

Corticosteroid-Associated Congestive Heart Failure in 12 Cats

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ABSTRACT

Cats are reported to be remarkably resistant to the adverse effects of exogenous corticosteroids. However, antecedent corticosteroid administration has been noted in cats with congestive heart failure (CHF) due to hypertrophic cardiomyopathy. Consequently, a study was conducted to describe the clinical and laboratory findings and outcomes in 12 cats diagnosed with CHF following corticosteroid administration. Methylprednisolone acetate was the most common corticosteroid administered. Time from initial corticosteroid administration to diagnosis of CHF ranged from 1 to 19 days. Mean respiratory rate was elevated, mean heart rate was relatively low for cats with CHF, and mean body temperature was subnormal. Systolic blood pressure and total serum thyroxine concentration were normal or below normal.

Vertebral-heart size on thoracic radiographs was increased. Mean interventricular septum thickness in diastole, mean left ventricular posterior wall thickness in diastole, and mean left atrial dimension at end-systole were above the reference range. Five cats died or were euthanized because of CHF. Seven cats recovered and were long-term survivors. Repeat echocardiograms disclosed partial or complete resolution of the M-mode abnormalities in these cases. All cardiac medications were eventually discontinued, and there was no recurrence of CHF. It was concluded that the 12 cats in this study suffered from a unique form of CHF associated with corticosteroid administration. Consequently, CHF should be listed as a potential adverse effect of corticosteroid administration in cats.

INTRODUCTION

Cats are reported to be remarkably resistant to the adverse effects of exogenous corticosteroids.^{1,2} Although there are reports of corticosteroid administration in cats leading to glucose intolerance (or “transient diabetes

mellitus”), skin fragility, iatrogenic hyperadrenocorticism, and recrudescence of mycotic lesions caused by *Sporothrix schenckii*, these are rare in the veterinary literature.³⁻⁸ Additionally, adverse cardiovascular effects attributable to corticosteroid administration in cats have not been reported. However, a recent retrospective study of cats with hypertrophic cardiomyopathy noted a history of antecedent corticosteroid administration in 13 of 160 cases (8%) with congestive heart failure (CHF).⁹ At the University of Minnesota Veterinary Medical Center (UMVMC), a conspicuous history of corticosteroid administration has been observed among many cats diagnosed with CHF.¹⁰ Consequently, a retrospective study was conducted to describe clinical and laboratory findings as well as short-term and long-term outcomes in cats diagnosed with CHF soon after corticosteroid administration. In just over half of the qualifying cases, CHF resolved, morphologic cardiac changes partially or completely normalized, and all cardiac medications were eventually discontinued. The temporal association between corticosteroid administration and the initial diagnosis of CHF, together with the clinical course of the disease, suggest that this is a unique form of CHF, which has been given the designation corticosteroid-associated CHF.

MATERIALS AND METHODS

Selection of Subjects

Medical records of cats diagnosed with CHF at the UMVMC from January 1992 to October 2001 were reviewed. The diagnosis of CHF was based on acute onset respiratory distress; radiographs that showed pulmonary infiltrates consistent with cardiogenic edema (with or without pleural effusion); and confirmed cardiac disease based on physical examination, thoracic radiography, electrocardiography, and echocardiography. Data were further analyzed if a history of corticosteroid administration preceded the diagnosis of CHF, and there was a reasonable temporal association

between corticosteroid administration and CHF. For the purposes of this study, a “reasonable temporal association” was defined as corticosteroid administration (oral, parenteral, or both) at any time during the 7 days preceding the initial diagnosis of CHF. Cases also were required to meet additional relatively conservative entry criteria to be included in the study population. Cases were excluded if corticosteroids had been chronically administered (i.e., for several months to years) prior to the initial diagnosis of CHF; if there was a history of pre-existing cardiac disease before corticosteroid administration; if clinical signs potentially ascribable to CHF were present prior to corticosteroid administration; if the history included confounding events or disorders that may have precipitated CHF; or if the case was lost to follow-up.

Evaluations

Data collected from the medical records of the study population cases included presenting complaint; signalment; type, dose, and reason for corticosteroid administration; and length of time from corticosteroid administration to initial diagnosis of CHF. Physical examination findings, systolic blood pressure measured by Doppler, and results of laboratory tests were recorded. Thoracic radiographs, electrocardiograms, and echocardiograms were reviewed by at least two (usually three) board-certified cardiologists (American College of Veterinary Internal Medicine). Additional data obtained from the medical record included treatment during the initial episode of CHF, survival to discharge, long-term medical management of cases that survived to discharge, and follow-up information, including the results of all rechecks. Finally, owners of all surviving cats were contacted by telephone during April 2004 to determine long-term outcomes.

Statistical Analysis

Normally distributed data are reported as mean \pm standard deviation. Data that were not normally distributed are reported as median (range). Variables that were meas-

ured at two time points in individual cats were compared by a paired Student's *t*-test, with $P < .05$ designated as the threshold for statistical significance. All statistical analyses were performed using NCSS 2004 Statistical Software (Number Cruncher Statistical System).

RESULTS

Study Population

From January 1992 to October 2001, 271 cats were diagnosed with CHF at the UMVMC. Among these 271 cases, 41 (15%) received corticosteroids at some time during the 7 days that preceded diagnosis of CHF. Of the 41 cases identified, 29 did not meet the entry criteria and were excluded. Among the excluded cases was one cat that had received daily oral corticosteroids for inflammatory bowel disease for more than 2 years prior to the initial diagnosis of CHF, suggesting that the development of CHF was unrelated to corticosteroid administration. One cat had a history of heart disease before corticosteroid administration. Corticosteroids had been administered to 21 cats because of respiratory abnormalities (coughing, wheezing, and labored breathing), which had been attributed to feline bronchial asthma. The diagnosis of feline bronchial asthma in these cases was based on history, physical examination, and occasionally on thoracic radiography, but thorough cardiac evaluations had not been performed before corticosteroid administration. Consequently, CHF could not be excluded as a cause for the respiratory signs that preceded corticosteroid administration. Corticosteroids were administered to two cats for vague clinical signs (anorexia and lethargy) that could potentially be ascribed to CHF.

The history for three cats included confounding events or disorders. One of these three cats had received corticosteroids shortly after being hit by a car. A murmur detected on physical examination prompted an echocardiogram, which disclosed severe hypertrophic obstructive cardiomyopathy.

Heart failure developed approximately 12 hours after an excessively high dose of atenolol was inadvertently administered. The second of these cats received a large volume of IV fluids and a methylprednisolone acetate injection for a 4-month history of weight loss and vomiting. Endoscopy under general anesthesia was performed 4 days after corticosteroid administration, and CHF developed 2 days thereafter. The third of these cats developed CHF following corticosteroid administration for a head tilt, and was subsequently found to be hyperthyroid. Finally, one cat was lost to follow-up immediately following discharge from the UMVMC. The remaining 12 cases formed the study population of cats with corticosteroid-associated CHF.

Presenting Complaint and History

Presenting complaints in the 12 study population cats were similar, i.e., acute onset lethargy, anorexia, respiratory distress, and tachypnea. Signalment, the type and dose of corticosteroid administered, reason for corticosteroid administration, and time from corticosteroid administration to initial diagnosis of CHF are presented in Table 1. Affected cats were 9.0 ± 3.4 years of age and weight was 5.5 ± 1.1 kg. Ten of the 12 cats were mixed breeds; seven were males and five were females. Parenteral methylprednisolone acetate was the most common form of corticosteroid used ($n = 8$); however, a variety of parenteral and oral corticosteroids and corticosteroid combinations were administered. Time from corticosteroid administration to initial diagnosis of CHF was as short as 1 day following an injection of methylprednisolone acetate to as long as 19 days in a cat that received a course of oral prednisolone followed by an injection of triamcinolone acetonide.

Four cats had previously received corticosteroids at times ranging from 72 days to approximately 1 year before their episode of CHF. Two of these cats had received corticosteroids on multiple occasions. None of the cats had shown prior

adverse effects for which veterinary attention had been sought. However, one owner reported that their cat “behaved as though tranquilized for 2 days” following each corticosteroid injection.

Physical Examination and Blood Pressure

Rectal temperature was $98.7^{\circ} \pm 2.2^{\circ}\text{F}$; respiratory rate was 70 ± 27 breaths per minute and heart rate was 145 ± 31 beats per minute. Heart rate was 150 beats per minute or slower in eight of the 12 cats. Heart rhythm was regular in 11 of the 12 cats and irregular in one. Auscultation revealed murmurs in two cats, diastolic gallop sounds in two, and both abnormalities were detected in one cat. Pulmonary auscultation disclosed increased intensity of breath sounds bilaterally in nine cats, fine crackles bilaterally in one, crackles and wheezes bilaterally in one, and ventrally muffled breath sounds in one.

Systolic blood pressure measured in six cats at the initial presentation was low (≤ 100 mm Hg) in all cases, with a mean of 82 ± 12 mm Hg. At subsequent examinations (2, 7, or 124 days after the initial presentation), systolic blood pressure for three other cats was 90, 134, and 126 mm Hg, respectively.

Table 1. Signalment, History, and Time to Onset of Congestive Heart Failure (CHF) in 12 Cats with Corticosteroid-Associated CHF

Cat No.	Age (yr)	Sex	Breed	Weight (kg)	Corticosteroid(s) Administered	Route	Dose (mg)	Reason for Corticosteroid	Days to CHF
1	8.2	Mc	DMH	4.7	Prednisolone	Oral	5 ^a	Pruritus, suspect allergy	19
					Triamcinolone acetonide	Parenteral	2.5		3
2	10.5	Fs	DSH	6.7	Methylprednisolone acetate	Parenteral	20	Shedding, suspect allergy	6
3	14.7	Mc	DLH	5.6	Prednisolone	Oral	7.5 ^b	Chronic diarrhea, suspect inflammatory bowel disease	13
4	12.4	Mc	DSH	8.2	Triamcinolone acetonide	Parenteral	2	Hindquarter pain and stiffness	5
5	5.6	Mc	DLH	6.1	Methylprednisolone acetate	Parenteral	15	Dermatitis, suspect allergy	4
					Betamethasone dipropionate	Parenteral	1		4
6	5.7	Mc	Ragdoll	4.3	Dexamethasone sodium phosphate	Parenteral	2	Back pain	5
					Dexamethasone sodium phosphate	Parenteral	12		3
					Dexamethasone sodium phosphate	Parenteral	8		2
					Prednisolone	Oral	5 ^b		1
7	8.2	Mc	DSH	5.2	Methylprednisolone acetate	Parenteral	24	Atopy	1
8	10.3	Mc	DSH	5.9	Methylprednisolone acetate	Parenteral	20	Chronic vomiting, suspect inflammatory bowel disease	1
9	11.7	Fs	Russian Blue	4.2	Methylprednisolone acetate	Parenteral	20	Recurrent pododermatitis	4
10	8.8	Fs	DSH	5.3	Methylprednisolone acetate	Parenteral	20	Alopecia, suspect allergy	5
11	2.0	Fs	DMH	4.8	Methylprednisolone acetate	Parenteral	20	Chin acne	5
12	9.7	Fs	DLH	5.3	Methylprednisolone acetate	Parenteral	12	Dermatitis, suspect allergy	7

^aEvery 24 hours for 4 days, then every 48 hours until 5 days before onset of congestive heart failure.

^bEvery 12 hours until onset of congestive heart failure.

DLH = domestic long hair; DMH = domestic medium hair; DSH = domestic short hair; Fs = female spayed; Mc = male castrated.

Additional Diagnostic Tests

Thoracic radiographs revealed mild to moderate pleural effusion in nine cats (identified as modified transudates in three of the cats), moderate to severe diffuse interstitial pulmonary infiltrates in 11, and a severe diffuse alveolar infiltrate in one. The cardiac silhouette was subjectively assessed to be large relative to the thorax in all 12 cats, although it was partially obscured by pleural effusion and pulmonary infiltrates in two. Vertebral-heart size calculated from lateral view radiographs was 8.5 ± 0.4 (reference range = 7.5 ± 0.3) in the 10 cats for which the cardiac silhouette could be adequately delineated.¹¹

Diagnostic electrocardiograms recorded in four cats disclosed sinus bradycardia (120 bpm) with a left anterior fascicular block-like conduction pattern and occasional ventricular premature complexes conducted with right bundle-branch block morphology; sinus bradycardia (80 bpm); atrial standstill with regular ventricular depolarizations (160 bpm) conducted with left bundle-branch block morphology; and atrial fibrillation (ventricular depolarization rate = 120 bpm), with occasional ventricular escape complexes conducted with left bundle-branch block morphology following any periods greater than or equal to 0.74 seconds of ventricular asystole.

Blood samples were collected from each of 10 cats for hematology and serum biochemistry analyses within the first 12 hours of presentation. Blood samples were collected prior to initiating treatment for CHF (other than providing supplemental oxygen) for seven cats, and three cats had blood samples collected at 1, 11, or 12 hours after therapy had been initiated. Hemograms were unremarkable. The mean white cell count ($16.3 \pm 7.1 \times 10^3/\mu\text{l}$; reference range = $3.4\text{--}15.7 \times 10^3/\mu\text{l}$) and segmented neutrophil count ($14.2 \pm 6.7 \times 10^3/\mu\text{l}$; reference range = $1.2\text{--}13.2 \times 10^3/\mu\text{l}$) were increased, and a stress leukogram was present in six of the 10 cats. Serum biochemistry analysis revealed increased mean concentrations of alanine aminotransferase, aspartate aminotransferase, blood urea nitrogen, cholesterol,

creatinine, glucose, and magnesium, and decreased mean concentrations of calcium and chloride. Additional details regarding serum biochemistry results are presented in Table 2.

Total thyroxine concentrations were measured in serum collected during the first 12 hours of presentation in seven cats and in serum collected at 1, 10, or 124 days after the initial presentation in three cats. Mean total serum thyroxine concentration was $1.1 \pm 0.6 \mu\text{g/dl}$ (reference range = $0.8\text{--}4.0 \mu\text{g/dl}$). None of the cats had an elevated total serum thyroxine concentration, and levels were below the reference range in five cats.

After a period of in-hospital stabilization, cardiac disease was confirmed by echocardiography in 11 cats. Median time from initial visit to echocardiography was 1 day (range = 0–5 days). On M-mode echocardiography, mean interventricular septum thickness in diastole, mean left ventricular posterior wall thickness in diastole, and mean left atrial dimension at end-systole were all above reference range (Table 3). Additional echocardiographic abnormalities were mild or moderate mitral regurgitation in six cats, mild tricuspid regurgitation in one, and systolic anterior motion of the mitral valve in three.

One of the cats in the study population (cat 9) died before an echocardiogram could be performed. A necropsy was not permitted by the owner, and no heart murmur, diastolic gallop sound, or arrhythmia was detected on physical examination. Despite the absence of echocardiographic confirmation of the presence of cardiac disease, data from this cat were included based on thoracic radiographs that disclosed a moderate pleural effusion, diffuse pulmonary interstitial infiltrates, and an enlarged cardiac silhouette relative to the thorax with a vertebral-heart size of 8.8.

Survival to Discharge, Treatment, and Outcome

Immediate therapy for CHF in all cases included supplemental oxygen, cage rest,

Table 2. Serum Biochemistry Values from 10 Cats with Corticosteroid-Associated Congestive Heart Failure

Biochemistry Variable	No. of Cats	Mean \pm SD	Reference Range	% Cases Increased	% Cases Decreased
Albumin (g/dL)	10	2.8 \pm 0.3	2.2–3.4	0	0
Alkaline phosphatase (IU/L)	10	37 \pm 19	1–80	0	0
Alanine aminotransferase (IU/L)	10	123 \pm 79	19–91	40	0
Amylase (IU/L)	9	934 \pm 244	362–1410	11	0
Aspartate aminotransferase (IU/L)	6	100 \pm 38	9–53	100	0
Bilirubin (mg/dL)	9	0.5 \pm 0.4	0.0–0.5	33	0
Blood urea nitrogen (mg/dL)	10	34 \pm 17	14–33	50	0
Cholesterol (mg/dL)	10	171 \pm 61	15–150	60	0
Total carbon dioxide (mEq/L)	6	20 \pm 3	12–21	50	0
Calcium (mg/dL)	10	8.8 \pm 0.7	8.9–11.3	0	60
Chloride (mEq/dl)	9	114 \pm 6	117–128	0	67
Creatinine (mg/dL)	10	1.5 \pm 0.4	0.6–1.4	60	0
Glucose (mg/dL)	10	256 \pm 114	50–150	80	0
Magnesium (mg/dL)	6	3.2 \pm 0.6	1.8–2.6	100	0
Phosphorus (mg/dL)	10	5.6 \pm 1.8	3.8–8.2	20	20
Potassium (mEq/L)	9	4.2 \pm 0.5	3.9–6.3	0	22
Sodium (mEq/L)	9	150 \pm 6	149–158	22	44
Protein (g/dL)	10	6.9 \pm 0.7	5.5–7.6	20	0

Table 3. M-mode Echocardiography Measurements from 11 Cats with Corticosteroid-Associated Congestive Heart Failure

Variable	Mean \pm SD	Reference Range	% Cases Increased	% Cases Decreased
Interventricular septum in diastole (mm)	6.5 \pm 1.2	<6.0	64	0
Left ventricular diameter in diastole (mm)	13.5 \pm 2.1	13.0–17.0	0	46
Left ventricular posterior wall in diastole (mm)	6.9 \pm 1.1	<6.0	82	0
Interventricular septum in systole (mm)	8.5 \pm 1.1	NA	NA	NA
Left ventricular diameter in systole (mm)	5.5 \pm 1.7	5.0–9.0	0	36
Left ventricular posterior wall in systole (mm)	9.8 \pm 1.3	NA	NA	NA
Left atrial dimension at end-systole (mm)	17.7 (15.4–22.6) ^a	10.0–14.0	100	0
Aortic root diameter (mm)	8.3 \pm 1.9	8.0–11.0	0	55

^aMedian (range) reported for data that are not normally distributed.

NA = not applicable.

and parenteral furosemide. Topical nitroglycerine was applied in one case. Five of the cats (cats 8–12) died or were euthanized because of CHF. One cat died in hospital within 1 day, and 3 were euthanized because of poor response to therapy 1 to 3 days after admission. One cat was discharged from the UMVMC after 6 days, and survived on car-

diac medications (furosemide, enalapril, and diltiazem) for 186 days before being euthanized because of uncontrolled CHF.

Necropsies were not permitted in any of these five cases.

Seven cats (cats 1–7) were long-term survivors that recovered from CHF and had no recurrences. These cats were discharged

Table 4. Treatments at Discharge and Outcomes in Seven Cats with Corticosteroid-Associated Congestive Heart Failure That Were Long-Term Survivors

Cat No.	Cardiac Medications at Discharge	Days to Examination That Prompted Drug Tapering	Tapering Period (Days)	Total Survival Time (Days)
1	Furosemide, diltiazem, aspirin	1216	16	>2078 ^a
2	Furosemide	338	18	>1608 ^a
3	Furosemide, diltiazem	203	19	457 ^b
4	Furosemide, atenolol	1550	13	2406 ^c
5	Furosemide, enalapril, aspirin	218	161	>1708 ^a
6	Furosemide, aspirin	10	26	>1432 ^a
7	Furosemide, enalapril	124	18	366 ^d

^aAlive at last contact in April 2004.

^bEuthanized due to gastrointestinal lymphoma.

^cEuthanized due to chronic renal failure.

^dEuthanized due to severe interstitial pancreatitis.

from the UMVMC with prescribed oral medications after a median of 3 days (range = 1–8). Details of their medications at discharge and outcomes are provided in Table 4. These seven cats were regularly rechecked by clinical examination, thoracic radiography, and echocardiography at the discretion of the consulting cardiologist and owner. Echocardiography performed a median of 218 days (range = 10–1,550) after discharge disclosed partial or complete resolution of the M-mode abnormalities that had been present during the initial episode of CHF. Physical examinations performed at the recheck examinations disclosed soft parasternal systolic murmurs in four of the seven cats. One cat showed mild and equivocal systolic anterior motion of the mitral valve on echocardiography. The cause(s) of the soft murmurs eluded detection in the remaining three cases. In one of the long-term survivors, an electrocardiogram performed during the initial episode of CHF had shown a left anterior fascicular block-like conduction pattern. A follow-up electrocardiogram was performed in that case after the echocardiogram had normalized, and it was unremarkable. Based on resolution of clinical and radiographic signs of CHF, partial to complete resolution of echocardiographic abnormalities, and normalization of the electrocardiogram in one case, all cardiac medications in these seven cats were cautiously discontinued by tapering the medications over a median of 18 days

(range = 13–161). Median duration of treatment with cardiac medications following discharge in these seven cases was 356 days (range = 36–1,563 days).

In four of the seven cats, the echocardiograms that prompted discontinuation of cardiac medications were the final echocardiograms performed. In the other three cats, the final echocardiograms were performed at 383, 529, or 571 days after their cardiac medications had been discontinued. The final echocardiograms showed significant decreases in interventricular septum thickness in diastole (from 6.6 ± 1.0 to 5.0 ± 0.9 mm; $P = .01$; reference range <6.0 mm), left ventricular posterior wall thickness in diastole (from 7.1 ± 0.5 to 4.7 ± 0.6 mm; $P = .01$; reference range <6.0 mm), and left atrial dimension at end-systole (from 17.7 ± 1.3 to 14.1 ± 0.7 mm; $P < .01$; reference range = 10–14 mm). There was also a significant increase in left ventricular diameter in diastole (from 13.9 ± 1.7 to 15.9 ± 1.0 mm; $P = .01$; reference range = 13–17 mm). The M-mode measurements that changed significantly between first and final echocardiograms in these seven cats are shown graphically in Figure 1.

At the time of last contact (April 2004), four of the seven cats were alive, and none of these cats had received any cardiac medications for at least 846 days. Additionally, CHF had not recurred, and the total survival time from date of discharge was 1,432 days or more.

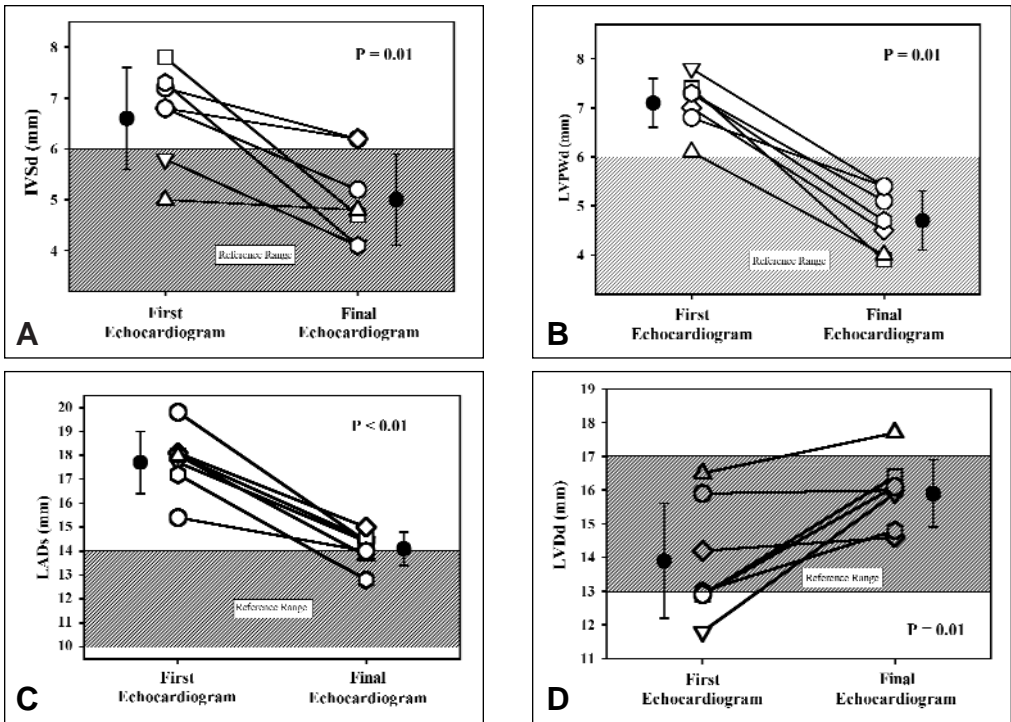


Figure 1. M-mode variables that changed significantly ($P \geq .01$) from first to final echocardiogram in seven cats that were long-term survivors. Interventricular septal thickness in diastole (IVSd) (**A**), left ventricular posterior wall thickness in diastole (LVPWd) (**B**), and left atrial dimension at end-systole (LADs) (**C**) all decreased; left ventricular diameter in diastole (LVdD) (**D**) increased. Shaded areas represent reference range for each variable.

Three of the seven cats were euthanized for reasons unrelated to cardiac disease (gastrointestinal lymphoma, chronic renal failure, and severe interstitial pancreatitis). At the time of euthanasia, these three cats had received no cardiac medications for 235, 843, or 224 days, there had been no recurrence of their CHF, and their individual total survival times were 457, 2,406, and 366 days.

A necropsy was performed in one of the long-term survivors (cat 7). The cat had received no cardiac medications during the preceding 224 days and had shown no recurrence of CHF when it was presented for vomiting. An abdominal mass was detected on palpation, and a soft parasternal systolic murmur was noted. The cat was euthanized after inflammation of the pancreas, with saponification of omental fat and extensive intestinal adhesions, were found during an exploratory laparotomy. A necropsy con-

firmed severe chronic active suppurative interstitial pancreatitis. With respect to the cardiovascular system, the heart:body weight ratio was normal (3.7 g/kg; reference range = 3–5 g/kg).¹² However, on histopathology, the left ventricle and interventricular septum contained hypereosinophilic myocytes with plump vesicular nuclei and perinuclear lipofuscin. There were also many areas of myofibrillar disarray and a mild increase in interstitial fibrosis. These histopathologic abnormalities led to a necropsy diagnosis of hypertrophic cardiomyopathy. Histopathology of the lungs showed multifocal acute pyogranulomatous bronchopneumonia. There was no evidence of CHF.

DISCUSSION

The cats described in this report presented with similar chief complaints, and many similar clinical, radiographic, and echocar-

diographic abnormalities associated with CHF due to various forms of feline idiopathic cardiomyopathy. When compared with results from a recent retrospective study of 106 cases of feline idiopathic cardiomyopathy, signalment was similar with respect to breed and gender.¹³ However, the cats in the study population described here were slightly older than those with feline idiopathic cardiomyopathy (9.0 ± 3.4 versus 6.8 ± 4.3 years). Serum biochemistry abnormalities in cats with CHF due to hypertrophic cardiomyopathy frequently include hypochloremia, hyponatremia, hypokalemia, a high total carbon dioxide, and elevated liver enzymes, and these abnormalities were detected in many of the cases of the present report.⁹ Indeed, based on the chief complaints, physical examinations, thoracic radiographs, electrocardiograms, echocardiograms, and serum biochemistry results, together with exclusion of hyperthyroidism and hypertension in most cases, the initial diagnoses in the 12 cases that comprised the study population were hypertrophic cardiomyopathy ($n = 6$), hypertrophic obstructive cardiomyopathy ($n = 3$), and feline unclassified cardiomyopathy ($n = 3$).

However, several features of the disease in these cases led to the eventual conclusion that this was a unique form of CHF associated with corticosteroid administration. The temporal association between corticosteroid administration and initial diagnosis of CHF was compelling. Selection of the study population was intentionally conservative. Consequently, some cases of corticosteroid-associated CHF may have been excluded. However, while readily acknowledging the limitations inherent in any retrospective study, there is a reasonable level of confidence that none of the population of cats suffered from CHF prior to corticosteroid administration.

Another feature that contributed to the conclusion was the strikingly slow mean heart rate (145 ± 31 beats per minute) among the study population. One cat was in atrial fibrillation, yet even in that case, heart rate was only 150 beats per minute on phys-

ical examination, and ventricular depolarization rate was 120 beats per minute on electrocardiogram. A previous study of cats with hypertrophic cardiomyopathy reported a mean heart rate of 173 ± 33 beats per minutes in 24 cases with CHF, and slow heart rates are unusual in cats with CHF due to other forms of cardiac disease.¹⁴ Low rectal temperature was common among the cases presented here, and hypothermia can lead to bradycardia. Although low rectal temperatures are frequently found among cats with CHF due to other cardiac diseases, heart rates are seldom as low as in the cases that comprised this present study population.

Furthermore, it is unlikely that a mean rectal temperature of $98.7 \pm 2.2^\circ\text{F}$ alone would be low enough to result in a mean heart rate of 145 ± 31 beats per minutes in cats in CHF. In a study that included 120 cats with CHF due to hypertrophic cardiomyopathy, mean rectal temperature was just 1°F higher than in cases presented here, but the mean heart rate was greater than 30 beats per minute higher.⁹ In the same study, average rectal temperature in cats with arterial thromboembolism ($n = 43$) was virtually identical to average rectal temperature in the present study population, and heart rate was 200 ± 36 beats per minute. Thus, slow heart rate in the present study population is not ascribable to hypothermia alone, but rather appears to be a feature of corticosteroid-associated CHF.

Several aspects of the progression of the disease in the seven long-term survivors in the present study population are unique. The first M-mode echocardiograms performed in all seven cats showed increased left atrial dimension at end-systole and increased thickness of the left ventricular posterior wall in diastole as well as increased thickness of the interventricular septum in diastole in five of the seven cases. Over time, these morphologic abnormalities normalized or approached normal, even when echocardiograms were performed for three of the seven cats several months after all cardiac medications had been discontinued. One cat

showed normalization of its electrocardiogram after initially having a left anterior fascicular block-like conduction pattern.

Cardiac medications were eventually discontinued in all seven cases without recurrence of CHF, and survival times were considerably longer than would be anticipated with CHF from other forms of cardiac disease, including feline idiopathic cardiomyopathy. The authors are not aware of any previously described form of cardiac disease in cats that follows this clinical course.

Naturally-occurring hyperadrenocorticism in humans is associated with echocardiographic abnormalities. Left ventricular diameter in diastole is significantly reduced, left ventricular mass index and wall thickness are significantly increased, and diastolic function measured by transmitral Doppler is impaired.¹⁵ Morphologic changes occur independently of the hypertension that frequently accompanies hyperadrenocorticism in humans.¹⁶ In the majority of affected human patients, there is complete regression of the left ventricular hypertrophy following successful therapy.^{17,18} The type of structural changes and the reversible nature of the left ventricular changes observed in the present feline population are similar to those observed in humans with hyperadrenocorticism. However, the ventricular remodeling described in humans is associated with chronically elevated corticosteroid concentrations (months to years), and the frequency of these changes is related to the duration of disease. Whether similar left ventricular changes occur much more rapidly in cats following exogenous corticosteroid administration remains to be established.

It is unclear whether the cats in this population had underlying heart disease that predisposed them to corticosteroid-associated CHF. Cats with known pre-existing heart disease were excluded from the study, but this does not preclude the possibility that occult or undetected heart disease existed prior to corticosteroid administration. The question about pre-existing heart disease is an extremely difficult one to answer defini-

tively in a retrospective study such as this, but it is an important issue and some speculation is necessary. In the opinion of the authors, several aspects of the data tend to support the existence of underlying heart disease in this study population. One piece of evidence is that it seems unlikely that corticosteroid administration alone could have resulted in heart disease of sufficient severity to result in atrial fibrillation and atrial standstill as was found in two cases. Also, although left atrial dimension at end-systole in 11 of the cases was moderately increased (15.4–19.8 mm), it was extremely large (22.6 mm) in one cat that did not recover from CHF. In all probability, the large left atrial dimension in that cat represented pre-existing heart disease. Further, soft systolic heart murmurs persisted in four of the seven cats that recovered from CHF and no longer required cardiac medications. Cardiac morphology among these seven cats normalized on echocardiography, but slight dimension abnormalities persisted in several cases. The final echocardiograms in five of the seven cats showed left atrial dimension at end-systole to be either at the upper end of the reference range or slightly above it (Figure 1C). In two of the seven cats, thickness of the interventricular septum in diastole was slightly above the reference range (Figure 1A). Systolic anterior motion of the mitral valve persisted in one of the cases, although it was mild and equivocal. Finally, histopathology in one case showed myocardial changes consistent with hypertrophic cardiomyopathy. Although the above findings suggest that underlying heart disease existed in the cats with corticosteroid-associated CHF, the possibility that they reflect adverse effects entirely attributable to corticosteroid administration cannot be excluded. Further studies are necessary to address this important issue.

Irrespective of the uncertainty regarding underlying heart disease, the data indicate that all cardiac medications can eventually be discontinued in many cats with corticosteroid-associated CHF, and that prolonged survival without recurrence of CHF can be

anticipated. This is crucial prognostically and has clear quality-of-life implications for both the cat and the owner. The study population evaluated here is too small to allow meaningful statistical analyses to distinguish between cats that will and those that will not recover from CHF. Rather, this distinction should be made based on response to time and therapy and findings on follow-up examinations that include echocardiography.

A study by the authors to investigate the pathophysiology of corticosteroid-associated CHF in cats is nearing completion; however, at the present time, it is not known. Several mechanisms could be involved, including left ventricular concentric hypertrophy with diastolic dysfunction, similar to what occurs in humans with hyperadrenocorticism; volume overload secondary to a mineralocorticoid effect of some corticosteroids; increased left ventricular preload and afterload secondary to the effects of corticosteroids to increase vascular reactivity; and plasma volume expansion, similar to what occurs in humans with hyperglycemia from diabetes mellitus, as a result of the diabetogenic effect of corticosteroids.^{3,15,19-26} In addition to the pathophysiology of corticosteroid-associated CHF, important questions remain, including the frequency of corticosteroid-associated CHF following corticosteroid administration and how best to predict and avoid this adverse effect. Until these questions are answered, it is recommended that any cat requiring corticosteroid therapy should be thoroughly evaluated for presence of pre-existing heart disease and that CHF should be listed as a potential adverse effect of corticosteroid administration in this species.

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