenic transcription factors such as Runx2, Msx2, and Sox9, which alters the cell and promotes an osteochondrogenic phenotype. These recent
highlights demonstrate that metastatic mineralization is an active cellular process and not a passive accumulation of mineral on tissue.

References:


Case History:

Case #: 18RD0840

Presenter: Gillian C. Shaw

Corresponding Institution: Comparative Ocular Pathology Laboratory of Wisconsin, School of Veterinary Medicine, Madison, WI

Signalment: 9-year 10-month-old neutered male schnauzer / poodle mix

History: Anterior lens luxation that led to glaucoma, duration of 4 days.

Gross findings: The globe was buphthalmic, there was a corneal ulcer with stromal infiltrate. The lens was cloudy and in its normal location. The iris and ciliary body were lined by white tissue/exudate. The aqueous humor and vitreous were cloudy and gelatinous. The optic nerve head was difficult to see.
Case Synopsis:

**Case #:** 18RD0840

**Presenter:** Gillian C. Shaw

**Corresponding Institution:** Comparative Ocular Pathology Laboratory of Wisconsin, School of Veterinary Medicine, Madison, WI

**Signalment:** 9-year 10-month-old neutered male schnauzer / poodle mix

**Histopathology:** Histologically, abundant lymphocytes and plasma cells infiltrate the entire uveal tract and multiple layers of epithelioid macrophages and neutrophils carpet the anterior uveal surfaces and the peripheral posterior cornea. Abundant macrophages along with lymphocytes and plasma cells infiltrate through the sclera into the episcleral tissues and an extraocular muscle and tendon. A fibrovascular membrane containing numerous inflammatory cells lines the anterior iris surface, crosses the iridocorneal angle causing peripheral anterior synechia and continues posteriorly as a postiridal fibrovascular membrane where it blends with a cyclitic membrane. The lens capsule is ruptured and there is extensive cortical lens fiber liquefaction with multifocal perinuclear lenticular mineralization. Lens fibers mingle with suppurative exudate within the anterior and posterior chambers. The anterior and posterior chambers, vitreous and subretinal space contain abundant fibrillar and homogeneous eosinophilic proteinaceous material with viable and degenerate neutrophils. Globules and “donuts” of homogenous eosinophilic material, interpreted as extralenticular leakage of liquefied lens protein, are present in the anterior and posterior chambers and vitreal space. Macrophages and neutrophils associated with these proteinaceous globules frequently contain similar brightly eosinophilic material, consistent with phagocytosis (“phakophagocytes”). The ciliary body exhibits focally extensive necrosis. The corneal epithelium is keratinized and axially ulcerated. The corneal stroma is infiltrated by neutrophils and peripherally vascularized. The retina is completely detached and diffusely necrotic and multifocally identifiable only by naked blood vessels. The optic nerve head is infiltrated by previously described inflammatory cells, deeply cupped, atrophied, and gliotic.

**Morphologic diagnosis:**
1. Anterior lens luxation, as per history
2. Severe pyogranulomatous and lymphoplasmacytic panophthalmitis with epithelioid macrophage carpeting and free lens proteins consistent with severe “lens-induced uveitis”
3. Buphthalmos
4. Corneal ulceration with moderate neutrophilic keratitis
5. Pre-postiridal fibrovascular and cyclitic membranes
6. Peripheral anterior synechia
7. Hypermature cataract with lens capsule rupture
8. Focally extensive ciliary body necrosis
9. Complete retinal detachment and diffuse retinal necrosis
10. Chronic secondary glaucoma

**Additional diagnostic tests:** None

**Comments:** It is known that if there is release of lens protein into the eye, it incites an inflammatory response, known as “lens-induced uveitis” (reviewed by van der Woerdt, 2000). Lens protein release can be the result of cataractous degeneration and leakage of liquefied lens.
fibers from a lens with intact lens capsule, or it can be caused by release of lens protein following lens capsule rupture, which can be either due to trauma or, in dogs, secondary to intumescent (and often “diabetic”) cataracts. In the majority of canine cases, the release of lens protein (whether from an intact or a ruptured lens) incites a "bland uveitis,” meaning a mild to moderate inflammatory response, manifesting as lymphoplasmacytic infiltration of the uvea and a small number of macrophages on the uveal surfaces with or without fibrovascular membrane and synechia formation. This has been termed “phacolytic” uveitis, when the lens capsule is intact and histologically obvious lens material is rarely found outside of the lens or “phacoclastic” uveitis when the lens capsule is ruptured. It can lead to secondary glaucoma due to fibrovascular membrane and synechia formation.

Another type of lens-induced uveitis, which is presented in this case of a 9-year-old schnauzer/poodle mix dog, represents a much more intense and severe lens-induced uveitis characterized by the presence of a carpet of granulomatous inflammation on the surface of the uveal tract in addition to lymphoplasmacytic uveal stromal infiltration and fibrovascular membrane and synechia formation. It is frequently accompanied, as in this case, by histologically apparent extralenticular leakage of liquefied lens protein and by retinal necrosis and secondary glaucoma. We believe that this disease is an exaggerated hypersensitive reaction against lens protein, which only certain dogs develop. It more often affects small breed dogs with poodle, dachshund and schnauzer topping the list. We have found that this diagnosis predicts problems in the second eye from what we consider to be hypersensitization of the immune system to lens protein. We warn clients that careful monitoring and prophylactic anti-inflammatory treatment is sometimes helpful in preventing serious disease in the second eye.

We have termed this type of severe lens-induced uveitis “asymmetric uveitis,” which was chosen to contrast it to the uveitis associated with canine uveodermatologic syndrome or VKH-like syndrome, another severe intraocular inflammatory response in which both eyes are affected “symmetrically” and simultaneously. In this severe lens-induced (i.e. “asymmetric”) uveitis it is more typical for one eye to develop the disease followed by the second eye at some point in the future unless, and sometimes despite, appropriate anti-inflammatory treatment. Occasionally, if an ophthalmologist is suspicious of this syndrome, he or she can attempt cataract removal from the remaining eye at the same time as enucleation of the affected eye, to try to prevent the inflammatory reaction to lens material and loss of vision.

A more severe variant of this disease is seen in diabetic dogs. In these cases, it is typical for both eyes to develop disease simultaneously, which we jokingly/confusingly refer to as “symmetric asymmetric uveitis,” when discussing cases around the multiheaded microscope. The miniature schnauzer breed is vastly over-represented in this diabetic variant of asymmetric uveitis, probably because of its propensity to develop diabetes mellitus.

The terms “phacolytic” and “phacoclastic” are somewhat confusing and fall under the “umbrella” classification of “lens-induced.” Thus, in COPLOW, when diagnosing the “bland” and less severe variety, we favor the broader and more self-explanatory term “lens-induced uveitis” and we diagnose “asymmetric uveitis” with this more severe form of lens-induced uveitis that predicts problems in the remaining eye.

We feel that “phacoclastic uveitis,” is more appropriate when there is trauma (blunt or penetrating) leading to lens capsule rupture and subsequent intraocular inflammation. As a result of a penetrating contaminated trauma causing lens capsule rupture, the globe might
develop a widespread severe endophthalmitis with intraocular bacteria in addition to uveal stromal inflammation. A specific type of penetrating injury with focal lens capsule rupture and seeding of microorganisms directly into the lens can be accompanied by relatively localized lens-centric endophthalmitis where bacteria can often be found in the lens. We call this specific lesion/phenomenon “septic implantation syndrome.” which is a story for another day.

A differential for globes with granulomatous or pyogranulomatous inflammation is a fungal infection, such as *Blastomyces dermatitidis* for example, and thus fungal infections should be ruled out.

For board prep histo-writing practice and exercise here is a suggested point break-down for a description and morphologic diagnosis. (Disclaimer – I’ve never served on the exam committee, so I have no idea if this is a reasonable point break down.)

Descriptive points:
- Ulcerative and suppurative keratitis with peripheral stromal vascularization (1 pt)
- Lymphoplasmacytic uveal stromal (1 pt)
- Lymphoplasmacytic and granulomatous scleral and optic nerve inflammation (2 pts)
- Macrophage and neutrophil carpeting uveal surfaces (1 pt)
- Pre- and postiridal fibrovascular membranes (1 pt)
- Peripheral anterior and posterior synechiae (2 pts)
- Ciliary body necrosis (1 pt)
- Hypermature cataract (liquefaction of lens cortex with mineral) with lens capsule rupture (2 pts)
- Free lens protein (1 pt)
- Diffuse retinal detachment and necrosis (2 pts)
- Optic nerve head cupping (1 pt)

Morphologic diagnosis: Severe pyogranulomatous and lymphoplasmacytic (1 pt) lens-induced/phacoclastic (1 pt) panophthalmitis with hypermature cataract (0.5 pt) and lens capsule rupture (0.5 pt), diffuse retinal detachment and necrosis (1pt) and chronic secondary glaucoma (1 pt)

References:

Case History:

Case #:  
A18-8135 and A18-8136

Presenter:  
Jessica Hanlon

Corresponding Institution:  
Purdue University

Signalment:  
Two, intact male, wild, adult, white-tailed deer

History:  
Two, intact male, wild, white-tailed deer were submitted by the Indiana DNR to the Animal Disease Diagnostic Laboratory for necropsy. The deer were reportedly spinning in circles with their tongues hanging out, and they were easily approachable.

Gross findings:  

Deer 1: Pale green, viscous, purulent material is ventral to the subcutaneous tissue at the dorsomedial aspect of the skull between the two antlers; the purulent material extends through the left parietal bone. The left cerebrum contains two, approximately 2.5 X 2 cm abscesses within the parenchyma.

Deer 2: A pale green, viscous, purulent material extends from the subcutaneous tissue between the antlers through the parietal bone, into the right cerebrum. The right cerebrum has an approximately 1 X 3 cm abscess. The parietal bone of the skull between the two antlers has two defects. The first is more rostral, approximately 0.5 X 0.2 cm, and extends through the entire bone into the brain parenchyma. The second is approximately 0.7 X 0.2 cm and does not extend through the entire thickness of the parietal bone.
Case Synopsis:

Case #:
A18-8135 and A18-8136

Presenter:
Jessica Hanlon

Corresponding Institution:
Purdue University

Signalment:
Two, intact male, wild, adult, white-tailed deer

Histopathology:
Brain (deer 1 and 2): A focally expansive abscess invades and replaces the white and gray matter of the cerebrum. The abscess is characterized by a large, necrotic center containing basophilic, bacterial clusters surrounded by many degenerate neutrophils, cellular debris, karyorrhectic debris, and few eosinophils. The necrotic center is surrounded by a thick band of fibrous connective tissue. Many macrophages, lymphocytes, plasma cells, and eosinophils infiltrate the band of fibrous connective tissue. A similar population of inflammatory cells cuffs the cerebral and meningeal arteries and veins. This inflammatory population traverses the vessel wall (vasculitis) of several of the vessels. The leptomeninges are invaded by many macrophages, lymphocytes, and plasma cells. The neuropil adjacent to the abscess is vacuolated and has increased clear space (edema) and is markedly infiltrated (multifocally) by mixed inflammation.

Morphologic diagnosis:
Brain: Cerebral abscess, focally expansive with lymphoplasmacytic and histiocytic meningoencephalitis, perivasculitis, and vasculitis

Additional diagnostic tests:
Deer 1: Representative samples of brain and a swab of the abscess were both positive for *Trueperella pyogenes* on bacterial culture. The brain also cultured positive for *Fusobacterium necrophorum*. CWD testing (IHC on lymph node and obex) was negative.
Deer 2: Representative samples of brain and a swab of the abscess were both positive for *Fusobacterium necrophorum* and *Proteus sp*. CWD testing (IHC on lymph node and obex) was negative.

Comments:
The clinical signs in both deer are attributed to the cerebral abscesses. Cerebral abscesses have been described as a cause of both morbidity and mortality in white-tailed deer in different areas of the United States and Canada. Clinical signs of infected deer may include one or more of the following: lack of fear, circling, blindness,
emaciation, weakness, incoordination, depression, lameness, and fever.\textsuperscript{1,4} Although the reported prevalence is low (2.2% in one study\textsuperscript{1}, 2.5% in another\textsuperscript{2}, and 4% in a third\textsuperscript{4}), the actual overall prevalence may be higher as intracranial abscesses can cause the clinical signs listed above which can lead to the deer being more susceptible to predation, being hit by a car, et cetera.

The risk factors for cerebral abscesses include trauma (i.e. antler fracture, sparring injuries, rubbing antlers on trees) and/or nutritional stress during the rut season.\textsuperscript{2,4} The rut season coincides with when the majority of cases of cerebral abscesses are seen in wild deer: between the months of October and March/April.\textsuperscript{1,4} Males are more likely to have an intracranial abscess (87% of the cases of the intracranial abscesses in the study by Baumann et. al.) compared to females.\textsuperscript{1} Infection can occur via direct extension (such as following trauma) or hematogenous spread.\textsuperscript{4}

Gross lesions can include the cerebral abscess +/- pitting/erosion most often of the frontal and/or parietal bones. The cerebral abscesses are typically 1-3 cm and contain yellow to pale green purulent material.\textsuperscript{4} When only skeletal remains are available, this pitting/erosion, could be used to identify deer that potentially died due to a cranial abscess.\textsuperscript{1,4} Histologically, the abscesses may also be accompanied by a meningoencephalitis.\textsuperscript{4}

In a study done by Baumann et. al.\textsuperscript{1}, \textit{Trueperella pyogenes} was isolated from 61% of the cranial abscesses. Other studies also found \textit{T. pyogenes} to be the most commonly isolated organism as well.\textsuperscript{3,4} Other bacteria cultured include the following (listed in no particular order): \textit{Proteus sp.}, \textit{Streptococcus sp.}, \textit{Staphylococcus sp.}, \textit{Escherichia sp.}, \textit{Serratia sp.}, \textit{Bacteroides sp.}, \textit{Klebsiella sp.}, \textit{Pasteurella sp.}, \textit{Citrobacter sp.}, \textit{Pseudomonas sp.}, \textit{Bacillus sp.}, \textit{Aeromonas sp.}, \textit{Fusobacterium sp.}, \textit{Enterococcus sp.}, \textit{Listeria sp.}, \textit{Salmonella sp.}, \textit{Alcaligenes sp.}, and \textit{Hafnia sp.}\textsuperscript{1}

Since the two deer submitted to the diagnostic lab were found circling in the same area, it is possible that they developed the cerebral abscesses after sparring with each other at a previous point in time.

References:

Case History:

Case #: 17RD3607

Presenter: Alex Harvey

Corresponding Institution: Comparative Ocular Pathology Laboratory of Wisconsin (University of Wisconsin – Madison)

Signalment: 2.5-year-old spayed female basset hound

History: The dog presented with a ~1 week history of conjunctivitis, uveitis with secondary glaucoma, and a lateral swelling of the sclera. Ultrasound revealed a mass within the ciliary body laterally.

Gross findings: The globe (OS) is sectioned slightly oblique from horizontal. Effacing and replacing the temporal ciliary body, there is a firm, white to tan, papillary mass which displaces the lens and distorts the temporal sclera. There is a moderate amount of hemorrhage in the posterior chamber and the retina is diffusely detached.
Case Synopsis:

Case #: 17RD3607

Presenter: Alex Harvey

Corresponding Institution: Comparative Ocular Pathology Laboratory of Wisconsin (University of Wisconsin – Madison)

Signalment: 2.5-year-old spayed female basset hound

Histopathology:

Histologically, an unencapsulated, extensively necrotic, poorly demarcated neoplastic population of cells is associated with the ciliary body and extends as a mass into the posterior chamber. The neoplasm extends through the limbal sclera. The neoplastic cells are polygonal to spindle shaped with variably distinct cell borders and are arranged in disorganized layers surrounding lamellated eosinophilic material interpreted as keratin. Within the lamellated keratin, there are very pale staining, amphophilic, and degenerate cells interpreted as ghost cells. More basal/inner layers exhibit smaller amounts of more basophilic cytoplasm, while more superficial/outer layers exhibit larger amounts of eosinophilic and keratinized cytoplasm, consistent with squamous differentiation. Nuclei are round, oval, or elongated with homogenous to finely stippled chromatin and one to two variably distinct nucleoli. Cellular pleomorphism is moderate, and there are 2-3 mitotic figures per 400x field. Occasional layers of more keratinized cells contain variably sized and amorphous brightly eosinophilic granular material, interpreted as trichohyalin granules, and variably sized deeply basophilic granular material, interpreted as keratohyalin granules. Extensive areas of necrosis affect approximately 90% of the tumor and pyogranulomatous inflammation infiltrates the necrotic areas.

The corneal epithelium is keratinized, and the stroma is infiltrated by a small number of neutrophils with peripheral stromal vascularization. A fibrovascular membrane covers the anterior iris surface and crosses the iridocorneal angle, causing peripheral anterior synechiae, and continues posteriorly causing posterior synechiae. Lymphocytes and plasma cells infiltrate the iris stroma. Homogenous, eosinophilic proteinaceous material fills the anterior chamber, and there is a moderate amount of hemorrhage in the posterior chamber. The lens exhibits cortical lens fiber liquefaction with morgagnian globule formation adjacent to the mass. (Lens protein in the posterior chamber is interpreted as artifact.) The retina is diffusely detached with minimal subretinal hemorrhage and subretinal macrophage, which occasionally contain pigment. The optic nerve head is mildly gliotic. Artifactualy, there is a segment of skeletal muscle within the posterior segments, just caudal to the ciliary body.

Morphologic diagnosis:

1. Intraocular metastatic pilomatricoma, clean margins
2. Minimal neutrophilic keratitis with epithelial keratinization and peripheral stromal vascularization
3. Moderate lymphoplasmacytic anterior uveitis with pre- and postiridal fibrovascular membranes with peripheral anterior and posterior synechiae
4. Focal cortical cataract
5. Mild intraocular hemorrhage
6. Diffuse retinal detachment
Additional diagnostic tests:

1. IHC for Papillomavirus (Animal Disease Diagnostic Laboratory, Purdue University)
   a. Papillomavirus antigen was not detected in the globe
2. Periodic acid–Schiff (PAS)
   a. Failed to highlight robust basement membranes associated with neoplastic cells
3. Picrosirius Red and Trichrome
   a. Confirmed the eosinophilic trabeculae were keratin

Comments:

Pilomatricomas are uncommon follicular neoplasms, comprising approximately 1% of cutaneous and subcutaneous tumors in dogs. Malignant pilomatricomas are even more rare, with only 20 cases reported in the literature.

A summary of benign pilomatricomas is extracted and modified here from The Skin Diseases of the Dog and Cat book (eds Gross, Ihrke, Walder and Affolter). Benign pilomatricomas are firm alopecic dome-shaped masses occurring most frequently on the legs and dorsal trunk (shoulders and caudal dorsum). Histologically, they are well-circumscribed masses within the dermis that lack a connection with the overlying epidermis. The neoplasm is composed of cystic lobules of neoplastic basaloid keratinocytes, resembling the matrix cells of the hair follicle, and have scant cytoplasm and large nuclei with little nuclear atypia. The cytoplasm of neoplastic cells can be granulated and occasionally contain brightly eosinophilic trichohyalin granules. The cells undergo abrupt keratinization toward the center of the lobules with keratinized cells (“ghost cells”) filling the cyst lumens. The mitotic activity can be high. Mineralization and osseous metaplasia are not uncommon in the center of the cysts. There can be a robust granulomatous response to free keratin associated with cyst rupture with multinucleated giant cells.

Pertinent differences of malignant pilomatricomas include grossly evident ulceration and metastasis. A variety of breeds and ages (ranging from 1 to 14 years of age) have been reported with no known age or breed predilections. There is an increased risk for benign pilomatricomas in the following breeds (listed in order); Kerry blue terrier, soft coated Wheaton terrier, standard poodle, old English sheepdog, and Bouvier de Flandres. Dogs with malignant pilomatricomas frequently present for lameness or neurologic signs associated with metastasis to bone.

Histologically, malignant pilomatricomas are poorly demarcated with invasion into surrounding tissues and may invade lymph vessels. There is a moderate amount of anisocytosis, mild anisokaryosis, and moderate mitotic activity (<10 mitoses per HPF). There are extensive areas of necrosis, and frequent dystrophic calcification or osseous metaplasia within the lobules. Keratinocytes containing trichohyalin granules and keratinocytes containing keratohyalin granules have also been reported. There is a marked pyogranulomatous inflammatory response. Lymphocytes and plasma cells can also be found infiltrating the stroma.

When diagnosing a malignant pilomatricoma, it is important to differentiate between pilomatricoma and other follicular tumors. Distinguishing pilomatricomas from tichoepitheliomas can be difficult, especially with less well differentiated neoplasms. Pilomatricomas tend to have larger aggregates of keratin and ghost cells with a greater predominance of basilar epithelial cells and more necrosis. Trichoepitheliomas tend to be comprised of squamous epithelial cells with inner root sheath, outer root sheath, and infundibulum differentiation (trichohyalin granules, agranular cells, and keratohyalin granules, respectively). There tends to be less keratinization
compared to pilomatricomas, and only rare calcification or ossification.\textsuperscript{1} Distinguishing malignant pilomatricomas from keratinizing basal cell carcinomas is somewhat easier. Basal cell carcinomas maintain connections with the epidermis and have a more plaque-like appearance.\textsuperscript{1}

The distinction between malignant and benign pilomatricomas is less clear. Some criteria that have been used are an increased ratio of basilar cells to keratinized ghost cells, infiltration into surrounding tissues, increased mitotic activity, increased nuclear atypia and lymphatic invasion.\textsuperscript{1,11} However, histologic appearance does not always predict clinical behavior. The most definitive criterion used to differentiate between the two is finding a metastatic lesion.\textsuperscript{2}

This case demonstrates the characteristic histologic features of a malignant pilomatricoma. Additionally, follow up provided by the rDVM confirmed the presence of other metastatic lesions in this patient. A CT showed nodules within the left cranial, left caudal, right cranial, and accessory lung lobes. Fine needle aspirate and cytologic evaluation of the mass within the left caudal lung lobe revealed a keratin-filled neoplasm supportive of hair follicle origin, likely metastatic pilomatricoma. The lung and bone are the most commonly reported sites of metastasis with 14/20 and 13/20 reports, respectively. To our knowledge, this is the first report of intraocular metastasis of a malignant pilomatricoma.

To be thorough, we considered the possibility of this being a metastatic malignant viral papilloma and thus pursued immunohistochemistry for papillomavirus, which was negative. The other changes in the globe are secondary to the intraocular neoplasm.

References:

Case History:

Case #: NE-18-471

Presenter: Gordon Ehrensing, DVM

Corresponding Institution: Michigan State University

Signalment: 4-year-old American paint gelding

History: This gelding had a 2 month history of hyporexia, sweating, polyuria, and polydipsia and a 2 week history of lethargy, diarrhea, and fever. The owners believe he had a seizure prior to presentation to the Michigan State University Large Animal Clinic. On presentation, he was tachycardic and febrile. Clinical examination revealed a large caudoventral abdominal mass, hepatomegaly, elevated hepatic enzymes, and hemoabdomen. Abdominal hemorrhage continued, and the horse was euthanized on 4/4/2018.

Gross findings: The abdominal cavity contains 30 L of partially clotted blood. The liver weighs 20.45 kg (4.0% of body weight, equine normal is estimated at 1.1%). The left lateral lobe of the liver is extensively effaced by a poorly demarcated, 30x25x15 cm, multilobulated, globoid mass with a mottled tan surface. The mass is regionally adherent to the gastric body or covered by firmly adherent omentum and fibrin tags. On cut section the mass contains abundant tan to grey to hemorrhagic inspissated necrotic tissue, fibrous connective tissue, and regions of amorphous mineralization. Glisson’s capsule is multifocally distended and focally ruptured, associated with partially extruded clotted blood. The right lateral lobe of the liver has an accentuated red to dark red reticular pattern. The subcapsular surface and superficial parenchyma are expanded by 4 randomly distributed, 3-5 cm in diameter, tan, moderately firm, centrally necrotic nodules which blend imperceptibly with the surrounding parenchyma and are grossly similar to the previously described mass. The caudate lobe of the liver is diffusely light tan, soft, friable, and sinks in formalin. The right cranial and caudal lung lobes each contain a single 3x2x1.5 cm tan, mildly firm peripheral nodule.
Case Synopsis:

Case #: NE-18-471

Presenter: Gordon Ehrensing, DVM

Corresponding Institution: Michigan State University

Signalment: 4-year-old American paint gelding

Histopathology: One representative section of liver mass and one section of lung are examined. Within the liver the hepatic architecture is widely effaced by a mass comprised of moderately well-differentiated neoplastic hepatocytes arranged in irregularly thick cords and sheets, supported by a scant fibrovascular stroma. No portal tracts are present within the mass. The neoplastic cells are polygonal, have moderate quantities of eosinophilic and frequently vacuolated cytoplasm, and have distinct cell borders. The nuclei are large, round to ovoid with coarsely stippled to vesiculate chromatin, and have 1-2 prominent nucleoli. Anisokaryosis is marked, and there are 11 mitotic figures in 10 high-power fields. Abundant necrosis, hemorrhage, fibrin deposition, accumulations of acicular clefts, and regions of amorphous mineralization are present within the mass. Small numbers of macrophages including hemosiderin-laden macrophages and aggregates of hematopoietic precursor cells are interspersed between the neoplastic population. Within the right lateral liver lobe (not submitted), hepatic parenchyma is multifocally infiltrated and compressed by aggregates of similar neoplastic cells. There is moderate bile duct proliferation within periportal and midzonal regions. Separately within the non-neoplastic liver, there is a region of moderate hepatic lipid accumulation characterized by large, well-demarcated intracytoplasmic clear spaces within hepatocytes. There is multifocal degeneration or necrosis of hepatocytes and large lakes of extravasated red blood cells.

Within the lung, pulmonary vessels are multifocally occluded by aggregates of the previously described neoplastic cells which often extend into adjacent lung parenchyma to form large, dense secondary masses composed of neoplastic hepatocytes, hematopoietic precursor cells, and necrotic debris with fibrin. There is mild congestion of the pulmonary parenchyma. Interlobular septae and subpleural surfaces are moderately expanded by edema fluid and a small quantity of loose fibrous connective tissue.

Morphologic diagnosis: Hepatocellular carcinoma with intrahepatic and pulmonary metastasis; regionally extensive hepatic lipidosis

Additional diagnostic tests: Immunohistochemistry for HepPar1

Comments: Hepatocellular carcinoma is a neoplasm arising from hepatocytes or hepatic stem cells which is reported in virtually every domestic species, including horses. While primary intrahepatic tumors of horses include hepatocellular carcinoma and hepatoblastoma, occurrence rates are poorly established in the literature. Blood chemistry changes associated with this condition are non-specific but may indicate a hepatocellular insult or cholestatic liver disease. Hypoglycemia as a paraneoplastic syndrome has been reported in dogs and horses with hepatocellular carcinoma, associated with release of insulin-like substance or glucose consumption by neoplastic cells\(^5,7\). Various inflammatory conditions are associated with
hepatocellular carcinoma in humans and in some veterinary species\textsuperscript{4,6}, though such a link has not been established in equines\textsuperscript{4,6}.

Hepatocellular carcinoma may be grossly massive, nodular, or diffuse with the latter form occurring least commonly and typically being the least amenable to surgical excision. Depending on degree of differentiation and the presence of secondary changes, these neoplasms are soft, friable, and somewhat resemble non-neoplastic liver. In this case, neoplastic tissue was grossly similar yet distinct from adjacent hepatic parenchyma, having severe regional expansion of the liver and wide regions of necrosis, hemorrhage, and mineralization. These changes reflected the degree of differentiation and rapid rate of growth relative to vascular supply. Histologically, hepatocellular carcinomas are composed of cords of hepatocytes greater than 4 cells thick or solid sheets of hepatocytes. Portal triads are not present within neoplastic parenchyma. Cavernous blood-filled spaces may develop (pelioid type), and scirrhous response is mild to marked. Metastasis usually occurs late in the disease and most commonly arise within lung, peritoneum, and lymph nodes\textsuperscript{1,2}.

Neoplastic cells typically demonstrate cytoplasmic immunoreactivity for alpha-fetoprotein and HepPar-1\textsuperscript{1}, though poorly differentiated tumors may lose HepPar-1 labeling and sparsely label with cytokeratin 19\textsuperscript{2}. While loss of HepPar-1 labeling tends to correlate with aggressive behavior and poor prognosis, diffuse immunolabeling of primary and metastatic carcinoma cells in this case provides counterpoint to this trend. Hepatocellular carcinoma must be differentiated from hepatocellular adenoma, cholangiocarcinoma, hepatoblastoma, and mixed tumors. Given that this tumor arose within a young adult horse, the primary differential diagnosis was malignant hepatoblastoma. Hepatoblastomas are typically benign tumors which arise as a single firm, lobulated, yellow to red mass less than 20 cm in diameter. As such, this neoplasm would be significantly less likely in this case even without histologic evaluation\textsuperscript{1,2,3}.

References:

Case History:

Case #: RE-17-95

Presenter: Eileen Henderson¹,², Dalen Agnew², Scott Fitzgerald², Matti Kiupel², Mohamed Faisal¹, Thomas Loch¹

Corresponding Institution: 1) Michigan State University Aquatic Animal Health Laboratory, 2) Michigan State University Veterinary Diagnostic Laboratory

Signalment: Adult female steelhead trout (Oncorhynchus mykiss)

History: Adult female steelhead trout collected during spawning migration/artificial gamete collection and evaluated as part of routine health screening.

Gross findings: Opercular cavity mass
Case Synopsis:

Case #: RE-17-95

Presenter: Eileen Henderson1,2, Dalen Agnew2, Scott Fitzgerald2, Matti Kiupel2, Mohamed Faisal1, Thomas Loch1

Corresponding Institution: 1) Michigan State University Aquatic Animal Health Laboratory, 2) Michigan State University Veterinary Diagnostic Laboratory

Signalment: Adult female steelhead trout (Oncorhynchus mykiss)

Histopathology:

Two representative sections of the submitted opercular mass specimen are examined. Examined sections are comprised of a lobulated, moderately cellular proliferation of thyroid follicular cells arranged in variably sized follicles containing homogenous amphophlic material (colloid). In some areas, these cells extend irregularly into the adjacent connective tissue. There is a large well-circumscribed, clear filled space lined by cuboidal to low columnar cells within the center of the mass (consistent with a cyst). There are several focal regions of necrosis, fibrosis, and hemorrhage scattered throughout the examined sections and there are variable numbers of lymphocytes randomly distributed among the follicles.

Morphologic diagnosis:

Opercular mass: Thyroid hyperplasia

Additional diagnostic tests: None

Comments:

Proliferative thyroid lesions are a common finding in teleosts. Differentiating thyroid hyperplasia from neoplasia, specifically thyroid carcinoma from thyroid hyperplasia, can be difficult as many of the criteria for malignancy used in mammals are not applicable to fish. Thyroid tissue in teleost fish is unique in that it is unencapsulated and can be distributed throughout the entire body. This is in contrast to elasmobranchs which have an encapsulated thyroid. Goiter or thyroid hyperplasia in fish often occurs in captive or managed fish and has been associated with numerous factors including iodine deficiency, genetic susceptibility, environmental factors (e.g. poor water quality), and exposure to goitrogenic substances (Fournie et al. 2005, Grizzle and Goodwin 2010). In mammals, numerous criteria are often used to differentiate thyroid hyperplasia from neoplasia including degree of invasiveness (e.g. invasion of the capsule), metastasis, and cytologic features. Thyroid hyperplasia in teleosts is often marked with extension into adjacent normal tissue. Concurrently, there is often proliferation of ectopic thyroid tissue in response to stimuli (e.g. iodine deficiency), which can often be mistaken for metastasis. Thyroid hyperplasia will typically resolve once the environmental stimuli have been removed; however, it has been proposed that these cells can undergo malignant transformation. In a paper by Fournie et al. 2005, specific criteria for distinguishing thyroid hyperplasia from neoplasia were proposed. Due to the difficulties in assessing invasiveness and metastasis in teleost fish, cytologic features of atypia are essential to differentiating thyroid hyperplasia from thyroid carcinoma.

References:
Grizzle JM, Goodwin AE. Neoplasms and related disorders. Fish Diseases and Disorders. 2nd ed. Cambridge, MA: CABI. 2010:19-84.
Case History:
Case #:
SP-18-0005249

Presenter:
Annie Marie Zimmerman, Dodd Sledge

Corresponding Institution:
Michigan State University Veterinary Diagnostic Laboratory

Signalment:
Approximately 6-year-old, castrated male, domestic medium hair cat

History:
This cat was found as a stray in 2013 and had a history of uveitis. An intraocular tumor OS was suspected at the time of enucleation.

Gross findings:
On gross examination of the formalin fixed eye upon receipt at the MSU VDL, the lens was small, appeared potentially anteriorly luxated, and there was a dense band of fibrous connective tissue bridging from the pars plana across the posterior aspect of the lens (suspected cyclitic membrane). There retina was diffusely detached and aggregated within the posterior compartment. The vitreous was mildly hazy, and there was a focal subretinal aggregate of tan, flocculent material.
Case Synopsis:  
Case #:  
SP-18-0005249  

Presenter:  
Annie Marie Zimmerman, Dodd Sledge  

Corresponding Institution:  
Michigan State University Veterinary Diagnostic Laboratory  

Signalment:  
Approximately 6-year-old male castrated domestic medium hair cat  

Histopathology:  
In the provided scanned slide from the sagittaly sectioned globe, the lens capsule is absent except for a small fragment of posterior capsule, and remnant lens material is prolapsed into the pupil and anterior chamber. The peripheral exposed lens fibers are extensively tattered and focally fragmented; fiber ends are occasionally surrounded by large multinucleate giant cells. Regions of fiber fragmentation are focally infiltrated by aggregates of neutrophils, plump histiocytes, and multinucleate foreign body type-giant cells containing intracytoplasmic eosinophilic lens fiber material. Within the remnant posterior lens capsule, there are numerous 10-12 um diameter septate fungal hyphae characterized by parallel walls and infrequent dichotomous branching. Abundant neutrophils and plump, foamy histiocytes aggregate amid loose strands of fibrovascular connective tissue are within the perilenticular posterior chamber. The iris and ciliary body stroma contain moderate perivascular to interstitial infiltrates of lymphocytes, plasma cells, and fewer neutrophils. There is diffuse retinal detachment and mild to moderate tombstoning hypertrophy of the underlying retinal pigment epithelium; the retina is corrugated within the vitreous posterior to the lens. Outer retinal atrophy is evidenced by diffuse loss of photoreceptors; inner retinal atrophy is characterized by loss of ganglion cells, rarefaction of the nerve fiber and plexiform layers, and segmental collapse of the inner nuclear layer. Arising from the base of the ciliary body and lining the inner aspect of the retina is a dense band of fibrous connective tissue containing moderate infiltrates of lymphocytes, plasma cells, and neutrophils that focally aggregate and form a densely cellular lymphofollicular aggregate. The expanded subretinal space contains abundant flocculent to homogenous eosinophilic proteinaceous fluid, and aggregates of necrotic debris, neutrophils, and histiocytes surrounding fungal hyphae similar to those within the lens capsule, which are often coated by thick, eosinophilic proteinaceous material.  

Morphologic diagnoses:  
Lens rupture with intracapsular fungal hyphae  
Pyogranulomatous endophthalmitis  
Fibrous cyclitic membrane  
Retinal detachment  
Diffuse outer and inner retinal atrophy  

Additional diagnostic tests:  
Additional GMS-stained sections highlight fungal hyphae within capsule remnants and identify loose aggregates of hyphae within the subretinal space.
Comments:
Histopathologic findings are consistent with fungal colonization of the lens capsule, lens rupture, and subsequent uveitis. Fungal endophthalmitis in felines is often associated with traumatic implantation; however, there was no gross or histologic evidence of previous corneal trauma. In follow-up with the submitting veterinarian, this animal had no clinical evidence of systemic involvement and was doing well following enucleation.

References:
Case History:

**Case #:** NO-18-406

**Presenter:** Leah Stein, Dodd Sledge

**Corresponding Institution:** Michigan State University Veterinary Diagnostic Laboratory

**Signalment:** 17-year-old, intact female American bison

**History:**

This American bison had a three week history of partial anorexia and weight loss. She had scant feces. There was no evidence of bloat and there were no parasites found on fecal examination. Physical examination under anesthesia revealed a firm, nodular, enlarged uterus. There was a marked abdominal effusion that was tan and cloudy, and that contained high numbers of lymphocytes on cytological examination. Due to her deteriorating condition, she was euthanized and submitted to the Michigan State University Veterinary Diagnostic Laboratory for post mortem examination.

**Gross findings:**

There were abundant amounts of subcutaneous and visceral fat, and the overall body condition score was 7/9. The abdominal cavity contained approximately 30L of red to tan, slightly opaque, watery fluid. Scattered over the surfaces of the omentum, mesentery, and peritoneal surface of the diaphragm, there were extensive plaques of thick, firm, tan to yellow, firm tissue that had a highly irregular, pitted and often umbilicated surface. The serosal surface of the reticulum was firmly adhered to the diaphragm by fibrous tissue. The capsular surface of the spleen was covered in hundreds of multifocal to coalescing, 0.5-3cm in diameter, yellow to tan, firm, plaques that extended less than 1mm into the parenchyma. There were lesser numbers of similar plaque-like lesions on the capsular surface of the liver and the serosal surface of the rumen. Additionally, the splenic capsule contained dozens of multifocal, 0.2-0.5cm in diameter, tan to red, firm nodules and a focal, 2x0.5x0.3cm, soft, red mass that did not extend into the parenchyma. A 30x15cm region encompassing the entirety of the cervix and extending into the uterus was diffusely thickened, nodular, hard, tan to red, and multifocally umbilicated. The body of the uterus was distended by approximately 5L of dark brown, opaque fluid. Within the wall of uterine body, there were less than one dozen, multifocal, 4-8cm in diameter, hard, nodular masses with tan, umbilicated centers over which the endometrial surface was often ulcerated. The renal pelvices of the right kidney were diffusely dilated to 0.5-2cm in diameter, and there was a 5x1x3cm supracapsular cystic space lined by firm, tan, fibrous tissue.
Case Synopsis:

Case #: NO-18-406

Presenter: Leah Stein, Dodd Sledge

Corresponding Institution: Michigan State University Veterinary Diagnostic Laboratory

Signalment: 17-year-old, intact female American bison

Histopathology:
In the cervix, there is transmural effacement of normal architecture by dense, haphazardly arranged fibrous connective tissue that surrounds multifocal, variably sized, fairly well differentiated tubules of neoplastic glandular epithelial cells. These cells are cuboidal to polygonal, have indistinct cell borders, and have moderate amounts of eosinophilic cytoplasm. Nuclei are round to ovoid, finely stippled to open faced, and have a variably distinct single nucleolus. Anisokaryosis is moderate, and there are no observed mitotic figures. Tubular lumens variably contain basophilic mucinous material or eosinophilic necrotic cellular debris. The peritoneal serosa of the diaphragm and spleen is markedly expanded by similar, thick bands of fibrous connective tissue that contain scattered, well differentiated neoplastic tubules.

Morphologic diagnoses:
Cervix: Uterine adenocarcinoma
Spleen and diaphragm: Metastatic uterine adenocarcinoma (carcinomatosis)

Additional Findings: Multifocally in the uterus, there are full thickness proliferations of a similar neoplastic epithelial cell population arranged in nests and tubules surrounded by dense fibrous stroma. Neoplastic cells in these foci exhibit marked anisokaryosis, nuclei are multifocally pleomorphic, and there are moderate numbers of binucleated cells. Dense sheets of fibrosis containing neoplastic cells also cover the liver, intestines, and mesentery. In the hepatic parenchyma, there is a single, nodular focus of dense fibrous connective tissue surrounding well differentiated neoplastic tubules. The capsule of one kidney is covered by dense fibrous connective tissue that lacks neoplastic tubules. In the same kidney, there are multifocal, radiating bands of interstitial fibrosis that extend from the medulla into the cortex and surround and individualize variably dilated tubules and glomeruli. There is marked atrophy of the renal pelvis characterized by loss of tubules, marked interstitial fibrosis, and pigmented debris in remaining tubular lumens. The medullary and pelvic tubules in both kidneys multifocally contain eosinophilic proteinaceous material.

Comments:
The gross and histopathologic findings were most consistent with a primary uterine adenocarcinoma with peritoneal carcinomatosis. The findings in the left kidney were considered secondary to ureteral obstruction caused by the extensive metastatic lesions. The clinical history was most concerning for lymphoma; however, the pattern of metastasis, degree of scirrhous reaction, and the umbilicated nature of the masses observed grossly did not support this diagnosis and instead favored a diagnosis of carcinoma. Histopathology revealed a proliferation of neoplastic glandular epithelial cells within the cervix, uterus, and covering the serosal surfaces of most of the abdominal viscera, consistent with an adenocarcinoma. The cervix was the only organ to be completely effaced by the neoplastic changes and there were no gross or histopathologic lesions to suggest a primary adenocarcinoma at a different site.

Lymphoma is the most common metastatic uterine neoplasm of cattle and the enzootic
form, caused by bovine leukemia retrovirus, commonly affects the heart, abomasum, lymph nodes and uterus. Uterine adenocarcinoma is rare in most domestic and wild species with the exception of rabbits and cattle. In cattle, uterine carcinoma is the most common primary uterine neoplasm, though still considered rare, and presents as multiple firm nodular masses in the uterine wall with a marked scirrhous response. There have been case reports of primary uterine adenocarcinomas with widespread metastasis in cattle, but none have been reported in bison. Reproductive tract abnormalities that have been reported in nonpregnant female bison include ovarian atrophy, cystic ovaries, bursal adhesions, hydrosalpinx, hydrobursitis, and paraovarian and uterine cysts.

References:
Case History:
Case #:
SP-18-0005543

Presenter:
Dodd Sledge¹, Annie Zimmerman¹, Jean Stiles²

Corresponding Institution:
1: Michigan State University Veterinary Diagnostic Laboratory
2: College of Veterinary Medicine, Purdue University

Signalment:
11-month-old, spayed female, domestic medium hair cat

History:
This patient’s owner noticed OS problems at 8 months old (February 2018). An exam performed on 2/6/2018 revealed negative intermittent menace, an intraocular pressure of 16 mmHg, slight mydriasis, a posterior cortical cataract, and possible persistent hyperplastic primary vitreous OS. OD was normal.

When seen by the referring veterinarian on 4/12/2018, OS had an intraocular ocular pressure of 45 mmHg, flare, rubeosis iridis, and mild mydriasis. The cataract did not appear progressed. The patient was started on prednisone acetate OS QID and Cosopt OS TID. On recheck examination by the referring veterinarian on 4/19/2018, the intraocular pressure measured 67 mmHg and the eye was buphthalmic. Treatment with latanaprost OS BID was initiated. Enucleation was performed by the referring veterinarian on 5/8/2018; a corneal ulcer was present at that time.

Gross findings:
On gross examination of the formalin-fixed globe, there was an axial superficial corneal ulcer affecting approximately ¼ of the total cornea. The lens was thinned in the anterior-posterior lane, and the posterior cortical lens was pale white and opaque. There was mild liquefaction of the vitreous. The retina was diffusely detached, and there was dark red and stringy pale tan material surrounding the inner and outer aspect of the detached retina near the optic disc.
Case Synopsis:
Case #:
SP-18-0005543

Presenter:
Dodd Sledge¹, Annie Zimmerman¹, Jean Stiles²

Corresponding Institution:
1: Michigan State University Veterinary Diagnostic Laboratory
2: College of Veterinary Medicine, Purdue University

Signalment:
11-month-old, spayed female, domestic medium hair cat

Histopathology:
In the provided scanned slide from the sagittaly sectioned globe, the globe is enlarged, and there is marked thinning of the posterior and limbal sclera. Protruding from the optic nerve head is a tuft-like gliovascular proliferation surrounded by a dense accumulation of flocculent, vascularized, basophilic material lined by a dense gliovascular membrane that bridges to the adjacent detached retina; thin extensions of such gliovascular membranes segmentally line the retinal inner limiting membrane. The surrounding vitreous contains scant loose strands of similar flocculent, vascularized material surrounded by abundant hemorrhage and rare scattered histiocytes. There is diffuse retinal detachment and moderate tombstoning hypertrophy of the underlying retinal pigment epithelium (RPE). Gliovascular proliferations and segments of RPE surround the outer aspects of the detached retina at the optic nerve head. Diffuse inner retinal atrophy is evidenced by loss of ganglion cells and regional rarefaction of the inner nuclear layer; outer retinal atrophy is characterized by loss of photoceptors and segmental collapse of the outer nuclear layer. There are no appreciable vessels within the neural retina in the examined plane of section. Mild optic nerve head degeneration is evidenced by increased prominence of the lamina cribosa and collapse of the neuroparenchyma. There is mild posterior cortical cataractous change including posterior migration of the lens epithelium, fragmentation and liquefaction of lens fibers, and formation of Morgagnian globules and bladder cells. The anterior aspect of the iris is lined by a thin fibrovascular membrane that bridges across the collapsed ciliary cleft and tracks along Descemet’s membrane, resulting in peripheral anterior synechiae. Corneal stromal fibers are diffusely moderately separated and individualized by edema fluid. The axial corneal epithelium is regionally absent; at the margin of the defect, the corneal epithelium is rounded and mildly elevated. The underlying exposed superficial stroma is mildly hyperesinophilic, and the intact perilimbal stroma contains mild perivascular to interstitial infiltrates of neutrophils.

Morphologic diagnoses:
Eye
Avascular neural retina and extraretinal gliovascular proliferation
Vitreal condensation and liquefaction
Retinal detachment
Optic nerve degeneration
Diffuse inner and outer retinal atrophy
Mild posterior cortical cataractous change
Pre-iridial fibrovascular membrane with peripheral anterior synechia
Indolent corneal ulcer
Comments:
This pattern of gliovascular proliferation along the inner and outer retina, and radiating into the vitreous along with lack of blood vessels within the neural retina has been previously recognized in young cats and has similarities to retinopathy of prematurity in humans. In humans, risk factors for development of retinopathy of prematurity include premature birth and low birthweight, although genetic factors have also been suggested. In cats, the risk factors for development of such neovascular proliferative vitreoretinopathy are unclear as this is a rare spontaneously occurring condition. This condition is often recognized in cats <1 year of age. Affected animals commonly have glaucoma associated with development of preiridal fibrovascular membranes and peripheral anterior synechia, and retinal detachment. Failure or dysregulation of retinal angiogenesis is likely the ultimate cause of these changes. Feline models of retinopathy of prematurity have been successfully made by exposing kittens to hyperoxic conditions immediately after birth suggesting that retinal oxygen tension plays a role in development of the condition.

References:

Case History:

Case #: SP-17-0011830

Presenter: Sarah Coe, Ed Rosser, and Erica Noland

Corresponding Institution: Michigan State University

Signalment: A 14-year-old female Standardbred horse

History:
The horse had presented for numerous raised circular lesions in the skin found diffusely on the body. The previous day, the horse had a dental float during which she was sedated with detomidine. It was noted at that time that there were several raised skin lesions around the left eye and muzzle. Some lesions appeared to be weeping. Silver sulfadiazine cream was applied. No additional lesions were noted that early evening; however, when the horse was checked on in the morning the lesions had spread over the whole body. The horse also had a history of severe chronic uveitis of the left eye and was being treated for a flare-up with atropine every 3 days and neo-poly-dex ointment twice daily. She had also been given oral dexamethasone.

Gross findings:
There were greater than 50 skin lesions that were raised, circular, and varied in size from approximately 1-5cm in diameter. Some of the lesions were oozing clear fluid and some lesions developed central ulcerations. The area ventral to the left eye was diffusely ulcerated.
Case Synopsis:

Case #: SP-17-0011830

Presenter: Sarah Coe, Ed Rosser and Erica Noland

Corresponding Institution: Michigan State University

Signalment: A 14-year-old female Standardbred horse

Histopathology:
Four specimens, including two acute, one intermediate, and one late stage skin lesion, were submitted to the MSU VDL. Eight sections representing the bisected and completely embedded four specimens are provided. In the most severely affected specimen representing the late stage skin lesion, there are marked perivascular and interstitial infiltrates of eosinophils, fewer neutrophils, and occasional histiocytes. Vessels throughout the full thickness dermis and hypodermis are multifocally obscured by red blood cells, aggregates of fibrin, and/or neutrophils. Such vessels are also occasionally surrounded by karyorrhectic debris. Discrete vessels are lined by plump, reactive endothelial cells. There is also extensive necrosis of the superficial dermis and portions of the epidermis as well as rare deeper foci of hypereosinophilic collagen bundles. In the lesser affected specimen representing the intermediate stage skin lesion, there are similar but lesser numbers of perivascular and interstitial inflammatory infiltrates. Occasional vessels are smudgy or obscured by red blood cells. In the two additional specimens representing the two acute stage lesions, there are no histologically remarkable lesions.

Morphologic diagnosis:
Haired skin: Eosinophilic dermatitis with fibrinoid and neutrophilic vasculitis

Additional diagnostic tests:
Bloodwork revealed a mild hyperlactatemia (2.3 mmol/L; ref range: 0.3-0.7 mmol/L) and a leukocytosis characterized by neutrophilia.

Comments:
The clinical and histopathologic findings in this case are demonstrative of urticarial vasculitis. Urticarial vasculitis is well reported in the human literature, and there are four reported cases in dogs. This process is a type III hypersensitivity reaction and can be triggered by concurrent disease, food hypersensitivity, drug reaction, and insect bites. Urticarial vasculitis is characterized clinically by erythematous plaques that last longer than common urticaria (48-72 hours). Definitive diagnosis can be made by histologic evaluation, which includes evidence of leukocytoclasia, swollen endothelial cells, fibrin deposition in and around vessel walls (fibrinoid degeneration), extravasated erythrocytes, and edema. In this case, the instigating cause is unknown; however, given the appearance of lesions around the time of detomidine administration, an adverse drug reaction is suspected.

References:
Case History:

Case Number: SP-18-0006936

Presenter: Wallaya Manatchaiworakul and Erica Noland

Corresponding Institution: Michigan State University

Signalment: A 3-year-old castrated male, German Shepherd dog

History:
The dog presented for lethargy and a high temperature (104.4F), and was placed on Amoxicillin and Rimadyl. Gabapentin was added seven days following presentation because the dog started limping. The dog had a recent history of vaccination.

Gross Findings:
Nine days following presentation, the feet were painful and multiple paw pads were sloughing off.
Case Synopsis:

Case Number: SP-18-0006936

Presenter: Wallaya Manatchaiworakul and Erica Noland

Corresponding Institution: Michigan State University Veterinary Diagnostic Laboratory, MI, USA

Signalment: A 3-year-old castrated male, German Shepherd dog

Histopathologic description:
Samples taken from the right front paw, right hind paw, and left hind paw were submitted to MSU VDL. Seven sections representing the completely embedded or bisected and completely embedded three specimens were provided. Within regions of the superficial dermis, collagen bundles were expanded by edema and blood vessel walls were variably obscured by neutrophils and fewer eosinophils. Surrounding some vessels, there was also fragmented nuclear debris or, less frequently, low numbers of extravasated red blood cells. Discrete vessels in these regions were lined by plump, reactive endothelial cells and frequently had marginating neutrophils and fewer eosinophils. Vessels throughout the remainder of the dermis were often lined by plump reactive endothelial cells. The overlying epidermis was segmentally atrophied or regionally lost and, in some regions, was covered by necrotic debris mixed with degenerate neutrophils.

Morphologic diagnosis:
Paw pad/haired skin: Superficial vasculopathy with regional epithelial atrophy and ulceration

Additional diagnostic tests: N/A

Comments:
In this case, occasional vessels were surrounded by fragmented nuclear debris; as such, a leukocytoclastic small vessel vasculitis was considered. However, no overt necrosis of vascular walls observed, thus vascular changes in conjunction with the overlying epithelial changes were most suggestive of at least a vasculopathy. Given the history of recent vaccine administration, an underlying cutaneous drug reaction is suspected. However, other causes of small vessel vasculopathy/vasculitis, such as systemic disease (bacteremia and tick borne disease) or a nonseptic idiopathic form of neutrophilic vasculopathy/vasculitis cannot be excluded.

Reference:
Case History:

Case #: 14-1959

Presenter: Margaret Martinez

Corresponding Institution: The Ohio State University

Signalment: 12-year-old spayed female mixed shorthair cat

History: An indoor only cat presented to The Ohio State University's (OSU) Neurologic service for progressive left hind limb weakness. On presentation the cat’s mentation and behavior were normal. She was ataxic, circling to the left, had a left head turn, decreased to absent conscious proprioception in all four limbs, and positional vertical nystagmus. She also had bronchovesicular sounds on physical examination. Prednisone and clindamycin were prescribed. The cat became completely non-ambulatory in the hind limbs and presented back to OSU.

The neurologic deficits were localized to the left central vestibular/ cerebellum. A brain MRI detected a subtle T2-weighted hyper-intensity and mass effect within the left brainstem. The area of the pons and medulla appeared fuller than normal causing flattening of the ventral cerebellum. There was attenuation of the dorsal subarachnoid space at the region of the obex due to a slight mass effect at the medullary/cervical junction. The central canal was dilated from the mid body of C1 through C5.

Gross findings: On post-mortem examination, the brainstem and cervical spinal cord at the level of C1 were diffusely and mildly enlarged with normal architecture and anatomy able to be appreciated.
Case Synopsis: Feline gliomatosis cerebri

Case #: 14-1959

Presenter: Margaret Martinez

Corresponding Institution: The Ohio State University

Signalment: 12-year-old spayed female mixed shorthair cat

Histopathology: There is a single cross section of half of the frontal cerebral cortex with associated lateral ventricle and a complete cross section of the cranial brainstem. On subgross the junction of the white and grey matter is blurred and less defined than usual by an increase in cellularity. Also throughout the grey and white matter, there is a diffuse, un-encapsulated, and poorly demarcated infiltrate of elongated neoplastic cells. No distinct mass is formed by the neoplastic cell infiltrate. The cells are characterized by mild anisocytosis and anisokaryosis, distinct cell borders, scant cytoplasm, and dense, hyperchromatic, elongated and occasionally tortuous or rounded nuclei with no distinct nucleoli. There are 0 mitoses in 10 high power fields (400x). In the affected white matter of the brainstem there are numerous swollen axons and axon sheaths (axonal degeneration). Within the affected grey matter several neurons were swollen and rounded with dispersed Nissl granules (central chromatolysis). There was also rounded foamy microglia (gitter cells) and enlarged astrocytes with eosinophilic glassy cytoplasm (gemistocytes) in severely affected foci.

Morphologic diagnosis: Brain frontal cerebral cortex and cranial brainstem: Gliomatosis cerebri

Additional diagnostic tests: CD45, GFAP, vimentin, and nestin immunohistochemistry. CD45 (microglial marker) and vimentin had negative staining, while GFAP (astrocyte marker) and nestin (progenitor cell marker) had variable positive staining.

Comments:

The cat was diagnosed with gliomatosis cerebri (GC). Also found on postmortem examination was a focus of neoplastic well-differentiated fibrous astrocytes (fibrous astrocytoma) at the lumbar spinal cord. The clinical signs were attributed to both the brainstem and lumbar spinal cord lesions.

The World Health Organization (WHO) defines gliomatosis cerebri as “a diffusely infiltrating glial neoplasm affecting at least three cerebral lobes.” In the present case a similar infiltrating neoplastic cell population was present not only in the frontal lobe and brainstem, but also the parietal lobe; therefore, fitting with the WHO definition. Gliomatosis cerebri can then be characterized as either type 1 (classical form) in which there is diffuse brain infiltration or type 2 in which there is a discrete mass, usually a high grade glioma, in addition to the diffuse brain involvement. Therefore, with this case is an example of type II gliomatosis cerebri in a cat. To the presenter’s knowledge this is the first report of this type of neoplasm in this species.

The cell of origin of GC is still under investigation, which is reflected in the variable immunohistochemical staining in both human and canine cases. In humans it is proposed that the neoplastic cells are most commonly of the astrocytic lineage, with fewer cases being of oligodendroglial or mixed phenotypes. In the several case reports of canine GC, some reported positive and others negative GFAP staining of neoplastic cells, variable CD18, nestin, and
vimentin staining, and one case of positive Olig2 staining.3-5; 7; 8 Therefore, immunohistochemistry should not be relied upon for diagnosing GC in veterinary species. A differential for the present case is microgliomatosis, which has been proposed to be of histiogenic origin.6 Similar to GC, the infiltrative neoplastic cells do not destroy pre-existing tissue; however, the neoplastic cells in humans usually stain positive for CD18 and negative for GFAP.6

References:

Case History:

Case #: SP-17-0006465

Presenter: Erica Noland\(^1\) and Vandre Clear\(^2\)

Corresponding Institution: \(^1\)Michigan State University, Lansing, MI; \(^2\)Animal Skin Clinic, Creve Coeur, MO

Signalment: An 11-year-old, spayed female Devon Rex cat

History:
The cat had been on steroids for the last 10 years for allergic skin disease. Despite being diabetic for the last 3 years, this cat was still receiving daily steroids. Hair loss progressed rapidly, and in the following month, had gotten much more widespread.

Gross findings:
There was hair loss over the ventral abdomen, ventral neck, and medial and caudal hind limbs. In addition, there were regions of hair loss over the lateral neck/shoulder and cheek region with thick adherent crusts.
Case Synopsis:

**Case #:** SP-17-0006465

**Presenter:** Erica Noland¹ and Vandre Clear²

**Corresponding Institution:** ¹Michigan State University, Lansing, MI; ²Animal Skin Clinic, Creve Coeur, MO

**Signalment:** An 11-year-old, spayed female Devon Rex cat

**Histopathology:**
Two 6mm punch biopsies, including one from an area of crusting over the left scapula and one from a region of alopecia in the left medial thigh region, were submitted to the MSU VDL. Four sections of haired skin, representing the two bisected and completely embedded punch biopsy specimens, are provided. In both specimens, there is follicular atrophy. Follicular ostia are often distended by dense keratin, and occasionally contain rare hair shafts. In one specimen, the epidermis is intact, 1-2 cell layers in thickness, and lined by basket weave keratin layers. In the other specimen, there is a focal neutrophilic crust forming a conical projection that is contiguous with the dermis. There are perpendicularly oriented collagen bundles that are extruding through the opening in the epidermis into this crust. The underlying superficial dermis contains large numbers of neutrophils and surrounding superficial fibrosis. The adjacent intact epidermis is moderately hyperplastic and lined by mild parakeratosis to mild compact orthokeratosis. There is a similar smaller perforating lesion forming a break within the adjacent hyperplastic epithelium.

**Morphologic diagnosis:**
Haired skin: Diffuse follicular atrophy and regional perforating dermatitis

**Additional diagnostic tests:**
Ultrasound examination revealed multiple pancreatic nodules, a mass on the jejunum, and diffuse hepatopathy.

**Comments:**
Given the follicular atrophy, normal stratum corneum, and normal to thinned epidermis in one specimen, iatrogenic hyperglucocorticoidism is favored over feline paraneoplastic alopecia. While there is epidermal hyperplasia and hyperkeratosis within the other specimen, the hyperplastic epidermis is bordering regions of inflammation; as such, this is considered a secondary finding. Interestingly, this other lesion resembles a perforating dermatitis. In dogs and cats, perforating dermatitis is thought to occur secondary to trauma in the context of allergic skin disease. This is unlike acquired perforating dermatosis in humans, which is predominately associated with chronic kidney disease and diabetes mellitus, but has been reported in association with other conditions as well.

**References:**
Case History:

Case #: Purdue-1

Presenter: Grant N. Burcham

Corresponding Institution: Heeke Animal Disease Diagnostic Laboratory, Purdue University

Signalment: 4-year-old St. Croix ewe

History: The ewe in this case lambed triplets in 2017. The lambs were weaned June 1, and the ewe’s udder remained large and continued swelling after weaning. During the last week of July, the ewe went off feed and died August 2 or 3. The ewe was examined on August 3.

Gross findings:

The ewe weighed 85 lbs and was thin. Blood was thin and watery.

The left half of the mammary gland was swollen. On cut section, the gland cistern mucosa of the affected side was dark red to purple. The gland cistern was filled with fibrinous exudate.

The thoracic cavity contained scant straw-colored fluid. The lungs were heavy and wet. The pericardial sac contained abundant straw-colored fluid.

Bilaterally, the renal pelves were dilated and filled with large (1.5 cm), yellow, chalky stones with concentric rings on cross-section. The kidneys were small and firm.

The abdomen contained scant, translucent, straw-colored fluid. The rumen contained partially digested feed material. The abomasum contained thick, dark red liquid. Irregular red foci, measuring 2-3 cm, were on abomasal folds. The colon contained dark, tar-like feces.

The liver was shrunken, firm, and had an enhanced lobular pattern. The bile duct was dilated and contained inspissated bile material.

Gross Diagnoses:

Whole body: thin, anemia
Mammary gland: fibrinous mastitis
Lungs: pulmonary edema
Pericardium: hydropericardium
Abdomen: ascites
Kidneys: nephrolithiasis
Abomasum: hemorrhage
Colon: melena
Liver: hepatopathy
Case Synopsis:

Case #: Purdue-1

Presenter: Grant N. Burcham

Corresponding Institution: Heeke Animal Disease Diagnostic Laboratory, Purdue University

Signalment: 4-year-old St. Croix ewe

Histopathology: Kidney: The medulla was shrunken, contained fewer collecting duct profiles, and had fibrous connective tissue expanding the interstitium. Several collecting ducts were dilated and contained proteinaceous liquid in their lumens. Renal cortex contained areas of interstitial fibrosis. Many glomeruli contained thickened urinary capsules; rare glomeruli were obsolescent. A few tubules were dilated and contained protein-rich fluid. Rarely, tubules contained brown-gold crystalline material that was birefringent with polarized light. Multifocally, renal cortex contained areas of atrophied tubules. Mild lymphocytic infiltrates were present throughout the tissue.

Morphologic diagnosis: interstitial fibrosis, medullary and cortical atrophy (obstructive nephropathy)

Additional diagnostic tests: Quantitative analysis indicated the uroliths were comprised of 100% xanthine. Mineral analysis measured hepatic molybdenum at 0.67 µg/g dry matter (reference range 1.70-6.50). Hepatic copper concentration was 121.43 µg/g dry matter (reference range 25-400), making the hepatic Cu:Mo 181:1. Two hay samples measured 2.6 and 2.8 ppm molybdenum, with Cu:Mo of 1.5 to 1.25:1.

Comments: Xanthinuria / xanthine urolithiasis is a rare condition in domestic animals, with reported cases in sheep, cattle, dogs, and cats. Two mechanisms of xanthinuria have been demonstrated in domestic animals: mutations of genes involved with purine metabolism and treatment with allopurinol. A third mechanism—molybdenum deficiency—was proposed by Henry Oscar Askew, a nutritionist working in New Zealand in the 1950’s, to explain the regular occurrence of xanthine uroliths in sheep grazing poor pasture in the Moutere Hills region. Citing the recent discovery that xanthine dehydrogenase required molybdenum as an “activator” for proper enzyme function, he measured the molybdenum in pasture, soil, and livers of sheep with xanthine uroliths. Low levels of molybdenum in livers and pasture were unifying factors in affected sheep. The ewe in the current presentation had decreased levels of molybdenum in the liver, suggesting deficiency of this micronutrient. Hay from the farm had adequate levels of molybdenum. Histologic lesions in the liver were compatible with acute, periacinar necrosis superimposed on chronic hepatic damage, suggesting ongoing copper toxicity may have also been contributing to illness in this ewe. The Cu:Mo was high in the liver, supporting this idea.

Histologic lesions within the kidney provided an excellent example of changes that occur secondary to obstruction of urine outflow. Ischemia is the underlying pathologic mechanism at work in this tissue. Interstitial and glomerular capsular fibrosis are important histologic features.

References:
1. Askew, HO. NZ J of Agricult Res. 1958
5. Ling et al. JAVMA. 1991
Case History:

**Case #:** 18-189

**Presenter:** Josh Lorbach

**Corresponding Institution:** The Ohio State University

**Signalment:** 13-year-old male-intact Akita dog

**History:** The animal presented to emergency care for complaints of vomiting, bloody diarrhea, and oliguria/anuria. Initial imaging and bloodwork revealed prostatomegaly and severe azotemia. Urinary catheterization and fluid support resolved azotemia, however following removal of urinary catheter the animal's anuric state resumed. Transfer to OSU Internal Medicine service and subsequent abdominal computed tomography (CT) imaging identified an expansile, lytic mass affecting the pubis and prostate, with lateral displacement of the urethra. CT also identified bilateral renal pelvis dilation (hydronephrosis).

**Gross findings:** Surgical debulking of the pelvic mass was performed by the OSU Surgical Oncology service. The intrapelvic mass expanded across the pelvic floor, and there was lysis of associated bone. The urinary bladder was distended with a thickened wall and diffusely dark red serosal surface, and severely-affected portions were resected during surgery. The urinary bladder failed to contract for the duration of surgery (approximately 3.5 hours).
Case Synopsis:

Case #: 18-189

Presenter: Josh Lorbach

Corresponding Institution: The Ohio State University

Signalment: 13-year-old male-intact Akita dog

Histopathology: The urinary bladder wall contains lakes of acute hemorrhage dispersed among bundles of smooth muscle fibers. There is patchy to diffuse acute coagulation necrosis of smooth muscle, characterized by hypereosinophilic sarcoplasm and condensed nuclei. Hemorrhagic and necrotic changes span the wall of the bladder from the submucosa to the serosa in some regions. In affected portions of smooth muscle there are prominent aggregates of reactive fibroblasts and neovascular profiles (granulation tissue). The submucosa is expanded by increased clear space (edema) with increased numbers of lymphocytes, plasma cells, and occasional neutrophils. One intravascular fibrin thrombus is present within the submucosa. The mucosa is hyperplastic with single cell necrosis, hemorrhage, and frequent vacuolar degeneration present in superficial urothelial layers.

Morphologic diagnosis: Marked subacute transmural urinary bladder coagulation necrosis and hemorrhage; mild lymphoplasmacytic to neutrophilic cystitis

Additional diagnostic tests: None

Comments: Microscopic findings were diagnostic for osteoblastic osteosarcoma of the intrapelvic mass. The urinary bladder lesions of transmural necrosis/hemorrhage are attributed to prolonged distension of the bladder described in the clinical history. Intrapelvic mass effect resulting in urethral obstruction is recognized in cases involving diagnoses of urinary malignancies, and in such cases vesicular necrosis has been described in literature. Primary intrapelvic damage of urinary bladder blood supply or innervation, as well as local hypoxia resulting from prolonged distension of the bladder and decreased circulation, are potential pathogenic mechanisms of bladder necrosis associated with urethral obstruction by malignancies.

References:


Case History:

Case #: 17-338-1

Presenter: Mallory DiVincenzo

Corresponding Institution: The Ohio State University

Signalment: 1-year-old, intact male Brown Norway rat

History: A 1-year-old intact male rat in foster care was being treated for lice infestation and was found dead after playing with a cage mate. No additional history was provided.

Gross findings: The peritoneal cavity contained 6 mL of dark red, watery, opaque fluid with a single, free floating, soft, dark red, opaque blood clot. The mesenteric vasculature was markedly dilated, tortuous, and dark red to gray, with 30 to 50 coalescing firm nodules positioned along the arcuate arteries. A dark red, soft, round to ovoid, smooth, loosely adherent clot was attached to the mesenteric aspect of the distal duodenum measuring 2 cm in diameter.
Case Synopsis:

Case #: 17-338-1

Presenter: Mallory DiVincenzo

Corresponding Institution: The Ohio State University

Signalment: 1-year-old, intact male Brown Norway rat

Histopathology:

Mesentery: Multiple cross sections of the mesenteric arteries are examined. The walls of the mesenteric arteries markedly and asymmetrically expanded by thick, concentric lamellations of reactive fibroblasts, collagen, erythrocytes, and eosinophilic extracellular material (fibrin). Multifocally infiltrating the media and adventitia are many degenerate and nondegenerate neutrophils and macrophages with fewer lymphocytes, plasma cells, extravasated erythrocytes (intramural hemorrhage), extracellular basophilic fragmented granular material (mineral), and karyorrhectic debris. The endothelium is frequently ulcerated and discontinuous, and the internal elastic lamina is frequently indiscernable throughout affected sections. The tunica intima and media are variably expanded by bands of smudgy, deeply eosinophilic, hyalinized extracellular material (fibrinoid change) admixed with cellular and karyorrhectic debris. Less cellular regions of the intima and media have marked expansion of the intima by layered collagen and fibrocytes resulting in marked narrowing of the arterial lumen.

Morphologic diagnosis:

Mesentery: Marked diffuse chronic-active fibrinosuppurative to necrotizing arteritis with fibrinoid change, transmural fibrosis, and multifocal arterial dissecting and aneurysmal hemorrhage.

Additional diagnostic tests: None

Comments:

The gross and histologic findings in this case are highly consistent with polyarteritis nodosa (PAN). PAN is a chronic progressive degenerative disease often observed in older, predominantly male rats. Medium arteries are most often affected, particularly those of the mesentery, pancreaticoduodenal artery, testes, and pancreas, as well as the hepatic, coronary, uterine, cerebral, adrenal, and renal arteries. Of note, PAN generally spares the pulmonary vasculature, as well as capillaries and glomeruli. Among the most affected rats are those in late stage chronic nephropathy, Sprague-Dawley rats, and spontaneously hypertensive (SHR) strains. PAN has also been reported previously in 1 non-laboratory, Norway rat, and was recently documented in a group of August Copenhagen Irish (ACI/SegHsd) rats. Affected rats often have no clinical signs unless arterial rupture is present, as in this case, resulting in sudden death due to abdominal hemorrhage. In addition to rats, similar syndromes to PAN have been reported in dogs, cats, mice, cynomologus macaques, pigs, horses, cattle, and sheep.

The pathogenesis of PAN has not yet been determined, but is thought to represent a type III hypersensitivity, with immune complex deposition in arterial walls and secondary activation of complement resulting in recruitment of leukocytes and subsequent in tissue damage. Lesions of PAN have also been observed in rats in association with exposure to estrogens, corticosteroids, and chemical carcinogens.
Gross findings generally include dramatically thickened, gray to red, firm to hard, medium sized arteries with marked tortuosity, focal hemorrhage, and/or aneurysmal dilatations. Common histologic findings include intimal fibrinoid degeneration with leukocyte infiltration of the intima and media by a mixture of mononuclear cells and neutrophils, which can progress to fibroplasia and gross thickening of the vessel wall with chronicity. Variation in the size and contours of the lumen may be present, with smudging and thickening of the normal medial architecture. Histologic lesions may also present in multiple phases of acuity simultaneously. Thrombosis is frequently observed with potential local infarction, hemorrhage, rupture, or recanalization occurring with chronicity.

References:

Case #: MSU-VDL-17-6426

Presenter: Tuddow Thaiwong, Michelle Magagna, Roger Maes, Matti Kiupel

Corresponding Institution: Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University, Lansing, MI

Signalment: 7-years-old, intact female, Beagle

History: This dog was reported to have a clinical presentation of acute bloody diarrhea and lethargy, despite up-to-date vaccination program.

Gross findings: N/A
Case Synopsis:

Case #: MSU-VDL-17-6426

Presenter: Tuddow Thaiwong, Michelle Magagna, Roger Maes, Matti Kiupel

Corresponding Institution: Veterinary Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University, Lansing, MI

Signalment: 7-years-old, intact female, Beagle

Histopathology:
Within the small intestine, there was marked villous blunting and fusion and segmental loss of superficial enterocytes. Remaining villous enterocytes varied from columnar to low cuboidal. The mucosal surface was overlain by pale eosinophilic flocculent material admixed with degenerate neutrophils, necrotic debris, and large rafts of bacterial bacilli. There was marked crypt dropout within the lamina propria, resulting in multifocal mucosal architectural collapse. Remaining crypts were frequently dilated, were lined by flattened to low cuboidal cells, and occasionally contained eosinophilic amorphous material admixed with karyorrhectic debris or sloughed epithelial cells. In multiple areas, crypt epithelium was disorganized, piled, and had increased mitotic activity and cytoplasmic basophilia, consistent with regenerative hyperplasia. There was mild multifocal necrosis of individual crypt epithelial cells, characterized by eosinophilic tinctorial change, cellular individualization, and nuclear karyorrhexis. Moderate numbers of lymphocytes, histiocytes and few neutrophils and eosinophils were scattered throughout the lamina propria. There was multifocal loss of central lymphocytes and replacement by accumulations of epithelioid macrophages with abundant eosinophilic cytoplasm and necrotic cellular debris within the mesenteric lymph node. The subcapsular and medullary sinuses of the lymph node contained multiple aggregates of histiocytes and few neutrophils.

Morphologic diagnosis:
Small intestine: Severe necrotizing enteritis with villus blunting and fusion and severe crypt necrosis
Lymph node: Moderate lymphoid follicular depletion; Multifocal granulomatous lymphadenitis

Additional diagnostic tests:
Immunohistochemistry:
  Canine parvovirus antigen detected
  Canine distemper virus antigen not detected
In situ hybridization: Canine circovirus DNA detected
PCR for canine parvovirus: Positive
PCR for canine circovirus: Positive

Comments:
The lesions in the small intestine and the lymphoid depletion are most consistent with canine parvovirus infection, as confirmed by the virology testing. Additionally in this case, there is a concurrent infection of canine circovirus as evinced by the prominent histiocytic infiltrates within lymphoid tissues and the presence of canine circoviral DNA and protein. We speculate the pathogenesis of this dual infection that infection with CPV-2, which caused crypt epithelial cell and lymphocyte necrosis and subsequent proliferation of regenerating epithelial cells and
lymphoblasts, provided the necessary target cells for CaCV-1 replication in these outbreaks and ultimately resulted in more severe and prolonged clinical disease. Alternatively, primary infection with CaCV-1 may cause immunosuppression and thus allow concurrent or secondary CPV-2 infection, despite previous vaccination and an unusual age.

References:
Case History:

Case #: SP17-0006285

Presenter: Raisa Glabman¹, Dodd Sledge¹, Michelle Magagna¹, Vandre Clear², and Erica Noland¹

Corresponding Institution: ¹Michigan State University, Lansing, MI; ²Animal Skin Clinic, Creve Coeur, MO

Signalment: An 11-year-old, male neutered domestic shorthaired cat

History:
The cat presented for a 3-month history of weight loss. Thinning of the hair coat started shortly thereafter. Routine blood work around that time, including serum chemistry and T4, was within normal limits. He then developed a 2-day history of nasal congestion/sneezing and lethargy. The owner reported he seemed “sweaty” after being immobile for long periods and had a sour odor. Over the next week, the animal lost 1lb. He seemed to have difficulty moving the back legs.

Gross findings:
At referral examination, the cat had a body condition score of 1.5-2/5. There was marked generalized scaling/flaking/crusting (adherent) and generalized hypotrichosis. There was brown interdigital debris, the ventral abdomen and medial thighs had patches of erythema, and the fur was stuck together with what appeared to be very light tan serous discharge.
Case Synopsis:

Case #: SP17-0006285

Presenter: Raisa Glabman1, Dodd Sledge1, Michelle Magagna1, Vandre Clear2, and Erica Noland1

Corresponding Institution: 1Michigan State University, Lansing, MI; 2Animal Skin Clinic, Creve Coeur, MO

Signalment: An 11-year-old, male neutered domestic shorthaired cat

Histopathology:
Three haired skin specimens respectively from representative lesions of the neck, dorsum, or right thigh were submitted to the MSU VDL. Six sections, representing the bisected and completely embedded specimens, were provided. The epidermis is moderately hyperplastic and is widely lined by mild to moderate parakeratosis. Such parakeratosis regionally contains large numbers of degenerative neutrophils and, in at least one specimen, colonies of coccoid bacteria. Hair follicles are variably atrophic, are often infiltrated by variable numbers of lymphocytes and histiocytes, and multifocally contain transepithelial apoptotic keratinocytes. There is similar change in predominately the deep keratinocyte layers of the epidermis immediately adjacent to follicular openings. The interfollicular epidermis is predominately unaffected. The superficial and periadnexal dermis contains moderate interstitial infiltrates of mast cell, lymphocytes, plasma cells, and histiocytes; fewer neutrophils and eosinophils; and low numbers of melanin laden macrophages consistent with pigmentary incontinence. Interspersed with this inflammatory population in the superficial dermis and variably noted within the follicular epithelium/epidermis, are large atypical round cells with hyperchromic to finely stippled nuclei and moderate amounts of eosinophilic cytoplasm. There are 6 mitoses in 10 high power fields. There is also widespread loss of sebaceous glands.

Additional diagnostic tests:
Thoracic radiographs performed at the rDVM were within normal limits.

Serial sections of above described haired skin specimens were immunohistochemically labeled for CD3, CD20, E-cadherin, or CD204. Many atypical round cells scattered throughout the superficial dermis and multifocally invading the overlying epidermis and follicular epithelium exhibited strong perimembranous immunoreactivity for CD3. There were lesser numbers of round to spindloid cells immunoreactive for CD204, consistent with histiocytes and dendritic cells, as well as low numbers of scattered CD20 positive small lymphocytes.

Morphological Diagnosis:
1. Lymphocytic interface dermatitis with transepithelial apoptotic keratinocytes, epidermal hyperplasia, hyperkeratosis, and diffuse sebaceous gland loss
2. Atypical CD3 positive round cell proliferation with multifocal epitheliotropism

Comments:
The clinical history and overall reaction pattern were suggestive of a thymoma associated exfoliative dermatitis; however, a thymoma was not found on thoracic radiographs. The described changes, alternatively, may reflect a similar reaction pattern of unknown cause. Lastly, given the large atypical T cell population noted in both the dermis and follicular epithelium, an epitheliotropic lymphoma was of concern.
References:
Case History:

Case #: XN16005

Presenter: Frank J. Simutis, DVM, PhD, Dipl. ACVP

Corresponding Institution: Bristol-Myers Squibb Company, Drug Safety Evaluation, Department of Pathology, New Brunswick, NJ.

Signalment: 5.5-year-old female cynomolgus monkey of Mauritian origin

History: Monkey from the stock colony was noted to have swelling around the face, neck, and inner thighs. Increasing abdominal distention and decreased body temperature (32.2°C) were noted during re-examination later the same day. Monkey was euthanatized due to poor clinical condition.

Gross findings: Moderate subcutaneous dependent edema in the cheeks, ventral abdomen, and inguinal region. Approximately 80-100 mL of clear, yellow fluid was present in the abdominal cavity, and 50-60 mL of clear fluid was present in the thoracic cavity. Renal cortices were markedly and diffusely pale. Fat depots in the heart, kidneys, and mesentery were gelatinous (serous atrophy of fat).

Hematology and serum chemistry:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC x 10⁶cell/µL</td>
<td>5.45-7.66</td>
</tr>
<tr>
<td>HGB (g/dL)</td>
<td>11.2-15.0</td>
</tr>
<tr>
<td>HCT (%)</td>
<td>36.9-54.6</td>
</tr>
<tr>
<td>PLT x 10³cell/µL</td>
<td>336-665</td>
</tr>
<tr>
<td>WBC x 10³cell/µL</td>
<td>5.33-20.67</td>
</tr>
<tr>
<td>Neutrophils x 10³cell/µL</td>
<td>1.60-17.23</td>
</tr>
<tr>
<td>Lymphocytes x 10³cell/µL</td>
<td>2.38-9.02</td>
</tr>
<tr>
<td>Monocytes x 10³cell/µL</td>
<td>0.15-0.78</td>
</tr>
<tr>
<td>Eosinophils x 10³cell/µL</td>
<td>0.01-0.85</td>
</tr>
<tr>
<td>Total Protein (g/dL)</td>
<td>7.0-8.6</td>
</tr>
<tr>
<td>Albumin (g/dL)</td>
<td>4.1-5.2</td>
</tr>
<tr>
<td>Globulin (g/dL)</td>
<td>2.6-3.8</td>
</tr>
<tr>
<td>BUN (mg/dL)</td>
<td>12-23</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>0.49-0.85</td>
</tr>
<tr>
<td>Phosphorus (mg/dL)</td>
<td>4.3-7.3</td>
</tr>
</tbody>
</table>
Case Synopsis:

Case #: XN16005

Presenter: Frank J. Simutis, DVM, PhD, Dipl. ACVP

Corresponding Institution: Bristol-Myers Squibb Company, Drug Safety Evaluation, Department of Pathology, New Brunswick, NJ.

Signalment: 5.5-year-old female cynomolgus monkey of Mauritian origin

Histopathology: Kidney: Multiple medium-sized arteries are either surrounded or segmentally infiltrated by accumulations of lymphocytes and plasma cells. Rarely, there is segmental disruption of the normal architecture of the tunica media and intima, and fragments of nuclear and cellular debris (likely degenerate neutrophils) are present. Approximately 75% of cortical tubules are lined by a cuboidal epithelium having increased cytoplasmic basophilia and crowded nuclei, with occasional mitotic figures present (tubular regeneration). Many affected tubules contain intraluminal cellular debris, neutrophils, or proteinaceous casts. Most glomeruli have segmental thickening of basement membranes and/or mesangial matrix and infiltration by occasional neutrophils. Many glomeruli fill the entire glomerular space and are surrounded by hypertrophic and/or hyperplastic parietal epithelium (glomerular crescents). Rare glomeruli are surrounded by increased amounts of fibrous connective tissue. Also present are occasional lymphocytic infiltrates within the tubular interstitium.

Morphologic diagnoses: Kidney: (1) arteritis and periarteritis, segmental, chronic, mild, consistent with polyarteritis nodosa; (2) tubular regeneration, multifocal, chronic, marked; (3) membranous glomerulonephritis, diffuse, chronic, mild, with glomerular crescent formation

Comments: Polyarteritis nodosa is a segmental necrotizing vasculitis of small- and medium-sized muscular arteries that is occasionally observed as an incidental finding in laboratory rats but is rare in monkeys. The lesions are often polyphasic, with acute and chronic changes present within the same vessel. Arteries in the pancreas, testes, and mesentery are most often affected in rats. In humans, renal vessels and other visceral arteries are frequently affected, and organ ischemia due to poor perfusion results in clinical illness. A specific inciting cause of polyarteritis nodosa in humans has not been established, although immune complex-mediated initiation of the complement cascade is thought to play a role as hepatitis B virus and other viral antigens have been detected in these vascular lesions.

Small- and medium-sized arteries in the pancreas, spleen (hilus), and heart (coronary artery) were also affected in this macaque. The pulmonary vessels were not involved, similar to the human form of the disease. Renal injury from chronic hypoperfusion due to segmental arteritis likely led to chronic renal failure, with accompanying clinical signs and gross pathology changes (dependent subcutaneous edema, ascites, and hydrothorax) and clinical pathology changes (hypoproteinemia, azotemia, and hyperphosphatemia). The clinical manifestations of renal failure in this monkey are similar to those reported for polyarteritis nodosa in another cynomolgus macaque. The glomerular changes in this animal have been reported as a background finding in monkeys and are likely unrelated to polyarteritis nodosa, as small vessels (including glomerular capillaries) are spared.
References:


Case History:

Case #: 50

Presenter: Pankaj Kumar, Bridget Lewis and Aaron Sargeant

Corresponding Institution: Charles River Laboratories, Spencerville, OH

Signalment: 5-month old, female, Sprague Dawley rat

History: The rat was a control animal from a 90 day oral gavage study. The rat exhibited no clinical signs before scheduled euthanasia.

Gross findings: There was a 0.5 x 0.5 x 0.4 cm, tan, firm, and solid mass at the cranial pole of the left kidney which effaced approximately 20% of the cortex and adjacent medulla.
Case Synopsis:

Case #: 50

Presenter: Charles River Laboratories, Spencerville, OH

Corresponding Institution: Charles River Laboratories, Spencerville, OH

Signalment: 5-month old, female, Sprague Dawley rat

Histopathology:

Approximately 20% of the renal tissue is replaced by a well demarcated, densely cellular, unencapsulated neoplasm that compresses the adjacent parenchyma. The neoplasm is composed of a disorganized mixture of three distinct cell populations: epithelial, blastemal and mesenchymal. The epithelial population is composed of cuboidal to columnar cells arranged in tubules with occasional densely cellular tufts that invaginate into the lumen (primitive glomeruli). These neoplastic cells have variably distinct cell borders, a moderate amount of eosinophilic cytoplasm, irregularly round to oval nuclei with densely clumped chromatin. The blastemal population is composed of ill defined, basophilic, densely aggregated, polygonal cells arranged in vague nests. These neoplastic cells have indistinct cell borders, a scant eosinophilic cytoplasm, a high nuclear to cytoplasmic ratio, round to oval nuclei with densely clumped chromatin. The mesenchymal population is composed of haphazardly arranged spindle cells in loose and lightly basophilic stroma (embryonal mesenchyme). These neoplastic cells are stellate to spindle with variably distinct cell borders, a scant amount of eosinophilic cytoplasm, oval to elongate nuclei with finely stippled chromatin. There are frequent mitotic figures in the epithelial and blastemal population. Interspersed within the neoplasm are a few cystic structures that are lined by flattened squamous epithelium and contains lightly basophilic material (mucus) with few sloughed epithelial cells.

Morphologic diagnosis: Kidney (left): Nephroblastoma

Additional diagnostic tests:

Comments:

Nephroblastomas or Wilms’ tumor are embryonal tumors of the kidneys that usually develop in young animals and children. These tumors arise from the rests of primitive metanephric blastema, a group of pluripotent cells that normally develops into both the nephrons and the renal interstitial tissue. A mutation in the Wilms tumor suppressor gene-1 (WT-1) on chromosome 11p13 is present in a subset of human nephroblastomas. The protein product of the WT-1 is a zinc-finger transcriptional factor that orchestrates the transition from epithelial to mesenchymal tissue during nephrogenesis. A genetic cause in animals has not yet been identified.

Grossly, nephroblastomas are most often unilateral and isolated to one pole of the kidney, encapsulated, multilobulated, white to tan, and firm with spongy/cystic areas of necrosis and hemorrhage. Microscopically, the epithelial component often forms abortive tubules or primitive glomeruli within tubules surrounded by the loose mesenchymal component which is organized in long interlacing streams and can differentiate into muscle, fibrous, adipose, cartilage or bone tissues. The blastemal component is often found in between the epithelial and mesenchymal components and are clusters of densely basophilic cells with high nuclear to cytoplasmic ratios.
The relative proportion of each component within a nephroblastoma can be highly variable. In this case, all three cell types are present (triphasic appearance) however, there is preponderance of epithelial and blastemal components over the mesenchymal component.

Spontaneous nephroblastomas occur rarely in young adult rats and are exceedingly rare in mice. These tumors have been induced in the rat only with genotoxic chemicals including dimethylnitrosamine, usually by transplacental, prenatal exposure. There are also certain rat strains that develop nephroblastoma and are utilized as an animal model. A related spontaneous lesion called nephroblastomatosis is encountered sporadically in Sprague-Dawley rats. Histologically, it is characterized by densely crowded blasts cells with ill-defined cytoplasm and basophilic nuclei located in the outer stripe of outer medulla. These foci of blast cells are remanants of metanephric blastemal cells and are considered preneoplastic.

Among domestic species, nephroblastoma is the most common primary renal tumor of swine, chickens and fish, the fifth most common primary renal tumor in dogs, and the fourth most common primary renal tumor in cats. In swine and poultry, metastases are rare, but in dogs and cats, metastasis is expected in > 50% of cases. Nephroblastoma can also occur in the thoracolumbar junction of the spinal cord and is seen most frequently in German shepherd dogs. These spinal cord tumors likely develop from remnants of renal rests trapped between the dura and developing spinal cord.

References:


Case History:

Case #: 18NX35

Presenter: Marie Pinkerton

Corresponding Institution: University of Wisconsin-Madison

Signalment: Free-ranging ~1 year old male white-tailed deer (Odocoileus virginianus)

History: Captured and sedated for tracking collar placement and rectal biopsy on 11 March 2018 in a Wisconsin county with endemic Chronic Wasting Disease. Mortality signal detected on 18 March 2018. Found dead by a shallow creek with no predation or scavenging lesions.

Gross findings:

This 34 kg yearling male white-tailed deer was in poor nutritional condition with scant subcutaneous and visceral adipose stores. Large regions of skeletal muscle were tan, dry, and friable, including: bilateral thigh and pelvic muscles (including semimembranosus, pectineus, rectus femoris, vastus lateralis, biceps femoris), and bilateral forelimb muscles (including subscapularis and serratus ventralis). The fascial planes of affected muscle had moderate to marked hemorrhage.

The pericardial sac contained 4 cc serous fluid. The epicardium and myocardium had multiple tan foci, including in the right ventricular wall at the apex and in the conus arteriosus, and in the right auricle. The endocardium of the left ventricle had moderate multifocal dark red ecchymoses in the septal wall and papillary muscle. There were broad thin fibrous adhesions of the left lung lobes to the thoracic wall, diaphragm, and each other.

Urine was dark red, watery, and translucent. Both kidneys were dark red brown with a dark red medulla. The lateral surface of the left kidney had a 4 mm diameter pale pink focus which extended 1 cm into the cortex as a pale pink wedge-shaped infarct.

The pylorus of the abomasum had two ~1 cm diameter dark red ulcers, and there were ~20 shallow ulcers throughout the rest of the abomasum, each 2-4 mm diameter. The proximal 15 cm of the duodenum contained dark red mucoid material; remaining intestinal contents were within normal limits. The rectal mucosa immediately orad to the anus had a focal 1 cm diameter shallow ulcer covered in a tan fibrinous membrane (rectal biopsy site).
Case Synopsis:

Case #: 18NX35

Presenter: Marie Pinkerton

Corresponding Institution: University of Wisconsin-Madison

Signalment: Free-ranging ~1 year old male white-tailed deer (*Odocoileus virginianus*)

Histopathology:

Skeletal muscle: Many scattered myocytes are degenerate or necrotic with one or more of the following: pallor or hypereosinophilia, cell swelling, loss of cross striations, fragmentation of sarcoplasm, infiltration by macrophages, replacement by macrophages and spindle cells with plump nuclei (satellite cells), or variable amounts of deeply basophilic stippled mineralization. The interstitium of affected muscle is multifocally mildly expanded by increased numbers of spindle cells with plump nuclei and small to moderate amounts of basophilic wispy to granular matrix. Few myocytes contain single sarcocysts, ~50-80 microns wide and up to 400 microns long, with a thin eosinophilic to amphophilic, occasionally striated wall, and containing many ~8x3 micron oval to crescentic bradyzoites.

Kidney: The cortex has a linear to wedge shaped area extending from the capsular surface to the medulla, in which all proximal convoluted tubules have loss of differential staining and retention of cellular outlines (coagulative necrosis), with multifocal moderate hemorrhage. Most glomeruli are viable and there is some survival around larger blood vessels. Multifocally the interstitium around the edge of the infarct contains few large plump spindle cells (macrophages +/- fibroblasts). In remaining renal tissue, few tubules contain small to moderate amounts of wispy to granular eosinophilic material, small amounts of cellular debris, rare neutrophils, and few sloughed tubular epithelial cells. Rare tubules have evidence of regeneration, including epithelial cells with basophilic cytoplasmic tincture, large nuclei with prominent nucleoli, attenuated cells, and occasionally a mitotic figure.

Morphologic diagnosis:

1. Skeletal muscle (and heart, not included):
   a. Severe subacute myonecrosis with mineralization (capture myopathy)
   b. Mild sarcocystosis

2. Kidney:
   a. Moderate subacute tubular necrosis with luminal pigment (myoglobin) and mild regeneration (myoglobinuric nephrosis)
   b. Moderate subacute focal cortical infarct

Additional diagnostic tests:

Immunohistochemistry for Chronic Wasting Disease on brainstem at obex and retropharyngeal lymph node: not detected.

Comments:

Capture myopathy, a type of exertional myopathy, is a common consequence of capture, handling, or immobilization of a variety of wild animals, including deer. Overexertion,
hyperthermia, metabolic acidosis, and especially increased stress-related circulating catecholamines may all play a role in the pathogenesis. Hypo- or hyperkalemia and low selenium levels may also play a role in some cases. Myonecrosis is usually multifocal and monophasic. Death can occur acutely due to cardiac failure caused by myocardial necrosis or hyperkalemia, or later due to myocardial fibrosis.

Death can also occur from renal failure due to myoglobinuria-associated acute tubular injury. Necrotic myocytes release myoglobin into the blood stream, which is excreted by the kidneys, causing myoglobinuria. Acute tubular injury with tubular epithelial degeneration and necrosis associated with myoglobinuria may be due to a combination of hypoxic/ ischemic damage, direct cytotoxic effect, and obstruction of tubules.

Sarcocystosis is a common incidental finding in wild white-tailed deer. Species that affect white-tailed deer include *Sarcocystis odoicoileocanis* and *S. odoi*, and the definitive hosts are most often domestic and wild canids.

**References:**


Case History:

Case #: 18-330

Presenter: Shelley J Newman DVM, DVSc, DACVP, Olufemi Fasina DVM, PhD

Corresponding Institution: Long Island University/University of Tennessee

Signalment: 2 of three perinatal Nigerian dwarf goat kids

History: Three goats kids were born without assistance to a three-year-old doe, bred previously to a 6 month old buck. Two goat kids, one doeling and one buck experienced respiratory difficulty at birth. Despite heroic efforts including CPR they both expired within the first five minutes of life. The third of the triplets, a doeling, died of respiratory difficulty at 1.5 weeks, but was not necropsied.

Gross findings:
The female kid had staining of meconium around the perineum. The lungs showed fetal atelectasis. There was a green to yellow mucoid content within both middle ears.
Case Synopsis:

Case #: 18-330

Presenter: Dr. Shelley Newman

Corresponding Institution: University of Tennessee

Signalment: 2 of three perinatal Nigerian dwarf goat kids

Histopathology: Slides contained a section of lung and a section of middle ear. The lung contained large numbers of alveolar macrophages, multi-nucleated giant cells and fewer neutrophils surrounding foreign material including intact and scrolled squamous epithelial cells and aggregates of amorphous yellow brown material (meconium). Alveolar spaces were marked filled by this material and bronchiolar lumina were similarly affected. Within the lumen, of the inner ear, here were moderate numbers of lymphocytes and plasma cells in the sub-epithelium, which was multifocally metaplastic. Additionally, there were focal areas of loose connective tissue containing large numbers of leaky small vessels (interpreted as granulation tissue). The lumen contained amorphous material resembling meconium and flakes of keratin.

Morphologic diagnosis:

Lung: Meconium aspiration bronchopneumonia, marked, subacute, diffuse

Middle ear: Otitis media, moderate, subacute, generalized, and lymphoplasmacellular

Final Diagnoses: Meconium aspiration syndrome (lung and ear)

Comments: Meconium release and aspiration is not considered part of normal parturition in the dog, sheep, dolphin, rabbit, human and/or non-human primate. In humans, contamination occurs in 10-15% of deliveries, 3% live births having meconium in lungs. Meconium aspiration syndrome, coined from a similar scenario in human infants, has been reported in foals as a cause of death at less than five days and in calves less than two weeks old.

The meconium is composed of bile, pancreatic enzymes, mucus, desquamated cells, lanugo, vernix caseosa, water, amniotic fluid and other cellular debris. Anything that would cause a hypoxic event in a fetus can cause peristalsis and the release of meconium in utero. Potential triggers include compression of the umbilical blood vessels, placentitis, umbilical cord knot, and placental insufficiency. It can also trigger the fetus to gasp and aspirate meconium and amniotic fluid into its lungs while in utero, or perhaps inhale meconium from the oropharynx at the time of the first breath of air.

Although sterile, meconium is locally irritative and obstructive and is a medium for bacterial growth. When aspirated, meconium is considered a toxin due to its damaging effect on surfactant and lung tissue. It is also directly toxic to the pulmonary epithelium, causing a haemorrhagic alveolitis with high concentrations of protein and albumin in the alveolar space. Meconium contains substances that are chemotactic to neutrophils and activate complement and may in addition be vasoactive. Moreover, meconium causes a potent dose-dependent inhibition of surfactant function and, along with fibrinogen and hemoglobin in the exudate, impairs the capacity of endogenous surfactant to reduce surface tension. Stability of alveoli at
end-expiration is thus compromised, as is the capacity to clear edema fluid from the airspaces. The resultant microatelectasis causes variable degrees of ventilation-perfusion mismatch or, worse still, intrapulmonary shunt.

Meconium also occludes the airways, from the upper airway to the alveoli, where during inspiration, air may be able to pass through but in the expiratory phase, air can become trapped behind meconium. This early mechanical obstruction gradually gives way to development of chemical pneumonitis over 48 hours. Meconium has many adverse biophysical properties, including high tenacity (stickiness), very high surface tension (215 mN/m), and potent inhibition of surfactant function.

Meconium aspiration pneumonia (MAS) is rare in veterinary medicine but has been reported in a dolphin, neonatal foals\textsuperscript{1,3} and calves that died following birth.\textsuperscript{2} In one study of 52 calves that died within two weeks of birth for infectious or noninfectious reasons, had evidence of meconium, squamous cells, or keratin was present in the lungs of 42.5 \%.\textsuperscript{2} Gross appearance varied from normal to suppurative bronchopneumonia to multifocal lobular atelectasis. The changes are more frequent than the cause of death in that 84\% had lesions, accounting for 18\% of deaths.\textsuperscript{2}

Microscopic changes were most consistent with a mild diffuse alveolitis with exudation of few neutrophil and fibrin.\textsuperscript{2} In rare cases, macrophages and multinucleated giant cells predominated around meconium particles, as in our case, and was accompanied by atelectasis, impaired gas exchange and ultimately acidosis.\textsuperscript{2} Acidosis can reduce colostrum intake and absorption. The lesions are often secondarily contaminated by bacteria (6/31) which are often organisms that would be seen in sepsis.\textsuperscript{2}

Older calves, have lesser amounts of meconium in lungs, which suggests that with time and no new exposure, they may be able to clear it. While squamous cell only aspiration exists, it is milder and only minimally mimics the foreign body reaction pattern of meconium.\textsuperscript{2}

To the best of our knowledge aspiration of meconium to the level of the middle ear to induce a foreign body otitis media, has not been reported. It is seen in the MAS in human infants. While there are conflicting reports, some suggest that being born through meconium contaminated fluids, increases the risk and incidence of ear infection in first two years of life\textsuperscript{8} where others say there is not an increased incidence. In one study of human infants, 55/130 had meconium aspiration and 17/130 had otitis media. Otitis media group could be grouped into those with suppurative inflammation and those with suppurative inflammation in addition to meconium debris. All cases with otitis media showed evidence of infection elsewhere, mainly pneumonia or meningitis. Virtually all cultured organisms were gram negative bacteria. Once in the ear, meconium may provide a culture media for bacterial growth and meconium may account for metaplastic epithelial changes. Intact auditory membranes do not hinder ascension of bacteria into middle ear. Inner ear is an important sample to help determine septicemia in peri-natal deaths.

References:


Case History:

Case #: 18-1124

Presenter: Ryan Jennings, DVM, PhD, Diplomate ACVP (Anatomic)

Institution: The Ohio State University, College of Veterinary Medicine, Columbus, OH 43210

Signalment: 8 year old MN English Setter

History: Intermittent bleeding from eyes, nose, prepuce and anus. Intermittent vesicular lesions on the nasal planum. No medications at time of biopsy. Biopsy from the left upper lip.
Case Synopsis:

Case #: 18-1124

Presenter: Ryan Jennings, DVM, PhD, Diplomate ACVP (Anatomic)

Institution: The Ohio State University, College of Veterinary Medicine, Columbus, OH 43210

Signalment: 8 year old MN English Setter

Histopathology:
Within the section of haired (facial, identified by vibrissae in section) skin, there is segmental marked irregular epidermal hyperplasia and mild compact orthokeratosis with a focal intraepidermal, subcorneal pustule containing neutrophils, erythrocytes, few macrophages and few acantholytic keratinocytes. At the base of the pustule, there is separation of individual and clusters of suprabasilar keratinocytes (acantholysis). There are increased numbers of mitotic figures within the associated basilar keratinocytes, which are frequently enlarged and reactive. There is mild, multifocal intercellular edema and low to moderate exocytosis of neutrophils and lymphocytes. The superficial dermis, predominantly surrounding superficial vessels but occasionally obscuring the dermo-epidermal junctions, contains moderate numbers of inflammatory cells predominantly composed of lymphocytes and plasma cells, with mild pigmentary incontinence. There are rare vacuolated or apoptotic basal keratinocytes. There are low numbers periadnexal (perivascular) lymphocytes and plasma cells.

Morphologic diagnosis:
Haired skin; suprabasilar pustular dermatitis with acantholysis

Additional diagnostic findings:
In sections of oral mucosa, there was prominent suprabasilar epidermal loss (ruptured vesicle/pustule) with segmentally intact and hypertrophied basilar keratinocytes.

Comments:
The histologic pattern of pustular dermatitis with acantholysis is typical of the pemphigus complex of diseases. Clinically, the lesion distribution of face and mucocutaneous junctions and hemorrhage, and as well as the histologic features of suprabasilar acantholysis were most supportive of a diagnosis of pemphigus vulgaris (PV). The differential diagnoses of cutaneous drug reaction and paraneoplastic pemphigus were considered less likely but nonetheless offered based on histopathology alone; however, these were considered unlikely following correspondence with the clinician based on the absence of previous medications (as triggers) and the absence of any abnormalities on thoracic radiographs and abdominal ultrasound.

PV is a rare manifestation of vesicular/bullous autoimmune disease targeting, primarily, the desmoglein 3 protein of suprabasilar keratinocytes, although the primary antigen may be
somewhat variable during the disease. Although considered a vesicular/pustular cutaneous
disease, much like in pemphigus foliaceus (PF), vesicles/pustules often rupture leading to the
clinical manifestation of crusts and ulcers. However, unlike PF, PV frequently affects the oral
cavity as well as mucocutaneous junctions (anus, vulva, prepuce, nasal planum). Other
cutaneous sites may be affected, including the concave pinna and elsewhere. Clinical
differential diagnoses (based on lesions and distribution) may include cutaneous drug reaction,
erythema multiforme, mucous membrane pemphigoid, and epidermolysis bullosa acquisita.

Histologically, PV is characterized by suprabasilar vesicles or pustules with acantholysis. Drug-
reaction and paraneoplastic pemphigus cannot be ruled out based on this lesion, and therefore,
the diagnosis should be rendered in the context of additional clinical information/diagnostics. It
is important, as is often the case with dermatopathology, that the pathologist recognizes that
specific histologic patterns may be observed in multiple disease processes, and that clinical
information is crucial in coming to a definitive diagnosis.

1. Gross, Thelma Lee., et al. Skin Diseases of the Dog and Cat: Clinical and