UNIVERSITY OF WISCONSIN
VMTH PATHOLOGY SERVICES/PH:(608)263-9934
2015 LINDEN DRIVE

MADISON, WI 53706
Phone #: 608-263-7600 **Fax #: 608-265-5626**

Owner: KOTOYO HOSHINA
5002 SHEBOYGAN AVE
APT 120
MADISON, WI 53705

Accession Number: N11-01010

Case Coordinator: Marie Pinkerton
Received: 09/19/2011 **Finalized:** 10/05/2011
Sampled: 09/18/2011

To: DR. DOMINIQUE KELLER
VMTH

History: RABIES SUSPECT? IF Y, SUBMIT RABIES FORM 4110: NO-N/A
DATE & TIME OF DEATH? -9/18/11, 11am
DEATH HOW? EUTHANIZED-IP Beuthanasia
PERMISSION FOR NECROPSY GRANTED? YES, VERBAL-
IS ANIMAL INSURED? NO-
TYPE OF NECROPSY? COMPLETE-
TYPE OF DISPOSAL? CREMATION WITH RETURN OF ASHES-
BODY IN/LABELED? A. YELLOW BAG/ORANGE TAG-
BRIEF HISTORY: -Aplastic anemia: anemia, thrombocytopenia, leukopenia. Bone marrow aspirate revealed hypoplasia in all three lineages. Also had autoagglutination on blood smear. Received a blood transfusion on 9/14, with cyclosporine administered 2 hours prior. Cyclosporine was continued twice daily after the transfusion. A temp of 104.6 was noted on 9/14, so enrofloxacin was administered twice daily. The morning of 9/15, the temp had decreased to 102.2 F (normal). He was eating and drinking very well with a normal mentation. lethargic. Syringe feedings of critical care was also administered to ensure proper GI motility. On the night of 9/15, the IV catheter was no longer patent. The overnight CCU crew had re-advanced the catheter into the vein and flushed. By 9/16, the rabbbit had a fever of 104.7 F. He was still eating and drinking, but did look a little more lethargic. The IV catheter was evaluated, and area around the catheter was wet with fluid and blood suggesting the catheter had slipped somewhat from the placement site despite re-advancement overnight. The IV catheter was immediately removed, the site cleaned and bandaged. Parenteral penicillin was added to the regimen to increase antibacterial spectrum. Since Mango was stable and eating and drinking, and since he was increasingly stressed at the clinic he was sent home. Medications were switched to oral enrofloxacin and cyclosporine. He was to be brought in the following morning to evaluate his temperature. The owners opted not to bring him that morning, but he was brought it on 9/18 due to lethargy, epistaxis rate, and anorexia. Owners opted for euthanasia, but the animal died just as the Beuthanasia solution was given intraperitoneal (no peripheral veins accessible).
CURRENT PHYSICAL FINDINGS: -Mango was QDR. T = 96.5 F RR = 80 bpm, with increased effort. HR = 160 bpm. He was bradycardic, tachypneic with increased effort, mentally innappriopriate and hypothermic. His lungs were harsh, mostly in the cranioventral lung fields. He also had epistaxis.
SURGICAL FINDINGS (IF ANY)? -N/A
PERTINENT LABORATORY RESULTS: -*Anemia, thrombocytopenia, leukopenia
9/13/11: PCV: 13% 9/16/11: PCV: 21% (improved)
HGB: 5.2 g/dL
RBC: 2.26*10^6/uL
MCV: 63.4 fL
MCH: 23.1 pg
MCHC: 36.5 g/dL
9/13/11: Platelet: 12*10^3/uL 9/16/11: Platelet: 36*10^3/uL (improved)

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Seg: 200/uL
Lymph: 1,940/uL
agglutination, not cleared by saline

*Non-regenerative anemia

RBC: 2.26*10^6/uL
% Reticulocyte manual: 0.2%
Absolute Reticulocyte manual: 0/uL

*Pancytopenia: marked erythrocytic, granulocytic, and megakaryocytic hypoplasia

IMAGING RESULTS X-RAY, ULTRASOUND: -N/A
IMAGING RESULTS CT, MRI: -N/A
CLINICAL DIAGNOSIS: -pancytopenia of unknown etiology
WHAT DETAILS/ANSWERS WILL NECROPSY PROVIDE? -bone marrow analysis, masses/macroscopic abnormmalities in the lungs and abdomen. Disease in the lungs causing the harsh lung sounds.
PREVIOUS BIOPSIES? IF Y, GIVE BIOPSY #S: NO-N/A
IF NONVMTH BX, PROVIDE COPY OF RESULTS: -N/A
MICROBIOLOGY ANALYSIS? IF Y, LIST TESTS: YES-E. caniculi positive. diagnosed in 2008.
VIROLOGY ANALYSIS? IF Y, LIST TESTS: NO-N/A
RABIES FA? NO-N/A
OTHER TESTING WANTED, DESCRIBE: -Bone marrow analysis to confirm the FNA (possibly a core)
CLIENT ASKS CLINICIAN TO CALL WITH RESULTS: YES-

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NECROPSY RESULTS

Necropsy

REQUESTED SMALL ANIMAL NECROPSY NO CHARGE

Gross Description

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NECROPSY RESULTS

REF CASE NO	123074
ANIMAL ID	Mango
SPECIES	Lapine
BREED	Other Lapine
SEX	Male
AGE	5y
WEIGHT GRAMS	0
GROSS DESCR	This is the body of a 5 year old rabbit weighing 2.8 kg, in moderate body condition, euthanized with an intraperitoneal injection at 11 am on 9-18-11 and necropsied at 1:53 pm on 9-19-11. The hair on the mid ventral abdomen is clipped and a 2 x 3 cm area of hair just above the right hind hock is clipped. There is blood on the muzzle. The body is in poor post-mortem condition with significant abdominal autolysis. There is minimal subcutaneous fat present and the skeletal muscles are very pale pink throughout the body. Several pinpoint areas of subcutaneous hemorrhage are over the right shoulder with the largest measuring 11 x 18 mm. A red, flat 11 x 18 mm area of subcutaneous hemorrhage is 3.5 cm cranial to the point of the hip on the right side. Two 0.5 cm in diameter areas of subcutaneous hemorrhage are 3 cm to the left of the ventral midline in the midabdonminal area. Seven ml of non-clotting serosanguinous fluid is in the thoracic cavity. The tracheal mucosa is pink to red. The right middle, left cranial, and cranial half of the left caudal lung lobes are firm, red and ooze blood on cut section. The right cranial lung lobe oozes fluid on cut section. In the margin between the left cranial and left middle lobes is an area of pale pink to grey firm tissue that extends roughly 1 cm into the parenchyma with indistinct margins. The heart weighs 59 g (2.1% body weight). The left ventricular wall measures 3 mm in thickness, the right ventricular wall measures 1 mm in thickness and the interventricular septum measures 3 mm in thickness. The liver is diffusely pale tan and weighs 71 g (2.5% body weight). The left lateral lobe is very firm and light grey throughout. A 1 cm in diameter focal area of hemorrhage is on the gastric mucosa 1 cm from the pyloric sphincter. Bone marrow is predominately red with a few tan areas.

Gross Findings

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NECROPSY RESULTS

REF CASE NO	123074
ANIMAL ID	Mango
GROSS FINDGS	1. Body as a whole: Marked generalized pallor 2. Gastrointestinal system a. Liver: Marked regionally extensive hepatopathy b. Stomach: Mild focal mucosal hemorrhage 3. Respiratory system: a. Lungs: a. Moderate focal left cranial lung discoloration (fibrosis vs. pneumonia vs. neoplasia) b. Mild regionally extensive congestion and edema b. Trachea: Mild diffuse mucosal hyperemia 4. Integumentary system a. Subcutaneous tissue: Mild multifocal subcutaneous hemorrhage 5. Thoracic cavity: Mild diffuse pleural effusion 6. Hematopoietic: Bone Marrow: Moderate diffuse reactive bone marrow
GROSS DX	1. Euthanasia 2. Marked generalized pallor 3. Hepatopathy 4. Pulmonary discoloration (pneumonia vs. fibrosis vs. neoplasia)
GROSS COMMENT	The cause of clinical signs are currently inconclusive with gross findings. Liver and lung lesions could potentially be related to the cause of pancytopenia.

Histopathology

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REF CASE NO 123074

ANIMAL ID Mango

HISTO DESCR

Bone marrow (Slide 1):
The bone marrow is severely hypocellular with an adipose to hematopoietic ratio of approximately 9:1. The majority of the cells are of mature lineage and include erythrocytes, plasma cells, macrophages, neutrophils, and lymphocytes. Myeloid and erythroid precursors are severely decreased and the myeloid to erythroid ratio is approximately 1:1. There are a few scattered megakaryocytes and many macrophages containing brown granular intracytoplasmic pigment.

Brain (Slides 2&3):
There are moderate numbers of scattered foci of melanocytes in the meninges (melanosis.) There are few lymphocytes around vessels within the brainstem.

Liver (Slide 4):
Multifocally there is centrilobular coagulative necrosis, with disruption of the walls of the central veins and occasional replacement and accumulation of homogenous amorphous eosinophilic material. Surrounding the central veins are swollen hypereosinophilic hepatocytes with loss of cellular detail and occasional poor to no nuclear staining (karyolysis). There are scattered small amounts of karyorrhectic debris. Hepatocytes containing large amounts of clear round to wispy cytoplasmic vacuoles which do not displace the nucleus (hydropic degeneration) are at the interface between necrotic hepatocytes and more normal appearing hepatocytes. Occasionally, necrotic and degenerating hepatocytes have deeply basophilic granules in their cytoplasm (mineralization.) Many lymphocytes, plasma cells, and few neutrophils surround and extend into bile ducts. The sinusoids contain few scattered lymphocytes. There are mild amounts of connective tissue around the portal triads (fibrosis).

Grossly abnormal liver (Slide 5):
Diffusely, hepatocytes are severely attenuated and have loss of cellular detail with poor or no nuclear staining, indistinct cellular borders, and occasionally hepatocytes contain few clear cytoplasmic vacuoles (hydropic change). There is severe congestion and widening of the sinusoids and nearly all vessels have disrupted walls and are filled with pale pink acellular material (thrombi.) There are large areas of hemorrhage and moderate multifocal areas of eosinophilic cellular and karyorrhectic debris scattered throughout the parenchyma and occasionally around and within vessels (necrosis). There is moderate decrease in the numbers of bile ducts and remaining ducts are partially collapsed and have disrupted epithelium. The capsule contains marked amounts of hemorrhage, eosinophilic cellular and karyorrhectic debris (necrosis), fibrin, and some fibrosis.

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There is severe distortion of lung architecture diffusely in 2 sections by hemorrhage and pale pink slightly granular fluid (edema) surrounding vessels, bronchi, and filling alveolar spaces. Alveolar spaces are multifocally filled with large amounts of fibrin, there is marked disruption of septa, and often pneumocytes are swollen and hypereosinophilic sometimes with poor to no nuclear staining. There is marked perivascular and some alveolar wall and lumen infiltration with lymphocytes, macrophages, and plasma cells. Several vessels in one section (Slide 5) are filled with eosinophilic acellular material (thrombi.) Other sections contain moderate multifocal areas of alveolar collapse (atelectasis) and occasional areas of peripheral emphysema. There are similar perivascular inflammatory cells and often bronchi and bronchiole have disrupted epithelium with large sloughed pieces in lumens.

Kidneys (Slide 6):
There is mild infiltration of lymphocytes around vessels, in the interstitium, and around glomeruli. There are few small multifocal areas of eosinophilic amorphous and cellular material (necrosis). The lumen of a few collecting ducts contain small amounts of purple granular material (mineral). There are small amounts of loose connective tissue occasionally around vessels (fibrin). There is mild congestion at the corticomedullary junctions.

HISTO DESCR

Trachea (Slide 6):
Vessels are moderately congested, and there is increased space between the elastic fibers (edema) in the lamina propria. The serosa contains mild scattered hemorrhage.

Stomach (Slide 6):
There is moderate multifocal hemorrhage in all layers of the mucosa extending into the submucosa. There is a focal area of coagulative necrosis with loss of cellular detail in glands containing golden brown pigment granules. There is a focal area of clear refractile circular material with thick walls (plant material) embedded in the necrotic glands and few scattered neutrophilic and lymphocytes. Few small vessels in the mucosa are filled with eosinophilic cellular material (thrombi).

Heart (slide 7):
In the right ventricle there is a large area of hemorrhage in the epicardium with a few small foci in the myocardium. The right atrial endocardium contains a large area of hemorrhage extending into the myocardium. Predominately in the epicardium and also extending into the myocardium are moderate amounts of adipocytes, macrophages, and fewer lymphocytes. There are many multifocal small areas of hypereosinophilic myocytes with loss of striations in the myocardium. Sometimes vessels contain plump reactive endothelial cells.
The left side of the heart contains moderate to marked areas of

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NECROPSY RESULTS

hemorrhage in all layers predominately in the left atrium. There is infiltration of adipocytes, macrophages and lymphocytes in the myocardium and endocardium. There are few small areas of hypereosinophilic myocytes with loss of striations in the myocardium.

HISTOPATH DX

1. Gastrointestinal:
a. Liver
i. Severe subacute lobar hepatic necrosis with thrombosis
ii. Marked subacute multifocal centrilobular hepatic necrosis
b. Stomach
i. Marked acute focal gastric mucosal necrosis with moderate multifocal hemorrhage and thrombosis
2. Respiratory:
a. Trachea
i. Moderate acute diffuse congestion and edema
b. Lungs
i. Marked subacute regionally extensive fibrinonecrotic and hemorrhagic lymphoplasmacytic pneumonia
ii. Marked subacute regionally extensive edema, moderate multifocal atelectasis, and mild multifocal peripheral emphysema
3. Hematopoietic
a. Bone Marrow
i. Severe diffuse pancytopenia/ trilineage hypoplasia
4. Cardiovascular
a. Heart
i. Marked acute multifocal hemorrhage and mild multifocal myonecrosis with moderate subacute multifocal lipogranulomatous myocarditis and epicarditis.

HISTO COMMENT

The lesion in the grossly abnormal liver lobe is most consistent with previous liver lobe torsion. This torsion would cause venous obstruction which would increase hydrostatic pressure and cause thrombosis. This caused hemorrhage, ischemia, and necrosis in the affected lobe, and likely created a cytokine cascade which affected other organs. In addition, anemia and hypoperfusion likely contributed to necrotizing lesions in multiple organs, particularly heart and liver.

The relationship of pancytopenia to the liver lesion is uncertain. This may be related to toxins or may have been a mild underlying chronic condition that was worsened by the multiorgan damage. Alternatively, but unlikely, demand for hematopoietic cells may have outstripped supply with no time for a regenerative response. Anemia but not pancytopenia has been reported in previous cases of liver lobe torsion in rabbits.

References:

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Pathologist

PATHOLOGIST Chamberlin, Tamara, DVM
PATHOLOGIST PINKERTON, MARIE, DVM, DACVP