

MYXOMATOUS MITRAL VALVE DISEASE IN A SHIH TZU DOG

Y.B. Teoh and K.H. Khor*

Faculty of Veterinary Medicine, University Putra Malaysia, UPM Serdang, Selangor, Malaysia

SUMMARY

An 11-year-old intact male Shih Tzu dog was referred to the University Veterinary Hospital (UVH) with history of coughing and laboured breathing. Auscultation revealed that the dog had a left systolic heart murmur grade V/VI at the base of the heart. Radiography showed findings of cardiomegaly and pulmonary oedema. Echocardiography findings revealed that dog has a myxomatous mitral valve disease. The mitral valve was severely thickened and prolapsed into the left atrium. Congestive heart failure (CHF) was treated with an angiotensin converting enzyme (ACE) inhibitor and diuretic. An anti-mucolytic agent was prescribed as a symptomatic treatment for the coughing that could be due to mild bronchitis. Dog did not respond well with treatment as the frequency of cough was not reduced and the duration was longer each time. Pimobendan was then added on to the initial treatment and there was a tremendous improvement seen from the patient after that. Episodes of productive cough were noticed greatly reduced and dog was much more active at home post two weeks of ACE inhibitor, diuretic and dual-acting inodilator. We successfully maintained the dog with minimal coughing episodes. However, the prognosis is moderate to poor in this case due to possibilities of refraction towards medications.

Keywords: coughing, echocardiography, heart, lungs, mitral valves, Shih Tzu

INTRODUCTION

Myxomatous mitral valve degeneration (MMVD) is the most common acquired type of canine heart disease. It is referred to as a non-infectious degeneration of heart valves commonly seen in older dogs. MMVD is a manifestation of a process that can affect all heart valves but usually it is detected in the mitral valve. Mitral valves are the most commonly reported valves affected in canine heart disease patient and followed by the tricuspid valves (Kittleston and Kienle, 1998; Vörös *et al.*, 2015).

MMVD can also be termed differently in various literatures such as chronic valve disease, degenerative valve disease and mitral valve endocardiosis (Petric, 2015). The disease is sequelae of a chronic degeneration of the mitral valves, for which the valves become thicker with irregular/nodular surface. The structural changes impede the valvular function to form a tight seal between the atrium and ventricle during cardiac contraction (Kittleston and Kienle, 1998). When mitral valves failed to close tightly, the blood flowing to the ventricle post atrial contraction will back flow to the left atrium, causing a regurgitation (MacGregor, 2014). Chronic regurgitation would induce enlargement of both the left atrium and ventricles. The compensatory mechanism of the heart due to increased leaked volume over time may cause pressure to build up in the left atrium, transmitting an upstream to the lungs leading to pulmonary oedema, which is a sign of congestive heart failure (CHF) (MacGregor, 2014). MMVD affects primarily small breed dogs later in life but can affect larger breed dogs. Breeds reported to be predisposed to MMVD includes small mixed breed dogs such as Cavalier

King Charles Spaniels, Cocker Spaniels, Pekingese, Dachshunds and also Shih-Tzu (Atkins *et al.*, 2009).

CASE REVIEW

An 11-year-old intact male Shih Tzu dog was referred to University Veterinary Hospital, Faculty of Veterinary Medicine (UVH-FPV) with history of coughing and laboured breathing. The dog had severe increased coughing and labour breathing for 3 months prior to presentation at UVH. The dog was treated with furosemide and benazepril for 7 days by the private veterinarian and the coughing episodes reduced. However, three days prior to presentation at UVH, the dog had relapsed episodes of coughing and laboured breathing. Again, the dog was prescribed with the same drugs and was then referred to the UVH for cardiovascular diagnostic workout.

Upon physical examination, the dog was quiet, alert and responsive. Temperature and heart rate were within normal limits with a body condition score of 2.5 out of 5.0. Vaccination and deworming status were up-to-date. Upon observation, the dog was panting heavily. Dog has severe halitosis due to gingivitis and severe accumulation of tartar built up on the surface of the bilateral molars and pre-molars. Heart auscultation revealed that patient had systolic heart murmur grade V/VI with maximum point of intensity at the left heart base. Further auscultation revealed crackled lung sounds and a productive cough was triggered post tracheal pinch. Thoracic radiograph of the right lateral view (Figure 1A) and dorso-ventral view (Figure 1B) revealed findings of cardiomegaly with the Vertebral Heart Score (VHS) of 11 with tracheal elevated dorsally, with the differential diagnosis of chronic degenerative valvular disease, MMVD, tricuspid endocardiosis and dilated cardiomyopathy. There was an increased opacity of the lung parenchyma from hilar to

*Corresponding author: Dr. Khor Kuan Hua (K.H. Khor);
Phone No: 03 86093926; Email: khkhor@upm.edu.my

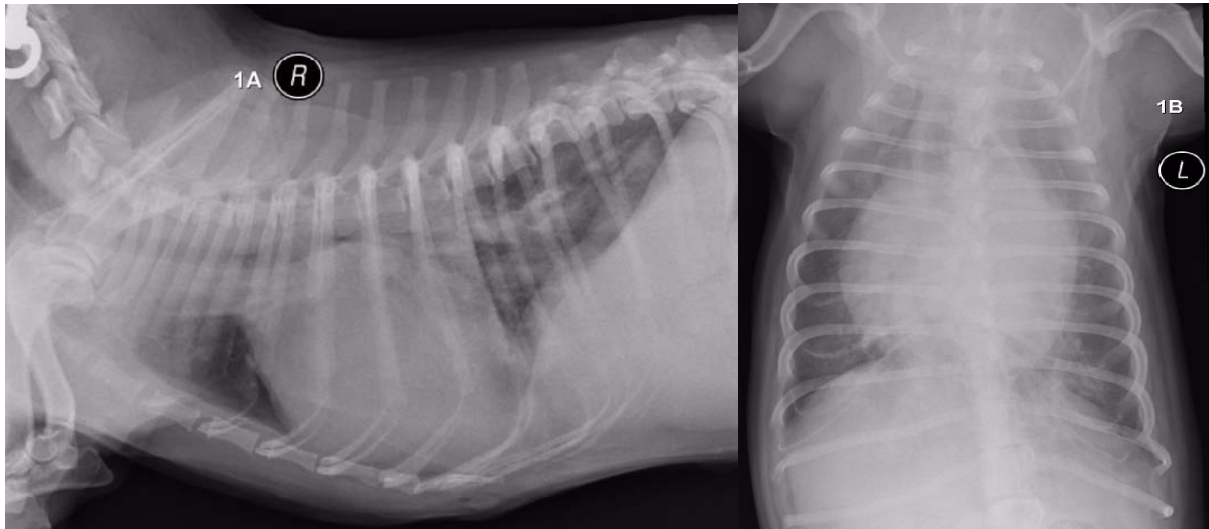


Figure 1A. (On the left) In the right lateral view of the chest radiograph, cardiomegaly was diagnosed with the presence of increased in sternal contact, elevation of trachea dorsally and vertebral heart score (VHS) of 13. Pulmonary oedema was diagnosed with the presence of increase in radio-opacity of caudal lung lobe with mixed interstitial pattern. **Figure 1B.** (On the right) In the dorso-ventral view of the chest radiograph, cardiomegaly was noted with the globoid heart shape and reduced space between the right and left heart outline to the thoracic ribs. There was a bilateral increased in radio-opacity of caudal lung lobe with mixed interstitial pattern suggestive of pulmonary oedema.

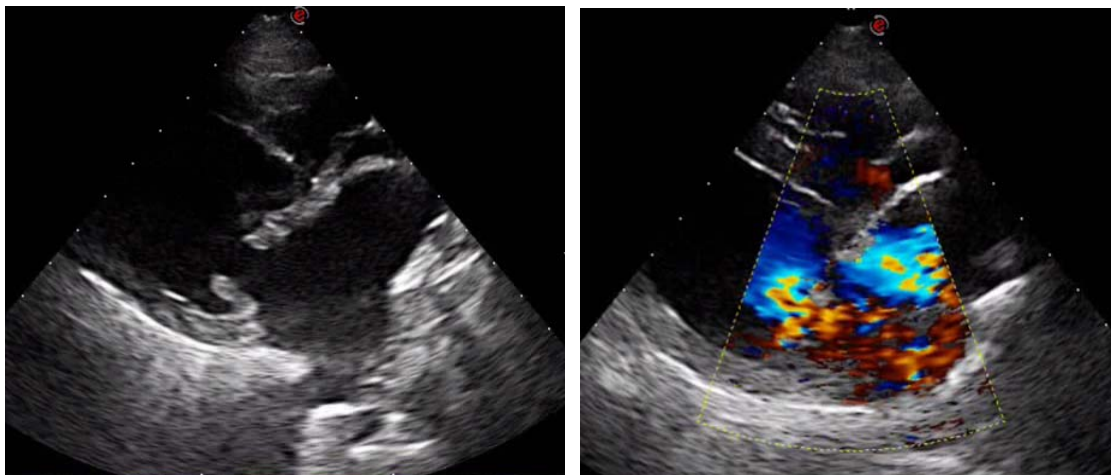


Figure 2. (On the left) Based on echocardiography of the right parasternal long axis view of the heart's image, there was a severe thickening of mitral valves. Upon contraction of the left ventricle, both the anterior and posterior leaflets were closed inadequately and have signs of mitral valve prolapse. (On the right) In the right parasternal long axis view with color flow Doppler of the heart in echocardiography, there were mixing of color seen in both left atrium and left ventricle which indicate a disruption of the blood flow from left ventricle in to the left atrium.

Table 1. Parameters of the left ventricle (LV) were collected from the M-mode of right parasternal short axis view at the papillary muscle level

Parameter	Average result	Reference range	Interpretation
LVID at diastole	47.8	29.0	Dilated ventricular lumen
LVID at systole	24.6	19.0	
LVPW at diastole	8.6	7.0	Thickened ventricular wall
LVPW at systole	11.3	10.0	
La:Ao ratio	2.27	1.60	Increase atrium size

LVID, Left ventricular wall internal dimension; LVPW, Left ventricular posterior/free wall thickness; La, Left atrium; Ao, Aorta

perihilar region of the dorsal lung field with alveolar pattern suggestive of pulmonary oedema. For confirmatory diagnosis of the heart condition, echocardiography was performed. The right parasternal long axis view of the heart image showed thickening of mitral valves, reduced in the proximity of the mitral valvular leaflets upon closure with sign of mitral valve prolapsed into the left atrium (Figure 2).

On the same view, the presence regurgitation of blood flow in both, the left atrium (LA) and left ventricle (LV) was evident using a color flow Doppler (Figure 2). Right parasternal short axis view at point the mitral valve level revealed similar thickening appearance of both, the anterior and the posterior leaflets of the mitral valve. Measurement of the LV were collected from the M-mode of right parasternal short axis view at the papillary muscle level. The abnormal findings were increased of the left ventricular internal dimension (LVID), increased of the left ventricular free wall thickness (LVPW) as well as the left atrium to aorta ratio (La:Ao) (Table 1). Final diagnosis for cardiomegaly in this case was MMVD.

Dog was treated with benazepril hydrochloride (Fortekor[®], Novartis Animal Health, Switzerland) at 0.5 mg/kg, once a day orally for 30 days. Benazepril hydrochloride is an angiotensin converting enzyme (ACE) inhibitor to suppress to renin angiotensin aldosterone system (RAAS) of the juxtaglomerular junction to prevent retention of fluid to control the heart murmur. Pulmonary oedema was treated with furosemide (Rasitol 40mg, Y.S.P. Industries (M) Sdn. Bhd., Malaysia) at 2 mg/kg orally thrice a day for 5 days and then tapered to twice a day for 5 days and then further reduced to once a day for 5 days. Furosemide is a loop diuretic which helps to reduce fluid and salt retention in the body by preventing antidiuretic hormone (ADH) action in the Loop of Henle. A symptomatic treatment of the coughing was prescribed with bromhexine hydrochloride (Bislan 8 mg, Y.S.P. Industries (M) Sdn. Bhd., Malaysia) at 1 mg/kg twice a day for 7 days. It is a mucolytic agent which aids in breaking down mucous in the respiratory tract. After 2 weeks of treatment with furosemide and benazepril hydrochloride, the frequency and the duration of the dog's cough did not improve over time. Hence, an additional medication of pimobendan (Vetmedin[®] Chew 5 mg, Boehringer Ingelheim, United Kingdom), a dual-acting inodilator was prescribed at 0.5 mg/kg (dose split to half morning and half at night) for 30 days in order to promote cardiac contractility and its vasodilation effect. At the same time, dog was also maintained on both benazepril hydrochloride and furosemide during the 30 days treatment.

After 4 weeks of pimobendan oral administration added to the treatment regime, the dog was reported to be very active at home with no signs of exercise intolerance. Episode of cough was only heard during excitement. Echocardiography was repeated and revealed that the parameters of the left side of the heart improved with LV wall thickness, LV lumen size and La:Ao ratio reduced. In the subsequent revisits at 10 weeks and 14 weeks after initial treatment, the dog was reported to coughed once at night. The treatment was continue as a life long regime to control CHF.

DISCUSSION

MMVD is the most common acquired type of heart disease in older dogs (MacGregor, 2014), primarily affecting the small breed dogs later at older age. However, this can affect larger breed dogs as well. Cavalier King Charles Spaniel being the most prominent breed described and diagnosed with MMVD (Beardow *et al.*, 1993, Kittleson and Kienle, 1998). Studies have shown that genetic factors play a large role in causing MMVD, due to the polygenetic inheritance especially in Cavalier King Charles Spaniel (CKCS) and Daschund dogs. Multiple genes which influence this trait that causes MMVD require a reach of certain threshold, for which male dogs have a lower threshold as compared to female; predisposing them to MMVD clinical manifestation at a younger age (Häggström *et al.*, 2004). Although studies have not been conducted extensively in the Shih Tzu dog, this breed has been frequently reported and correlations with the genetic factor was suggested (Petric, 2014). Older, small breed dogs of less than 20 kg have been reported to be more commonly affected with MMVD, but it is not limited to small breed dogs only (Margiocco, 2010). Large breed dogs may be affected by MMVD but disease progression was reported to be much rapid as compared to small breed dogs (Atkins *et al.*, 2009). Hence, dog owners need to be aware and educated about the possible risk upon adoption of breeds mentioned above. Awareness and knowledge of canine heart disease would allowed immediate attention when clinical signs manifest.

MMVD is a manifestation of a process that can affect all heart valves but usually it is detected in the mitral valve. In a normal condition, the LA is the chamber that oxygenated blood flows into after passing through the lungs. Blood then passes through the mitral valve into the LV and gets pumped out into the body circulation. The mitral valve closes when the LV contracts and thus preventing blood from flowing back into the LA. An unaffected mitral valve is thin and supple, anchored in place by strands of tissue called the chordae tendinae. The pathophysiology of MMVD have been well described in dogs. MMVD is a process that occurs when the mitral valves becomes thickened. Grossly, the mitral valvular leaflets appears thicker with nodular pattern at the edge of the valvular leaflets. Histologically, the thickening of the spongiosa and the degeneration of fibrosa layer remain as the classical feature of MMVD (Maxie, 2015).

As the degeneration of the mitral valvular leaflet progresses, the abnormal structure will then prevent effective coaptation (closing) of the valves and hence resulting in regurgitation of blood back flowed (leak) into the LA, known as mitral regurgitation. The regurgitation leads to an increase in cardiac work, remodeling of ventricle and finally ventricular dysfunction (Atkins *et al.*, 2009). Clinically, cardiac remodelling will cause ventricular dilatation as well as LV wall hypertrophy. Over time, LA will be dilated due to the progressive backflow of the blood which have worsened and often dogs will not show signs of CHF if the atrium still can contain the regurgitated blood. The exact time course for the clinical sign of CHF varies from patient to patient. The

increasing volume of the leak along with long-term compensatory mechanisms eventually leads to an increase in the pressure within the atrium. The increase pressure in the LA is transmitted upstream to the lungs leading to fluid exuding from the capillaries into the alveoli of the lungs, causing pulmonary oedema (Rozanski *et al.*, 2012). Besides that, the increase of pressure in LA can also happen suddenly if the corda tendinae ruptures and produces a partially unanchored mitral valve, known as mitral valve prolapse (Jeresaty *et al.*, 1985). In this case, we suspected that the corda tendinae was weaken hence the mitral slightly prolapsed into the LA upon closure.

Symptoms of CHF generally do not appear for 3 to 4 years after the diagnosis of heart disease. Often the first outward sign of worsening MMVD is a cough, which was the primary complaint for this patient. Coughs often occurred due to two reasons. In the advanced stage of MMVD, general cardiac enlargement or the increment in LA chamber size may cause the trachea to be elevated dorsally. It was speculated to cause a degree of airway collapse in the trachea, or even contributing to concurrent bronchitis due to severe injury to the lungs and bronchi from the severe coughing (Rush, 2002). Cough in patients with MMVD due to the congestion in the lungs (signs of CHF) requires immediate medical attention. A recent study has documented that rising breathing rates during sleep are likely to be indicative of worsening heart disease. As seen in this case, crackles were heard upon auscultation and findings were consistent with the chest radiograph with the evidence of pulmonary oedema (Rush, 2002). Radiograph of the the thoracic often provides information about the severity of the disease by looking at heart size and are often the definitive means in diagnosing CHF (Atkins *et al.*, 2009).

Systolic murmur with a maximum point of intensity at the left heart base was characteristics of MMVD during cardiac auscultation. A diagnosis of MMVD using echocardiography provides the definitive ante mortem diagnosis and distinguishes MMVD from other murmurs of cardiac causes. The leak in the mitral valve can be detected by colour flow Doppler echocardiography.

Severity or the stages of heart condition can be made based on the Classification of Chronic Degenerative Valvular Disease (CDVD) (Atkins *et al.*, 2009) (Table 2). The patient in this case was classify as Stage C in which the dog showed clinical sign of CHF with evidence of abnormal findings in the radiograph and echocardiography. Some patients have been reported to have life-threatening clinical signs at Stage C but this dog was only presented for excessive coughing and lethargy. Chronic (or home-based) therapy for Stage C patients was recommended based on the consensus which includes prescription of furosemide (1–2 mg /kg q12 hr to 4–6 mg/kg q8 hr orally), ACE-inhibitor (dose depends of the drug used), pimobendan (0.25–0.30 mg/kg q12 hr). Furosemide is a very potent loop diuretic and it acts on the kidneys to help reduce lung congestion by reducing fluid retention. Pimobendan helps the heart work more effectively and has been shown to improve survival in MMVD patients (Boswood, 2016). ACE-inhibitors and spironolactone block deleterious compensatory mechanisms that occur with severe heart disease and have

been shown to prolong survival as well (Lefebvre, 2007). Other medications that are sometimes used in treatment of CHF include hydrochlorothiazide, amlodipine and torsemide (de Madron, 2011). Often the onset of congestive heart failure is sudden and may require hospitalisation. When patients are hospitalised, patients generally receive supplemental oxygen and intravenous furosemide therapy. This therapy usually allows patients to get past the initial crisis stage and most patients are able to survive the crisis and resume normal life with the assistance of medication. Dietary modification including sodium restriction is useful at this stage to prevent the recurrent of pulmonary oedema (Atkins *et al.*, 2009).

Cardiac cachexia may be of concern, hence maintenance of adequate calorie intake is required. Controlled salt intake is extremely crucial in order to control the clinical signs of CHF. The consensus have suggested that modest restriction of sodium intake in all dietary sources with avoidance of processed or salted food if possible (Atkins *et al.*, 2009). Hence, the patient was maintained with the Royal Canin Cardiac diet which provides vascular support, early renal support, electrolyte balance and cardiac support. Goals in treatment and diet control in MMVD patients are to prolong lifespan and improve quality of life with less stressful episodes as result of clinical signs.

Table 2. The four stages for classification of chronic degenerative valvular disease (CDVD) (Atkins *et al.*, 2009)

Stage	Definition
Stage A	Dogs at risk for CDVD but have no identifiable cardiac structure disorders (i.e. Cavalier King Charles Spaniel, Dachshunds)
Stage B1	Dogs with CDVD, that have never developed clinical signs and do not have radiographic or echocardiographic evidence of cardiac remodelling
Stage B2	Dogs with CDVD, that have never developed clinical signs have radiographic or echocardiographic evidence of cardiac remodelling (i.e. left-sided heart enlargement)
Stage C	Dogs with CDVD and past or current clinical signs of heart failure associated with structural heart remodelling. <ul style="list-style-type: none"> • Dogs presenting heart failure for the first time may present severe clinical signs and may require hospitalisation • These dogs needs treatment to stay free from symptoms of hear failure
Stage D	Dogs with end-stage CDVD and heart failure that is refractory to standard therapy (i.e. furosemide, ACEIs, pimobendan +/- spironolactone)

Generally, it is recommended to review the heart condition every 6-12 months during the pre-clinical phase

of MMVD to monitor progression of the disease. Once clinical signs develop, rechecks may occur more frequently - every 3 to 4 months or as needed depending on patient's condition (Olson, 2014). Rechecks might involve blood tests to monitor kidney function and electrolyte levels as these can be negatively affected by the medications used to treat CHF. Radiograph of the chest are utilised to assess the recurrence of CHF and echocardiograms to monitor heart size and blood flow related to conditions in the heart. Recently, the cardiac biomarker N-terminal pro b-type natriuretic peptide (Nt-proBNP) has been developed as an aid for the diagnosis and monitoring of disease progression in MMVD. It is a species specific cardiac biomarker which have been developed into instant test kits to detect elevated serum NT-proBNP levels, helping clinicians to determine the severity of the disease. As the cardiac muscles stretch during a pressure overload, the peptides will be released, hence being detected by the test kits (Wolf *et al.*, 2013).

The prognosis for newly diagnosed MMVD varies widely. While the average time from when a murmur is first heard until CHF is present is approximately four years, the speed of progression of the disease is difficult to predict for individual patients. Once a patient has developed congestive heart failure, the average survival span is 12-14 months, although this can vary as well (Gompf, 2011). This dog survived 344 days and had enjoyed an extended days of good quality of life. The most frequent cause of death for MMVD patients in congestive heart failure is euthanasia due to either inability to control the signs of congestion such as ascites, coughing, dyspnea, anorexia or weightloss regardless of medication dose given or inability of the patient to tolerate the amount of medication needed to control congestion (Mallery, 1999).

CONCLUSION

MMVD is a manageable disease with diligent medication and dietary monitoring, but is incurable due to the irreversible effect of the chronic degeneration of the mitral valves. Owners need to be aware that it would be a life long commitment to maintain the quality of life of the dog, with full compliance to the treatment regime for the best effects on reaching the treatment goals; prolonging lifespan and improving quality of life by controlling clinical signs of CHF.

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CONFLICT OF INTEREST

None of the authors have any potential conflicts of interest to declare.

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