Feline Acquired Cardiac Disease

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Introduction

Cardiac disease affects approximately 10-15% of the entire feline population[1]. This percentage dramatically increases to 33% in patients over eight years of age. Therefore, it is imperative general practitioners understand the common characteristics of feline acquired heart disease. The most common form of acquired cardiac disease in the cat is cardiomyopathy. Cardiomyopathy poses some challenges in diagnosis, especially given echocardiogram remains the gold standard diagnostic test. This session will summarize the updated classifications of feline cardiomyopathies as well as review the characteristics of each cardiomyopathy. In addition, diagnostic and medical therapy guidelines will be discussed.

Updated Classification of Feline Cardiomyopathies

The ACVIM Consensus Statement from 2020 describes the most current classification of feline cardiomyopathy, diagnosis, and treatment[2]. The underlying theme to the classification scheme utilizes the "phenotype" of the disease. This highlights the fact there are numerous systemic conditions which may result in subsequent cardiomyopathy. Perhaps the most clinically relevant is the hypertrophic cardiomyopathy (HCM) phenotype. A patient with a thick left ventricle cannot be diagnosed with idiopathic hypertrophic cardiomyopathy without first ruling out the many other causes for left ventricular hypertrophy. Additionally, a restrictive cardiomyopathy (RCM) phenotype describes a patient with significantly impaired diastolic function but does not necessarily mean the patient has restrictive cardiomyopathy caused by idiopathic changes to the ventricle. There can be overlap between groups as cardiomyopathy progresses and patients that were once clearly an HCM phenotype develop a restrictive filling pattern or reduced systolic function (i.e. dilated cardiomyopathy phenotype) secondary to infarction.

Hypertrophic cardiomyopathy (HCM)

HCM is the most common feline cardiomyopathy, representing 60% of the cardiac patients[1-5]. It has a male predisposition and most commonly affects middle aged patients. Some pure breeds such as Domestic Shorthair, Maine Coon, Sphynx, Ragdoll, Persian, etc. can be affected even younger and more severely. Idiopathic HCM is defined as a thickness of at least six millimeters of any portion of the left ventricle in the absence of other disease/abnormal loading conditions. The ventricle may be diffusely or asymmetrically affected. Therefore, careful 2-dimensional evaluation is required from a trained sonographer. The right ventricle can also be variably affected[6,7]. Once a diagnosis of a thick left ventricle is made, all causes for an HCM phenotype must be excluded before making a final diagnosis of HCM. These include systemic hypertension, hyperthyroidism, acromegaly, myocarditis, infiltrative disease, and

pseudohypertrophy (i.e. relative hypovolemia). This workup usually involves a blood pressure and T4. Cardiac troponin I can be considered to rule out myocarditis or transient myocardial thickening.

HCM and the HCM phenotype are classically accompanied by a degree of ventricular diastolic impairment that tends to progress overtime. As this occurs, the left atrium will dilate and the combination of endothelial disruption and blood stasis in the enlarged left atrial/auricular chamber predisposes the patient to thrombus formation. Therefore, an important part of the echocardiographic examination is also an assessment of left atrial size and function. Once the patient meets criteria for increased risk of thrombus formation, antiplatelet therapy in the form of clopidogrel is recommended.

There is a subset of patients with HCM that also have an obstructive component to their disease. This obstruction is usually a left ventricular outflow tract obstruction (LVOTO) that results in a heart murmur and leads to the diagnosis. The LVOTO may be caused by a false tendon, systolic anterior motion of the mitral valve apparatus (SAM), or a prominent septal bulge. SAM is one of the more common forms of LVOTO and occurs when the anterior mitral valve leaflet and/or chordae tendineae interfere with the blood being ejected from the left ventricle[8]. SAM results in increased LVOT velocities and a classic eccentric jet of mitral regurgitation. LVOTO results in an audible murmur that is typically dynamic (i.e. intensity changes with patient stress and heart rate). A large retrospective study (REVEAL) showed HCM and HOCM cats have similar quality and quantity of life[9]. Another study showed atenolol therapy had no significant difference on five-year mortality rate in cats with confirmed HOCM[10]. This is contrary to what is seen in people. Many cardiologists now reserve atenolol therapy for severe HOCM cases (i.e. where peak LVOT velocity is > 3.5-4 m/s).

Arrhythmias are seen relatively commonly in cats with HCM. One Holter study showed there was no significant difference in ventricular ectopy between Stage B and C cats[11]. Furthermore, the presence of ectopy did not necessarily predict sudden death. The threshold for treating arrhythmias in cats is higher than dogs due to the reduced feasibility of medicating the patient, the limited treatment options, and limited ability to measure daily arrhythmia burden/response to treatment. Ventricular arrhythmias may be treated with sotalol or atenolol. Atrial arrhythmias may be treated with atenolol or diltiazem. Ideally, anti-arrhythmic therapy should be prescribed with the help of a cardiologist.

The rate of disease progression is variable for each patient. Therefore, recheck assessments via echocardiogram are usually recommended every 12 +/- 6 months or so. Fortunately, while HCM is a very common disease, the overall cardiac mortality rate is 25%[2,9,10]. Recurrent congestive heart failure (CHF) is the most common cause for cardiac death in these patients followed by euthanasia post ATE and finally, sudden death presumably from an arrhythmia or coronary event[12]. Still, it is important to educate clients that the median survival time for HCM/HOCM cats with first-time CHF is approximately 12 months. If these patients have an HCM phenotype secondary to hyperthyroidism or systemic hypertension, the prognosis can be better as long as the underlying disease is treated[5].

Restrictive Cardiomyopathy

RCM is the second most common form of cardiomyopathy, representing about 25% of patients. This disease is defined by normal ventricular wall thickness, atrial or bi-atrial enlargement, and impaired diastolic function. There are two forms of the disease: diffuse myocardial form that is commonly associated with infectious conditions and the endomyocardial form where scar/fibrotic tissue is visible on echocardiogram and gross pathology. This disease carries a worse prognosis compared to HCM. This

may be due to the fact that these patients are more commonly diagnosed once they experience Stage C disease (i.e. CHF of an ATE). There is no breed nor sex predisposition and the median age of diagnosis is 10 years.

Dilated Cardiomyopathy (DCM)

DCM is defined as a dilated left ventricular internal chamber with reduced left ventricular systolic function. Prior to the late 1970s, DCM from taurine deficiency was a common feline cardiomyopathy. Since that discovery, diets have been adjusted and DCM is rare. However, some patients may still be at risk; particularly those cats on vegan/vegetarian, home cooked, or high pulse ingredient diets. Diagnosis of DCM usually occurs late in the disease process (i.e. Stage C) and the prognosis is guarded to poor. There is no breed nor sex predisposition and the median age at diagnosis is 10 years. These patients usually live weeks to months once CHF has occurred, even with pimobendan therapy. Sudden death is relatively more common in this group of cardiomyopathy.

Arrhythmogenic Right Ventricular Cardiomyopathy (ARVC)

ARVC is another rare form of feline cardiomyopathy. Cats with ARVC classically develop a very dilated and thin right ventricle due to fibrofatty replacement of the cardiomyocytes. These patients often present with right sided congestive heart failure that can be challenging to treat. Median age of ARVC patients is 10 years. Unlike dogs with ARVC, cats with ARVC are not as commonly afflicted with severe arrhythmia burdens although arrhythmias do still occur.

Non-specific Phenotype (NCM)

The final category of feline cardiomyopathy is NCM. This used to be termed “unclassified cardiomyopathy.” The terminology has changed to allow the clinician to describe the phenotype of the patient more accurately. As the name suggests, NCM is reserved for patients who have an abnormal echocardiogram but their pathophysiology does not meet the diagnostic criteria of any of the aforementioned classes. There may be a slight female predisposition and most cats are between eight and 10 years of age. Approximately 50% of cats present in CHF when they are first diagnosed with this cardiac disease[13].

Miscellaneous Category

A relatively new condition that is gaining recognition is transient myocardial thickening (TMT). This is an HCM phenotype that normalizes over time. Cats with TMT typically have a higher measured cTnI and it is believed these patients have a stressor that leads to the thickening[14]. Some cats have tested positive for infectious etiologies such as *Bartonella sp* and *Toxoplasma.* The cats behave similar to a myocarditis but do not always require specific treatment aside from CHF therapy. The prognosis for these patients is excellent as long as they make it through the period of CHF.

Another instance of partially reversible cardiac disease or CHF is the steroid-induced pathology. There are cats who may or may not have underlying cardiac pathology that receive steroid therapy and then present with CHF days later. It is thought that the combined mineralocorticoid and corticosteroid effects are responsible for causing plasma volume expansion, diastolic impairment, and worsened afterload due to vascular stiffness[15,16]. These patients do not always have significant remodeling post CHF and their

prognosis can be less certain than TMT patients. Overall, clients should be educated about this possible side effect of steroids and given appropriate guidance for monitoring their pet.

Diagnostic Tools for Feline Cardiomyopathies

Echocardiogram is still the gold standard for diagnosing the etiology of cardiac disease. Cats can be challenging to image due to their size, temperament, and fast heart rates. Furthermore, fractions of millimeters can make the difference of a normal versus diseased diagnosis. Therefore, the echocardiogram should ideally be performed by a cardiologist or a well-trained sonographer.

Tools available at a general practice level include physical exam findings, electrocardiography (ECG), thoracic radiography (TXR), and biomarkers, +/- point of care ultrasound (POCUS). Physical exam findings such as a murmur, gallop sound, or arrhythmia may indicate an underlying cardiomyopathy. Murmurs can be physiologic and a gallop sound can be normal in older patients, however they still warrant further workup. An ECG is helpful to classify any rhythm disturbance or diagnose a left anterior fascicular block pattern (deep S wave in leads II, III, and aVF with a larger R wave in leads I and aVL). TXR are a specific but insensitive test due to the way the cat heart remodels with disease. The NT-proBNP and SNAP proBNP have shown to have the best sensitivity and specificity when used in patients that have evidence of underlying disease or are in respiratory distress, respectively[17,18]. cTnI has limited use in screening for cardiac disease but is most helpful for diagnosing myocarditis in this cardiologist's opinion. HCM genetic testing is available for Maine Coon, Ragdoll, and Sphynx breeds. However, this is not appropriate for diagnosing disease and is better used for breeding programs and risk assessment. POCUS is not a replacement for echocardiogram but POCUS can be used to assess left atrial size, B lines, and the presence of pericardial or pleural effusion[19].

Staging of Feline Cardiomyopathies

There is now a staging scheme that mirrors the ACVIM Stages for dogs with myxomatous mitral valve disease. Stage A cats are those at risk for developing cardiomyopathy due to their signalment or family history. These patients should be screened appropriately. Stage B cats are those cats that have echocardiographic evidence of disease. B1 are cats that do not have left atrial enlargement and therefore have a low risk of developing clinical signs from their disease in the near future. Stage B2 includes cats who have left atrial enlargement that warrants medication (i.e. thrombus prevention). These cats are at a higher risk of adverse events due to more progressive disease. Stage C includes cats who have experienced an episode of congestive heart failure (CHF) and/or an aortic thromboembolic event (ATE). These patients require more medical therapy and more frequent monitoring. Finally, Stage D patients are cats whose CHF is considered "refractory" to standard doses of therapy.

Congestive Heart Failure (CHF) Therapy

CHF is a common outcome for cats with cardiomyopathy. Clinical signs, resting respiratory rate, and thoracic radiographs/POCUS remain the main tools for making the diagnosis[19,20]. Once CHF is diagnosed, diuretic therapy is required. Loop diuretics such as furosemide or torsemide are the mainstay of treatment. The aim of therapy is to find the lowest needed dose to control clinical signs while minimizing negative side effects of the drug. Renal values and electrolytes need to be checked prior to therapy, a few weeks post-therapy, and ideally every few months thereafter. Spironolactone has a weak diuretic effect due to its aldosterone antagonism. A prospective study found cats tolerated the dose of 2 mg/kg/day and seemed to do well with spironolactone therapy in addition to their loop diuretic[21]. ACE-inhibitors have proven their place in canine management of CHF. However, that same evidence is lacking in cats. ACE-inhibitors have many theoretical benefits, but this therapy may be withheld if the patient has concurrent azotemia, inappetence, or is difficult to medicate. If the patient is not already on an anti-platelet or anti-coagulant, that should be initiated and is considered crucial to reduce the risk of ATE[25]. Pimobendan has been investigated in various studies[22-24]. Pimobendan may promote left atrial function but whether this translates to lower ATE risk is unclear. Pimobendan seems to be well tolerated by most cats that can be medicated. The exception is cats with significant LVOTO. Therefore, most cardiologists do not prescribe pimobendan to cats with obstructive disease. This cardiologist will consider pimobendan for cats with renal disease, systolic dysfunction, or pleural effusion in the absence of LVOTO. It is important to also treat any other systemic disease as appropriate treatment will result in prolonged survival.

Aortic Thromboembolism (ATE) Prevention

ATE is a devastating complication of feline cardiomyopathy. Any cat with cardiomyopathy is at risk. The risk is considered increased once the left atrium has at least moderate remodeling. The FAT CAT study showed clopidogrel was superior to aspirin in preventing a recurrent ATE[26]. This has been extrapolated and the recommendation is to treat B2 cats with clopidogrel over aspirin when possible. A review of anti-platelets and anti-coagulants is outside the scope of this lecture. However, once an ATE event has occurred or if there is still increased risk of ATE despite clopidogrel therapy (such as spontaneous echo contrast or a forming thrombus), addition of another agent is recommended. This is typically in the form of a heparin or anti-Xa drug. These drugs tend to be more expensive and low molecular weight heparin requires injection, which usually makes them second line therapies. Cats seem to tolerate combination therapy and more studies are ongoing to determine if anti-Xa drugs may be superior to clopidogrel. In this cardiologist's experience, the combination of an anti-platelet and a low molecular weight heparin or an anti-Xa have worked well if the client can afford the anti-Xa.

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