Canine Laryngeal Rhabdomyoma

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Introduction

Primary tumors of the larynx are rare in dogs; they account for 0.02% of all biopsy and necropsy specimens.^{2, 12} Numerous histologic types of laryngeal neoplasms have been described in canines and include rhabdomyomas, rhabdomyosarcomas, squamous cell carcinomas, osteosarcomas, mast cell tumors, fibrosarcomas and others. Although laryngeal tumors encompass a wide variety of histologic types, they all have nearly identical clinical signs of voice changes, dyspnea, and coughing. Laryngeal tumors in humans are associated with cigarette smoking; however, no risk factors have been identified in companion animals.^{10, 11} Laryngeal tumors have been reported in various purebred dogs as well as mixed breeds, and there does not appear to be any specific breed predilection, although males do appear to be at increased risk.^{1, 5, 10} Most patients that develop laryngeal tumors are older, with a median age of eight years at the time of diagnosis.⁵ However, rhabdomyomas are more common in young to middle-aged dogs ages two to eight years old.^{5, 10}

History

Max, a 6-year-old male neutered Boxer, presented to MSU-CVM Internal Medicine Department on January 11, 2018 for a 3-4 month duration of change in voice (bark) and chronic respiratory issues including coughing, mild exercise intolerance, and intermittent gagging while eating. The owner reported that Max had a dry, nonproductive cough that was worse in the mornings, but resolved as the day progressed. He was previously diagnosed with heartworms at the time of his adoption, approximately two years prior to presentation at MSU-CVM. Max was treated for heartworm disease and tested negative for heartworm antigen after completion of his treatment. He currently has no clinical signs associated with the prior heartworm infection. Before Christmas of 2017, Max was evaluated for his respiratory issues by his referring veterinarian who noted an erythematous airway. Max was then treated with an injectable antibiotic, but showed no improvement.

Presentation

Upon presentation, Max was bright, alert, and responsive. He had a body condition score of 7/9. His heart rate (116 beats per minute), respiratory rate (36 breaths per minute), and temperature (101.4° F) were all within normal limits. His mucous membranes were pink with a capillary refill time <2 seconds. His heart and lungs auscultated normally. Nuclear sclerosis was noted bilaterally. Cranial abdominal palpation elicited a mild pain response. A small, hairless, round, dermal pink mass was noted in the area of his left cranial scapula. All peripheral lymph nodes palpated normally in size and consistency. The remainder of his physical exam was within normal limits.

Differential Diagnoses

Based on Max's history and clinical signs, the primary differential was laryngeal paralysis with possible concurrent lower airway disease. In order to further evaluate Max's laryngeal function, an upper airway examination was scheduled. During this anesthetic event a bronchoscopy and bronchoalveolar lavage were performed to assess his lungs and rule out lower airway disease. Routine bloodwork was performed (CBC/Chemistry), which revealed a mild eosinophilia, but was otherwise unremarkable. Thoracic radiographs revealed a diffuse bronchial and interstitial pulmonary pattern. Given Max's clinical signs, history, and eosinophilia, chronic bronchitis was the proposed etiology for these findings. A Baermann fecal float was performed to rule out possible lung parasites, and no parasites were seen.

On laryngeal examination, bilateral laryngeal paralysis was confirmed. Also, a 0.5 cm x 0.5 cm erythematous nodular mass was identified at the base of the arytenoids ventrally, causing

a partial upper airway obstruction. At this time an incisional biopsy was taken via a cauterizing snare which was submitted for histopathology. Following Max's laryngeal examination, a bronchoscopy was performed which revealed severe lower airway disease. The bronchi collapsed easily on suction due to severe bronchomalacia. In the right lung lobes, the respiratory mucosa appeared irregular with small, raised erythematous nodules noted throughout the bronchioles. The airways were also diffusely inflamed. Airway sampling was performed followed by evaluation with cytology and culture/sensitivity. Bronchoalveolar cytology of the right lung lobes demonstrated few macrophages, but no atypical cell population or etiologic agents were found. However, the sample contained few cells and may not have been a representative sample of his concurrent lung pathology. The left lung lobes had degenerate neutrophils and eosinophil numbers were moderately increased. No atypical cell population or etiologic agents were found. The presence of macrophages and neutrophils from Max's bronchoalveolar cytology indicated a chronic inflammatory process with the presence of eosinophils indicating a possible underlying allergic component. The culture revealed faint growth of mixed bacteria including Stenotrophomonas maltophilia and Pseudomonas pseudoalcaligenes. However, these bacteria are not considered respiratory pathogens so Max was not treated for infection.

While Max was still under anesthesia, computed tomography (CT) was performed with contrast to further characterize the mass. On CT, the mass was found to extend further caudally into surrounding laryngeal soft tissues, measuring approximately 2 cm x 1.5 cm x 2 cm on the right side of the larynx. Histopathology of the mass revealed laryngeal mucosa expanded by a densely cellular, infiltrative neoplasm composed of one cell type. Cells were arranged in small bundles and fascicles. Based on these findings, Max was diagnosed with laryngeal rhabdomyoma.

Pathophysiology

Rhabdomyomas are rare benign tumors that originate from striated muscle. They occur most commonly in the myocardium, skeletal muscles of the larynx, and in the head region. Rhabdomyomas in dogs can become large, but are minimally invasive and do not metastasize.¹¹ They are less common than rhabdomyosarcomas.² One study reported that rhabdomyomas and rhabdomyosarcomas combined account for only 0.07% of all diagnosed neoplasms in animals.² Despite its rare occurrence, the most common site for development of rhabdomyoma in animals is the larvnx.² The primary clinical signs in dogs with larvngeal tumors are due to the physical presence of the mass, which obstructs the airway as it grows. Symptoms may also be present from the accumulation of secretions in the airway due to the presence of the mass. Clinical signs of laryngeal tumors may include progressive exercise intolerance, dysphonia, stridor, stertor, dysphagia, coughing, halitosis, hemoptysis, oral hemorrhage, and pytalism.^{1, 3, 5, 10} Some animals may present with signs of acute upper airway obstruction, including severe dyspnea, tachycardia, and cyanosis.¹⁰ The severity of clinical signs depends directly on the extent of airway obstruction.³ Tumors of the larynx may also be noted as an incidental finding during physical examination or intubation for routine general anesthesia.

Diagnostic Approach & Considerations

In patients with laryngeal tumors, physical examination findings may vary depending on the size and location of the primary tumor. Auscultation of the cervical region may reveal stridor, which is associated with a partial airway obstruction. In animals with an acute upper respiratory obstruction, tachypnea, dyspnea, and crackles (presumably due to aspiration pneumonia) may be present. Palpation of the larynx may reveal a discrete mass, asymmetry, or diffuse swelling.¹⁰ Direct visualization of the larynx via a laryngoscope is the most helpful tool in differentiating various diseases of the larynx.³ A flexible fiber optic endoscope may be used to assess the distal larynx.³ Other diagnostics include radiography, ultrasonography, computed tomography, magnetic resonance imaging, and histopathology.

Plain survey radiographs may aid initial diagnosis by demonstrating laryngeal distortion and increased soft tissue opacity.⁵ Radiographs may also provide information regarding the size and extent of the tumor. Thoracic radiographs are useful to identify evidence of metastasis and changes that accompany chronic and severe upper airway obstruction, such as aspiration pneumonia.³ Ultrasonography may be useful for identifying a mass or secondary functional problem, such as laryngeal paralysis, but is not superior to direct laryngeal visualization.⁵ Advanced imaging with computed tomography or magnetic resonance imaging allows the most accurate assessment of local invasion and regional lymph node status prior to surgical intervention.¹⁰

The definitive diagnosis of rhabdomyoma can only be confirmed with histopathology. A biopsy of the mass can be obtained using alligator forceps, needle biopsy instruments, loop snares, or bronchoscopic biopsy forceps and examined by microscopy and immunohistochemistry. Demonstration of the muscle-specific intermediate filament protein, desmin, with immunohistochemical staining confirms that neoplasms are of muscle origin; however, this staining cannot differentiate between skeletal muscle and smooth muscle cells.⁴ A definitive diagnosis of a skeletal muscle tumor is made using myoglobin, which is a specific marker for skeletal muscle.⁴ Other immunohistochemical markers used for diagnosis of rhabdomyoma include muscle-specific actin, myosin, vimentin, and Z-protein.^{4, 7} Cytologically, rhabdomyomas are considered a "granular cell tumor" composed of individual round or polygonal cells containing numerous fine pink cytoplasmic granules and a

central round nucleus.¹¹ Electron microscopy reveals the pink granules to be numerous mitochondria.¹¹ Cross-striations can be discerned in most cases, as well as intracytoplasmic crystalline structures, but both are identified much more readily with phosphotungstic acid-hematoxylin (PTAH) stain than with hematoxylin-eosin stain.^{2, 6}

Treatment & Management

Treatment options for laryngeal neoplasia include surgical excision, chemotherapy, radiation therapy, or a combination thereof.¹⁰ The type, location, and stage of the tumor influences which of these treatment modalities would be most appropriate. Small, benign masses can be resected using endoscopic techniques (laser) via a transoral approach or through a ventral laryngotomy.^{1, 10} Larger or more invasive tumors may require a partial or total laryngectomy with a permanent tracheostomy.^{1, 10} Removal of a portion of the tumor in an attempt to preserve laryngeal function is an option when follow-up chemotherapy is possible, such as with lymphoma or mast cell tumors. Resection of the neoplasm and the submucosa or a partial laryngectomy is the most appropriate treatment for benign laryngeal neoplasms. However, due to the invasiveness of Max's tumor, a total laryngectomy would be the most appropriate therapy. Both partial and total laryngectomies are associated with several post-operative complications such as dysphagia, nausea and fistula secondary to wound dehiscence.⁸ Inappropriate closing of the larynx during swallowing may lead to aspiration pneumonia.⁸ In addition, excessive and intermittent coughing may be present due to the production of granulation tissue at the surgical excision site.⁸ As the tracheostomy site heals, some degree of stomal stenosis is normal but excessive stenosis can result in hypoventilation.¹³ Preventing wound infection or self-trauma is important in reducing stomal stenosis and may initially require the use of paw bandages or hobbles.¹³

A complete laryngectomy with a permanent tracheostomy requires careful management and daily care which can be cumbersome to the owner. The stoma should be inspected every one to three hours during the postoperative period for accumulation of mucus and cleaned when mucus begins to occlude the stoma or causes increased respiratory effort. This interval gradually increases as healing continues to progress. The owner should be advised that the animal should not be subjected to dust, dirt, cigarette smoke or burning wood as these environmental irritants may cause increased tracheobronchial secretions that can result in stomal obstruction.¹³ Owners must inspect the stoma on a regular basis, approximately every four to six hours, and carefully remove any mucous secretions using a clean moistened cottonball, swab, or gauze.¹³ The cleaning interval gradually increases to approximately once a day after the first month postoperatively. Good stoma hygiene also includes the application of petroleum ointment around the stoma to prevent the mucus from adhering to the skin and obstructing the stoma. Owners also need to clip the hair around the stoma once or twice a month to prevent matting. Skinfold occlusion of the stoma is the most common long-term complication after permanent tracheostomy.¹³ This complication occurs in animals with excessive skinfolds or subcutaneous fat that occlude the stoma. Occlusion can also occur when the neck is flexed. Animals with a permanent tracheostomy should be walked with harnesses rather than collars or any restraint on the neck. Aspiration pneumonia or drowning can occur during bathing. Also, owners should be advised that animals with a permanent tracheostomy should never be allowed to swim.

Case Outcome

Max recovered well in hospital and was discharged on January 13, 2018 with Amoxicillin, Tylenol 4, and instructions to return for a recheck examination. A surgical consult was recommended to discuss options for removal of Max's laryngeal rhabdomyoma. The prognosis for most laryngeal tumors is guarded due to advanced disease present at the time of diagnosis.⁵ However, benign tumors, as in this case, have a good prognosis with surgical excision. Most dogs with operable rhabdomyomas live longer than 1 year and may be presumed cured with proper margins.¹¹ Max has not yet returned to MSU-CVM for his surgical consult but the owners report that he has been doing well at home. Since Max's first visit, his respiratory effort has been much improved. His voice has returned to normal and they have not noted any gagging.

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