Her Heart Grew Three Times in Size

Hypertrophic Cardiomyopathy in a Cat

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Introduction

Hypertrophic Cardiomyopathy (HCM), is the most commonly diagnosed cardiac disease in cats[1]. In a retrospective study of 287 cats with heart disease, 67.6% were diagnosed with HCM. Cats who present with HCM may be as young as 6 months of age to as old as 7 years of age. Males tend to develop the disease earlier and more severely than females. In the same study with 287 cats, 65.8% of those diagnosed with HCM were male[4]. The most common breeds associated with hypertrophic cardiomyopathy include Maine Coons, Ragdolls, and Sphinxes, where it is believed to have a genetic component[8].

Cats with mild HCM can have no clinical signs, but cats in which the disease has progressed may present with respiratory distress, a grade 2-3 systolic murmur, and a gallop rhythm. Cats with HCM may also present with a peracute onset of paresis or paralysis of the hindlimbs due to thromboembolism. The most drastic consequence of HCM is sudden death[8]. Cats presenting with clinical signs of heart failure tend to have a poor prognosis and most die within 8 months[6]. However, most cats with HCM remain asymptomatic, and heart disease is only detected as an incidental finding during routine screening or necropsy[1].

History and Presentation

Khloe was an approximately 5-year-old, female spayed, red and white domestic longhaired cat who presented to MSU-CVM emergency service on 7/23/19 for increased respiratory effort. She initially presented to her referring veterinarian, who took radiographs that revealed fluid within her thoracic cavity. Lasix was administered and she was referred to MSU-CVM if she did not improve.

Khloe presented to MSU-CVM ICU quiet and dull. Her body condition score was ideal at 4/9, and she weighed 6.4 kg. She had a rectal temperature of 100 degrees Fahrenheit. Khloe was tachycardic with a heart rate of 240 beats per minute and had muffled heart sounds. She had an increased respiratory effort with a respiration rate of 60 breaths per minute. She had a mild skin tent and was estimated to be 5% dehydrated. Khloe had a pendulous abdomen. On tFast there was fluid found in the pleural cavity and an enlarged left and right atrium. On aFast, there was fluid in the abdomen. A thoracocentesis was performed, and 60 mls of fluid was removed from her chest. A NOVA was also performed which revealed a severe metabolic acidosis. Due to her bloodwork findings, Khloe was moved to the oxygen cage overnight. She was maintained overnight on butorphanol (0.2mg/kg IVQ4), Cerenia (1mg/kg IVQ24), Lasix (1mg/kg IV once), enalapril (0.4mg/kg POQ24), and clopidogrel (1/4 tab per cat Q24). The next morning Khloe remained quiet and dull and oxygen dependent. She became hypothermic with a temperature of 91.5 degrees F. She was also ataxic and non-weight bearing in her hind end but was non-painful. Due to her poor prognosis, humane euthanasia was elected and her remains were submitted for necropsy.

Necropsy Findings

On physical exam, Khloe's forelimbs were both shaved over the cephalic veins, the abdomen was distended, and a fluid wave was appreciated.

The thoracic cavity contained approximately 50-100 ml of clear red tinged fluid. The lungs were collapsed and small, diffusely dark red to purple, and heavy and wet. The caudal vena cava and aorta were diffusely enlarged. Approximately 5-10 ml of red tinged fluid was present in the pericardial sac. The heart was diffusely enlarged and weighed 26.7 grams. A 5cm x 2cm pale to tan sharply demarcated oval zone of myocardium surrounded by a 2mm-3mm zone of dark red

to purple hyperemia was present on the right ventricle. There was moderate subcutaneous edema over the jugular region.

The abdominal cavity contained approximately 250-350 ml of yellow tinged clear fluid. The liver was enlarged with rounded margins and had a diffuse reticulated pattern across all lobes.

Histopathology revealed multifocal and locally extensive severe chronic myocardial fibrosis with myocyte degeneration as well as diffuse severe acute left ventricular papillary muscle necrosis. The alveoli of the lungs were filled with homogenous eosinophilic fluid and fibrin, consistent with pulmonary edema. Within the liver, there was diffuse paracentral, moderate acute hepatocellular degeneration.

Pathophysiology

Familial, or primary HCM, is associated with Maine Coons and Ragdolls. In both Ragdolls and Maine Coons, it is caused by genetic mutations in the cardiac myosin binding protein C, referred to as the A31P mutation in Maine Coons and the R820W mutation in Ragdolls. This mutation is incorporated into sarcomere in both homozygous and heterozygous individuals[8]. However, the penetrance of this mutation tends to be much lower in those individuals who are heterozygous, so the incidence and severity of disease is decreased. In an echocardiographic study of 332 Maine Coon cats, HCM was diagnosed in 50% of cats homozygous for the A31P mutation, while only 6% of heterozygous cats were diagnosed with HCM[5].

The A31P mutation affects the ability of the sarcomeres of the cardiomyocytes to contract and relax, leading to increased systolic stress on the sarcomeres. The heart then tries to

replace the affected sarcomeres by producing new sarcomeres. However, if a mutation is present, the ability of the heart to produce a normal sarcomere is decreased. If the new sarcomere is abnormal as well, more sarcomeres will be produced until there is a normal one[8]. This causes severe concentric hypertrophy of the chambers of the heart, especially the left ventricle. The thickening of the left ventricular walls leads to decreased lumen size and reduces adequate filling during diastole. Therefore, stroke volume is decreased. These factors lead to enlargement of the left atrium and, subsequently, blood backs up into the pulmonary vein. The increased blood volume increases hydrostatic pressure and causes fluid to leak out of the blood vessels, resulting in pulmonary edema as well as pleural effusion. Additionally, hypertrophied, anteriorly displaced papillary muscles may be present, leading to displacement of the chordae tendineae and anterior leaflet of the mitral valve into the left ventricular outflow tract (LVOT). This is referred to as systolic anterior motion (SAM) of the mitral valve and can result in a LVOT obstruction, which further increases the pressure inside the left ventricle, worsening the hypertrophy[9]. If the disease becomes severe enough, right sided heart failure may also be observed. Passive congestion occurs in the caudal vena cava and can cause ascites as well as hepatomegaly with secondary centrilobular congestion[8].

Thromboemboli are a devastating sequelae to HCM. The inadequate filling of the heart can lead to turbulent blood flow, which can predispose the blood to clotting. Clots most commonly develop in the left atrium or auricle[9]. They most commonly travel with blood flow and lodge in the aortic bifurcation, occluding adequate flow to the hind limbs and resulting in hindlimb paresis or paralysis[8]. However, in this case, a thromboembolism not only lodged within the aortic bifurcation but also within the coronary arteries. The myocardium supplied by the coronary artery became hypoxic and resulted in a myocardial infarct.

It is important to note that left ventricular hypertrophy can also occur secondary to several diseases, such as aortic stenosis, systemic arterial hypertension, hyperthyroidism, and acromegaly**.** Generally, if the underlying disease is treated, the cardiomyopathy will improve[8]. However, this cat did not show any signs of these diseases, and the changes seen involved the entire heart, so it is more likely that her HCM was primary rather than secondary. Additionally, the irregular branching of the myocytes seen histologically in Khloe's case also suggest primary HCM rather than secondary.

Diagnostics

If Khloe's owners had elected to continue her treatment and workup, several diagnostic tests would have been performed to confirm and diagnose HCM. The most common and definitive method of diagnosis is echocardiography. Features such as ventricular wall thickness, valvular anatomy, and turbulent blood flow can be evaluated with an echocardiogram. An end diastolic ventricular wall that is greater than 6mm in thickness is defined as left ventricular concentric hypertrophy. It is important to note that measurement of the ventricular wall is best done using 2-dimensional echocardiography. It is also important to note that measurement of the left atrium is also critical in cats, as the left atrium can dilate due to increased diastolic filling pressure and identifies a significant risk of developing congestive heart failure or arterial thromboembolism. A left atrial diameter of greater than 16mm or a ratio of left atrial diameter to aortic diameter of greater than 1.5 is considered abnormal. Another important aspect of the echocardiogram of cats with HCM is identification of systolic anterior motion of the mitral valve, a hallmark pathologic feature of HCM. Characteristic double turbulent jets of mitral regurgitation and turbulent systolic ejection blood flow arising from the same location in the LVOT can be visualized using color-flow doppler[6].

Another diagnostic tool that can be utilized for diagnosis of HCM is thoracic radiographs which are critical for evaluation of congestive heart failure and can be used to monitor disease progression and response to treatment[6]. However, cats with mild or moderate HCM may have no radiographic evidence of disease, so normal cardiac size on radiographs does not rule out HCM. Left atrial enlargement can be visualized as a bulge on a dorsoventral or ventrodorsal projection at the 2-3 o'clock position. Additionally, cats may have evidence of pulmonary edema or pleural effusion[7].

A third diagnostic tool used to diagnose HCM and to monitor the prognosis of myocardial disease is serum cardiac troponin 1 and N-terminal pro-B type natriuretic peptide (NT-proBNP). Natriuretic peptides counter-regulate the renin-angiotensin-aldosterone system and are produced specifically by cardiac atriums that are stretched or overfilled. Natriuretic peptides increase the heart's diastolic function by promoting natriuresis, blood flow to the kidneys, diuresis, and vasodilation[3]. An ELISA SNAP test is available and is useful to differentiate between heart failure and primary respiratory disease in cats[6]. It is also useful in screening for cardiac disease in asymptomatic cats, with a high sensitivity and specificity. Cardiac troponin 1 is a myocardial protein that is increased in patients with myocardial necrosis, indicating active myocardial damage[8]. While cardiac troponin has been shown to be a sensitive biomarker for cats with heart disease, it does not distinguish cats that are symptomatic from asymptomatic, so its use as a screening test is limited[6]. Additionally, cardiac troponins are more effective to evaluate ischemic lesions, which are not always present in cats with HCM[3].

Upon necropsy, several characteristic lesions are indicative of HCM. The left ventricular lumen is significantly reduced, and the free wall is thickened to greater than 6mm[1]. However, as the disease progresses, cardiomyocytes are lost, and the ventricles may become thin and fibrotic.

Most cats will succumb before this stage of disease[6]. Additionally, the left atrium is moderately to severely dilated. Frequently, the right atrium is also enlarged, and the right ventricle hypertrophied. Affected animals will also have an increased absolute and relative heart weight. Normal cats have an average relative cardiac weight of 4.8g/kg, while cats affected with HCM have an average cardiac weight of 6.4g/kg. Cats affected with HCM may also have an absolute cardiac weight of greater than 20 grams. Furthermore, in more than half of necropsied cases, pulmonary edema is present and in twenty percent of cases, pleural effusion is also present. Histopathologically, the hallmark feature of HCM is myofiber disorientation which is visualized as a bizarre, disorganized cellular architecture. Myocytes are hypertrophied and have large, rectangular hyperchromatic nuclei. Replacement fibrosis of small intramural coronary arteries is also commonly present[1].

Treatment and Prevention

Treatment of asymptomatic cats is controversial and can depend on the degree of hypertrophy of the left ventricle, severity of left ventricular outflow tract obstruction in cats with systolic anterior motion of the mitral valve, and the left atrial size. The most utilized medication for these patients is either a calcium channel blocker or a beta blocker. Beta blockers, while worsening early ventricular relaxation, also slow the heart rate and help to prolong diastole to increase left ventricular filling and stroke volume. Beta blockers can also help in reducing LVOT due to SAM of the mitral valve. Calcium channel blockers work by improving early diastolic relaxation by reducing isovolumic relaxation time[6].

In symptomatic cats presenting with chronic heart failure, the most lifesaving treatment of choice is furosemide to reduce pulmonary edema. The initial dose should be between 2-4mg/kg and can be repeated within 1 hour if given intravenously, or 2 hours if given

intramuscularly. Cats presenting with signs of respiratory distress should be placed in an oxygen-enriched environment and a butterfly catheter should be used to perform thoracentesis to look for pleural effusion as soon as possible[8]. ACE inhibitors may also be given to decrease pulmonary edema[6]. Pimobendan, while initially considered contraindicated in cats with HCM, has not shown to worsen hypertrophy or clinical signs of cats with a LVOT. Pimobendan can be beneficial in these patients due to its positive inotropic effects, increasing vasodilation[2]. Lastly, since patients with HCM are prone to intracardiac thrombus formation, anticoagulants such as clopidogrel may be administered to help prevent incidence of thromboemboli[6]. Prognosis of HCM is highly variable and depends on clinical presentation and echocardiographic findings. Cats with no clinical signs and mild disease have a good long term prognosis[8]. However, once heart failure and significant left ventricular hypertrophy develops, the prognosis worsens, and they typically succumb within 3 months to 1 year[6].

Prevention of HCM focuses on removing affected individuals from breeding pools. Echocardiographic screening is used in an attempt to identify affected cats. However, most breeders perform this at a young age, before cats would have evidence of HCM, so the utility of this approach is limited. Additionally, genetic testing is available for Maine Coons and Ragdolls. If a cat is homozygous for the mutation, it is recommended that the cat not be bred, and that heterozygous individuals should only be bred if they are an outstanding example of the breed. Even in this case, these individuals should only be bred once[7].

In Khloe's case, she was probably born with the genetic mutation to cardiac myosin binding protein C and her HCM became progressively worse as she aged, until she developed left sided and eventually right sided congestive heart failure. She developed pulmonary edema and pleural effusion, and thromboemboli due to turbulent blood flow lodged in the coronary

arteries perfusing her right ventricle. A myocardial infarct occurred, affecting the right ventricle's ability to contract, and worsening the already present right sided congestive heart failure. Even if her owners had pursued treatment, her prognosis would have been guarded, and it is unlikely she would have lived much longer.

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