Eosinophilic Bronchopneumopathy in a Newfoundland

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Abstract

A 2.5-year-old female spayed Newfoundland was presented to the Cornell University Hospital for Animals (CUHA) Emergency Service for evaluation of coughing, lethargy, and suspected bronchopneumonia. Failure to respond to antibiotic and antitussive therapy, as well as increasing clinical signs, prompted the patient's primary care veterinarian to refer her to the CUHA for further diagnostic workup. Clinical findings, diagnostic imaging, and cytological evaluation of the respiratory tract confirmed a diagnosis of eosinophilic bronchopneumopathy. Treatment consisted of corticosteroid therapy and nebulization therapy. Clinical improvement and response to therapy occurred shortly after the initiation of treatment and the patient was discharged with good prognosis. Eosinophilic bronchopneumopathy, previously referred to as pulmonary infiltrates with eosinophils (PIE), is an inflammatory disease caused by a suspected hypersensitivity reaction. This case study will review the clinical presentation, diagnosis, and management of canine eosinophilic bronchopneumopathy.

Introduction

Respiratory diseases are commonly seen in dogs. While some are treated empirically and respond successfully to therapy, some respiratory conditions require further diagnostic evaluation to determine adequate therapy and resolve clinical signs. At minimum, a diagnostic evaluation for canine respiratory disease includes a physical examination, complete blood count, chemistry profile, and diagnostic imaging such as radiographs. In some cases, evaluating for the presence of respiratory parasites may prompt fecal testing. Diagnostic procedures for the visualization and sampling of the airway, as well as for cytological evaluation, are necessary in animals with a persistent cough or radiographic evidence of respiratory disease.[1] Airway

sampling is vital in order to determine and characterize the inflammatory response and to identify any infectious agents or neoplastic processes present in the respiratory system.[1] These procedures are usually minimally invasive. Tracheobronchoscopy is a common technique that allows the direct visualization of larger airways to assess pathology and allow for guided airway sampling via bronchial brushing or biopsy.[1] Tracheal washes are typically used for sampling larger airways, while bronchoalveolar lavages are useful for the evaluation of smaller airways and alveoli.[1] These sampling techniques become especially important when other diagnostics have not determined a cause for underlying respiratory disease.

Eosinophilic bronchopneumopathy (EBP) is an uncommon disease that requires further work-up for definitive diagnosis. EBP is typically suspected when other therapies have failed and respiratory signs persist. Though the clinical presentation of EBP may mimic other diseases such as bronchitis, bacterial pneumonia, or infectious tracheobronchitis, the treatment for EBP is very different. In cases where an animal fails to respond to empirical treatment, it is critical that further evaluation is conducted so that the proper therapy is instituted promptly.

Signalment and Chief Complaint

A 2.5-year-old female spayed Newfoundland presented to the Cornell University Hospital for Animals (CUHA) Emergency Service for evaluation of a productive cough and suspected bronchopneumonia of one-week duration.

Case History

The patient presented to her primary care veterinarian for a one-day history of coughing, gagging, and lethargy. At this time the patient was treated empirically for bronchitis with an antibiotic and a cough suppressant. Four days later, she returned to her primary care veterinarian for a continued cough, bilateral serous nasal discharge, and lack of clinical improvement.

Thoracic radiographs revealed a diffuse bronchointerstitial lung pattern and the patient was started on an additional antibiotic. Within two days, the patient became lethargic and anorexic and began coughing up increased amounts of phlegm. Failure to respond to antibiotic and antitussive therapy, accompanied with the patient's declining condition, prompted her referral to the Cornell University Hospital for Animals (CUHA) Emergency Service for further diagnostic workup.

The patient had no previous medical history and was up-to-date on all vaccinations. She was also current on all flea, tick, and heartworm preventatives. Her most recent heartworm negative antigen test was two months prior to presentation.

Clinical Findings

On presentation, the patient was quiet, alert, and responsive with normal cardiothoracic auscultation, with the exception of harsh lung sounds heard bilaterally. No murmurs, arrhythmias, crackles or wheezes were appreciated. A cough was easily elicited by palpation of the trachea and the patient had bilateral serous nasal discharge. The remainder of the physical examination was unremarkable. Quick assessment tests evaluating the patient's packed cell volume (PCV), total solids, and renal function were all within normal limits. A blood smear showed normal red cell morphology and a subjective peripheral eosinophilia. Blood gas analysis revealed a mild respiratory alkalosis and moderate hypoxemia. A focused ultrasound of her thorax showed B lines bilaterally in her mid-ventral thorax and a positive glide sign, indicating an infiltrative process within the lung parenchyma. Three-view thoracic radiographs showed a moderate bronchointerstitial lung pattern suggestive of a bronchopneumonia or hematogenous spread infectious pneumonia. The patient was not oxygenating sufficiently on room air and was maintained on nasal prong oxygen. At this time, the patient was also started on empirical

anthelminthic therapy to treat for potential primary parasitic lung infection and migrating gastrointestinal parasites. Maintenance intravenous fluids were also initiated at this time and the patient was monitored in the intensive care unit overnight.

The following morning, she was transferred to the Internal Medicine Service for further diagnostic evaluation to determine the underlying cause of the cough, bronchointerstitial lung disease, and hypoxemia. A complete blood count (CBC), chemistry panel, and disseminated intravascular coagulation panel were all unremarkable with the exception of a peripheral eosinophilia (2.4 thou/uL; reference range=0.1-2.1 thou/uL) that was confirmed via a peripheral blood smear. An endotracheal wash (ETW) was performed and a sample of the wash was submitted for cytological evaluation and analysis. Cytological evaluation of the fluid from the tracheal wash revealed a highly cellular population of greater than ninety percent eosinophils and increased numbers of goblet cells. These findings were consistent with severe eosinophilic inflammation with evidence of increased mucus production. Aerobic, anaerobic, mycoplasma, and fungal cultures of the tracheal wash fluid were all negative for growth and no microorganisms were observed.

Problem List

At this time, the patient's primary problem list included severe eosinophilic infiltration of the lungs with increased mucus production. Additional problems, likely secondary to the primary problem, were coughing, bilateral harsh lung sounds, hypoxemia, exercise intolerance, anorexia, and peripheral eosinophilia.

Differential Diagnoses

Signs of productive coughing, bilateral hash lung sounds and moderate hypoxemia were all considered secondary to the diffuse bronchointerstitial lung disease. Exercise intolerance and

anorexia were attributed to discomfort from the ongoing disease process and hypoxemia. Primary differential diagnoses for bronchointerstitial disease and other associated clinical signs included cardiogenic and non-cardiogenic pulmonary edema, allergic or hypersensitivity reaction, trauma or foreign body, primary neoplasia or secondary metastasis, infectious or inflammatory conditions, and parasitic infection. The peripheral eosinophilia in this patient raised the suspicion of parasitic infection, hypersensitivity and allergic disease, warranting further evaluation of the respiratory tract. The eosinophilic inflammation seen via cytological evaluation of the respiratory tract further supported these suspicions of parasitic, hypersensitivity, and allergic disease. Additionally, no parasites or ova were seen on fecal examination. Lack of evidence of parasites in the respiratory or gastrointestinal system and rapid response to therapy made parasitic disease less likely and supported EBP as the more likely cause of the patient's clinical signs. Based on all clinical findings and the exclusion of other known causes of eosinophilic infiltration of the lower airways, a diagnosis of eosinophilic bronchopneumopathy (EBP) was made.

Treatment

Following the results of the endotracheal wash, the patient was started on intravenous immunosuppressive corticosteroid therapy and saline nebulization therapy every six hours. Oxygen therapy via nasal prong was continued until the patient's peripheral oxygen saturation reached 96% on room air. The patient was also continued on the current anthelminthic therapy plan.

Outcome

The patient responded well to the instituted treatment plan and her respiratory effort, peripheral oxygen saturation, and energy level improved within twenty-four hours. Three days

after presentation, the patient was discharged to the care of her owners on immunosuppressive corticosteroid therapy with good prognosis and the plan to reassess response to therapy in a few weeks to determine a tapering protocol until the lowest effective dose of steroid is reached. Like most cases of EBP, the inciting cause of the patient's eosinophilic bronchopneumopathy was not determined in the case.

Discussion

Eosinophilic bronchopneumopathy (EBP), previously referred to as pulmonary infiltrates with eosinophils (PIE), is an inflammatory disease caused by a suspected hypersensitivity reaction to aeroallergens.[2] The disease is characterized by eosinophilic infiltration of the pulmonary parenchyma and bronchial mucosa.[3] While Siberian Huskies and Alaskan Malamutes are predisposed to EBP, the disease can be seen in any breed.[2] Age of onset has been reported most commonly in young adults ages four to six years of age, but has been seen in animals ranging from three months to thirteen years old.[2] Females are believed to be more commonly affected with EBP than males.[2]

On presentation, 95-100% of animals have a harsh cough that is usually followed by a gag.[2] Fifty percent of animals have some form of nasal discharge - either serous, mucoid, or mucopurulent.[2] Increased or adventitious lung sounds are often found, though some affected animals may have normal cardiothoracic auscultation.[2] The remainder of the physical examination is typically unremarkable and most animals are systemically healthy. Exercise intolerance and anorexia are seen with progression of disease. Lab work for most animals with eosinophilic bronchopneumopathy is usually unremarkable. Although a peripheral eosinophilia is helpful in prioritizing EBP, only 50-60% of cases demonstrate this finding, making it a poorly sensitive test.[2] Since the clinical signs and lab work are nonspecific and not always present, these

entities are not enough to definitively diagnose eosinophilic bronchopneumopathy. Typically, diagnostic imaging, airway sampling, and exclusion of other diseases are required for definitive diagnosis.

Radiographic findings are typically a mixed moderate to severe bronchointerstitial lung pattern. The severity of lung disease seen radiographically usually correlates directly to the level of lung infiltration.[2] Bronchoscopic examination usually shows abundant yellow-green mucus with thickening of the mucosa.[3] Respiratory samples with primarily eosinophilic inflammation increase the suspicion of parasitic and allergic diseases. Tracheal wash samples from normal airways usually contain respiratory epithelial cells, small amounts of mucus, occasional inactive macrophages, and rare neutrophils and lymphocytes.[4] Cytological evaluation of respiratory secretions from animals with EBP typically have a cytological analysis of greater than 20-50% eosinophils.[1]

The pathology associated with eosinophilic bronchopneumopathy likely occurs from repeated antigenic exposure which results in chronic irritation and inflammation in the airways.[5] This results in epithelial desquamation and mucous gland hyperplasia that can lead to airway obstruction.[5] Studies suggest that eosinophils are recruited into the bronchial mucosa as a result of cytokines and eotaxin chemokines which are released as a part of a CD4 T helper 2 cells immune response to specific aeroallergens.[6] Additionally, respiratory epithelial cells and alveolar macrophages are believed to produce increased amounts of matrix metalloproteinases (MMPs).[2] These MMPs have collagenolytic and proteolytic properties which lead to the destruction of the lower airway and pulmonary parenchyma.[2]

Since an etiology is usually not identified, most cases are considered idiopathic. Intradermal allergen skin tests have been suggested to determine the cause of the triggering

allergen, but these tests have been unreliable at identifying the causative agent, likely due to differences in localized and systemic immune responses to specific allergens.[2] Although the exact etiology and pathogenesis are not fully understood, prognosis is considered good with adequate immunosuppressive therapy and most animals show improvement in clinical signs within a few days of therapy.[2] Complete resolution of all clinical signs is rare and treatment should be tailored to the individual animal. Many animals eventually relapse after complete discontinuation of therapy and will need to be maintained on low dose corticosteroid therapy for life-long disease management.[3] Some studies have shown that inhaled corticosteroids can be a form of treatment for animals in which oral corticosteroids are contraindicated or not tolerated due to side effects.[5] Advantages of inhaled corticosteroids include an increase in local concentration of drug and a reduction in systemic side effects. However, in some animals, inhaled corticosteroid therapy fails to control the cough and oral treatment is eventually required.[7] Further studies are required to determine a protocol for inhaled corticosteroid treatment of EBP.

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