Cardiomyopathies in small animals

Yoko Fujii, DVM, Ph.D, DACVIM (Cardiology),
Azabu University, Japan

Cardiomyopathies were previously defined as "an idiopathic myocardial disease that is not secondary to any other type of congenital/acquired heart disease or systemic diseases." With increasing understanding of etiology and pathogenesis in human medicine, the difference between cardiomyopathy and specific heart muscle disease has become indistinct.[1] Cardiomyopathies are now classified by the dominant pathophysiology or, if possible, by etiological/pathogenetic factors. The American Heart Association recently advocated the following new definition of cardiomyopathy: Cardiomyopathies are a heterogeneous group of diseases of the myocardium associated with mechanical and/or electrical dysfunction that usually (but not invariably) exhibit inappropriate ventricular hypertrophy or dilatation and are due to a variety of causes that frequently are genetic. Cardiomyopathies either are confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disability.[2] Because the understanding of etiology or pathogenesis of cardiomyopathy has been limited in veterinary medicine, the previous classification is generally used. It is considered a dilated, hypertrophic and restrictive group on the basis of the predominant morphological and functional abnormalities. In addition, arrhythmogenic right ventricular cardiomyopathy and unclassified cardiomyopathy were also recognized in dogs and/or cats.

Feline cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is the most common form of heart disease in cats. In humans, HCM is inherited in 50-70% of the cases, and numerous causative mutations have been identified. In veterinary medicine, a causative mutation in the cardiac myosin-binding protein C (MYBPC^3) sarcomeric gene has been identified in Maine Coon cats[3] and Ragdoll cats with HCM,[4] although modifier genes or environmental triggers have been suspected in the development and progression of the disease. American shorthair cats and Persian cats were also reported to have a familial incidence of HCM.

HCM is characterized by left ventricular (LV) hypertrophy with diastolic dysfunction. The pattern of hypertrophy has been known to be heterogeneous; symmetric hypertrophy, asymmetric

hypertrophy (the septum more hypertrophied that the free wall or vice versa), apical hypertrophy and so on. Diffused septal hypertrophy was reported as the most common type of HCM classified by echocardiogram.[5] However, the results may not represent the prevalence in the whole cat population because the cats underwent echocardiographic examination due to cardiac murmur, gallop, arrhythmia or showing clinical signs. Septal hypertrophy was usually taken to be accompanied with LV outflow obstruction (so-called hypertrophic obstructive cardiomyopathy; HOCM), which resulted in cardiac murmur. It was reported that about 64% and 33% of HCM cats had cardiac murmur and gallop, respectively.[6] Therefore, cats with HCM but no murmur or gallop may not be able to be diagnosed as HCM until obvious clinical signs break out in the relatively severe stage.

Echocardiography is usually necessary to confirm the morphological and functional assessment of LV. Echocardiography can demonstrate not only the morphological changes of LV but also left atrial dilation, systolic anterior motion (SAM) of mitral valve, diastolic dysfunction, mitral regurgitation, etc. In order to make a diagnosis, it is important to rule out other systemic disorders resulting in LV hypertrophy such as systemic hypertension most commonly due to chronic kidney disease and hyperthyroidism. In addition, the hydration status of the patients should be considered in order to interpret the echocardiographic findings.[7]

It is sometimes difficult to know the etiology of LV hypertrophy. Regional myocardial function assessed by strain analysis may be able to differentiate the etiology of LV hypertrophy.[8,9] In addition, tissue Doppler imaging (TDI) would be a useful modality to make an early diagnosis in cats with suspected HCM[10,11] and to evaluate diastolic function.[12,13]

Affected cats are at risk of sudden death, development of congestive heart failure (CHF) and systemic arterial thromboembolism (ATE). The factors associated with poor prognosis were reported; CHF, high heart rate, arterial thromboembolism, marked left atrial dilation, severe LV hypertrophy, absence of SAM, low fractional shortening, young age, thoracocentesis, etc.[5,6,14] Sudden onset of clinical signs in cats with cardiomyopathy is not uncommon, although the cats may have subclinical disease for a long time.

The evidence for the choice of treatment for feline HCM is limited. Previous studies failed to demonstrate the obvious benefit of an early therapeutic approach to subclinical HCM.1[5-17] Angiotensin converting enzyme inhibitor showed some benefits in cats with symptomatic HCM in two non-controlled investigations.[18,19] Fox et al conducted a multicenter feline chronic heart failure study, and preliminary results were orally presented (unpublished). Cats with CHF due to HCM were divided into 4 treatment groups (furosemide, furosemide+atenolol, furosemide+diltiazem, furosemide+enalapril), and some favorable results were seen in a group of cats with furosemide

plus enalapril. However, results should be interpreted with caution since there were several limitations. Thromboembolic complications need several therapeutic considerations such as analgesics, thrombolytic therapy, anticoagulants, management of CHF and reperfusion syndrome if present.

Other forms of cardiomyopathies were also documented in cats. Restrictive cardiomyopathy (RCM) is characterized by no obvious morphological LV changes with impaired diastolic function, and is less commonly seen than with HCM. Dilated cardiomyopathy (DCM) is a more common disease in dogs, although it used to be a common disease in cats until an association was reported between taurine deficiency and reversible myocardial failure, mimicking primary DCM.[20] DCM could also be the end-stage of HCM, called dilated HCM.[21] Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a heart muscle disorder characterized by supraventricular and ventricular tachyarrhythmias, sudden cardiac death, and in some patients, CHF.[22] Some myocardial disease that does not fit into any category or one category of cardiomyopathy is classified as unclassified cardiomyopathy. Moderator band cardiomyopathy is a rare and unique condition characterized by thickened large false tendon across the mid-LV.[23] These cardiomyopathies are less common in cats, and thus, unlike HCM, their etiology and clinical characteristics are not well known.

Canine cardiomyopathy

Dilated cardiomyopathy (DCM) is a most common form of cardiomyopathy in dogs, especially large-breed dogs.[24-26] Doberman Pinscher, Newfoundland, Great Dane, Boxer, Portuguese water dog, Irish wolfhound, and Cocker spaniel etc. are among the breeds known to be predisposed to DCM.

Several previous reports indicated breed-associated differences in natural history, clinical course and outcome among dogs with DCM. High prevalence of ventricular tachyarrhythmia was reported in Doberman with DCM. Ventricular tachyarrhythmia is usually observed when animals develop more severe heart failure, however, a high incidence rate of ventricular ectopy was reported in Doberman with asymptomatic stage.[27] Boxer is well known to be predisposed to ARVC, characterized by manifesting ventricular tachyarrhythmia originating from the right ventricle. Some percentage of affected dogs will progress to DCM. ARVC in Boxers was suspected to be caused by defects and dysfunction in their ryanodine receptors and calstabin abnormalities.[28]

Investigation of the molecular basis for the disease has been attempted by several investigators. Since DCM has been known as a familial disease with the breed-specific characteristics described above, some of the genes responsible for the human DCM were assessed in dogs. However, most of

the study failed to identify a causative mutation 29-34 except for one report.[35]

By revealing the genetic basis of DCM, a new approach to treatment such as gene therapy may possibly provide favorable outcomes for this fatal disease in future.

Because of limited population of giant/large breed dogs probably due to housing circumstances in Japan, DCM is less commonly seen, compared with the western countries. In this lecture, feline cardiomyopathy will be more focused on.

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