

**An Esophageal Mass in a Beagle Dog**  
**Senior Seminar Paper**

**By: Lina N. Mohamed**  
**DVM Class of 2008**

**Advisor: Dr. H. Jay Harvey, DVM, Diplomate ACVS**  
**Associate Professor of Small Animal Surgery**

**College of Veterinary Medicine**  
**Cornell University**

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## **Summary**

This clinical report describes a rhabdomyosarcoma, diagnosed by histopathology, in the esophagus of an 11 year old male castrated beagle dog. Clinical signs associated with the mass were progressive regurgitation of food and liquid. The patient also suffered from chronic bronchitis, chronic coughing and recurring pneumonia. Diagnostic testing included bronchoscopy, endoscopy, trans-tracheal wash evaluation (cytology and culture), thoracic radiographs, abdominal ultrasound, CT scan, fluoroscopy, bloodwork, urinalysis and histopathology. The surgical excision and post-operative treatment/diagnostic testing are described, as well as the histopathology process of diagnosis. Canine esophageal histology, previously documented canine esophageal tumors and canine rhabdomyosarcoma is discussed.

## **Signalment, Chief Complaint & Case History**

Smokey Kukla, an 11 year old male castrated beagle, presented to the Cornell University Hospital for Animals Soft Tissue Service on January 30<sup>th</sup>, 2007 for further evaluation of an esophageal mass. His clinical signs consisted of progressive regurgitation of food and a phlegm-like liquid as well as chronic coughing.

Smokey was adopted from a Virginia rescue organization in 2004, with a history of chronic bronchitis. For the next two years, he was treated by his referring veterinarian (rDVM) for chronic bronchitis and recurring bouts of pneumonia with various antibiotics, steroids and theophylline. In July of 2006, Smokey presented to the Cornell Internal Medicine Service for chronic coughing and a 3 week history of vomiting. Orthogonal thoracic radiographs, bronchoscopy and trans-tracheal wash evaluation confirmed the previous diagnosis of chronic

bronchitis. A round, firm, vascularized mass arising from the dorsal esophageal wall was visualized at approximately the level of the thoracic inlet via endoscopy. Fine needle aspiration of the mass was non-diagnostic. Endoscopic biopsies of the stomach and small intestines showed mild inflammation, not deemed severe enough to cause vomiting. Abdominal ultrasound revealed hepatomegally with a 3.5 cm hyperechoic hepatic nodule of unknown clinical significance, a 0.83 cm hypoechoic splenic nodule and mild prostaomegally with mottled echogenicity. Bloodwork showed mild thrombocytosis and mildly elevated ALT, AST, Alk Phos and cholesterol levels. Lastly, an ACTH stimulation test and fecal analysis were negative. No cause for the vomiting was determined and Smokey was discharged with the recommendation to pursue further work-up of the esophageal mass with the Cornell Soft Tissue Service. Smokey's clinical signs improved over the next 3 months and then began to worsen. In December of 2006, the rDVM excised a malignant melanoma from the medial canthus of Smokey's right eye. In January of 2007, Smokey was diagnosed with aspiration pneumonia by the rDVM and began antibiotic therapy.

### **Clinical Findings**

On presentation to the Soft Tissue Service on January 30<sup>th</sup>, 2007, Smokey was nervous, but bright, alert and responsive. He weighed 12 kg with a body condition score of 4/5. Physical examination revealed moderate to severe dental disease, and a lobulated, pink, alopecic mass on the inferior medial canthus of the right eye. Unfortunately, precise thoracic auscultation was difficult due to Smokey's nervous disposition, but harsh lung sounds were thought to be detected. The remainder of the physical examination was unremarkable. Complete blood count showed mild thrombocytosis and a chemistry panel showed mildly elevated ALT, AST, Alk Phos, GGT and cholesterol levels. Urinalysis revealed mild-moderate proteinuria and an elevated

cortisol:creatinine ratio. Based on these findings, further diagnostics testing for hyperadrenocorticism after recovery was recommended. Smokey was sedated with midazolam and butorphanol. Orthogonal thoracic radiographs showed mildly improved mixed cranioventral airspace & airway pattern, compared to radiographs taken 8 days prior at the rDVM. This was interpreted as resolving aspiration pneumonia. Radiographs also showed a focally thick & irregular ventral esophageal wall, either due to the mass or a normal fold/peristaltic wave. The trachea was mildly deviated ventrally cranial to the heart. A tracheal stripe was present along with moderate amounts of gas and fluid distending esophagus, indicative of aerophagia or esophageal dysfunction. Abdominal ultrasound revealed a second, smaller nodule cranial to the first nodule seen the previous summer. The previously observed splenic nodule was not visualized and the prostate appeared normal in size and echogenicity. The following day, Smokey was anesthetized for advanced imaging procedures. Endoscopically, the mass appeared subjectively larger compared to the previous July but was otherwise unchanged. CT scan revealed a 22mm focal soft tissue mass arising from the dorsal/right esophageal wall, extending 1.5 cm cranial to the first rib to 2.5 cm caudal to the first rib. The mass protruded into the esophageal lumen and caused mild tracheal compression. It was slightly heterogeneous and mildly contrast enhancing. Additionally, there was severe left lung atelectasis and the heart was shifted to the left, attributed to left lateral recumbency of the patient. Next, the Cornell Ophthalmology Service surgically excised the palpebral mass and applied a dose of strontium 90 radiation therapy to the surgical site. This mass was diagnosed as an incompletely excised malignant melanoma by histopathology. Smokey recovered in the Intermediate Nursing Care Unit where his treatment plan involved triple antibiotic ophthalmic ointment (1/4<sup>th</sup> strip OD QID 10 days), enrofloxacin (11.3 mg/kg PO SID) and an Elizabethan collar.

## **Problem List**

Smokey's problem list related to his chief complaint included the esophageal mass, regurgitation, aspiration pneumonia, chronic coughing and chronic bronchitis. It is theorized that the esophageal mass led to regurgitation (due to esophageal obstruction), increasing the risk of aspiration pneumonia. The pneumonia, along with the chronic bronchitis and tracheal compression by the mass could all contribute to Smokey's coughing. The problem list also included dental disease, elevated liver values (ALT, AST, GGT, ALP and cholesterol), two hepatic nodules, proteinuria, increased urine cortisol:creatinine, and a palpebral mass.

## **Esophageal Mass Differential Diagnoses**

Inflammatory/granulomatous disease and neoplasia were the two broad differential diagnoses for the esophageal mass. Due to Smokey's age, the appearance of the mass and its growth pattern, neoplasia was the presumed diagnosis. The following tumors have been documented in the canine esophagus: adenocarcinoma, squamous cell carcinoma, fibrosarcoma, neuroendocrine carcinoma, leiomyoma, leiomyosarcoma, multinodular plasma cell tumor, plasmacytoma and osteosarcoma.<sup>1, 2</sup> Based on the smooth, non-ulcerated, rounded, well-defined, sub-epithelial and solitary appearance of Smokey's esophageal tumor and its growth rate, the top differential diagnosis was a smooth muscle tumor.<sup>3, 4</sup>

## **Surgical Treatment**

Due to the strong suspicion of neoplasia and Smokey's progressive clinical signs, the decision was made to surgically excise the esophageal mass. The morning of the surgery, PT and aPTT in-house tests were within normal limits. A partial cranial sternotomy and ventral midline esophagotomy was performed to excise the tumor from the dorsal wall of the esophagus.

Smokey was anesthetized, clipped, prepped and draped in a standard manner for the procedure. An approximately 20 cm ventral midline skin incision was made from the caudal cervical region to the cranial sternal region and the underlying subcutaneous tissue was sharply dissected. The superficial and deep pectoral musculature along with the sternocephalicus and sternohyoid muscles were separated along midline. The first and second sternabrae were transected longitudinally using a sagittal bone saw. The rib cage and surrounding soft tissue were retracted along with the trachea, exposing the esophagus, left carotid artery and left vagosympathetic trunk. At that time, the lesion was visualized as a mass within the esophagus. 3-0 silk stay sutures were placed in the esophagus and the ventral wall of the esophagus was incised, exposing the mass. 3-0 stay sutures were placed in the mass before excising it by sharp dissection at its base attachment to the dorsal wall esophageal wall. The mass was then submitted as an excisional biopsy to the Cornell Pathology Service.

The mucosa of the excision site was closed using 3-0 silk in a simple interrupted pattern. The esophagotomy was closed in a two-layer manner, first closing the mucosa and submucosa using 3-0 silk and then closing the muscularis using 3-0 PDS. Both layers were closed using a simple interrupted pattern. All stay sutures were removed before using size 18 surgical steel to close the partial sternotomy in a figure eight pattern between the first and second ribs. 3-0 PDS was used to close the sternohyoid muscle in a continuous pattern. 3-0 was also used to close the sternocephalicus muscle with one simple interrupted suture caudally and to reattach the muscle to the soft tissue surrounding the manubrium using a cruciate suture.

The incision was then extended approximately 10 cm caudally and the linea alba was incised. A gastrostomy tube placement by laparotomy was performed in the standard surgical manner. A 16 french tube was placed through the omentum and sutured to the left ventral portion

of the greater curvature of the stomach using 3-0 silk in a purse-string pattern. 3-0 nylon was used to suture the tube to the omentum in a simple interrupted pattern. The tube was secured to the left external abdominal wall using 3-0 nylon in everting mattress and Chinese finger-trap patterns. During the laparotomy, the liver appeared subjectively enlarged with multiple hepatic nodules present. The surgeon elected not to biopsy the nodules at that time. The linea alba was closed using 3-0 nylon in a continuous pattern. The subcutaneous tissues were closed using 3-0 monocryl in a continuous pattern and 3-0 nylon was used to close the skin in a cruciate pattern. Smokey recovered rapidly and uneventfully from anesthesia.

### **Post-operative Treatment**

Smokey recovered from surgery in the Intensive Care Unit. His treatment protocol involved IV fluids (P-lyte A + 15 mEq KCl at 60 ml/kg/day), fentanyl continuous rate infusion (5 mcg/kg/hr), tapering continuous rate infusion of medetomidine (2 mcg/kg/hr for 4 hours, then 1 mcg/kg/hr for 2 hours, then 0.5 mcg/kg/hr through to the next morning), cefazolin (22 mg/kg IV TID), enrofloxacin (10 mg/kg IV SID), famotidine (0.5 mg/kg IV BID) and the previously described ophthalmic ointment treatment. The surgical incision was iced for 10 minutes every 6 hours and an Elizabethan collar was placed on Smokey to prevent self-trauma. Quick assessment tests performed 7 hrs post-operatively were considered normal for a post-surgical patient.

The following morning at 8 am, the medetomidine was discontinued and the fentanyl dose was decreased to 3 mcg/kg/hr. The surgical bandages were removed revealing a healthy incision with moderate bruising of the surrounding soft tissues. A neck wrap was applied to protect the incision from the Elizabethan collar and a non-adhesive bandage was applied to the abdominal portion of the incision under a soft-bandage belly wrap. That evening, the fentanyl was replaced with hydromorphone (0.1 mg/kg SQ q 4 hrs) for analgesia. Smokey began

receiving 1/4<sup>th</sup> of his daily caloric requirement every 6 hrs through the gastrostomy tube. The feeding protocol was as follows: (a) flush tube with 5 ml of warm water, (b) syringe feed 100 ml of Hill's a/d blended with 75 ml of water, warmed over 10-15 min, (c) flush tube with 10-15 ml of warm water.

Two days post-operatively, Smokey was transferred to the Intermediate Nursing Care Unit. The hydromorphone dose was decreased to 0.5 mg/kg and the IV fluids were decreased to 30 ml/kg/day. Three days post-operatively, IV fluids were discontinued. Four days post-operatively, the hydromorphone was discontinued and Smokey was discharged to the care of his owners. His owners were instructed to administer 136 mg of crushed enrofloxacin daily and the contents of a 250 mg cefalexin capsule through the gastrostomy tube every 12 hours for 4 days. These antibiotics were prescribed to combat the pneumonia and prevent infection at the incision site, respectively. Smokey was to receive 5 mg of famotidine every 12 hours for 14 days to protect the esophageal lining from gastric reflux. Smokey's incision was to be checked for signs of inflammation or infection and he was to wear the Elizabethan collar at all times. The owners were taught how to use the gastrostomy tube and instructed to follow the previously described feeding protocol. They were advised to stop feeding immediately and contact a veterinarian if Smokey began vomiting or regurgitating.

### **Follow-up Diagnostic Testing & Care**

Eleven days post-operatively, follow-up imaging was performed. Orthogonal radiographs revealed no abnormalities. A fluoroscopic esophagram examination was negative for esophageal leakage but did demonstrate mild irregularity of thoracic esophageal lumen, minimal gastroesophageal reflux and an esophageal motility disorder. The latter was characterized by failure of primary peristaltic waves to move the contrast boluses the length of the esophagus, into

the stomach. Thus, contrast material accumulated in the thoracic esophagus until it was moved to the stomach by secondary peristaltic waves. Since there was no leakage of contrast material into the mediastinum, the esophagotomy was deemed fully healed. The gastrostomy tube was removed under general anesthetic the following day. While under general anesthesia, the Cornell Ophthalmologists resected the incision from the palpebral mass excision along with some of the surrounding tissue. Cryoablation was then performed at the periphery of the surgical margins in an attempt to prevent re-growth of the malignant melanoma. Smokey was fed a diet of canned and dry food mixed with the a/d slurry and offered water ad libitum. He had a healthy appetite and did not demonstrate any vomiting or regurgitation. Three days later, he was discharged to the care of his owners with famotidine (5 mg PO BID for 14 days) and triple antibiotic ophthalmic ointment (1/4" strip applied to the right eye QID for 5 days).

### **Esophageal Mass Histopathological Findings**

Histopathological evaluation of the tumor revealed a neoplastic process with neoplastic cells extending to the surgical margins. There was marked pleomorphism, anisokaryosis and numerous multinucleated giant cells. No mitotic figures were observed at 10x magnification. The neoplastic cells stained positive for vimentin and negative for cytokeratin and alcian blue, indicating a mesenchymal origin. It was negative for cit-kit, ruling out a fibrosarcoma, and positive for desmin, eliminating all non-muscular tumors. The tumor did not stain for smooth muscle actin, a stain specific for smooth muscle. It did stain positive for myoglobin, a stain specific for skeletal muscle.<sup>5</sup> Thus, the tumor was diagnosed as a rhabdomyosarcoma. To the author's knowledge, this type of tumor has not been previously documented in the canine esophagus.

## **Prognosis**

Due to the extreme rarity of observed rhabdomyosarcomas in dogs, and particularly the non-documented status of such tumors in the canine esophagus, the prognosis is currently unknown. Estimating from soft part sarcomas in general and leiomyosarcomas specifically, it was inferred that the metastatic potential was relatively low and complete surgical excision would be associated with a prolonged survival.<sup>6</sup>

## **Up-date**

In March of 2008, Smokey's owner reported that he has not had any problems with regurgitation or pneumonia since the surgery. He still coughed occasionally and had developed orthopedic problems which were managed with prednisone. The palpebral mass had not recurred.

## **Discussion**

### *Canine Esophageal Histology*

The canine esophagus is composed of four main layers, or "tunicas". Starting from the lumen, these tunicas are the mucosa, submucosa, muscularis and adventicia/serosa. The tunica mucosa is made up of three layers: the lamina epithelialis, the lamina propria and the lamina muscularis. The lamina epithelialis is formed by non-keratinized, stratified squamous epithelial cells. The lamina propria is fibrous in nature and is denser than the submucosal connective tissue. It is composed of fine collagen fibers and elastic fibers. The lamina muscularis lies furthest from the lumen. In the dog, it is absent cranially and appears as a continuous sheet of longitudinally-oriented smooth muscle bundles from the mid-region of the esophagus to the stomach. The tunica submucosa is made up of loose connective tissue, blood vessels, lymph vessels, nerves and seromucous glands throughout the length of the esophagus. This is the surgical holding

layer of the esophagus. The tunica muscularis consists of two layers of skeletal muscle. At the most cranial portion of the esophagus, these layers are interdigitated. However, for the majority of the esophagus, the muscles are oriented as inner circular and outer longitudinal layers. The tunica muscularis of the cervical esophagus is surrounded by the tunica adventicia. This outer tunica consists of blood and lymph vessels along with nerve bundles. The thoracic and short abdominal portions of the esophagus are covered by a tunica serosa (mediastinal pleura and abdominal peritoneum, respectively).<sup>7,8</sup>

#### *Documented Tumors in the Canine Esophagus*

The occurrence of esophageal neoplasia in companion animals is extremely rare, thus, it is difficult to accurately determine the incidence rates of such tumors. One source has stated that esophageal tumors compose less than 5% of all feline and canine cancers.<sup>9</sup> Another review of 49, 229 dogs over an 11 year period observed only 8 esophageal tumors, 2 of which were primary in nature while the other 6 were secondary.<sup>1</sup> The most commonly reported primary tumors are: squamous cell carcinoma, adenocarcinoma, leiomyosarcoma, fibrosarcoma and osteosarcoma. Rarer tumors which have been reported are neuroendocrine carcinoma, plasma cell tumor, undifferentiated carcinoma, plasmacytoma, and leiomyoma.<sup>1,9</sup> There are esophageal sarcomas associated with *Spirocerca lupi* in regions where this esophageal worm is present, but this will not be the focus of this discussion.<sup>2,10</sup> Thymic, heart base, thyroid, respiratory tract and gastric neoplasms have been observed to secondarily invade the esophagus.<sup>1,9</sup> Esophageal tumors are typically diffusely invasive but there have been cases of well-circumscribed tumors protruding into the esophageal lumen. Large masses may become ulcerated, as is often seen with squamous cell carcinomas.<sup>1,2</sup> Common clinical signs seen with all of these tumors are associated with esophageal obstruction due to the tumor encroaching on the lumen. Such signs are progressive in

nature and include dysphagia, painful deglutition, regurgitation (possibly containing fresh blood), respiratory signs due to aspiration pneumonia secondary to regurgitation, weight loss and dehydration.<sup>2</sup> Documented sites for metastasis include the gastric wall, trachea, lymph nodes (mid-cervical, bronchial, retropharyngeal, and pre-scapular) and the lungs.<sup>2</sup> Metastasis to the kidneys, spleen and thyroid has also been noted with esophageal squamous cell carcinoma.<sup>1</sup>

### *Rhabdomyosarcomas*

Rhabdomyosarcomas are malignant tumors arising from striated muscle cells and their precursors.<sup>11</sup> They are relatively rare in companion animals and are estimated to be less than 1% of all spontaneous neoplasms, despite striated muscle tissue making up a large portion of the animal body. There are no apparent breed, sex or regional risk factors, in addition to no known causes, in domestic animals.<sup>4,12</sup> Interestingly, most canine rhabdomyosarcomas arise in tissues normally lacking striated muscle cells. It has been proposed that such tumors originate from either embryonic remnants of myotomes, pluripotent cells of embryonic structures or primitive mesenchymal cells capable of differentiating into striated muscle cells.<sup>5,12</sup> Thus, canine rhabdomyosarcomas have the potential to form in any part of the body and have been reported in the pharynx, gingiva, urethra, urinary bladder, myocardium, greater omentum, larynx, trachea, tongue, appendicular musculature, oral cavity and the skin. Unlike the tumor described in this clinical report, rhabdomyosarcomas tend to be invasive, diffuse and poorly circumscribed.<sup>4</sup>

Histopathological findings show well-differentiated or pleomorphic polyhedral cells with anisokaryosis and multinucleated giant cells. Cross-striations may or may not be present and may require electron microscopy to be visualized. Electron microscopy may also reveal sarcoplasmic filaments. Maturation of the tumor cells seems to be consistent with the process of normal myogenesis. Specifically, the transformation of primitive rhabdomyoblasts to striated muscle

cells is accompanied by particular actin and myosin filaments as well as normal cross striations.<sup>4,5</sup> Definitive diagnosis, particularly distinction from other tumors originating from muscle, often requires immunohistochemistry.<sup>11, 12, 13</sup> A typical rhabdomyosarcoma stains negative or weakly positive for vimentin, cytokeratin negative, desmin and muscle specific actin positive, smooth muscle actin negative, alpha-sarcomeric actin positive and myoglobin positive. Staining characteristics may vary depending on degree of differentiation or stage of maturation. Also, some rhabdomyosarcomas express smooth muscle actin, a stain normally specific for smooth muscle. Of the above stains, alpha-sarcomeric actin and myoglobin are the only markers specific for striated muscle. Two other markers, *myoD1* and myogenin are used in human medicine and are also considered specific for striated muscle.<sup>5</sup>

Rhabdomyosarcoma metastatic sites include the lungs, lymph nodes, heart, spleen, adrenal glands, kidneys and skeletal muscle.<sup>11, 12</sup> There is inconsistency in the veterinary literature surrounding the metastatic rate of these tumors. Some papers document extremely aggressive rhabdomyosarcomas that metastasize early in the course of disease via the lymphatic or venous system. Conversely, there are reports of low or moderate rates of metastasis via hematogenous routes.<sup>12, 5</sup> Other authors reason that metastatic rate cannot be accurately determined due to the infrequency of diagnosis in veterinary medicine.<sup>10</sup>

Prognosis is currently unknown in veterinary medicine, because of the low rate of diagnosis combined with the even lower occurrence of treatments intended to be curative.<sup>13</sup> This is in contrast with human medicine, where multimodal treatment protocols involving surgery, radiation therapy and/or chemotherapy are being actively applied and documented, leading to the collection of prognostic data.<sup>14</sup> Prognosis in people is also dependant on a histological classification scheme, which has yet to be researched in veterinary medicine.<sup>10, 13</sup> This scheme

classifies rhabdomyosarcomas as either embryonal, boytroid, alveolar or pleomorphic, each of which has preferred anatomical locations, unique gross morphology and behavior. One promising note in the veterinary literature is that disease-free intervals and overall survival times have been relatively positive in the few documented cases of rhabdomyosarcomas treated with surgical excision, radiation therapy and/or chemotherapy.<sup>13</sup>

Unfortunately, there are still many unknowns relating to rhabdomyosarcomas in veterinary medicine. This is largely due to the extremely low incidence of this tumor in all domestic animals, and dogs in particular. A consistent histological classification scheme needs to be universally adopted and used to relate histopathological findings with the clinical aspects of the tumor (anatomical location, course of disease and outcome) in order to gather prognosis-oriented information. Complete surgical excision is the gold standard for all soft tissue sarcomas; however, further work is need for the development of radiation and chemotherapy protocols, for cases where complete surgical excision is either not possible or not advisable.<sup>12</sup>

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