

Echocardiographic Findings in 11 Cats with Acromegaly

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Background: Information regarding cardiac changes in domestic cats with acromegaly is limited.

Hypothesis/Objectives: The objective of this study was to describe the echocardiographic findings in cats with acromegaly.

Animals: Eighteen cats diagnosed with acromegaly at Colorado State University between 2008 and 2012. Of these 18 cats, 11 had echocardiography performed.

Methods: A retrospective review of medical records was made to identify cats with acromegaly that also had echocardiography performed.

Results: Of the 11 cats identified, 7 had left ventricular concentric hypertrophy, 6 had left atrial enlargement, and 7 had evidence of abnormal diastolic function. All 11 cats had evidence of structural or functional cardiac disease.

Conclusions and Clinical Importance: Cardiovascular abnormalities frequently are present in cats with acromegaly, and a complete cardiac evaluation should be considered in these patients.

Key words: Acromegaly; Cardiomyopathy; Endocrinopathy; Feline.

Acromegaly (hypersomatotropism) is an uncommonly diagnosed endocrine disease in domestic cats, but there is evidence it may be underrecognized.¹ The syndrome is most commonly caused by oversecretion of growth hormone (GH) by a functional adenoma or hyperplasia of the pars distalis of the cranial pituitary gland, leading to secondary increased concentrations of circulating insulin-like growth factor-1 (IGF-1).^{1,2} Excessive GH secretion has catabolic and diabetogenic effects; IGF-1 has anabolic effects; and, if a macroadenoma is present, space-occupying effects of the mass also may occur. Commonly reported abnormalities in cats with acromegaly include insulin-resistant diabetes mellitus; growth of bone, cartilage, and soft tissues; organomegaly; inferior prognathia; and neurologic signs.^{2–4} Acromegaly has been reported most commonly in middle-aged to older, castrated male cats.

In human patients with acromegaly, cardiovascular abnormalities have been documented consistently, and are a major cause of morbidity and mortality. Studies report that up to 90% of acromegalic people have concurrent cardiomyopathy and up to 25% develop congestive heart failure. In addition to cardiomyopathy, approximately 33% of human patients with acromegaly have concurrent systemic hypertension.⁵

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Abbreviations:

2D	2-dimensional
Ao	aorta
E/A	ratio of peak early to peak late left ventricular inflow velocities
FS	fractional shortening
GH	growth hormone
IGF-1	insulin-like growth factor-1
IVRT	isovolumic relaxation time
IVS	interventricular septum
IVSd	interventricular septum thickness at end-diastole
IVSs	interventricular septum thickness, systole
LA/Ao	left atrium-to-aortic ratio
LA	left atrium
LV	left ventricle
LVFWd	left ventricular free wall thickness at end-diastole
LVFWs	left ventricular free wall thickness, systole
LVIDd	left ventricular internal dimension at end-diastole
LVIDs	left ventricular internal dimension, systole
LVOT	left ventricular outflow tract

There is little information, however, regarding the cardiovascular changes present in cats with acromegaly. An early case series that described the clinical findings in cats with acromegaly briefly mentioned cardiac abnormalities in 8 cats, but this study reported primarily left ventricular wall thicknesses with no description of other echocardiographic features.⁴ A more recent study, investigating the prevalence of acromegaly in cats with diabetes mellitus briefly described the echocardiographic features of 5 affected cats as variable, and reported atrial enlargement, left ventricular hypertrophy, diastolic dysfunction, systolic anterior motion of the mitral valve, and mild increases in left ventricular outflow tract velocity, but the frequency of these findings was not reported.¹

The present study was undertaken to more thoroughly evaluate the structural and functional cardiovascular abnormalities in cats with acromegaly and to determine the prevalence of these abnormalities in cats with acromegaly.

Materials and Methods

Animals

The medical records of the Colorado State University Veterinary Teaching Hospital of cats presented between January 2008 and December 2012 were retrospectively reviewed to identify cats with acromegaly that received an echocardiographic evaluation at or around the time of evaluation for potential treatment of acromegaly. A confirmed diagnosis of acromegaly was defined by the following: (1) insulin-resistant diabetes mellitus requiring management with >6 units of insulin q12h;⁶ (2) absence of other causes of insulin resistance (eg, hyperthyroidism, nonpituitary neoplasia, infection, concurrent medications); (3) physical changes consistent with acromegaly; and (4) increased resting serum IGF-1 concentration (>184 nmol/L; reference range, 12–92 nmol/L). The serum IGF-1 assay was performed at the Diagnostic Centers for Animal and Population Health at Michigan State University, using a commercially available radioimmunoassay. Two times the upper limit of the reference range for IGF-1 was used as a cut-off value to decrease the possibility of a false-positive test result.⁷ A visible pituitary mass on computed tomography or magnetic resonance imaging was not required for inclusion in the study as long as the other criteria were fulfilled. Serum GH analysis was not required because of limited availability of the assay.

Echocardiographic Measurements

Cardiac structure and function were characterized using conventional transthoracic 2-dimensional and M-mode echocardiography with both color and spectral Doppler. The Doppler echocardiographic evaluations were performed by an experienced operator or cardiology resident in awake, nonsedated cats. Examinations were performed with a GE Vivid 7 ultrasound machine with a 7 MHz multifrequency phased-array transducer[®] as previously described.^{8,9} Data from the original echocardiographic reports were collected. All structural measurements were made from 2D-guided M-mode images according to the recommendations of the American Society of Echocardiography using the average of 3 measurements for each value.¹⁰

Left ventricular (LV) free wall thickness at end-diastole (LVFWd) and during systole (LVFWs), interventricular septal thickness at end-diastole (IVSd) and during systole (IVSs), LV internal dimension at end-diastole (LVIDd) and during systole (LVIDs) were measured, and fractional shortening (FS) then was calculated. Pathologic hypertrophy was defined as a diastolic LVFWd or IVSd thickness ≥ 6 mm or both.^{11–14} Papillary muscles were subjectively assessed as hypertrophied or normal by the operator. When appropriate echocardiographic images were available, papillary muscle size was assessed objectively by direct tracing of the muscles to obtain papillary muscle area.¹⁵ Papillary muscle hypertrophy was identified as a combined papillary muscle area >0.8 cm².

The left atrium-to-aortic ratio (LA/Ao) was calculated from M-mode measurements made on the long axis inflow/outflow right parasternal view. Left atrial enlargement was defined as an LA/Ao of ≥ 1.7 or a left atrial measurement ≥ 17 mm.¹⁴

Pulsed-wave Doppler parameters included peak early and late diastolic transmitral flow velocities, isovolumic relaxation time (IVRT), and peak pulmonary venous flow velocities (systolic, early diastolic, atrial systolic). Maximal systolic aortic and pulmonary arterial blood flow velocities were measured with pulsed-wave or continuous-wave Doppler. Left ventricular outflow tract (LVOT) obstruction was defined as maximal systolic aortic flow velocity >1.6 m/s. The presence of systolic anterior motion (SAM) of the

mitral valve, defined as motion of the septal mitral valve leaflet toward the LVOT, was assessed by both 2D and M-mode imaging.

Systemic Arterial Blood Pressure Measurement

Systolic arterial blood pressure was measured indirectly on the tail, hindlimb, or forelimb in awake cats by the individual performing the echocardiogram by the Doppler sphygmomanometry method as previously described.¹⁶ At least 3 measurements were obtained and averaged. Systemic hypertension was defined as a systolic blood pressure measurement ≥ 170 mmHg.¹⁶

Statistical Analysis

Data are presented as percentages, except for age, IGF-1, and insulin dose, which are expressed as medians and ranges.

Results

Animals

Eleven cats that met the inclusion criteria were identified. Of these, 7 (63.6%) were domestic short hair, 3 (27.3%) were domestic long hair, and 1 (9.1%) was a Siamese. Nine cats (81.8%) were castrated males and 2 (18.2%) were spayed females. The median age was 11 years (range, 7–14 years). The most common physical findings consistent with acromegaly were broad facial features (10 cats), weight gain despite unregulated diabetes mellitus (6 cats), and enlarged paws (5 cats). Serum IGF-1 concentration ranged from 192 to 641 nmol/L (median 469 nmol/L). The median insulin dose was 12 units (range, 8–26 units). Insulin types included glargine (6 cats), detemir (4 cats), and protamine zinc insulin (1 cat). One cat was receiving diltiazem and amlodipine for previously diagnosed arrhythmia and systemic hypertension, respectively.

Physical Examination

On physical examination, a murmur was detected in 4 (36.4%) cats, a gallop heart sound was noted in 3 (27.3%) cats, and an arrhythmia was noted in 1 cat (9.1%). One cat was noted to have both a murmur and a gallop heart sound. One cat without a history of known cardiac disease was presented for evaluation of tachypnea and dyspnea, and based on radiographic findings was diagnosed with left-sided congestive heart failure. Four cats had no abnormal findings noted on auscultation (36.4%).

Systemic Blood Pressure

Of the 11 acromegalic cats, 10 had an indirect, Doppler blood pressure measurement performed. Only 1 cat (10%) was identified as being overtly hypertensive (systolic blood pressure ≥ 170 mmHg). However, 1 cat was receiving amlodipine that had been prescribed before evaluation for the current study for previously noted systemic hypertension. If this cat is included, 2 cats (20%) had systemic hypertension. The mean systolic blood pressure was 149 mmHg (range, 132–182 mmHg).

Echocardiography

Left ventricular concentric hypertrophy was identified in 7 cats (63.6%). Of these, hypertrophy of both the IVS and LVFW (symmetric hypertrophy) was noted in 4 cats (57.1%), hypertrophy of the IVS alone was noted in 1 cat (14.3%), hypertrophy of the LVFW alone was noted in 1 cat (14.3%), and the papillary muscles alone were subjectively hypertrophied in 1 cat (14.3%). In the cat with subjective papillary muscle hypertrophy, the images necessary to perform papillary muscle area measurements were not available. Papillary muscle area could not be calculated in 4 patients. Of these, 1 cat that also had symmetric LV hypertrophy was noted to have papillary muscle hypertrophy. All cats had normal LVIDd despite presence of concentric hypertrophy. The left atrium was enlarged in 7 cats (63.6%) and in 1 cat (9.1%) echocardiographic contrast was noted spontaneously in the left atrium.

Peak aortic blood flow velocity was normal in all but 3 cats (27.3%), and in these 3 cats the aortic flow velocity was only mildly increased (<2.0 m/s). Systolic anterior motion of the mitral valve was not noted in any cat.

Diastolic function was assessed in all cats. Abnormal diastolic function was identified in 8 cats (72.3%). Of these, 5 cats had impaired relaxation and 3 had a restrictive left ventricular filling pattern. Impaired systolic function was noted in 1 cat.

In all cats assessed by echocardiography, evidence of structural cardiac disease, functional cardiac disease, or both was noted.

One cat had a follow-up echocardiogram performed 6 months after stereotactic radiotherapy for a pituitary adenoma. At the time of initial evaluation of this cat, a subjectively hypertrophied left ventricular papillary muscle was noted and diastolic dysfunction was evident. At the time of the follow-up echocardiogram, diastolic dysfunction characterized by impaired relaxation was noted and papillary muscle hypertrophy persisted.

Discussion

Acromegaly in cats is caused by a functional somatotrophic adenoma or hyperplasia of the pituitary gland that causes chronic excessive growth hormone secretion and consequently increased plasma IGF-1 concentrations.^{1,2} The direct anabolic effects of IGF-1 oversecretion cause growth and enlargement of several organs, including the heart. The effect of somatomedins such as IGF-1 on the myocardium can include interstitial fibrosis, hypertrophy of individual cardiomyocytes, and increased collagen content.² In addition, systemic hypertension is a common consequence of acromegaly in human patients, and hypertension likely contributes to the development of left ventricular hypertrophy and diastolic dysfunction.

The constellation of cardiac changes identified in human patients with acromegaly has been termed acromegalic cardiomyopathy and is divided into 3 stages: hyperkinetic syndrome (early cardiac hypertrophy and increased cardiac output), middle phase (more

severe hypertrophy, impaired diastolic function and possible systolic dysfunction), and end-stage disease (severe diastolic dysfunction and congestive heart failure with possible severe systolic dysfunction).⁵ The cardiac changes in feline acromegaly have been less thoroughly described.

Growth hormone and IGF-1 exert their effects on the heart directly by autocrine, endocrine, and paracrine mechanisms, and indirectly as a consequence of systemic hypertension.⁵ Insulin-like growth factor-1 increases the intracellular calcium content of myocytes and enhances the calcium sensitivity of myofilaments. Stimulation of cardiomyocytes by GH and IGF-1 is associated with an isoform change from high ATPase myosin to low ATPase myosin, and GH and IGF-1 have a direct effect on myocardial contractility.¹⁷⁻¹⁹ These effects lead to the LV hypertrophy that is noted in many acromegalic patients. Interstitial fibrosis is the main abnormality found on histology in human patients along with myofibrillar derangement, myocyte necrosis, and lymphomononuclear cellular infiltration.²⁰

The results presented here demonstrate that cardiac abnormalities also are common in acromegalic cats. The most common changes noted included concentric left ventricular hypertrophy, diastolic functional abnormalities, and left atrial enlargement. Systemic hypertension also was noted in the cats in this study at a frequency similar to that noted in human acromegalic patients.⁵ Routinely performing echocardiography in cats with acromegaly should be considered, particularly if anesthesia for radiotherapy or hypophysectomy is being considered.

This study has several limitations. Not every cat presented for acromegaly during the study period had a cardiac evaluation performed, and those cats with physical examination evidence of possible cardiovascular disease (eg, heart murmur, gallop heart sound) probably were more likely to receive additional testing. Consequently, the prevalence of cardiac changes in the study population may have been higher than that of the general acromegalic cat population.

Another limitation is study size. Only 11 cats met the inclusion criteria of the study and these cats may not have been an accurate representation of the general population. Unfortunately, the fact that acromegaly is uncommonly diagnosed makes the evaluation of a large number of patients difficult. Some of the cats included in this study may have had primary cardiomyopathies rather than cardiomyopathy related to acromegaly. Although it is impossible to state definitively that all of the cardiac changes noted in this study were directly caused by acromegaly, the high prevalence of cardiac changes in the study population suggests a possible causative mechanism, particularly because these cardiovascular abnormalities are known manifestations of acromegaly in people.

Additional studies of acromegalic cardiomyopathy in cats would be beneficial for determining the most appropriate therapeutic recommendations for these patients. In human patients with acromegaly, cardiac changes may improve with successful hormonal control,

but this improvement may take many months to be noted.^{21–26} At this time, it is unknown to what extent the cardiac changes noted in cats with acromegaly may improve with time.

Footnote

^a GE Medical Systems, Milwaukee, WI

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Conflict of Interest: Authors disclose no conflict of interest.

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