Canine Dilated Cardiomyopathy

A Case Report

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Class of 2018

Clinicopathologic Conference

October 27, 2017

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Introduction

Diseases of cardiac muscles are one of the most common causes of cardiac failure in dogs. Heart failure results from degenerative changes, including chamber enlargement and decreased myocardial contractility.[6] Dilated cardiomyopathy (DCM) is a disease of heart muscle characterized by systolic dysfunction and ventricular chamber enlargement .[4] DCM results in clinically important morbidity and mortality[5], including congestive heart failure (CHF), and sudden death secondary to ventricular arrhythmias.

Idiopathic (primary) dilated cardiomyopathy is the most common etiology; however, DCM can be secondary to a number of infectious causes (trypanosomiasis), nutritional deficiencies (taurine), hereditary traits, and drugs (doxorubicin).[9]

Etiology

Primary dilated cardiomyopathy, also known as idiopathic dilated cardiomyopathy, is the most common form of DCM seen in canine patients.[8] Breeds with suspected genetic predisposition to the development of DCM include Doberman Pinschers, Irish Wolfhounds, Great Danes, German Shepherds, Newfoundlands, Cocker Spaniels, and Portuguese Water dogs.[9] Familial DCM in Portuguese water dogs is reported to have an autosomal recessive mode of inheritance, and clinical signs occur in patients typically < 1year of age.[11] The mode of inheritance in Irish Wolfhounds is thought to be autosomal-dominant.[12]

In some cases the causative mutation has been suggested[10], whereas in most cases the exact underlying mutation remains elusive[11-14]. Many studies today are centered around identifying specific genes that predispose patients to DCM. Further investigation

of genetic markers for canine DCM may lead to earlier diagnosis and treatment of DCM.[2] Initiating treatment for these patients earlier in the occult phase of DCM may lead to better prognosis and quality of life.

There are also many forms of secondary DCM, including genetic, toxic, infectious, nutritional, and metabolic etiologies.[9] It is important to determine the underlying cause of a patient's DCM as it can affect the treatment and prognosis. Toxic and infectious causes of canine DCM are important because if the underlying cause is identified it may either be prevented or reversed, or at least treated more specifically. The main toxic cause of DCM in canine patients is associated with certain chemotherapeutic agents.[2] Anthracyclines, such as doxorubicin, can lead to several different forms of cardiac dysfunction including DCM.[2] The toxicity is dose dependent and can usually be prevented by monitoring cardiac function via echocardiography before administration of these drugs.[9] Infectious myocarditis is not well understood in the canine patient and is usually associated with viral etiologies.[9] However, one known infectious cause of myocarditis is Chagas disease.[2] This disease caused by *Trypanosoma cruzi* leads to three different types of myocarditis: acute, intermediate, and chronic.[9] The chronic form is associated with DCM in canine patients.[9] Nutritional cardiomyopathy has been reported in a number of breeds on urolytic diets (Hills Prescription Diet u/d) [15], and in cases of taurine deficiency. Reports also exist of a carnitine-responsive cardiomyopathy in boxers.[16]

Pathophysiology

Regardless of the cause of DCM, the overall pathophysiology of disease is similar. The primary morphologic change in DCM is ventricular eccentric hypertrophy, which occurs as a result of systolic deficiency in the heart.[4] As the ventricles lose their contractility, they eject less blood and decrease the stroke volume.[9] The body responds to the decreased stroke volume by trying to increase the preload of the ventricle.[9] Continuous remodeling of the ventricle leads to thinning of the walls and worsened contractility of the heart.[4] As the cardiac output continues to decrease, renal blood flow also decreases, which activates the renin-angiotensin-aldosterone system (RAAS).[4] This system causes fluid retention at the level of the kidneys which leads to further increases in preload.[5] As the preload continues to increase, and the contractility continues to worsen, the heart is not able to push enough of the fluid through the circulatory system.[6] This leads to congestive heart failure (most commonly left-sided), respiratory distress, and pulmonary edema.

Histopathology of affected patient's hearts reveals two distinct histologic types of canine dilated cardiomyopathy.[2] The first and most common type of DCM seen via histopathology is the attenuated wavy fibre type.[9] This type of DCM is characterized by thin myocytes that have a wavy appearance and are separated by clear edematous fluid.[2] This histologic change is very sensitive and specific for DCM because it is not seen in specimens of animals with cardiac chamber dilation caused by a disease other than DCM.[2] The other type of DCM seen on histopathology is the fatty infiltration-degenerative type that is mainly seen in Boxers.[9] The changes seen in this type include degeneration of the myofibers, myocyte atrophy, and fibrosis with fatty infiltrates.[2]

History & Signalment

The most common signalment for a patient with DCM is a middle-aged, large or giant breed dog.[6] Male dogs are also more likely to develop DCM than female dogs of the same breed and age.[6] DCM is classified as an adult onset genetic disorder[5], so most patients that present with this condition will be middle aged to older.[5] DCM is characterized by a prolonged asymptomatic phase (occult DCM), which may last from 2-4 years. Once clinical signs of DCM develop it is referred to as overt DCM. In the occult stage of DCM, cardiomegaly is seen, particularly left ventricular enlargement, and arrhythmias may be noted (atrial fibrillation). Clinical signs result from left ventricular dysfunction, arrhythmias, or congestive heart failure. Owners may notice signs of cardiovascular compromise such as shortness of breath, weakness, exercise intolerance, and syncope.[6] If DCM is severe enough and has led to congestive heart failure, signs such as coughing, ascites, and dyspnea may be noted.[5] In animals with DCM, sudden death may occur before clinical signs are reported, typically associated with ventricular arrhythmias.[9]

Physical Examination

Just like the presenting complaints, the physical exam of a patient with DCM can vary, and patients with occult DCM may have no physical exam abnormalities.[2] In patients with physical examination abnormalities, decreased cardiovascular output can lead to pale mucous membranes and delayed capillary refill time.[5] Cardiac auscultation may reveal a low grade left systolic heart murmur, or an audible third heart sound[2] (i.e. gallop rhythm) due to increased left ventricular filling pressure. Heart sounds may also

appear decreased due to impaired ventricular contractility. Irregular heart rates are commonly found because of either premature ventricular contractions or atrial fibrillation.[9]

Weak femoral pulses may be palpated due to reduced contractility or due to arrhythmias. If a patient develops left-sided CHF, crackles may be heart on thoracic auscultation and tachypnea may be present. If a patient also develops right-sided CHF, jugular vein distension and/or enlargement of the spleen or liver may be appreciated on abdominal palpation.[6]

Diagnostic Approach/Considerations

A complete and thorough physical exam is an important basis for the diagnosis of DCM in the canine patient. Tachycardia, arrhythmias, and signs of congestive heart failure are all physical exam findings that, along with a patient's signalment, can help make a presumptive diagnosis of DCM.[2] The workup for a definitive diagnosis of DCM includes a minimum database and diagnostic imaging including radiographs and echocardiography.[9] ECG and BP are important, as well.

Blood work such as a complete blood count and chemistry profile are usually performed but not necessary for the diagnosis of DCM. The most common changes seen on these tests are pre-renal azotemia due to poor renal perfusion, hyponatremia, hypokalemia, and mild elevations in liver enzymes due to congestion of the liver.[2] Complete blood count may be consistent with a stress leukogram.[2] Electrocardiography (ECG) can also have various different findings in dogs with DCM. Sinus arrhythmias are a common finding and atrial fibrillation is sometimes seen in giant breeds.[2] Twenty-four

hour Holter monitoring can be a useful tool in detecting DCM while it is still in the occult phase, especially in boxers and Doberman Pinschers.[2] Several studies have shown that the presence of greater than fifty ventricular premature contractions, or any couplets or triplets, within twenty-four hours is thought to predict future DCM in canine patients.[9]

Echocardiography is the gold standard for a definitive diagnosis of DCM.[9] Echocardiography will allow cardiac function and structure to be assessed and for other cardiac diseases to be ruled out as well. The main functions of echocardiography in the diagnosis of DCM include assessing chamber size and myocardial function.[9] All chambers may be dilated, but the left ventricle and atrium are usually the most affected.[2] Normal chamber size differs among species and the cut-off for diagnosing dilation is still under debate. In human medicine, the cut-off is at greater than 112% the size of a normal chamber size for a person of that height and age.[2] Systolic myocardial function is most commonly assessed by fractional shortening measurement.[9] This is a measure of the difference between end diastolic volume and end systolic volume, and a value of less than 20-25% in dogs is considered abnormally low.[2] Mitral valve insufficiency can be seen in DCM cases because the dilation of the left ventricle keeps the valve leaflets from being able to close completely. Mitral regurgitation may cause falsely decreased fractional shortening, so mitral valve function should be assessed before making a diagnosis of DCM.[9]

Radiographs are not as useful of a diagnostic test when a patient is suspected to have DCM. However, chest radiographs may reveal signs of congestive heart failure secondary to DCM or other cardiac abnormalities.[9] Changes that can be seen on radiographs in patients with DCM include general cardiac silhouette enlargement,

globoid heart, pulmonary edema, pleural effusion, or distended pulmonary vasculature.[9] A globoid heart may be confused with pericardial effusion and should be differentiated via the use of ultrasound.[5]

Certain blood tests can be used to help diagnose and monitor progression of DCM in canine patients. One of these tests is a test that measures for proBNP, an enzyme that indicates active myocardial stretching.[17] Over the past few years several studies have been done to determine the clinical utility of pro-BNP snap ELISA tests in diagnosing DCM in patients without overt clinical signs.[17] One study showed that elevated pro-BNP levels in Dobermans predisposed them to development of occult DCM.[17] Another test that can be used is blood taurine levels, especially in patients with unbalanced or unusual diets.[15] Taurine deficiency has been proven to predispose patients to the development of occult DCM.[15]

Treatment / Management

Treatment of canine DCM varies from case to case and is dependent on how advanced the disease is at time of diagnosis. Angiotensin-converting enzyme (ACE) inhibitors are a mainstay of treatment in both acute and chronic cases of DCM.[6] These medications are indicated once any chamber enlargement is noted. ACE inhibitors such as enalapril are effective in treating heart failure because they decrease the activation of the RAAS system.[6] The mechanism of action of these drugs is involved in inhibiting the conversion of angiotensin I to angiotensin II.[9] Enalapril is dosed at 0.25-0.5 mg/kg every 12 hours.[7] The most common side effects include GI symptoms such as vomiting and diarrhea or azotemia.[6]

Inotropic therapy is another cornerstone medication for the treatment of DCM and accompanying congestive heart failure. Inotropes are used to increase the contractility of the heart and are important in diseases that affect the myocardium of the heart, such as DCM.[9] Digoxin is an inotrope that has been used classically for treatment of DCM, but recently, pimobendan has become the new first choice of inotropes for these patients.[7] Pimobendan is a phosphodiesterase III inhibitor that improves contractility of the heart and also has vasodilating effects.[6] The dosage for pimobendan is 0.15-0.3 mg/kg every 12 hours.[6] Digoxin is still used sometimes in conjunction with pimobendan because of its anti-arrhythmic properties and its neurohormonal modulation.[9] The dose for digoxin is usually 0.22 mg/m^2 and should be based on lean body weight.[7] Digoxin can be toxic in canine patients, especially the Doberman Pinscher, and can either cause cardiac or non-cardiac toxicity.[9] Therapeutic drug monitoring of digoxin is required.

Diuretics are commonly used in congestive heart failure patients and this holds true in patients with DCM. Loop diuretics, usually furosemide, are an important therapeutic because they retain water in the renal tubular lumen and decrease the fluid buildup in the heart and other organs.[6] Furosemide is the most commonly used and has a very wide dosing range.[9] The usual starting dose is around 1-2 mg/kg every 12-24 hours but needs to be used at the lowest possible dose for chronic therapy.[6] In acute congestive heart failure, furosemide can be used more aggressively in order to stabilize a patient because the toxic dose is 3-4x the therapeutic dose.[6]

Spironolactone is the last of the main therapeutic drugs used in patients with DCM and secondary congestive heart failure. The mechanism of action of spironolactone is a potassium-sparing diuretic that works at the level of the distal convoluted tubule and

collecting duct. Spironolactone is considered a weak diuretic but may have synergistic effects while used alongside a loop diuretic. This drug also inhibits aldosterone and decreases myocardial fibrosis. The dose for canine patients is 2-4 mg/kg every 12 hours.

Treatment of canine DCM is centered around controlling clinical signs and slowing the progression of disease. The disease process is irreversible, so owner education is an important part of managing a case of DCM. After all diagnostics are performed and a treatment plan is implemented, it is important to recheck the patient in a week to reassess.[2] Blood work should be performed at this time to check for medication side effects and an electrocardiogram (ECG) can be performed to check for any arrhythmias.[9] Owners should be educated about clinical signs of heart failure to watch for at home including labored breathing, elevated resting respiratory rate (over 35 breaths/minute), syncope, and severe lethargy.[6] Once stable, echocardiography should be rechecked every 3-6 months depending on the patient.[9]

Prognosis

Prognosis historically in patients with DCM has been guarded to poor, and average survival time was around 3 months.[2] However, with the implementation of newer drugs, particularly pimobendan, and earlier detection, recent studies have shown a survival rate as high as 12-24 months.[9] Assessing the progression of a patient's DCM is essential to deciding the prognosis of an individual patient because several diagnostic findings are negative prognostic indicators.[1,3] One study showed that decreased LVDs (left ventricular diastolic)-index (a measure of LV contractility), presence of pulmonary edema, presence of VPCs, Great Dane breed, high plasma creatinine, and low plasma

protein were all considered negative prognostic indicators in patients with DCM.[3] Positive prognostic indicators include no signs of CHF at the time of diagnosis and good response to initial medical therapy.[2]

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