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Chronic obstructive pulmonary disease (COPD) in a blue and gold macaw (*Ara ararauna*) secondary to cockatoo dander exposure

Introduction

This report describes a 2-year-old blue and gold macaw (*Ara ararauna*) with a history of chronic lower respiratory disease. Lung and air sac biopsies confirmed chronic obstructive pulmonary disease (COPD) and that the etiology of the respiratory disease was not viral, fungal or bacterial, but was consistent with chronic exposure to an environmental irritant or allergen. Additionally, an elevated packed cell volume was consistent with chronic respiratory disease. The bird was treated medically and environmental changes were made to reduce the bird's clinical signs.

Respiratory distress is a common presentation of a sick bird. Lower respiratory disease in birds is typically characterized by coughing, abnormal breathing sounds, open-mouth breathing, increased respiratory rate, labored breathing, dyspnea, tail bobbing, and cyanosis and can have numerous etiologies.[1] Additional clinical signs may include sneezing and nasal discharge. Etiologies may include infectious, metabolic, nutritional, toxic, physical or neoplastic causes. Infectious etiologies include gram-negative bacteria (*E. coli, Klebsiella pneumoniae, Pasteurella multocida, Pseudomonas aeruginosa, Salmonella spp., Yersinia pseudotuberculosis,* other), gram-positive bacteria (*Streptococcus spp., Staphylococcus aureus, Mycobacterium, Enterococcus,* other) , *Chlamydophila psittaci, Mycoplasma spp., Aspergillus spp., Cryptococcus spp.*, viruses (Pacheco's disease virus, Amazon tracheitis virus, reovirus, Newcastle disease virus, poxvirus, avian viral serositis form of eastern equine encephalitis, infectious

laryngotracheitis, and avian influenza), and parasites (*Cytodites nudus, Sternostoma tracheocolum, Syngamus trachea, Knemidokoptes pilae, Sarcocystis falcatula, Toxoplasma, Atoxoplasma*).[1] Metabolic etiologies include hepatic disease, renal disease, heart failure, coagulopathies, anemia, gout and hemochromatosis.[1] Malnutrition (hypovitaminosis A), obesity and thyroid hyperplasia (goiter), as well as toxins including polytetrafluoroethylene (Teflon®), zinc, inhaled gases such as methane and smoke inhalation can also lead to respiratory disorders.[1] Silicosis and resulting respiratory clinical signs associated with peat moss bedding has been reported in one blue and gold macaw.[2] Aspiration pneumonia, trauma (ruptured air sac, humeral fracture with infection, hemorrhage), tracheal foreign body, ascites from either liver disease or heart failure, peritonitis or a tracheal stenosis are also differentials for respiratory problems in avian patients.[1] Primary neoplasia either in the lungs or in the form of masses that mechanically reduce ventilation, as well as metastases to the lungs, could also lead to respiratory disease. Conure bleeding syndrome can lead to respiratory difficulties but was not a differential in this case. Also, chronic respiratory disease that is associated with exposure to the feather dust or dander of cockatoos or African grey parrots has been reported in blue and gold macaws.[3-5]

The initial diagnostic plan for a bird with respiratory disease should include a physical examination, complete blood count, plasma biochemistry panel, whole body radiographs, and screening for antibodies to or antigen of *Chlamydophila psittici* and *Aspergillus spp.* A plasma protein electrophoresis may also be performed. Fungal and bacterial cultures and cytology can be performed on lung, air sacs, spleen, liver or mass samples obtained with either lavage of the upper airways or endoscopy. Histopathology

can be performed on lung, air sacs, spleen, liver or mass samples obtained with endoscopy or exploratory surgery. Treatment regimens for respiratory disease vary greatly depending on the etiology.

The anatomy of the avian lower respiratory system differs from the mammalian lower respiratory system. The lungs of birds are dorsally located in the cranial coelomic cavity and are similar in proportion of body weight to mammals, however, they are proportionately smaller in volume and more rigid than the lungs of mammals.[6] Air capillaries are narrow tubes that form an extensive network for oxygen exchange and have a greater surface area for oxygen exchange than the alveoli of mammals. The pressure gradient of oxygen across these stationary (non-expanding) capillaries allows for greater diffusion of oxygen across these membranes in birds than across the alveolar surface of mammals.[6] Mammals have distensible alveoli at the terminal end of their respiratory system and because the alveolar wall is thicker than the wall of the avian air capillary, oxygen exchange is less efficient in mammals than in birds. Additionally, birds have air sacs that allow inhaled air to continuously flow over the air capillaries allowing more oxygen diffusion. In general, the respiratory system of birds is more efficient than the respiratory system of mammals and may allow for greater respiratory compensation with advanced disease.

Macaw pulmonary hypersensitivity (MPH), a form of COPD, typically occurs in blue and gold macaws following chronic exposure to an environmental allergen or irritant such as feather dander from a cockatoo or African grey parrot. This disease rarely occurs in other macaw species. Clinical signs include dyspnea when excited, wheezing, facial skin cyanosis, and a dry cough.[3] Polycythemia is a common clinical pathological finding

in birds with clinical signs. This polycythemia results from decreased oxygen exchange in the lungs because the air capillaries are thickened and fibrous. Radiographic changes can include thickened bronchial walls, right-sided cardiomegaly, great vessel enlargement, and hyperinflation of the air sacs.[3] Diagnosis of COPD in macaws is based on histopathology of lung tissue (obtained with rigid endoscopy of the coelomic cavity) which shows consolidated and thickened interstitium, eosinophilic material in the interstitium, increased fibrous tissue and a mixed cellular infiltrate. Smooth muscle hypertrophy is common and atrial loss may also be present. Proliferation of lymphoid tissue and lymphoid nodule formation may occur.[7] Bronchoscopy can also be performed although it can be difficult to obtain diagnostic lung samples in this manner.

The exact pathophysiology of COPD in macaws is not well understood and has not been described in the literature. There is an inflammatory response, resulting in secretions, infiltrates and smooth muscle hypertrophy. Typically, inflammation in the lungs consists of lymphocytes and plasma cells, but not eosinophils. Research on the avian immune system has been conducted, but most studies focus on commercial poultry and immune responses to diseases of economic concern such as infectious bronchitis, coccidiosis and salmonellosis.[8,9] Information on the psittacine immune system, pathways involved in the inflammatory response and what cells and mediators contribute to chronic respiratory disease, is scant, and the role of cytokines and immunoglobulins in the pathophysiology of avian COPD is still unknown. Reversal of histological changes and resulting improvement of clinical signs without treatment is unlikely. Medical therapy and environmental changes can result in mild improvements of clinical signs.

Treatment of macaws with COPD typically includes daily anti-inflammatory treatment with a non-steroidal anti-inflammatory (NSAID) medication, such as meloxicam or carprofen, and environmental changes that reduce exposure to feather dust. In mammals, non-steroidal anti-inflammatory medications exhibit analgesic, anti-inflammatory, and antipyretic activity through inhibition of cyclooxygenase, phospholipase A_2 and inhibition of prostaglandin synthesis. Possbile adverse effects associated with NSAID administration include gastro-intestinal ulceration, renal toxicity or hepatotoxicity.[10] Gastroprotectants such as sucralfate, cimetidine or omeprazole should be used in conjuction with long term NSAID therapy to prevent gastro-intestinal ulceration. Sucralfate is an anti-ulcer agent, but the exact mechanism of action is not known. Adverse effects associated with sucralfate administration are rare but could include constipation.[10] Cimetidine is a histamine-2 blocker which reduces gastric acid production and possible adverse effects include CNS effects (confusion) in patients with renal or hepatic compromise.[10] Omeprazole is a proton pump inhibitor and reduces the production of acid in the stomach. Possible side effects associated with omeprazole administration include gastro-intestinal distress, CNS disturbances, hematologic abnormalities, urinary tract infections and proteinuria.[10] Long-term corticosteroids (more than approximately 5 days) are typically contraindicated because they can rapidly cause severe immuno-suppression in the avian patient. Other possibilities for treatment include medications traditionally used in humans with COPD, asthma, and allergies. These medications include bronchodilators (β agonists), such as albuterol, clenbuterol or salmeterol, or leukotreine antagonists, such as montelukast sodium. Bronchoconstriction occurs during an asthma attack in humans, and a β agonist will act by stimulating the

production of cyclic AMP through the production of adenyl cyclase which in turn leads to relaxation of smooth muscle in the lungs, uterus, and vessels and therefore reduces bronchoconstriction. Possible side effects associated with β-agonist administration include tachycardia, tremors, central nervous system excitement and dizziness.[10] Although there may be smooth muscle contraction in macaws with COPD, the main histological lesion is hypertrophy which is unlikely to be corrected with a β agonist. Bronchodilators may provide mild relief of clinical signs in the avian patient. Leukotreine antagonists are a newer class of medications used in humans to treat asthma and allergic rhinitis. Leukotrienes are cell mediators that are associated with the pathophysiology of asthma and allergies including inflammation. Leukotrienes can be released from a number of inflammatory cells including mast cells and eosinophils in the asthmatic or allergic patient. Montelukast sodium (Singulair®), the most commonly prescribed leukotriene antagonist, is an antagonist for the receptor of the leukotriene, LTD_4. Leukotriene, LTD_4, has been associated with mucus secretion, airway edema, and bronchoconstriction in asthmatic patients.[11] No research has been performed in avian species to examine the efficacy or safety of leukotreine antagonists, but this new class of drug could be useful in the treatment of inflammatory diseases such as COPD in birds. Possible side effects associated with montelukast sodium administration include eosinophilia, hepatotoxicity and pyuria.[11]

Chronic obstructive pulmonary disease (COPD) has been reported in many species but most commonly humans and horses.[12,13] Most research into the pathogenesis of respiratory disease has been performed in mammals and significant differences from mammalian pathology may exist in avian species. Chronic respiratory disease in

mammals is often associated with a chronic exposure to an irritant or allergen such as cigarette smoke, hay dust and mold.[12,13]

Chronic obstructive pulmonary disease (COPD) in humans refers to a group of conditions including chronic bronchitis, bronchiectasis, asthma and emphysema, which are typically slowly progressive and poorly reversible. Pathological findings consist of fibrosis and obstruction of the small airways, enlargement of airspaces and destruction of lung parenchyma and loss of elasticity of the small airways.[14,15] Additionally, there is an increased inflammatory cell infiltration in central airways, consisting of T- lymphocytes and macrophages. This local inflammation also leads to the production of mucus in the airways which can limit airflow. Additionally, cigarette smoking causes elevated circulating neutrophil levels.[12] COPD in humans is often resistant to anti-inflammatory treatment with corticosteroids, and therefore other treatment regimens are currently being investigated.[16] Additional treatments include inhaled long-acting bronchodilators and theophylline, which is a smooth muscle relaxant.[10] Theophylline administration can lead to CNS stimulation and gastro-intestinal irritation.

Recurrent airway obstruction (RAO), previously known as COPD, often occurs in horses that are stabled and fed hay most of the year, and often presents clinically as exercise intolerance. The incidence of RAO increases with age and disease seems to be related to chronic exposure to allergens such as hay dust and mold. As in humans, inflammation, bronchoconstriction and mucus secretion are key components of disease progression. Medical treatment may include corticosteroids, bronchodilators, and cromolyn sodium. Corticosteroids at anti-inflammatory doses decrease circulating levels of T-lymphocytes, inhibit lymphokines, reduce interferon production, and antigen

processing, and decrease the number of mast cells and histamine production.[10] Possible side effects of corticosteroid administration include immuno-suppression, polyuria, polydipsia, increased appetite and gastro-intestinal ulceration. Cromolyn sodium (Intal®) reduces mast cell degranulation, decreases bronchoconstriction, and attenuates bronchospasm.[17] Possible adverse effects associated with cromolyn sodium administration include throat irritation, cough, wheeze and nausea. In addition to medical therapy, environmental changes must also be made including reducing exposure to environmental allergens. Medical therapy alone rarely leads to clinical improvement without accompanying environmental changes.[13,18] Both COPD in humans and RAO in horses have similarities to the chronic respiratory disease that occurs in blue and gold macaws following chronic exposure to cockatoo or African grey parrot dander. These diseases result from chronic exposure to an environmental allergen or irritant and inflammation is involved in disease progression and clinical signs. Regression of clinical signs is difficult to achieve and numerous medications and environmental changes may be required. Long term prognosis for macaws with COPD is guarded and significant improvements in clinical signs, even with medical therapy and environmental changes, are unlikely.

Clinical Report

A 2-year-old male, blue and gold macaw was referred with a nine month history of lower respiratory disease. The bird was housed indoors in a cage (1m x 1m x 1m) with a grate above the substrate and fed a mix of a pelleted diet for psittacine birds, dried fruit mix, table food and occasional nuts (almonds, peanuts) as treats. Newspaper was used as substrate on the bottom of the cage and was changed 2-3 times per week. The owner did

not smoke, but the bird lived in a room with a scarlet macaw and a Moluccan cockatoo. The other birds were apparently healthy.

The bird was initially presented to a veterinarian for increased respiratory effort, especially when excited, and a "clicking" noise when breathing. The bird had a weak positive *Aspergillus sp.* antibody titer and a packed cell volume (PCV) of 59%. The veterinarian treated the bird with an unknown dose of ciprofloxacin and itraconazole. The bird improved mildly with treatment but clinical signs did not resolve completely. The veterinarian repeated treatment for aspergillosis two more times. Specifics of the diagnostics and treatments were not available.

The bird was then presented to a second veterinarian 8 months later because clinical signs were still present. The referring veterinarian performed radiographs that were within normal limits and a *Chlamydophila psittaci* antibody titer was negative. An elevated creatine kinase was present on plasma chemistry (1167 IU/L; normal 50-400 IU/L). This elevated CK may have been due to muscle damage or sample hemolysis.[19] No other abnormalities were noted and no complete blood count was performed. The veterinarian referred the bird for further diagnostics.

On presentation, the bird weighed 1.2 kg and was extremely stressed when handled. A brief physical examination was performed before the bird needed to be placed in an oxygen cage. On physical examination, the bird had a keel score of 3/5 and increased respiratory effort on both inspiration and expiration. No respiratory "clicking" was heard on initial auscultation. No other abnormalities were noted. As stated previously, differential diagnoses for lower respiratory disease may include exposure to

environmental allergens/irritants (inflammatory), infectious, metabolic, nutritional, toxic, physical or neoplastic causes.[1]

Initial diagnostics included a complete blood count (CBC), plasma biochemistry analysis, whole body radiographs and an *Aspergillus sp.* panel sent to the University of Miami. The *Aspergillus sp.* panel includes antigen and antibody levels as well as a plasma protein electrophoresis (EPH). An elevated PCV and a stress leukogram (heterophilic leukocytosis with a monocytosis and lymphopenia) were present (Table 1). Polycythemia in birds typically results from either dehydration or from an underlying disease such as hemochromatosis, respiratory disease or heart disease.[1] The plasma proteins were not elevated and no other signs of dehydration were present in this patient. Macaws are not a species prone to developing hemochromatosis and no evidence of cardiac disease was ausculted on physical examination. Based on the patient's clinical signs, respiratory disease is the most likely etiology for the polycythemia. A stress leukogram likely resulted from either transport to the clinic or handling in the clinic prior to venipuncture. No other significant abnormalities were noted on the CBC or biochemistry panel. The *Aspergillus spp.* antigen and antibody levels were negative and the albumin and A:G ratio were slightly low on the EPH (Table 2). Hypoalbuminemia is associated with chronic liver disease, chronic inflammation, renal disease, protein malnutrition, gastrointestinal disease, parasitism, or sequestration.[1] Other than chronic inflammation, there was no evidence of any of the above diseases in this patient. The albumin was only mildly decreased and is interpreted here as a result of chronic inflammation. Because of the hypoalbuminemia and normoglobulinemia, the A:G ratio was also low.

Table 1: CBC and plasma biochemistry results of a 2-year-old blue and gold macaw (*Ara arauna*) with chronic obstructive pulmonary disease

	Visit 1 2/16/06	Visit 2 5/9/06	Visit 3 7/14/06	Normals for adult macaws*
PCV (%)	65 ↑	69 ↑	68 ↑	39-48
WBC (x 10^3/UL)	15.7 ↑	13.8 ↑	10.1	6-12
Heterophils (%)	82 ↑	72	67	58-78%
Lymphocytes (%)	12.7 ↓	26	15.8 ↓	20-45%
Monocytes (%)	4.4 ↑	2.1	13 ↑	0-3%
Total Protein (g/dl)	4.0	3.7	4.2	2.1-4.5
Albumin (g/dl)	1.4	1.3	-	1.24-3.11
Glucose (mg/dl)	278	311	-	145-345
Calcium (mg/dl)	8.6	8.5	-	8.5-13
Phosphorus (mg/dl)	4.8	4.3	-	2-12
Alkaline Phos. (IU/L)	98	67	-	20-230
AST (IU/L)	102	94 ↓	-	100-300
LDH (IU/L)	83	71	-	70-350
CK (IU/L)	193	103	-	100-300
Cholesterol (mg/dl)	177	171	-	100-390
Uric Acid (mg/dl)	3.7	4.7	-	2.5-11

*Bloodwork was analyzed by the in-house clinical pathology laboratory and no established reference ranges are available; reference values obtained from Harrison & Lightfoot[20]

Table 2: *Aspergillus* sp. panel including plasma protein electrophoresis (EPH) results for a 2-year-old blue and gold macaw (*Ara arauna*) with chronic obstructive pulmonary disease

	Visit 1	Visit 2	Normals for adult macaws*
Total protein (g/dl)	3.0	3.0	2.1-4.5
A/G ratio	1.34 ↓	1.49 ↓	1.5-3.5
Pre-albumin (g/dl)	0.52	0.58	0.05-0.7
Albumin (g/dl)	1.20 ↓	1.22 ↓	1.24-3.11
Alpha 1 (g/dl)	0.07	0.07	0.04-0.25
Alpha 2 (g/dl)	0.16	0.13	0.04-0.31
Beta (g/dl)	0.59	0.55	0.48-0.68
Gamma (g/dl)	0.46	0.46	0.2-0.5
Aspergillus sp. antibody	0.8	-	<1.4 negative
Aspergillus sp. antigen	1.0	-	< 1.4 negative

*Normals provided by the Avian and Wildlife Laboratory, University of Miami School of Medicine, Miami, FL 33136.

On radiographs obtained with a direct capture digital X-ray sensor,[a] mild splenomegaly and areas of intramedullary opacities in both humeri were present (Figures 1 & 2). Differentials for splenomegaly include systemic infection or inflammation, neoplasia, and metabolic disease, such as hepatic lipidosis or hemochromatosis.[1] Systemic inflammation was the likely cause of mild splenomegaly in this case. Differentials for the opacities in the humeri included infectious, due to *Aspergillus sp.* or *Mycobacteria sp.*, neoplastic or traumatic.[1] Because of the well-demarcated margins and eventual resolution, a traumatic etiology was most likely. Venipuncture and radiography were performed under isoflurane anesthesia.[b]

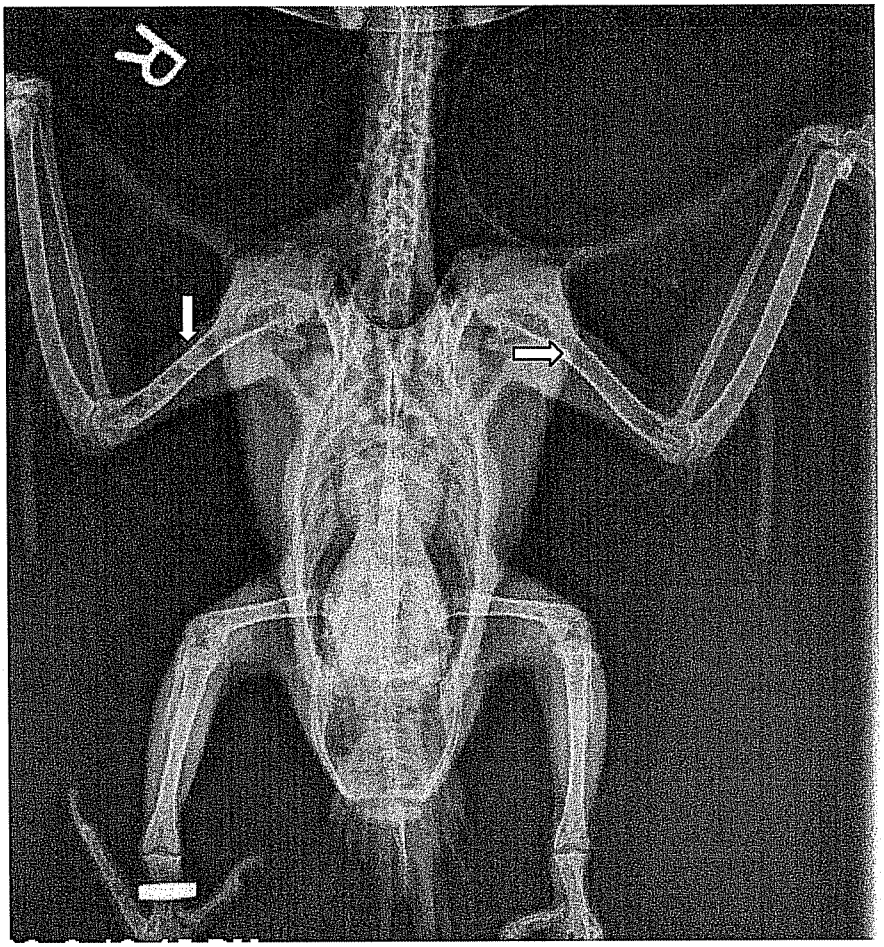

Figure 1: Ventrodorsal view of whole body radiographs of a 2-year-old male blue and gold macaw (*Ara ararauna*) with lower respiratory disease . Intramedullary lesions are present in both humeri (arrows). No other abnormalities are noted.

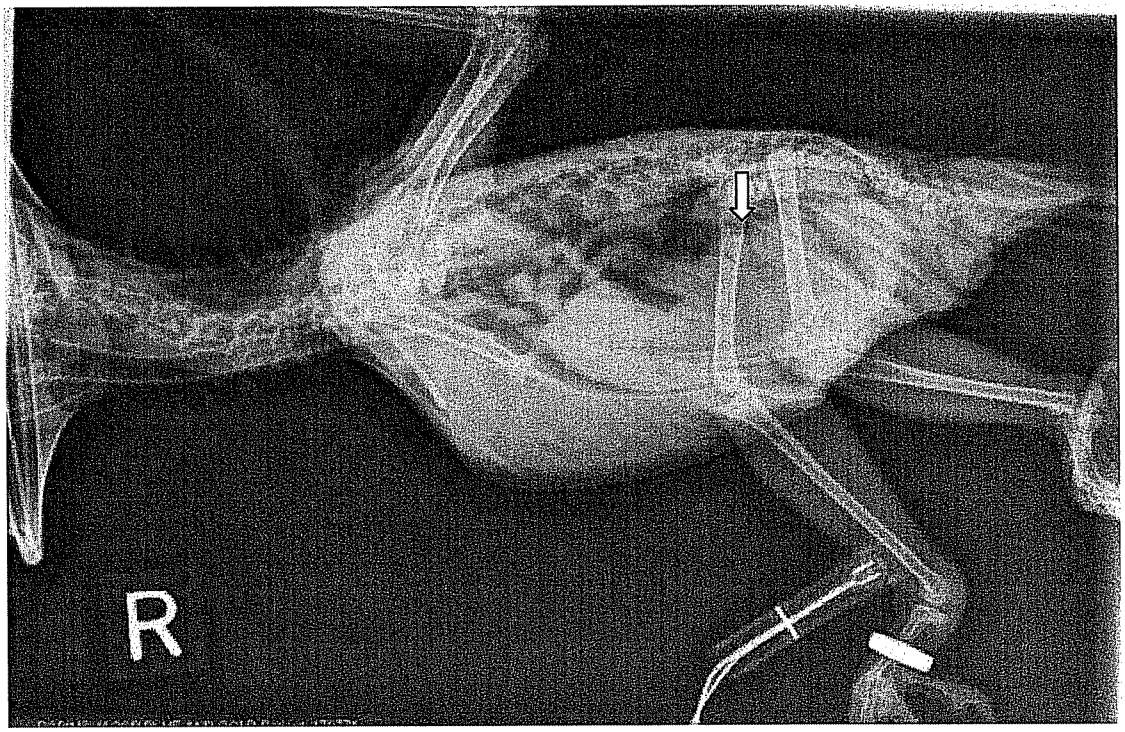

Figure 2: Right lateral view of whole body radiographs of a 2-year-old male blue and gold Macaw (*Ara ararauna*) with lower respiratory disease. Mild splenomegaly is present (arrow). The bird is slightly rotated in this radiograph, however, the rotation was not considered significant enough to affect interpretation of the respiratory system.

Additional diagnostics included rigid endoscopy of the coelomic cavity, cytology, bacterial and fungal cultures and histopathology. Rigid endoscopy of the coelomic cavity was chosen in order to obtain samples to determine if an infectious agent was present or if the chronic respiratory disease was due to an environmental irritant or allergen. Additionally, a bone biopsy was recommended to determine the nature of the intramedullary lesions in the humeri but was declined by the owner.

The bird was mask induced with isoflurane[b] (3% in 2 L/min O_2) and then intubated with a 4.5 mm non-cuffed endotracheal tube and placed in right lateral recumbency on a heated table. The bird was given butorphanol[c] (2 mg/kg IM[21]) for analgesia after intubation. The feathers between the last rib, the sacrum and the iliotibialis cranialis muscle were plucked and the skin surgically prepared with chlorhexidene scrub and sterile saline. A one centimeter (cm) incision was made in the skin approximately 0.5 cm behind and parallel to the last vertical rib on the left. Curved mosquito hemostats were used to bluntly penetrate through the muscle of the body wall and enter the coelomic cavity. A rigid endoscope[d] was introduced into the left abdominal air sac and the coelomic cavity was explored with the endoscope. The air sacs were cloudy and thickened, and biopsies of the left lung and air sacs were taken with a biopsy forcep.[e] Differential diagnoses for cloudy air sacs include infectious (bacterial, fungal, viral), inflammatory or chronic exposure to environmental allergens or irritants. There was minimal bleeding resulting from these biopsies. Samples were submitted for histopathology, aerobic and anaerobic bacterial and fungal culture. A 2 mm x 2 mm, pale mass was visualized caudal to the ventriculcus on the ventral left abdominal air sac. Samples of this mass were aspirated for culture and cytology but because it was filled

with a thick white fluid, a solid sample could not be submitted for histopathology. Differential diagnoses for this mass included infectious, neoplastic, and inflammatory, such as an old, inactive granuloma or walled off foreign body. All other organs appeared grossly normal. The muscle layers were closed with 4-0 polydioxanone suture[f] (PDS) with one cruciate suture and the skin was closed in a similar manner. The bird was given 120 mL warm Normosol-R®[g] subcutaneously and recovered from anesthesia in a heated cage (85°F) with oxygen (5 L/min). Recovery from anesthesia was slightly prolonged but uneventful. The bird recovered well from surgery and went home the following day on meloxicam[h] (0.2 mg/kg q12h for 7 days)[21] for post-operative pain.

Cytology of the fluid aspirated from the mass was consistent with degenerate cellular material with no evidence of inflammation, infection or neoplasia. There was no growth on bacterial or fungal cultures of this fluid, and there was also no growth on bacterial or fungal cultures of lung biopsies.

Histopathology of the air sacs revealed a moderate amount of interstitial edema with hemorrhage. Lymphoplasmacytic infiltration in the parabronchi with mild hypertrophy of smooth muscle was present in lung biopsies (Figures 3 & 4). Special stains (hematoxylin & eosin, silver, acid fast) for fungi, bacteria and acid fast bacteria in lung samples were negative. No viral inclusions were seen. These biopsy results are consistent with an inflammatory reaction resulting from exposure to a persistent environmental allergen.[7] COPD in macaws has been previously reported in blue and gold macaws that were exposed to cockatoo or African grey parrot dander.[3-5]

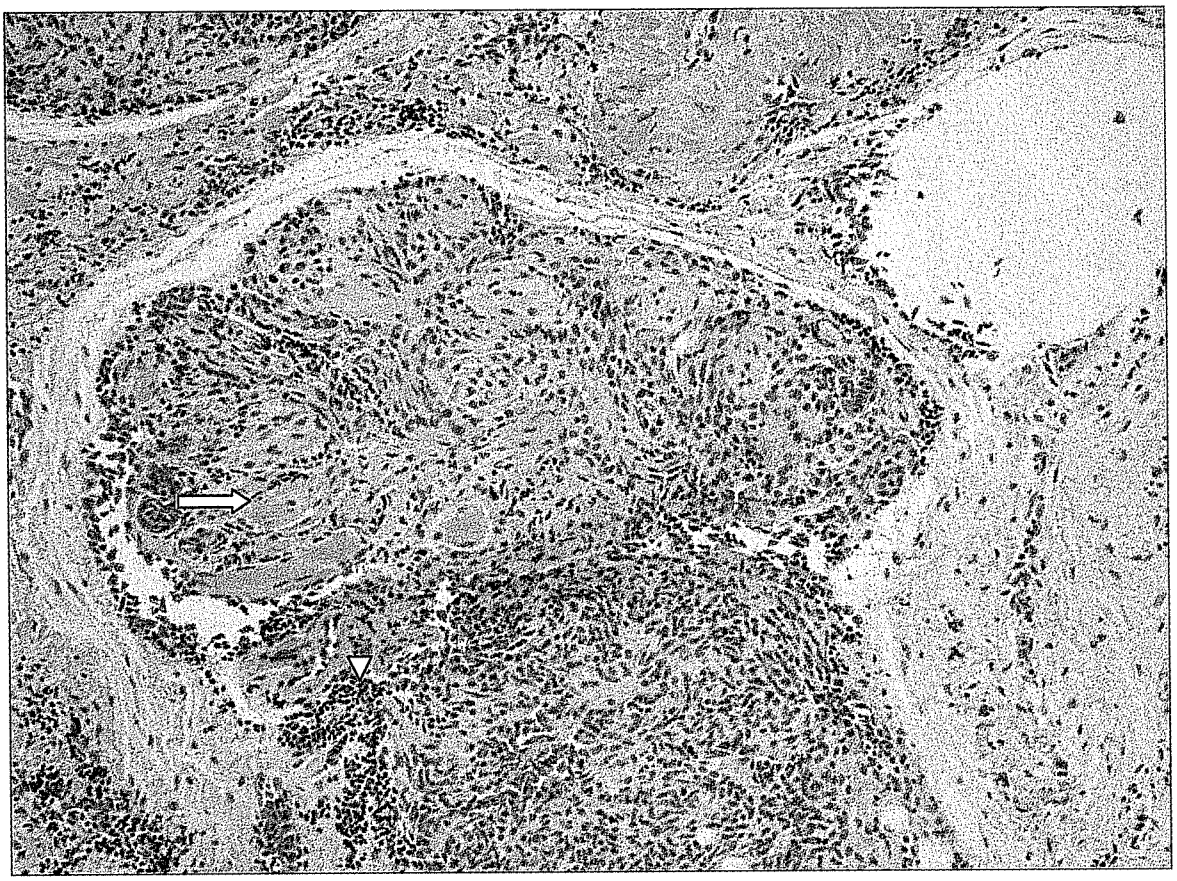

Figure 3: Hematoxylin and eosin stained section of lung from a 2-year-old male blue and gold macaw (*Ara ararauna*) with chronic respiratory disease (10X). There is mild smooth muscle hypertrophy (arrow) present and mild lymphoplasmacytic inflammation (arrow head).

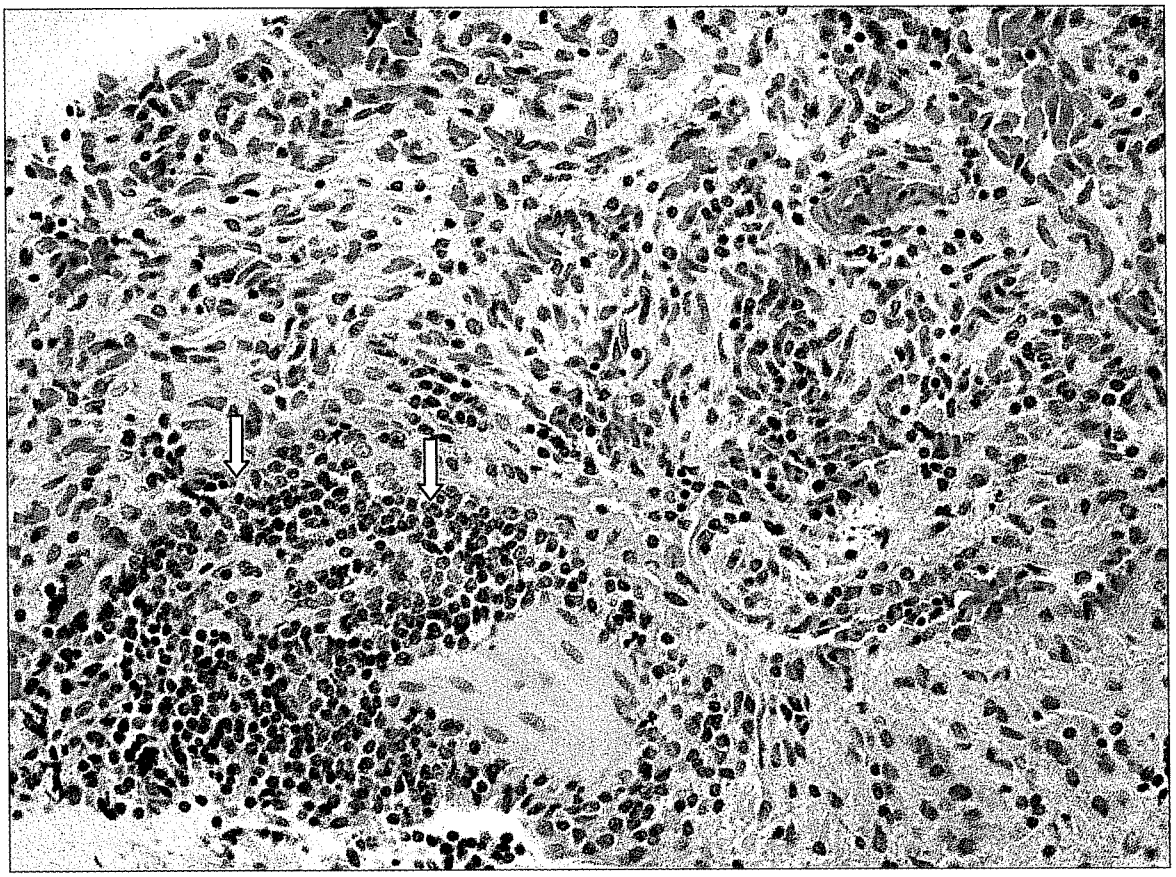

Figure 4: Hematoxylin and eosin stained section of lung from a 2-year-old male blue and gold macaw (*Ara ararauna*) with chronic respiratory disease (40X). There is a moderate amount of lymphoplasmacytic infiltration in this section of lung (arrows).

The client was advised to continue the bird on meloxicam at the current dose (0.2 mg/kg PO q12h) until the following visit in an attempt to reduce the inflammatory reaction in the lungs and sucralfate[i] (25 mg/kg PO q12h)[21] was added to reduce the likelihood of gastrointestinal side effects. Additionally, the client was advised to, 1) keep the blue and gold macaw in a room separate from the cockatoo, 2) increase cleaning in the house to reduce dander on surfaces, 3) add numerous HEPA air filters throughout the house, and 4) bathe the birds regularly to reduce feather dander in the house. The client was asked to schedule a recheck exam in 4 weeks.

The bird returned for a recheck examination 12 weeks later (visit 2). The owner had increased the meloxicam dose to 0.25 mg/kg PO q12h a few weeks before this visit (without consultation from a clinician) and had completely removed the cockatoo and scarlet macaw from the household 2 weeks prior to the visit. The owner had placed numerous HEPA filters throughout the house and increased the frequency of cleaning the house. There was no significant change on physical examination and a CBC, plasma biochemistry, EPH and whole body radiographs were repeated. Venipuncture and radiography were performed under isoflurane anesthesia. The PCV remained increased at 69% (Table 1), a mild leukocytosis was present (possibly stress related) and the albumin was still slightly decreased (Table 1 & 2). There was a mildly decreased AST, but no other clinically significant abnormalities were present on the plasma biochemistry panel. A decreased AST could be due to decreased liver mass, individual patient variation or variation of laboratory normals.[19] There was no evidence of liver disease and the AST was only mildly decreased and therefore interpreted as individual patient variation. Repeat radiographs showed substantially resolved humeral intramedullary lesions. The

spleen was still slightly enlarged but was smaller than on the previous visit and no other abnormalities were noted (Figures 5 & 6). Due to the increasing PCV and lack of clinical improvement, the dose of meloxicam was increased (1 mg/kg q12h).[21] Additionally, the bird was prescribed montelukast sodium[j] (1.25 mg PO q24h) in an attempt to reduce inflammation in the lungs. The owner was again asked to return in 4 weeks. The owner called 3 weeks after visit 2 to schedule visit 3 and advised the receptionist that she had not been giving the montelukast sodium as prescribed to the patient. Additionally, the patient's clinical signs had not improved. She was advised of the importance of giving the prescribed medications and was scheduled for an appointment 4 weeks after starting the montelukast sodium.

The bird returned for a recheck exam nine weeks after visit 2. The owner reported that since the last visit, the bird's clinical signs had improved but were still present. The owner had been giving meloxicam as prescribed for 4 weeks (1 mg/kg PO q12h) but had increased the montelukast sodium to twice daily (1.25 mg PO q12h) without consulting a clinician. Additionally, the other birds were still living in another house with a friend. The bird was examined and although increased inspiratory and expiratory respiratory efforts were present, they were not as severe as during the first two visits. Blood was taken from the right jugular while the bird was awake with an oxygen mask over his face. The bird took several minutes to recover after handling but did not need to be placed into an incubator with oxygen. There were no significant findings on physical examination (other than increased respiratory effort) and the PCV remained increased (68%). A mild lymphopenia and monocytosis were present but the overall leukocyte count was within normal limits (Table 1). These leukocyte abnormalities were

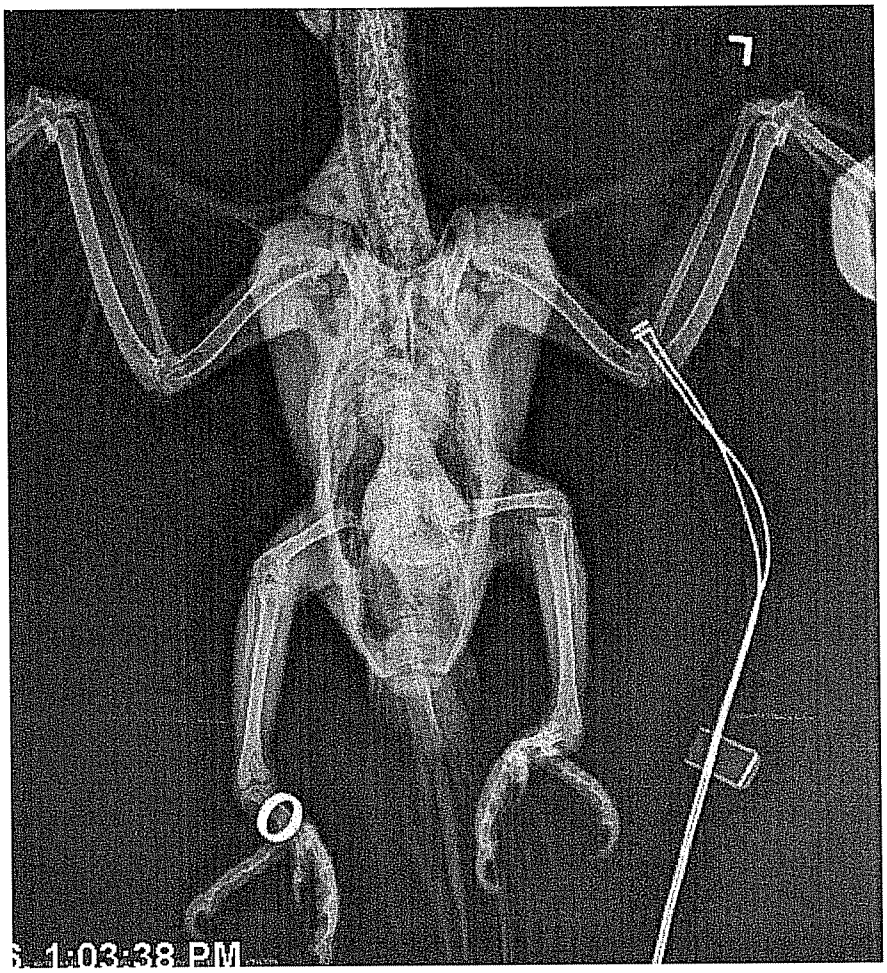

Figure 5: Ventro-dorsal view of whole body radiographs of a 2-year-old male blue and gold macaw (*Ara ararauna*) with chronic obstructive pulmonary disease. No abnormalities are noted. The lesions previously present in both humeri have resolved. The bird in this radiograph is slightly rotated, however, the rotation was not considered significant enough to affect interpretation of the respiratory system.

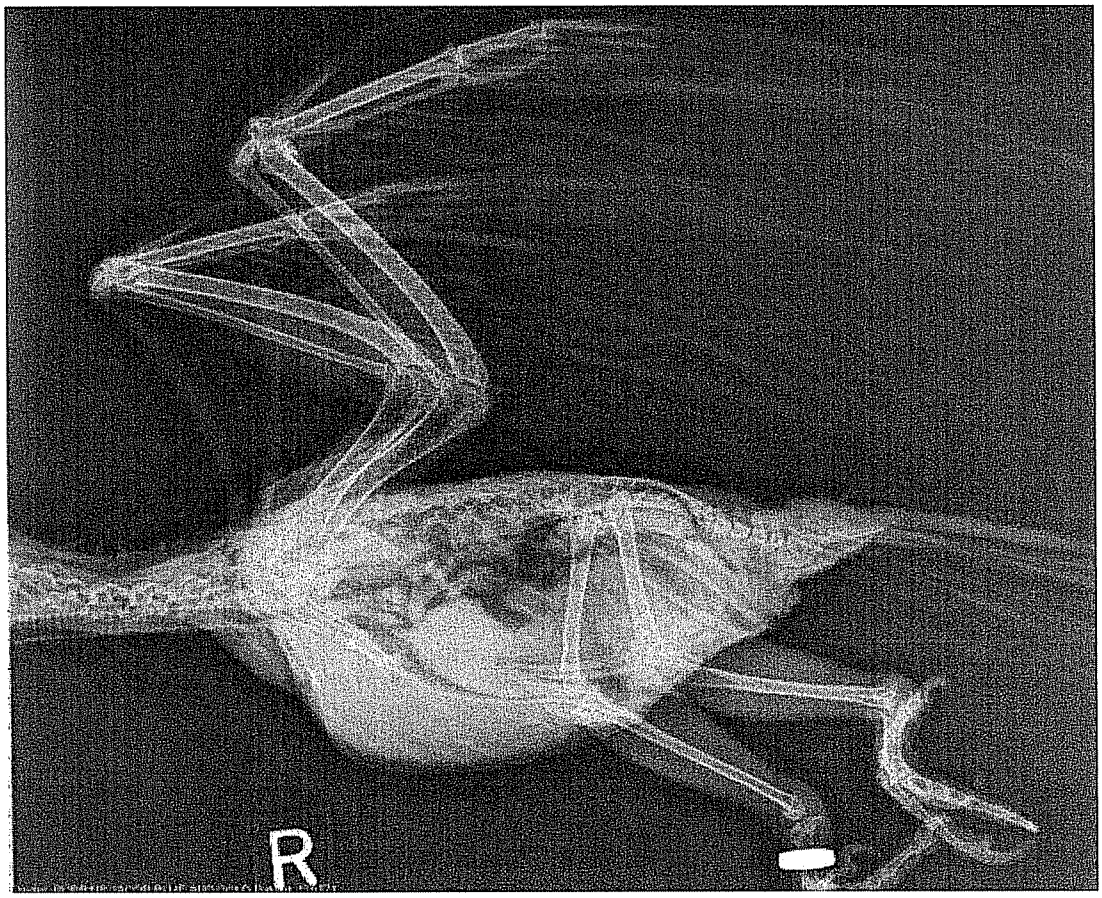

Figure 6: Right lateral view of whole body radiographs of a 2-year-old male blue and gold macaw (*Ara ararauna*) with chronic obstructive pulmonary disease. Mild splenomegaly is still present, but no other abnormalities were noted. The bird in this radiograph is slightly rotated, however, the rotation was not considered significant enough to affect interpretation of the respiratory system.

attributed to a stress response. Chronic inflammation could also have lead to a monocytosis. The owner was advised to continue on the current dosing regimen of meloxicam (1 mg/kg PO q12h), sucralfate (25 mg/kg PO q12h) and montelukast sodium (1.25 mg PO q12h) and to return for a recheck in another 2 months. Although a 1% decrease in PCV is likely not significant, stopping the upward progression of the PCV and the mild improvement in clinical signs was seen as a positive indicator of slowing disease progression. Planned follow up for this patient includes physical examinations and complete blood counts every two months. Adjustments in dosing of current medications will be made based on clinical signs and changes in the PCV, and additional medications, such as Vitamin E, may be added if clinical signs worsen. Repeat lung biopsies may be considered in the future.

Discussion

This blue and gold macaw represents a classic case of macaw pulmonary hypersensitivity, a form of chronic obstructive pulmonary disease. This disease most commonly occurs in blue and gold macaws, but the exact pathophysiology of the disease is not well understood. The macaw had lived with a Moluccan cockatoo for two years prior to presentation and the feather dander from the cockatoo most likely contributed to the patient's disease. The patient's primary clinical sign was respiratory distress when handled or stressed. Additionally, the bird had polycythemia.

Chronic obstructive pulmonary disease was diagnosed by performing an examination, complete blood count, plasma biochemistry panel, whole body radiographs, an *Aspergillus sp.* panel, fungal and bacterial cultures, cytology and histopathology of the air sacs and lungs. No infectious organisms were isolated on culture or seen on cytology

or histopathology; it is possible that samples were taken from regions that did not have infectious organisms present. Histopathology revealed hemorrhage and edema in the air sacs and lympoplasmacytic infiltration and smooth muscle hypertrophy of the lungs. These histopathology findings and a history of a two- year exposure to a bird which produces copious feather dander (Moluccan cockatoo) are consistent with COPD in a blue and gold macaw.[7]

Medical therapy, which included non-steroidal anti-inflammatory medications, gastro-protectants and anti-leukotrienes, was instituted in this patient. NSAIDs, such as meloxicam and carprofen, and gastro-protectants, such as sucralfate, cimetidine and omeprazole, are the most common treatment for COPD in macaws. Because, NSAIDs alone did not lead to any clinical improvement in this patient and the polycythemia continued to worsen, therapy with montelukast sodium, a leukotriene antagonist, was instituted. An initial lack of improvement in clinical signs could be due to inadequate dosing, owner non-compliance or the resistance to treatment of the primary disease. Although no research has examined the use of leukotriene antagonists in avian species, mild improvement in clinical signs and polycythemia was achieved after a month of treatment with montelukast sodium. The meloxicam, sucralfate and montelukast sodium were continued indefinitely. Other possible treatments in this bird could have included vitamin A and E supplementation. Recent studies in people with COPD have shown that oxidative damage to the lungs can result during exacerbations and anti-oxidant (vitamin A & E) supplementation may help reduce this damage.[22,23] Additional medications were not added to this patient's treatment regimen due to ongoing owner compliance problems.

Perhaps with better owner compliance, the patient would have shown improvement in clinical signs earlier. Unfortunately, owner compliance is a common challenge in veterinary medicine. The addition of montelukast sodium seemed to help the bird clinically, however, prior to dosing, possible side effects resulting from this medication were unknown. Very few adverse effects result from use in humans and include headache, dizziness, nausea, fatigue and rash. There are no reports of clinical use of montelukast sodium in avian species. Discussions are present on some veterinary forums, however, many doubt the efficacy of montelukast sodium in macaws with COPD because of the lack of eosinophils or mast cells on histopathology of the lungs.

Environmental changes were made to reduce continued exposure to cockatoo feather dander. Changes included removing the cockatoo from the house, increasing cleaning of the house, and adding numerous HEPA air filters throughout the house. HEPA air filters are more effective than non-HEPA filters at removing small airborne particles which may have contributed to this bird's disease. Due to the chronic nature of COPD in macaws, reversal of histopathologic lesions and improvement of clinical signs rarely occurs. Repeat lung biopsies have not been performed. After six months of medical treatment and environmental changes, mild improvement in clinical signs was achieved in this patient.

Summary

A 2-year-old male blue and gold macaw (*Ara araruna*) was referred with a nine-month history of lower respiratory disease. On physical exam, the bird was easily stressed and quickly developed respiratory difficulty when handled. Polycythemia was the most clinically significant abnormality on blood work. Radiographs and an

Aspergillus sp. panel did not reveal the etiology of respiratory disease. Rigid endoscopy was performed to obtain samples for culture, cytology and histopathology. Fungal and bacterial cultures were negative and cytology was non-diagnostic. On histopathology, samples of the lung and air sacs revealed that the clinical respiratory disease was due to chronic exposure to an environmental irritant or allergen. Medical therapy and environmental changes led to mild improvement of clinical signs in this patient.

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ENDNOTES

[a] Eklin EDR6, Eklin Medical Systems, Inc., Sunyvale, CA, 94089, USA

[b] Iso Flo®, Abbot Laboratories, North Chicago, IL, 60064, USA

[c] Torbugesic®, Ft. Dodge Animal Health, Overland Park, KS, 66225, USA

[d] Storz 2.7 mm, 30° rigid endoscope (18cm length) with a 14.5 French instrument channel, Karl Storz Endoscopy – America, Inc., Culver City, CA, 90230, USA

[e] Storz 5 French elliptical biopsy forceps, Karl Storz Endoscopy – America, Inc., Culver City, CA, 90230, USA

[f] PDS II®, Ethicon, Inc., Somerville, NJ, 08876, USA

[g] Normosol-R®, Abbot Laboratories, North Chicago, IL, 60064, USA

[h] Metacam®, Boehringer Ingelheim, Ridgefield, CT, 06877, USA

[i] Carafate®, Axcan Scandipharm, Inc., Birmingham, AL, 35242,USA

[j] Singulair®, Merck & Co. Inc., Whitehouse Station, NJ, 08889,USA