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**ADDL Case #:** A12-10440    **Other ID:** 757-0182    **Date Received:** 3/29/2012

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SUSAN MCGRATH  
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|---------------------------------|-------------------------------|------------------------------|
| <b>Vet Phone:</b> 494-1107      | <b>Species:</b> Canine        | <b>Sex:</b> FS-Female Spayed |
| <b>Vet Fax:</b> 496-1025        | <b>Breed:</b> German Shepherd | <b>Age:</b> 6.5 Years        |
| <b>Animal ID:</b> (1)MAGGIE     |                               |                              |
| <b>Tests Requested in:</b> Path |                               |                              |

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**Final Report**  
4/30/2012 9:52:04 AM

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**Pathology** by Laura Baseler and Steve Lenz

**Case Summary** (4/27/2012 )

**Diagnosis:**

Neuroendocrine carcinoma with multiorgan metastases

**Comment on Diagnosis:**

Immunohistochemistry for protein gene product 9.5, synaptophysin and chromogranin A were performed on sections of liver, spleen and pituitary gland. Diffusely, neoplastic cells in the liver, spleen and pituitary gland have strong granular cytoplasmic labeling with protein gene product 9.5. Synaptophysin moderately labels the cytoplasm of approximately 80% of neoplastic cells in the pituitary and spleen and weakly labels the cytoplasm of approximately 60-90% of neoplastic cells in the liver depending on the liver section. Chromogranin A weakly labels the cytoplasm of approximately 40% of neoplastic cells in the pituitary gland, moderately labels cytoplasm of 50% of neoplastic cells in the liver and weakly labels the cytoplasm of 50% of neoplastic cells in the spleen.

The immunohistochemistry results are consistent with a neuroendocrine tumor; however, the origin of the tumor is unknown. Additional immunohistochemistry may help determine the tissue origin of the tumor.

Decalcified sections of humerus and femur were examined microscopically. In a section of the humeral head, the articular cartilage is irregularly thinned (erosions) with diffuse loss of metachromatic staining. Multifocally, chondrocytes are sparse and widely separated in the cartilage. Multifocally, nests of neoplastic cells efface the bone marrow. In a section of decalcified femoral condyle, there is complete loss of articular cartilage with replacement by fibrous connective tissue. The adjacent synovium exhibits villous hyperplasia with rare hemosiderophages in the subsynovial connective tissue. Multifocally, bone marrow hematopoietic cells are effaced by packets of neoplastic neuroendocrine cells. Focally, the bone marrow is effaced by hemorrhage mixed with lesser amounts of edema, fibrin and hemosiderophages.

## **Histopathologic Examination (4/6/2012 )**

### **Description of Histopathology:**

Multiple tissues are examined microscopically, including the lung, omentum, thyroid gland, parathyroid gland, liver, spleen, kidney, trachea, pancreas, urinary bladder, lymph nodes, stomach, heart, mediastinal mass, small intestine, large intestine, adrenal glands, bone marrow and brain. Tissues with lesions are described.

Approximately 90% of the pituitary pars intermedia and pars distalis is effaced by an infiltrative, non-encapsulated neoplasm composed of packets of polygonal cells supported by a fine fibrovascular stroma with multifocal to coalescing areas of necrosis and hemorrhage. Multifocally, neoplastic cells form rosettes. Neoplastic cells have an elongated oval nucleus, dispersed chromatin, an indistinct nucleolus and a moderate amount of eosinophilic cytoplasm. There are 17 mitotic figures in 10 400X fields. There is mild anisocytosis and anisokaryosis

Bilaterally, adrenal glands are almost completely effaced by neoplastic cells, similar to those in the pituitary, and multifocal to coalescing infarcts characterized by necrotic cellular debris, hemorrhage, fibrin and edema. Few zona glomerulosa cells remain, which allows for tissue identification.

In the liver, neoplastic cells (similar to those in the pituitary) efface approximately 40% of the hepatic parenchyma and are arranged in packets with a fine fibrovascular stroma or fill and distend sinusoids which compress hepatocytes. Packets of cells are separated by bridging necrosis and hemorrhage mixed with fibrin and edema. Multifocally, neoplastic cells are present in the lumen of portal and central veins and form packets in the connective tissue of portal triads. Focally, portal veins contain intraluminal fibrin thrombi. Multifocally, hepatocytes are atrophied or contain cytoplasmic lipofuscin or bile.

Approximately 80% of the splenic parenchyma is effaced by similar neoplastic cells. Rarely, neoplastic cells are multinucleated with up to 4 nuclei. Multifocally, necrotic neoplastic cells are mixed with fibrin, hemorrhage and edema. Hemosiderophages and megakaryocytes are scattered throughout the spleen.

Approximately 90% of the pancreas is effaced by the neoplasm; there is marked loss of endocrine and exocrine pancreas with lobular collapse and closely spaced pancreatic ducts lined by hypertrophied epithelial cells. Fibrosis surrounds remaining ducts and pancreatic lobules. Within the neoplasm there is focal necrosis with central mineralization; the necrosis is surrounded by lymphocytes and macrophages. Multifocally, there is abundant hemorrhage, fibrin and edema. Neoplastic cells, lymphocytes and plasma cells infiltrate the peripancreatic adipose tissue.

Approximately 40% of the renal cortex is effaced by the neoplasm. Neoplastic cells also expand the cortical interstitium, fill the lumen of venules in the cortex and corticomedullary junction and capillaries in glomerular tufts and rarely infiltrate the medulla. Scattered renal tubular epithelial cells contain cytoplasmic bile. Scattered medullary tubules have mineralized epithelium.

Diffusely, alveolar capillaries and pulmonary arterioles and venules are filled with intraluminal neoplastic cells which also distend alveoli. Multifocally, there are alveolar hemorrhages and clusters of foamy macrophages. Focally, yellow pigment is found in the cytoplasm of alveolar macrophages, in alveolar lumina and within the alveolar septa.

Neoplastic cells efface approximately 10% of the left atrial and ventricular myocardium. Cardiomyocytes adjacent to the neoplasm often have vacuolated sarcoplasm (degeneration), are atrophied or have fragmented sarcoplasm and a pyknotic nucleus (necrosis). Focally, in the ventricular myocardium, hemorrhage surrounds and separates cardiomyocytes, some of which are degenerate or necrotic. Two medium-sized myocardial arteries in the ventricle have eosinophilic granular material that expands the tunica media; affected vessels have compressed lumina (arteriosclerosis).

The enlarged lymph node near the stomach and duodenum is completely effaced by the neoplasm. Multifocally, neoplastic cells infiltrate the capsule and rarely invade capsular capillaries. Multifocally, neoplastic cells are necrotic and mixed with abundant hemorrhage, fibrin and edema. Few hemosiderophages are scattered in the neoplasm. A second lymph node, presumed to be a mesenteric lymph node, is similarly affected.

The cranial mediastinal mass seen at necropsy is composed of adipose tissue infiltrated by multiple nests of neoplastic cells and a marked infiltrate of perivascular lymphocytes and plasma cells. Multifocally, neoplastic cells are necrotic and mixed with hemorrhage, fibrin and edema.

The small intestinal mesenteric nodule seen at necropsy is composed of neoplastic cells.

In a section of femoral bone marrow that contains rare mineralized bony trabeculae, there is multifocal effacement of the marrow by packets of neoplastic cells.

In a section of tissue containing the two uterine horns near the site where the perimetrium of the uterine horns was attached to omentum and to each other; the perimetrium of both uterine horns are focally adhered together by connective tissue. The myometrium of both horns is circumferentially moderately infiltrated by histiocytes and lymphocytes mixed with edema. The uterine lumina contains either sloughed epithelial cells and rare basophilic mineralized debris or cellular debris.

There is mild focally extensive urinary bladder propria submucosa hemorrhage.

In the area of omentum that had hemorrhage at necropsy, adipocytes are surrounded and separated by hemorrhage.

**Morphologic Diagnosis:**

Pituitary gland, adrenal glands, liver, spleen, pancreas, kidney, lung, heart, lymph nodes, cranial mediastinum, small intestinal mesentery, bone marrow: neuroendocrine carcinoma

**Comment on Histopathology:**

The origin of the multicentric widely disseminated neoplasm could not be definitively determined at necropsy or histologically. Differentials for the tissue of origin include: pituitary gland, adrenal gland or liver. Histologically, the neoplasm appears to be a neuroendocrine carcinoma; immunohistochemistry will be performed to confirm this diagnosis and results will be placed in the case summary.

Decalcified sections of femur and humerus are pending; lesions will be detailed in the case summary.

**Necropsy Examination** (4/6/2012 )

**Gross Findings:**

A 31.4 kg, reportedly six-year-old spayed female white German Shepherd dog was submitted for necropsy on 3/29/12. According to the submitter, the dog had a history of thrombocytopenia, peripheral lymphadenopathy, and splenic and hepatic nodules.

The animal was in good body condition, autolysis was minimal. Diffusely, adipose tissue and subcutis were icteric. Overlying the abdominal cavity, there were multiple hemorrhages in the skin and underlying skeletal muscle. The following lymph nodes were enlarged and red on cut-surface: left axillary, right retropharyngeal, mesenteric, all tracheobronchial and mediastinal lymph nodes and a lymph node adjacent to the stomach and duodenum.

The abdominal cavity contained approximately 75 mL of unclotted blood. The liver was markedly enlarged

with scattered numerous tan to red, 0.1 to 0.5 cm in diameter slightly raised nodules throughout all liver lobes. Diffusely, the spleen was markedly enlarged with numerous scattered 0.2 to 1.0 cm diameter, tan nodules. Bilaterally, renal cortices were diffusely pale brown with numerous, round, scattered, 0.2 to 0.4 cm diameter, tan to pink nodules in the cortex occasionally with interspersed cortical petechiae. Variably-sized hemorrhages were scattered in the gastric serosa. There were multiple widely scattered 0.2 to 0.4 cm, round, gastric mucosal erosions and many anastomosing linear depressions in the mucosa. There were several tan, 0.2 to 0.4 cm, round nodules scattered throughout the pancreas. There was a raised, red, 0.4 cm diameter nodule in the distal duodenal serosa; a similar lesion was present in the jejunal mesentery. There was a focal distal duodenal mucosal ecchymosis. There were a few jejunal mucosal erosions. Diffusely, the small intestinal lumen was gas-filled. Multifocally, the large intestinal mucosa was congested. Focally, there was hemorrhage in the omental adipose tissue adjacent to mesenteric vessels. Both adrenal glands were markedly enlarged and dark red on cut-surface; the right adrenal gland was friable.

There were numerous tan, round, 0.2 to 0.5 cm, firm nodules in the epicardium, myocardium and endocardium of the left and right atrium, left and right ventricle, and left papillary muscles. Multifocally, hemorrhages were interspersed between the nodules. Focally, a tan, slightly raised irregularly-shaped plaque (0.4 cm x 0.6 cm) was present in the mitral valve. There was approximately 8 mL of unclotted blood in the pericardial sac. Diffusely, left lung lobes were pale pink with multiple widely scattered round hemorrhages and numerous firm, tan, round variably-sized nodules; similar nodules were also found in the congested right lung lobes. The cranioventral aspect of the left cranial lung lobe was mottled dark red to black. Diffusely, the trachea was collapsed and flattened dorsoventrally with a widened trachealis muscle. Petechiae were scattered in the costal pleura.

Bilaterally, the femoral heads were mildly misshapened and flattened with multiple cartilage erosions. Bilaterally, there were multiple articular cartilage erosions, osteosclerosis and osteophyte formation on the medial and lateral trochlear ridges of the distal femoral condyles, the head of the humerus, medial humeral condyle and ulnar olecranon and coronoid processes. The stifle and elbow joint capsules were diffusely thickened by fibrosis, and the synovium was dark yellow and thickened.

There was a single hemorrhage in the urinary bladder mucosa. A segment of omentum and the distal portions of the left and right uterine horns were fused together.

The pituitary was diffusely enlarged (1 cm x 0.6 cm x 0.2 cm) and dark red.

Gross lesions were not observed in the brain, eyes, oral cavity, larynx, thyroid gland, parathyroid glands, esophagus, gall bladder or midshaft femoral bone marrow.

**Gross Diagnosis:**

Liver, spleen, kidney, heart, lung: nodules (neoplasia)  
Lymph nodes (mesenteric, right retropharyngeal, left axillary, tracheobronchial and mediastinal):  
lymphadenopathy  
Pericardial sac: mild hemopericardium  
Abdominal cavity: mild hemoperitoneum  
Pancreas: nodules  
Skin, adipose tissue: diffuse icterus  
Stomach: serosal hemorrhages, mucosal erosions  
Trachea: tracheal collapse  
Elbows, stifles, hips, scapulohumeral joints: degenerative joint disease

**Comment on Necropsy:**

Final diagnosis is pending the results of histopathology.