

Advances in Feline Cardiology

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Cardiovascular diseases are common in cats.¹⁻³ Myocardial disorders are the major cause of heart failure and thromboembolism, with idiopathic hypertrophic cardiomyopathy the most important of the primary myocardial diseases.⁴⁻⁷ Extensive myocardial fibrosis leading to a restrictive cardiomyopathy or a right ventricular cardiomyopathy is now recognized on a regular basis in mature cats. Conversely, dilated cardiomyopathy is rare today because feline diets are supplemented with taurine. Nonsuppurative myocarditis is identified sporadically in cats; however, the diagnosis is difficult and often based on suspicion (or necropsy). The cardiac manifestations of hyperthyroidism, hypertension, and anemia are well known in this species, but these conditions must be distinguished from primary cardiomyopathies, as management and prognoses differ. Primary acquired valvular disease is very rare in cats. Herein is a summary of clinical aspects of the most important of the feline myocardial diseases.

HYPERTROPHIC CARDIOMYOPATHY

Feline hypertrophic cardiomyopathy (HCM) is characterized by hypertrophy of the left ventricle (LV) that cannot be explained by congenital heart disease, hypertension, or endocrinopathy.^{4,5} Hypertrophy in cats is typically concentric, including the entire LV. Regional hypertrophy, however, is also common, often involving the upper septum, the ventricular free wall, and the papillary muscles. In most cases of symptomatic HCM, the left atrium is dilated. Mitral regurgitation may be evident because of papillary muscle hypertrophy or accelerated blood flow in the LV outlet that leads to mitral valve–septal contact (systolic anterior motion). Atrial and systemic thrombi are often encountered in cats with this disease. Small vessel coronary artery disease, as well as areas of myocardial fibrosis and infarction, also has been

reported in some cats. The natural history of feline HCM is quite variable and can be benign or lethal. Clinical signs are explained by left-sided congestive heart failure (CHF), complications of thromboembolism, outflow tract obstruction, or arrhythmias.

Clinical Pathophysiology

The cause of CHF in cats with HCM is thought to involve mainly ventricular diastolic dysfunction.^{4,5,8,9} Abnormalities of ventricular filling are characterized by either abnormal myocardial relaxation (an active, oxygen-dependent process) or reduced LV compliance (distensibility). These problems are related to abnormal cardiac muscle, myocardial ischemia, or oxygen imbalance (reduced delivery relative to demand), increased chamber stiffness (thick wall to lumen ratio), and myocardial fibrosis. Higher than normal pulmonary venous and left atrial pressures are required to fill a stiff ventricle, predisposing to pulmonary edema. A vigorous atrial contraction may be needed to maintain ventricular preload; accordingly, the development of atrial fibrillation can be disastrous, causing severe CHF. The roles of myocardial ischemia and stress (sympathetic activity) in the pathogenesis of diastolic dysfunction require further study. It is well known, however, that stress predisposes affected cats to CHF. Certainly, protracted tachycardia increases myocardial oxygen demand, decreases coronary perfusion time, and elevates left atrial pressure. These factors may explain the sudden development of left-sided CHF (flash pulmonary edema), so often observed in this disorder.

Cats with HCM also may suffer from abnormal ventricular systolic function.^{4,10} Dynamic and labile pressure gradients between the LV and the aorta are often found as blood is ejected rapidly across a bulging ventricular septum. Increased systolic pressure in the LV may stimulate further hypertrophy and predispose to ventricular subendocardial ischemia. These systolic gradients are due to the combination of septal hypertrophy and mitral-septal contact. The latter stems from systolic anterior motion (SAM) of the mitral valve that begins once ejection has been initiated. The presence of significant SAM is invariably associated with mitral regurgitation (MR). Mitral incompetency also can be traced to geometric changes in the LV, papillary muscle dysfunction, or, possibly, atrial dilatation.

Clinical Features

Male cats are predisposed to HCM. Young cats (5 months–6 years of age) are often affected, although

cats of any age may have the disease. The possibility of HCM may be prompted by auscultation of a cardiac murmur or gallop sound in a cat that has no other signs of heart disease.^{2,4,11} When symptomatic, most cats are presented for tachypnea and dyspnea attributable to CHF with pulmonary edema or pleural effusion. CHF may be precipitated by stress, fever, moderate to severe anemia, thyrotoxicosis, anesthesia, or fluid therapy. Urgent presentation may follow arterial thromboembolism to the terminal aorta. Signs related to embolism of the right forelimb or the cerebrum are more subtle or vague. A coronary embolus can lead to infarction or sudden death. Nonspecific signs such as lethargy or anorexia are less common. Syncope is an infrequent sign.

Typical physical examination features of HCM include various combinations of the following: gallop, murmur of MR (along the left apical sternal border), arterial thromboembolism, pulmonary edema, or biventricular CHF (pleural effusion). When present, the systolic murmur can vary, often increasing in intensity with higher heart rates. This finding suggests that dynamic outlet obstruction and SAM are present. The apical impulse can be prominent. Arrhythmias can occur but are not common. Arterial blood pressure is normal.

Laboratory tests can be useful.^{2,3,5,12} The electrocardiogram (ECG) may be abnormal but results are inconsistent. Increased amplitude R waves in lead II or a left axis deviation compatible with concentric hypertrophy or left anterior fascicular block may be observed. Radiographs can be normal but in advanced cases demonstrate cardiomegaly (elongation) and left atrial enlargement (most evident as an auricular bulge on the ventrodorsal view). Prominent pulmonary vascular patterns may indicate pulmonary hypertension secondary to elevated left ventricular diastolic pressure. Increased lung densities are compatible with pulmonary edema. Pleural effusion is common in acute CHF and in chronic, longstanding cases of heart failure. Routine complete blood count and clinical chemistries are unremarkable in most cases unless thromboembolism or intercurrent disease is present. Serum thyroxine is normal.

HCM is characterized echocardiographically by increased ventricular thickness (generally 6 mm or more), normal to decreased intraluminal size, and normal or increased systolic shortening fraction.^{3,5,10,12} However, 2-dimensional (2-D) echo may show regional LV hypertrophy that is not homogeneous; thus, overreliance on one measurement (i.e., the LV wall between the papillary muscles) is discouraged. Some cats have prominent ventricular septal hypertrophy

with varying obstruction of the LV outlet; others have prominent papillary muscles (representing an early sign of HCM in some cats). The size of the left atrium bears prognostic significance, as it usually relates to the severity of diastolic failure or MR and can predict the risk for CHF and thromboembolism. In chronic HCM, LV contractility may decrease, the chamber can dilate, and evidence of progression to restrictive disease may be seen (see Feline Restrictive Cardiomyopathy section). Systolic anterior motion of the mitral valve is observed quite often, increasing in severity with increased sympathetic tone. Doppler studies may demonstrate abnormal relaxation or compliance of the LV, MR, or high-velocity LV outflow caused by dynamic obstruction.

Drug Therapy for Hypertrophic Cardiomyopathy

A number of cardiovascular drugs are used in the management of feline HCM. These drugs also may be of value for treatment of other feline cardiovascular disorders. It is emphasized that no large, controlled studies indicate a superior treatment for asymptomatic disease, for cats with recurrent bouts of CHF, or for advancing heart failure. Prevention of arterial thromboembolism is a persistent problem. Pharmacologic therapy for cats with HCM may include combinations of furosemide, diltiazem, a beta-adrenergic blocker, an angiotensin-converting enzyme (ACE) inhibitor, or drugs that impair coagulation. Relevant clinical pharmacology of these drugs in cats is discussed next.

Beta-adrenergic blockers (atenolol 12.5 mg PO once or twice daily or propranolol 5 mg PO tid) are most often used to block the adverse effects of sympathetic efferent traffic on the heart.¹³ Once daily atenolol often controls heart rate at <150/minute for almost 24 hours, although pharmacokinetic studies suggest that bid treatment may be better. Beta-blockers prevent sinus tachycardia and prolong diastole, increasing time for both coronary and ventricular filling. Myocardial oxygen demand is reduced through decreases in heart rate, contractility, and blood pressure. Beta-blockade is especially helpful for reducing pressure gradients caused by dynamic LV outflow obstruction. One can administer the ultra-short beta-blocker esmolol at a 0.5 mg/kg loading dose followed by a 0.1 mg/kg/minute infusion as a provocative treatment during Doppler examination of the LV outlet. A simpler approach is to administer 12.5 mg of atenolol orally and to repeat the Doppler study 1½ to 2 hours later. The murmur of MR when caused by SAM of the valve may partially abate with beta-blockade. In a small European study, beta-blockade

with propranolol was associated with regression of LV hypertrophy, but this has not been a consistent finding. Unfortunately, the net effect of beta-blockade on diastolic function in cats with HCM is unknown. The direct effect on myocardial relaxation is unfavorable; however, indirect effects, such as reduced myocardial oxygen demand, decreases in intraventricular gradients, and prolongation of diastole also should be important and could benefit diastolic function. Adverse effects include severe sinus bradycardia (examination heart rate <100/minute), depression, and precipitation of CHF. Because of the nonspecific blocking effects of propranolol, it is not recommended in cats with uncontrolled pulmonary edema or in cats with arterial thromboembolism until collateral circulation has been restored.

Diltiazem, a calcium channel antagonist, is a popular drug for chronic management of HCM, according to the clinical report of Bright and associates.^{8,9} Calcium channel blockers are thought to improve LV relaxation. The precise mechanism for this benefit has not been elucidated. Indirect effects through reduction of blood pressure and reflexive increase of sympathetic tone could be involved. Alternatively, myocardial perfusion may increase with diltiazem because the drug is a coronary vasodilator that also decreases resting heart rate, although less effectively than a beta-blocker. Overall, diltiazem should reduce myocardial oxygen demand by decreasing heart rate, contractility, and blood pressure. Effects on reducing dynamic outflow tract gradients have been disappointing at the doses commonly used. Although the chronic administration of diltiazem has been reported to decrease LV hypertrophy in cats with *very severe* HCM, we rarely observe regression even after prolonged therapy with diltiazem, especially in the typical case. Overall, diltiazem is usually preferred in our practice when a cat has *already experienced* CHF or when it has moderate to severe LV hypertrophy and left atrial dilatation as demonstrated by echocardiography. Diltiazem is also reasonable therapy for the cat with HCM and concurrent atrial fibrillation. Preparations of diltiazem vary and include the following: (a) diltiazem ¼ of a 30-mg tablet PO tid, (b) Dilacor XR® (Watson Laboratories) brand of diltiazem (note: the 240-mg Dilacor XR capsule is opened to reveal four 60-mg drug tablets, which are split into halves with a pill cutter; the dose is 30 mg once or twice daily), or (c) Cardizem® CD (Hoechst Marion Roussel) brand (120-, 180-, 240-mg capsules, compounded in capsules or in a palatable syrup to provide 30 mg once daily). Anorexia, skin reactions, and erythema/edema have been observed in some cats receiving this drug. Depression, weakness,

and hypotension may indicate sinus bradycardia, atrioventricular (AV) block, or arterial vasodilation from an overly high dose or drug sensitivity (e.g., in older cats with inherent AV conduction disease). A *combination* of atenolol and diltiazem may be considered in cats with HCM and dynamic LV outflow tract obstruction (30 mg Dilacor XR in the evening; 6.25–12.5 mg atenolol in the morning); however, heart rate and blood pressure should be monitored with this combination therapy because of the combined effect of these drugs on heart rate, contractility, and blood pressure.

Furosemide is the initial treatment of choice for cats with pulmonary edema (2–4 mg/kg intravenously [IV] or intramuscularly [IM] as an initial dose; thereafter, 1–2 mg/kg IV, IM, or subcutaneously [SC] q 8–12 h for 24–48 hours). Oral therapy is prescribed for home care of cats that have experienced pulmonary edema; however, the maintenance dosage is often titrated down to a relatively low 1 to 2 mg/kg every second to third day. This can be accomplished over a period of 2 to 3 weeks. In some cases, furosemide can be discontinued completely. Conversely, doses of 2 mg/kg or higher bid to tid may be needed to treat progressive pulmonary edema or pleural effusion in cats with chronic CHF. These problems are detected by client monitoring of exercise activity and resting respiratory rate and through periodic examinations and thoracic radiographs. Dietary sodium restriction can be combined with furosemide, provided that the cat will eat a new diet. Efficacy of diuretic therapy is monitored using respiratory rate, level of activity, thoracic examination, and chest radiograph. Overzealous diuresis can be detected by periodic measurement of blood pressure, serum blood urea nitrogen (BUN), creatinine, and electrolytes. Azotemia, hypokalemia, and hyponatremia are very common in cats receiving furosemide on a daily basis. Mild to moderate azotemia (e.g., BUN 40–70 mg/dl) is not necessarily an indication to alter furosemide therapy in a cat with persistent fluid accumulation, because the edema is likely to worsen if furosemide dosage is decreased. In contrast, in a cat with azotemia and a completely clear chest cavity, the dose of furosemide should be reduced to prevent unneeded volume contraction.

ACE inhibitors such as enalapril (Enacard® [Merck AgVet]) and benazepril (Lotensin® [Novartis Pharmaceuticals]) can be administered at a dosage of 0.25 to 0.5 mg/kg q 24 h for recurrent or progressive pulmonary edema or pleural effusion. Whether the ACE inhibitors will reduce myocardial hypertrophy in this disease is unknown, but clinically these drugs seem to benefit the fluid accumulation of CHF. Therapy is monitored by measuring arterial blood pressure indi-

rectly and with periodic monitoring of renal function and serum sodium and potassium concentrations. Angiotensin inhibition, when combined with diuretic or aspirin therapy, can cause acute renal failure that is reversible with fluid therapy or upon discontinuation of drug therapy. If systolic blood pressure (the easiest to measure indirectly) is <85 mm Hg or if BUN increases significantly above pretreatment levels, the dose of enalapril, furosemide, or both should be reduced by 33% to 50%.

Nitrates (nitroglycerin ointment ¼ inch topically once or twice daily) may be used for hospital therapy of CHF in conjunction with furosemide and oxygen administration. Nitrates may also be used for home care of cats, particularly if the cat experiences unexplained bouts of dyspnea or if the client has trouble medicating the pet.

Digoxin is rarely used in cats with HCM. There are no data supporting use of cardiac glycosides in this disease. The principal indications for digoxin (given with diltiazem or a beta-blocker) are development of atrial fibrillation or CHF associated with echocardiographic evidence of progressive LV systolic failure and cardiac dilatation. Digoxin is eliminated by renal mechanisms, and the elimination half-life, even in healthy cats, is very long (often 2–3 days). Digitalization in cats is initiated at a dose of ¼ of a 0.125-mg Lanoxin® (Glaxo Wellcome) tablet every 48 hours. A serum digoxin concentration is measured about 14 days later, with the blood sample drawn 10 to 12 hours posttreatment. The therapeutic goal is a trough serum concentration between 1 and 1.5 ng/ml.

Antithrombotic drug therapy can be prescribed in an attempt to reduce the chance of arterial thromboembolism.^{14–16} There are no prospective studies demonstrating efficacy of any treatment. Two approaches have developed empirically. Aspirin (1 baby aspirin or ¼ of an adult aspirin every 3 days) or warfarin (Coumadin® [DuPont Merck Pharmaceuticals], starting at ½ of a 1-mg tablet daily) may be prescribed to inhibit thrombogenesis. *Aspirin* may inhibit platelet function in some cats. The dose is probably critical, but good guidelines are lacking. Anorexia, vomiting, and gastric erosions are potential complications of therapy. *Coumadin* represents a more aggressive approach to treatment of cats with severe atrial dilatation, prior embolization, or other risk factors (e.g., atrial fibrillation).¹⁵ Because warfarin initially enhances coagulation, cotherapy with heparin (100 IU/kg SC) should be given for the first 48 to 72 hours. A baseline one-stage prothrombin time (PT) should be obtained. A recommendation¹⁵ has been made to calculate the international normalized ratio (INR) to

achieve a value of between 2.0 and 3.0 (with the blood sample drawn approximately 2 hours posttreatment). The $INR = (\text{patient PT} \div \text{control PT})^{ISI}$, where ISI = international sensitivity index of the thromboplastin used in the PT assay. The control value is obtained from a control *population* (not a single cat). The validity of using this approach in cats has not been completely determined, but it represents the most rational approach thus far. Warfarin should not be used with aspirin, and other drug interactions must be considered. Should bleeding occur at any body site or in the litter box, therapy must be discontinued immediately and the INR reestablished at 2.0 to 3.0. Vitamin K therapy is used to treat a bleeding diathesis.

Treatment Approaches

No data indicate any substantial benefits of therapy in asymptomatic cats with HCM. Increasingly, cats with asymptomatic or mild HCM and normal left atrial size are left untreated. Many show little progression of disease at follow-up. Thus, in the asymptomatic cat, the veterinarian could reasonably consider prescribing no therapy, or, empirically, a beta-adrenergic blocker or diltiazem. Some clients indicate that their cat is more active when receiving therapy, but this may simply represent a placebo effect. Beta-blockers are recommended by many in the setting of moderate to severe LV outflow tract obstruction, and atenolol is most often prescribed for this purpose. Marked LV hypertrophy, especially with concurrent left atrial dilatation, suggests significant diastolic dysfunction or MR, and diltiazem is usually prescribed. Anticoagulant therapy may also be recommended, especially when left atrial dilatation is present (see following). Initially, cats with asymptomatic disease are examined by repeated thoracic radiographs or by echocardiography every 3 to 6 months. Echocardiography has the advantage of providing objective measures of wall thickness and left atrial size, and a Doppler study can be used to document reduction in dynamic obstruction and associated MR if these flow disturbances are present at initial examination. Thereafter, the stable cat is seen every 6 to 12 months. In many cases, the disease is quite stable, and there is little justification for excessive reevaluation after the 1-year follow-up.

Management of acute heart failure in cats with HCM is a challenge. Initial efforts are directed at improving tissue hypoxia, relieving stress, and reducing the venous and pulmonary capillary pressures. Thoracentesis is performed if a large pleural effusion is present. Intubation and artificial ventilation best manage impending respiratory arrest. Fortunately, most cats can be managed medically. The cat is placed at rest,

oxygen (40%–50%) is administered by cage oxygenator, and sedation is given if necessary (butorphanol 0.15 mg/kg mixed with acepromazine 0.05 to 0.1 mg/kg SC). Furosemide is administered and the dose is reduced as previously described once diuresis occurs. Two percent nitroglycerin ointment is also administered q 12 h when moderate to severe pulmonary edema exists. Treatment is continued for 24 to 72 hours. Subsequently, oxygen is withdrawn, nitrate ointment is discontinued, and furosemide dosage is lowered and titrated to the severity of pulmonary edema or pleural effusion. Many cats develop hypokalemia and prerenal azotemia during such intensive therapy. Mild cases need not be treated, but if the cat refuses to eat and drink after 24 to 36 hours of therapy, judicious fluid therapy (e.g., 20 ml/kg/day) and potassium supplementation (IV or oral) are needed.

Chronic management of CHF in cats with HCM often involves home therapy of furosemide, diltiazem, and treatment to prevent thromboemboli. If the dosage frequency of furosemide is more than 1 mg/kg once daily, enalapril 0.25 mg/kg daily for 2 weeks can be added with the intent of increasing the dose to 0.5 mg/kg daily if blood pressure, renal function, and electrolytes are adequate. Initial reevaluation is in 1 to 2 weeks, then again in 1 month. Periodic reevaluations (at least every 3 to 6 months for 2 years) are recommended and include history and examination, arterial blood pressure measurement, thoracic radiographs, serum biochemical profile, and, often, a focused recheck echocardiogram. The timing of specific examinations depends on clinical circumstances and economic considerations.

Treatment and Prevention of Arterial Thromboembolism

Although some reports have indicated the importance of collateral vasoconstriction and the value of inhibiting platelet-derived vasoconstrictors, there are no controlled studies demonstrating improvement of collateral flow with therapy in spontaneous cases. Surgery generally has been avoided because these cats usually have disseminated intravascular coagulopathy (DIC) and many develop (or have) lung edema after anesthesia (although there have been some surgical successes following embolectomy). A significant number of cats (approximately 40%) with HCM will walk within 3 weeks of the thrombotic event, provided heart failure is controlled and the limbs undergo spontaneous revascularization.¹⁶ Sufficient time (at least 1 week) should be allowed for improvement. Severe ischemic muscle necrosis does develop in some cases, and these cats are usually euthanized. The cat

with a single functionless or edematous limb may do well after limb amputation, but this is rarely recommended or requested.

The initial treatment of cats with thromboembolism involves analgesia and sedation with butorphanol 0.2 to 0.3 mg/kg SC q 8 h combined with acepromazine 0.1 mg/kg. An alternative therapy is the 10-cm² fentanyl patch; 25 µg/hour release may also be considered but will not work as quickly as butorphanol. The acepromazine/butorphanol combination is effective sedation/analgesia for the cat in distress. Sodium bicarbonate 1 mEq/kg IV over 10 to 20 minutes is sometimes administered at first presentation, as metabolic acidosis and/or hyperkalemia may result from muscle necrosis and reperfusion. Heparin 200 to 300 IU/kg IV, then 200 IU/kg SC every 8 hours for 48 to 72 hours may be administered to prevent further thrombosis. Beta-blockers, especially propranolol, should be avoided until the cat is walking without difficulty. If CHF is controlled, maintenance fluid therapy is administered (with furosemide) to maintain urinary output and prevent hyperkalemia. Excitement has waned for IV streptokinase (90,000 IU over 30 minutes, followed by 45,000 IU/hour for 3–6 hours) and IV tissue plasminogen activator (0.25–1 mg/kg/hour to a total dose of 1–10 mg/kg), as these expensive treatments are difficult to control and carry a very high mortality rate.¹⁴ Reperfusion—be it spontaneous or induced by a thrombolytic drug—can lead to fatal hyperkalemia from rapid reperfusion of necrotic muscles.

Prevention of thromboemboli is recommended when atrial enlargement is present. When the left atrium is enlarged (>16 mm on 2-D echo), aspirin is prescribed every 3 days. Warfarin is recommended when the cat has one of the following: (a) prior documented thromboembolism, (b) left atrial dimension exceeding 20, (3) evidence of spontaneous echocardiographic contrast (smoke) in the left atrial cavity, or (4) atrial fibrillation. One must have a cooperative client for warfarin therapy to succeed.

FELINE RESTRICTIVE CARDIOMYOPATHY

Feline restrictive cardiomyopathy (RCM) has also been called intermediate cardiomyopathy and endomyocardial fibrosis.^{1,5,17,18} The pathogenesis of these lesions is undetermined. Antecedent myocarditis seems a likely, although unproven, initiating cause. RCM in some cats clearly represents a late stage of HCM complicated by myocardial failure or myocardial infarction. A variety of necropsy lesions have been observed in cats demonstrating clinical features of RCM. LV endomyocardial fibrosis may be patchy,

multifocal, or diffuse in distribution. The LV may be mildly or regionally hypertrophied, mildly dilated, or normal in size. Often there is regional thinning or infarction of the LV free wall or LV apex, interspersed with focal or regional wall hypertrophy. Prominent papillary muscle hypertrophy or fibrosis is evident in some cats. Extreme endocardial fibrotic scarring is occasionally evident and can involve the mitral valve apparatus, cause midventricular constriction or stenosis, or obliterate the LV apex. A common feature is striking biatrial dilatation. Systemic thromboemboli are common and left atrial and ventricular mural thrombi may be observed. Histologic lesions include endocardial thickening, endomyocardial fibrosis, myocardial interstitial fibrosis, myocyte hypertrophy, and focal myocytolysis and necrosis. Arteriosclerosis of intramural coronary arteries may be recognized.

Pathophysiology

The pathophysiology of RCM in the cat is unresolved. Echocardiography generally demonstrates a low normal to mildly reduced shortening fraction (ejection fraction). When decreased ejection fraction is present, it is probably caused by a loss of functional myocardium, and the systolic dysfunction may progress over time. Regional LV wall dysfunction may be observed, characterized by diminished LV free wall thickening and excursion. Doppler studies may demonstrate mitral insufficiency, but regurgitation usually is mild. Because the abnormalities of ejection fraction and mitral valve function do not sufficiently explain the marked left atrial dilatation characteristic of this disease, it is assumed that impaired LV distensibility is the principal pathophysiologic disorder. Myocardial or endomyocardial fibrosis is the most likely explanation for this diastolic dysfunction. Myocardial ischemia, relaxation abnormalities, cardiac arrhythmias, or ventricular dilatation can further impair ventricular diastolic function. Progressive increases of left atrial pressure develop to fill the stiff LV and thereby predispose the cat to elevated pulmonary venous pressure and pulmonary edema. One can also speculate that the marked left atrial dilatation and fibrosis increase the resistance to right ventricular ejection. These factors probably lead to chronic pulmonary hypertension, cause the progressive enlargement of the right side of the heart, and contribute to the elevated central venous pressure that is so often observed in advanced cases. Pulmonary edema, pleural effusion, and hepatic congestion are typical manifestations of CHF and can be explained by the aforementioned cardiac lesions along with neurohumoral and renal compensations activated in response to lim-

ited cardiac output. Stasis of blood in a dilated left atrium undoubtedly predisposes affected cats to atrial thrombi and systemic thromboembolism.

Clinical Findings

Most cats with RCM are middle aged or older, although young cats with this condition also have been recognized. History and clinical signs of RCM are similar to those described for HCM. Examination of the cat with RCM can reveal a variety of physical manifestations. The most consistent auscultatory finding is a gallop sound, indicative of ventricular diastolic dysfunction. A soft to moderately loud systolic murmur of mitral or tricuspid regurgitation may be detected near the left or right sternal borders but is not always evident. Premature ventricular or atrial beats may be heard, leading to an irregular rhythm and arterial pulse. The femoral pulse is otherwise normal or slightly reduced in amplitude. Palpable hepatomegaly or pleural effusion with elevated jugular venous pressure or prominent jugular pulsations is suggestive of concurrent right ventricular failure. Pulmonary edema or pleural effusion is most often manifested as tachypnea, although orthopnea, respiratory distress, and cyanosis may develop in severe cases of CHF. Thoracic auscultation is variable, but careful auscultation may reveal loud bronchial sounds, fine crackles, or a fluid line. Blood pressure usually is normal. Signs of aortic thromboembolism may be evident.

Diagnostic studies are helpful in recognizing heart disease and establishing the diagnosis of RCM. The ECG is frequently abnormal. Ventricular enlargement and myocardial disease can be manifested as a widened QRS complex (>0.04 seconds), increased amplitude R waves (>0.7 mV) in leads II, aV_F, or III, splintered R waves, right axis deviation, or left bundle branch block, and ventricular extrasystoles. Atrial enlargement is characterized by widened (>0.035 seconds) or tall (>0.2 mV) P waves, atrial ectopic rhythms, or atrial fibrillation. Thoracic radiographs are often impressive and characterized by left atrial dilatation and cardiac elongation that is typical of LV enlargement. The cardiac apex can be pointed or rounded. Some cats manifest astounding left atrial enlargement that, on the lateral projection, can be seen to separate the mainstem bronchi and create a convex dorsocaudal border. Some cases demonstrate a valentine-shaped heart reminiscent of HCM. Pulmonary hypertension may be evident radiographically as dilatation of both lobar arteries and veins. Interstitial and alveolar infiltrates indicative of pulmonary edema or bilateral pleural effusions indicate the development of CHF. LV angiography is rarely performed but can

delineate a number of anatomic lesions: Marked left atrial dilatation, mild LV dilatation, and irregular filling defects of the LV lumen seem most characteristic of this disease. In some cases, the LV cavity is distorted by fibrotic papillary muscles, endocardial plaques, or prominent moderator bands; midventricular cavity obliteration may be evident.

Marked left atrial or biatrial dilatation is the most characteristic echocardiographic feature of RCM. The LV, in typical cases of RCM, is neither as hypertrophied nor as dynamic as that observed in HCM. In contrast to cats with dilated cardiomyopathy, ventricular shortening fraction is either normal or just mildly reduced (generally >25%) and the mitral opening (E point) to septal distance is minimally increased. However, marked regional wall dysfunction may be noted, most often affecting segments of the LV free wall. Examination by 2-D echocardiogram may reveal a ventricle that is mildly dilated just below the mitral valve; yet, apically, the LV may appear hypertrophied and the papillary muscles thick or rigid. Discrete thinned areas of ventricular atrophy, infarction, or scar may be imaged. Focal or diffuse, subendocardial, hyperechoic wall segments probably denote fibrosis or endomyocardial plaques. In extreme cases of endocardial fibrosis, imaging of the mid to apical LV lumen may demonstrate thickened, hyperechoic, fibrous tissue that bridges the septum, papillary muscles, or free wall, obliterates the apical LV cavity, or confers an appearance of diminished systolic motion or restricted filling. Prominent LV moderator bands (false tendons) also may span portions of the lumen. Left atrial or ventricular mural thrombi are observed infrequently. The right ventricle is often dilated in symptomatic cats but is otherwise devoid of structural lesions. Doppler studies can indicate AV valve regurgitation, but the condition is rarely severe. Because of the rapid feline heart rate, Doppler assessment of diastolic function is very difficult, but it can demonstrate a restrictive LV filling pattern with rapid deceleration time and small A wave. When CHF has developed, pleural and pericardial effusions usually will be present. The pericardial effusion can be substantial but decreases markedly after successful treatment of heart failure.

Clinical laboratory studies of cats with RCM are not specific, and most abnormalities are attributable to CHF, diuretic therapy, or thromboembolism. A plasma or whole blood taurine should be measured. Decreased concentrations have been noted in some cats and could contribute to reduced myocardial contractility. Analysis of pleural effusates indicates a transudate, modified transudate, or chyle. Macrophages,

mesothelial cells, and small lymphocytes predominate unless there is chylothorax, in which case well-preserved neutrophils may be more numerous.

Therapy of Restrictive Cardiomyopathy

Respiratory distress in this condition is attributed to pulmonary edema, pleural effusion, or both, and initial treatment should be directed accordingly. When pleural effusion is present and sufficient to cause atelectasis, thoracentesis should be performed while the cat is sternally recumbent. A sample of the effusate should be retained for chemical and cytologic analysis. Pulmonary edema can be severe in some cats with RCM. Initial therapy includes supplemental oxygen, furosemide 2 to 4 mg/kg IM or IV q 8 h, and 2% transdermal nitroglycerin paste ¼ inch topically q 12 h. Once diuresis has been observed, the diuretic dose is decreased to 1 to 2 mg/kg SC q 8 to 12 h. Following initial diuresis, the cat should be given fresh water ad libitum. If water is refused or continual weight loss occurs, maintenance IV or SC fluids should be given (0.45% NaCl–2.5% dextrose solution 40–50 ml/kg/24 hours; add 8–12 mEq KCl per 500 ml fluid). In cats with aortic thrombosis, both serum potassium and renal function should be monitored at least daily, more often if thrombolytic therapy is given. Liquid nutritional support given by an indwelling nasogastric tube may be considered if anorexia persists; however, most cats begin to eat after effective resolution of CHF. Systemic thromboembolism is managed as described previously for feline HCM.

Chronic therapy of the cat with RCM centers on medical management of CHF and prevention of thromboembolism. Drugs used in management of CHF have been discussed previously. A sodium-restricted diet should be dispensed if the cat will eat it. We have had the best results in treating CHF using a combination of furosemide, enalapril, and digoxin. The daily furosemide dosage depends on the severity of fluid accumulation and must be individualized. Initial doses between 1 and 2 mg/kg q 12 h are reasonable; however, doses as high as 4 mg/kg q 8 h have been tolerated. The ACE inhibitors have been used frequently in cats with RCM. The initial dosage is low, 0.25 mg/kg PO q 24 h, but can often be increased to as high as 0.5 mg/kg q 12 h. Aspirin (1 baby aspirin every 3 days) or Coumadin (starting at 0.5 mg daily) may be prescribed to inhibit thrombogenesis. Should progressive pleural effusion develop despite digoxin, furosemide, and enalapril therapy, the clinician can perform thoracentesis and consider one or more of the following strategies for refractory CHF: (1) Increase enalapril to a maximal dosage of 0.5 mg/kg q 12 h, (2)

increase furosemide to 4 mg/kg q 8 h, (3) add nitroglycerin paste at a dose of ¼ inch topically q 12 h, (4) add spironolactone 2 to 4 mg/kg PO daily, or (5) substitute one oral furosemide treatment for an SC injection two or three times weekly. The cat should be reassessed by clinical examination and radiography in 3 to 7 days. Should all of these treatments fail, euthanasia should be considered.

The value of other treatments such as diltiazem or beta-blockers in feline RCM is unresolved. Rutin® (Lederle) is prescribed when there is evidence of recurrent pleural effusion with chylothorax. Treatment of complicated and rapid ventricular tachycardia in cats with RCM is problematic. Propranolol 2.5 to 5.0 mg q 8 h or procainamide ¼ of a 250-mg capsule mixed in the food q 8 h has been used, but negative inotropic effects, poor client and patient compliance, and lack of efficacy studies suggest that such treatments be reserved for symptomatic (i.e., syncopal) patients or for those with dangerous ventricular arrhythmias.

The long-term prognosis of RCM is guarded and quite variable. Some cats have been successfully managed for CHF for more than 2 years, and such cases have been rewarding to clients and clinicians alike. One-year survival is not uncommon after onset of heart failure. Unfortunately, relentless CHF, refractory pleural effusion, or systemic thromboembolism each presents formidable obstacles to long-term survival.

OTHER MYOCARDIAL DISEASES

Dilated cardiomyopathy is recognized by echocardiographic demonstration of reduced LV shortening (ejection) fraction, absence of ventricular wall thickening, and absence of congenital or valvular cardiac disorder.^{4,5,19-22} Consequences of this disorder, which is now uncommon in cats because of supplementation of the amino acid taurine in cat foods, are CHF and thromboembolism. Previously, taurine deficiency accounted for the large number of cases of dilated cardiomyopathy in the cat. Sporadic cases of dilated cardiomyopathy still occur, possibly a consequence of myocarditis. Cats with dilated cardiomyopathy are evaluated for taurine deficiency (breeds particularly at risk include the Burmese, Abyssinian, and Siamese) and treated with taurine 250 to 500 mg twice daily for 12 weeks. Heart failure is managed with furosemide, digoxin, and enalapril or benazepril.

Hyperthyroid heart disease is common²³⁻²⁵ and leads to biventricular hypertrophy, with the LV becoming quite thickened in chronic cases. While hyperthyroidism remains an important differential diagnosis for other forms of cardiomyopathy, affected cats infrequently develop CHF because veterinarians are now

very cognizant of this disorder. If thoracic radiographs show only mild to moderate cardiomegaly, further studies are unlikely to add to the management of the disorder, and treatment of the hyperthyroidism is pursued with no additional cardiac medication prescribed. Infrequently, biventricular CHF develops in cats with moderate to severe cardiomegaly and evidence of reduced global LV systolic function. This situation is managed medically with furosemide, enalapril, and methimazole. Once the cat is stable, it should be referred for treatment with iodine 131 (¹³¹I) or possibly ultrasound-guided injection of a unilateral hyperthyroid nodule with ethyl alcohol. The cardiac manifestations of thyrotoxicosis usually abate following definitive treatment of hyperthyroidism (except for those with overt cardiac failure or those with true intercurrent HCM). Thromboembolism is exceedingly rare in isolated thyrotoxic heart disease. Cardiac disease and clinical signs can be partially controlled with atenolol 6.25 to 12.5 mg PO once daily in cats with long-standing thyrotoxicosis that cannot be managed definitively and without tolerance for methimazole or carbamazepil.

Hypertensive heart disease should be included in the differential diagnosis of any cat with a gallop, murmur, or echo-proven LV hypertrophy.^{26, 27} The clinical condition can resemble mild HCM. Heart failure and thromboembolism are rare. Diagnosis is generally straightforward if the clinician obtains a device to measure arterial blood pressure. Treatment is directed at controlling hypertension and progressive renal injury and at preventing ocular complications. Amlodipine (Norvasc® [Pfizer Labs] ¼ of a 2.5-mg tablet once or twice daily; increase dosage as needed up to ½ tablet tid) is the current medication of choice for controlling hypertension in cats. Beta-blockers or ACE inhibitors are reasonable alternatives, although not as effective. Furosemide is also indicated in short-term hospital therapy of cats with retinal hemorrhage/detachment.

Acromegaly and growth hormone excess have been incriminated as causes of feline heart disease.²⁸ Cats with diabetes and other signs of acromegaly should be considered as potential candidates for this syndrome. For optimal management, a specialist in internal medicine or endocrinology should be consulted.

Nonsuppurative myocarditis occurs sporadically in cats.⁵ The cause is unknown. Some cats are presented for ventricular arrhythmias, while others develop fulminant heart failure, restrictive cardiomyopathy (chronic, healing phase), or thromboembolism. The diagnosis is difficult and often based on suspicion. Because myocardial biopsy is difficult in cats and en-

zyme changes are nonspecific, the diagnosis is usually tentative or made at necropsy.

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