

Exercise Intolerance & Chronic Cough in a Geriatric Dog

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Ernest, a 10-year-old, 9.8-kg neutered West Highland white terrier, was presented for dyspnea and cyanosis that was preceded by 3 months of cough and exercise intolerance.

History

Ernest's nonproductive cough sounded harsh, occurred at a frequency of 5 to 10 times per day, and appeared induced by handling and excitement. Both cough and exercise intolerance gradually worsened. Dyspnea and cyanosis had appeared over the past 3 weeks in association with stressful situations or during any kind of exercise. Treatment with furosemide

(2 mg/kg PO once a day for 3 days) did not improve signs.

Examination

Ernest was tachypneic and displayed a severe expiratory dyspnea with a pronounced expiratory abdominal push. Bilateral diffuse inspiratory crackles were noted on thoracic auscultation. Buccal mucosal membranes were cyanotic. Heart rate, cardiac auscultation, and rectal temperature were within limits. Body condition score was 6/9. Before further investigation, the patient received an injection of butorphanol (0.2 mg/kg IM), and flow-by oxygen was administered.

Diagnostic Results

Serum chemistry panel and CBC results were within range except for alkaline phosphatase (280

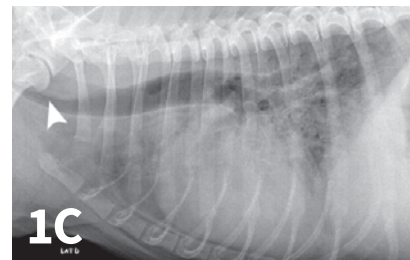
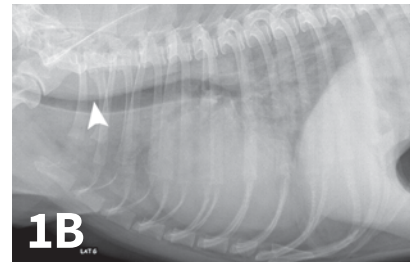
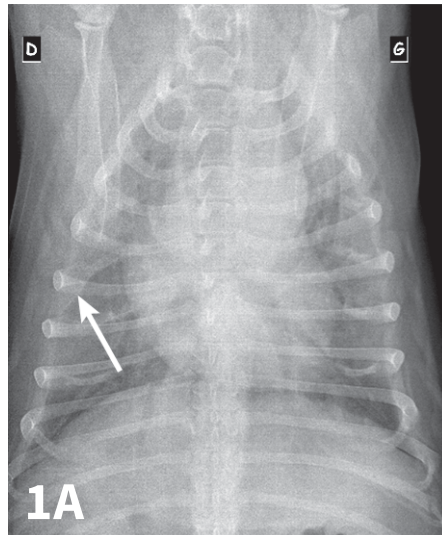
IU/L; range, 27-74) and hematocrit (57%; range, 37%-55%). Thoracic radiographs showed a severe bronchointerstitial pattern, right cardiomegaly, and prominent pulmonary artery trunk (**Figure 1**, next page).

Echocardiography revealed severe arterial pulmonary hypertension estimated at 67 mm Hg in systole (range, <20) based on the peak velocity of the tricuspid regurgitant flow (V_{max} TR 3.95 m/s; range, <2.9); severe right ventricular hypertrophy and septal flattening were also subjectively assessed. Arterial blood gas analysis indicated severe hypoxemia (pO_2 47 mm Hg; range, 80-100) and hypocapnia (pCO_2 27 mm Hg; range, 35-45).

A fecal Baermann analysis was negative.

ASK YOURSELF

- ▶ What is the clinical presentation of canine idiopathic pulmonary fibrosis (CIPF)?
- ▶ Are bronchoscopy and bronchoalveolar lavage (BAL) useful in the diagnosis of CIPF?
- ▶ How is a diagnosis of CIPF confirmed?
- ▶ What is the treatment for CIPF?



▲ Ventrodorsal (A) and left and right lateral (B, C) thoracic radiographs of a 10-year-old West Highland white terrier showing a redundant tracheal membrane (1B, arrowhead; 1C, arrowhead), a severe generalized bronchointerstitial pattern, and a pleural fissure line (1A, arrow) between right pulmonary lobes.

Diagnosis

Suspicion of canine idiopathic pulmonary fibrosis (CIPF) with severe secondary pulmonary hypertension.

Treatment

Ernest was hospitalized in an oxygen cage for 3 days and treatment with sildenafil (2.5 mg/kg PO twice a day) was initiated, which led to significant improvement in the dog's clinical condition (progressive disappearance of the dyspnea and pink color of the mucous membranes). Ernest was discharged at day 5 after a progressive oxygen withdrawal, which was well-tolerated.

Outcome

At recheck evaluation 7 days later, Ernest was clinically improved with resolution of both dyspnea and cyanosis. Exercise was limited to two 15-minute walks per day, which were well-tolerated.

Cough was still present but did not impact his quality of life. Pulmonary crackles were still heard. Treatment was continued without adjustments. After 6 months of treatment, exercise tolerance had improved (three 30-minute walks per day, well-tolerated) and cough was present only occasionally. On echocardiography, subjective parameters of pulmonary hypertension were improved (absence of septal flattening), but the absence of a tricuspid regurgitant flow at this time precluded the objective assessment of pulmonary artery pressures. Blood gas analysis was not available (poor patient compliance).

After 1 year of treatment, signs of CIPF and pulmonary hypertension were still under control. Lung crackles were still present on thoracic auscultation. A thoracic computerized tomography scan was performed under sedation to assess

BAL = bronchoalveolar lavage
CIPF = canine idiopathic pulmonary fibrosis

the distribution of lung parenchymal lesions (**Figure 2**). Lesions observed were compatible with those described in CIPF.^{1,2} Arterial blood gas analysis was performed under sedation and showed a pO₂ of 51 mm Hg and a pCO₂ of 41 mm Hg. The low arterial pO₂ value is likely secondary to the severe underlying parenchymal lung disease and may have been compounded by the influence of sedation on the ventilation pattern (reduction in amplitude of respiratory movements).

Ernest was still alive 18 months after the initial workup. However, because of the cardiopulmonary debilitation and low likelihood of biopsy results influencing clinical management, antemortem biopsies were considered too invasive. The owner consented to confirmation of diagnosis by histopathology on a lung tissue biopsy sampled after death or euthanasia.



- ▲ Transverse thoracic precontrast CT images (lung window) of the same patient at the level of the caudal lung lobes. Scans revealed an almost generalized ground-glass opacity (**red asterisks**), visible as an increase in overall opacity of the lung parenchyma without obscuration of the underlying vessels in the accessory and caudal lung lobes.

DID YOU ANSWER?

- ▶ CIPF is a progressive lung disease of unknown origin which usually affects middle-aged to older dogs of the West Highland white terrier breed.⁴ Classic signs are exercise intolerance and chronic cough in otherwise bright and alert dogs, but some dogs may be presented with history of syncope, cyanosis, respiratory difficulties, panting, or tachypnea. Bilateral inspiratory crackles are commonly noticed on lung auscultation and may be heard without a stethoscope when the dog is breathing with an open mouth. An abdominal breathing pattern consisting of an excessive expiratory push is commonly present. A right-sided systolic murmur can be heard in dogs with tricuspid regurgitation due to pulmonary hypertension, but because of the presence

of crackles, adequate auscultation may be difficult.

- ▶ Bronchoscopy and BAL fluid analysis provide useful information about lungs and airways. In dogs with CIPF, these complementary procedures often rule out infectious causes of disease and permit assessment of other respiratory abnormalities. In the present case, anesthetic risk was considered too high to perform a bronchoscopy and a BAL. Bronchoscopic findings in dogs with CIPF are not specific. Anomalies such as tracheal collapse, bronchial mucosal irregularity, increased amounts of bronchial mucus, bronchomalacia, or bronchiectasis may be observed, alone or in combination. Analysis of BAL fluid

usually shows an increase in the total cell count because of increased numbers of macrophages and neutrophils. Bacterial growth is not commonly seen in CIPF.¹

- ▶ Impaired arterial blood oxygen in a geriatric West Highland white terrier with progressive clinical signs and crackles audible on thoracic auscultation can lead to a clinical suspicion of CIPF. However, definitive diagnosis of CIPF is challenging and relies on histopathologic examination of lung tissue,³ although thoracic high-resolution computed tomography (HRCT) may have a high specificity.^{1,2} HRCT findings include ground glass opacities, parenchymal bands, subpleural lines, subpleural interstitial thickening, peribronchovascular interstitial thickening, traction bronchiectasis, and honeycombing.^{1,2}

- ▶ There is currently no specific effective treatment for CIPF. Management mainly aims at reducing clinical signs on an individual basis and to alleviate comorbidities, such as pulmonary hypertension, when present. Oral corticosteroids might relieve cough in some dogs with secondary airway inflammation. Antitussives can be used if cough is irritating. Bronchodilators such as theophylline may be used to promote bronchodilation, enhance mucociliary clearance, and increase contractibility of the diaphragmatic muscle. When pulmonary hypertension is present, treatment with sildenafil may improve exercise tolerance and quality of life. ■

CIPF = canine idiopathic pulmonary fibrosis
HRCT = high-resolution computed tomography

See page 92 for references.

Brief Summary of Prescribing Information

convenia[®]
(cefovecin sodium)

Antimicrobial for Subcutaneous Injection in Dogs and Cats Only

CAUTION: Federal (USA) law restricts this drug to use by or on the order of a licensed veterinarian.

INDICATIONS:

Dogs

CONVENIA is indicated for the treatment of skin infections (secondary superficial pyoderma, abscesses, and wounds) in dogs caused by susceptible strains of *Staphylococcus intermedius* and *Streptococcus canis* (Group G).

Cats

CONVENIA is indicated for the treatment of skin infections (wounds and abscesses) in cats caused by susceptible strains of *Pasteurella multocida*.

CONTRAINDICATIONS: CONVENIA is contraindicated in dogs and cats with known allergy to cefovecin or to β -lactam (penicillins and cephalosporins) group antimicrobials. Anaphylaxis has been reported with the use of this product in foreign market experience. If an allergic reaction or anaphylaxis occurs, CONVENIA should not be administered again and appropriate therapy should be instituted. Anaphylaxis may require treatment with epinephrine and other emergency measures, including oxygen, intravenous fluids, intravenous antihistamine, corticosteroids, and airway management, as clinically indicated. Adverse reactions may require prolonged treatment due to the prolonged systemic drug clearance (65 days).

WARNINGS: Not for use in humans. Keep this and all drugs out of reach of children. Consult a physician in case of accidental human exposure. For subcutaneous use in dogs and cats only. Antimicrobial drugs, including penicillins and cephalosporins, can cause allergic reactions in sensitized individuals. To minimize the possibility of allergic reactions, those handling such antimicrobials, including cefovecin, are advised to avoid direct contact of the product with the skin and mucous membranes.

PRECAUTIONS: Prescribing antibacterial drugs in the absence of a proven or strongly suspected bacterial infection is unlikely to provide benefit to treated animals and may increase the risk of the development of drug-resistant animal pathogens.

The safe use of CONVENIA in dogs or cats less than 4 months of age and in breeding or lactating animals has not been determined. Safety has not been established for IM or IV administration. The long-term effects on injection sites have not been determined. CONVENIA is slowly eliminated from the body, approximately 65 days is needed to eliminate 97% of the administered dose from the body. Animals experiencing an adverse reaction may need to be monitored for this duration.

CONVENIA has been shown in an experimental *in vitro* system to result in an increase in free concentrations of carprofen, furosemide, doxycycline,

and ketoconazole. Concurrent use of these or other drugs that have a high degree of protein-binding (e.g. NSAIDs, propofol, cardiac, anticonvulsant, and behavioral medications) may compete with cefovecin-binding and cause adverse reactions.

Positive direct Coombs' test results and false positive reactions for glucose in the urine have been reported during treatment with some cephalosporin antimicrobials. Cephalosporin antimicrobials may also cause falsely elevated urine protein determinations. Some antimicrobials, including cephalosporins, can cause lowered albumin values due to interference with certain testing methods.

Occasionally, cephalosporins and NSAIDs have been associated with myelotoxicity, thereby creating a toxic neutropenia⁴. Other hematological reactions seen with cephalosporins include neutropenia, anemia, hypoprothrombinemia, thrombocytopenia, prolonged prothrombin time (PT) and partial thromboplastin time (PTT), platelet dysfunction and transient increases in serum aminotransferases.

ADVERSE REACTIONS:

Dogs

A total of 320 dogs, ranging in age from 8 weeks to 19 years, were included in a field study safety analysis. Adverse reactions reported in dogs treated with CONVENIA and the active control are summarized in Table 2.

Table 2: Number of Dogs* with Adverse Reactions Reported During the Field Study with CONVENIA.

Adverse Reaction	CONVENIA (n=157)	Active Control (n=163)
Lethargy	2	7
Anorexia/Decreased Appetite	5	8
Vomiting	6	12
Diarrhea	6	7
Blood in Feces	1	2
Dehydration	0	1
Flatulence	1	0
Increased Borborygmi	1	0

*Some dogs may have experienced more than one adverse reaction or more than one occurrence of the same adverse reaction during the study. Mild to moderate elevations in serum γ -glutamyl trans-ferase or serum alanine aminotransferase were noted post-treatment in several of the CONVENIA-treated dogs. No clinical abnormalities were noted with these findings.

One CONVENIA-treated dog in a separate field study experienced diarrhea post-treatment lasting 4 weeks. The diarrhea resolved.

Cats

A total of 291 cats, ranging in age from 24 months (1 cat) to 21 years, were included in the field study safety analysis. Adverse reactions reported in cats treated with CONVENIA and the active control are summarized in Table 3.

Table 3: Number of Cats* with Adverse Reactions Reported During the Field Study with CONVENIA.

Adverse Reaction	CONVENIA (n=157)	Active Control (n=163)
Vomiting	10	14
Diarrhea	7	26
Anorexia/Decreased Appetite	6	6
Lethargy	6	6
Hyper/Acting Strange	1	1
Inappropriate Urination	1	0

*Some cats may have experienced more than one adverse reaction or more than one occurrence of the same adverse reaction during the study.

Four CONVENIA cases had mildly elevated post-study ALT (1 case was elevated pre-study). No clinical abnormalities were noted with these findings.

Twenty-four CONVENIA cases had normal pre-study BUN values and elevated post-study BUN values (37–39 mg/dL post-study). There were 6 CONVENIA cases with normal pre- and mildly to moderately elevated post-study creatinine values. Two of these cases also had an elevated post-study BUN. No clinical abnormalities were noted with these findings.

One CONVENIA-treated cat in a separate field study experienced diarrhea post-treatment lasting 42 days. The diarrhea resolved.

FOREIGN MARKET EXPERIENCE: The following adverse events were reported voluntarily during post-approval use of the product in dogs and cats in foreign markets: death, tremors/ataxia, seizures, anaphylaxis, acute pulmonary edema, facial edema, injection site reactions (alopecia, scabs, necrosis, and erythema), hemolytic anemia, salivation, pruritus, lethargy, vomiting, diarrhea, and inappetence.

For a copy of the Material Safety Data Sheet, (MSDS) or to report a suspected adverse reaction call Zoetis Inc. at 1-888-963-8471.

STORAGE INFORMATION:

Store the powder and the reconstituted product in the original carton, refrigerated at 2° to 8° C (36° to 46° F). Use the entire contents of the vial within 56 days of reconstitution. PROTECT FROM LIGHT. After each use it is important to return the unused portion back to the refrigerator in the original carton. As with other cephalosporins, the color of the solution may vary from clear to amber at reconstitution and may darken over time. If stored as recommended, solution color does not adversely affect potency.

HOW SUPPLIED:

CONVENIA is available as a 10 mL multi-use vial containing 800 milligrams of cefovecin as a lyophilized cake.

NADA# 141-285, Approved by FDA

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Distributed by
Zoetis Inc.
Kalamazoo, MI 49007

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