Journal of Cardiology and Cardiovascular Research

Monge Utrilla O, et al., 2022- J Cardiol Cardiovasc Res
Case Studies

Canine Dilated Cardiomyopathy Secondary to Hypothyroidism: Review of 3 Clinical Cases

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Received Date: 10-20-2022
Accepted Date: 10-31-2022
Published Date: 11-18-2022

Abstract

Canine dilated cardiomyopathy is characterized by ventricular systolic dysfunction with eccentric hypertrophy. Can be primary or secondary to other disorders such as hypothyroidism. Different cardiac changes, due to the inotropic and chronotropic alterations, can appear in these patients. Mainly affecting the left ventricle, although both ventricles may be affected. Electrocardiographic alterations may appear, as in the cases described, needing different therapeutic strategies for its control. Many times, we are able to achieve a complete resolution of the cardiac alterations once the hypothyroidism is stabilized, but this is not always possible, leaving permanent alterations.

Keywords: Dilated cardiomyopathy; Hypothyroidism; Dog.

Abbreviation: Ao: Aorta; EDVI: End-Diastolic Volume Index; EF: Ejection Fraction; ESVI: End-Systolic Volume Index; FS: Fractional Shortening; LA: Left Atrium; LVIDNd: Left Ventricle Internal Diastolic Diameter Normalized; T4: Thyroxine; TSH: Thyrotropin; RV FAC: Right Ventricular Fractional Area Change; RVEDAi: Right Ventricle End-Diastolic Area Index.

Introduction

Dilated cardiomyopathy is characterized by systolic dysfunction of the left ventricle or systolic dysfunction of both ventricles. Also, eccentric hypertrophy of the affected cardiac chamber. No other cardiac alteration that justifies these changes, such as valvular problems or systemic hypertension, appears [1].

A strong predisposition to suffer from dilated cardiomyopathy is observed in the canine specie, mainly in large or giant breeds, highlighting the Doberman breed [2]. It is the second most common heart disease in this

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DOI: https://doi.org/10.37191/Mapsci-JCCR-3(3)-068

species [2]. This disease can appear due to genetic causes, having found different genetic mutations linked to the development of the disease, although other causes have been observed, such as arrhythmogenic problems, systemic or infectious diseases, toxic and dietary causes [3].

Hypothyroidism can produce alterations at the cardiovascular system, such as decreased heart rate, decreased contractility, and secondary eccentric hypertrophy [4]. In addition, can cause alterations in the electrical conductivity, subserve the appearance of arrhythmias such as atrial fibrillation or ventricular arrhythmias [5].

Case 1

Canine patient, American Staffordshire terrier, 9 years old, neutered male, with exercise intolerance. On physical examination, the presence of a mitral murmur is detected, and weak femoral pulse. Blood tests are performed, revealing a non-regenerative, hypochromic, and microcytic anemia.

Due to these findings, an abdominal ultrasound was performed, finding a 5 cm diameter splenic mass. The study is completed with an echocardiography. Echocardiography revealed left ventricle eccentric hypertrophy with increase of LVIDNd 2, EDVI 147 ml/m², ESVI 78,6 ml/m².

Left atrium dilatation with LA/Ao ratio of 2.23 and left systolic dysfunction with SF 22% and FE 46% (Figure 1). Concentric mitral regurgitation.

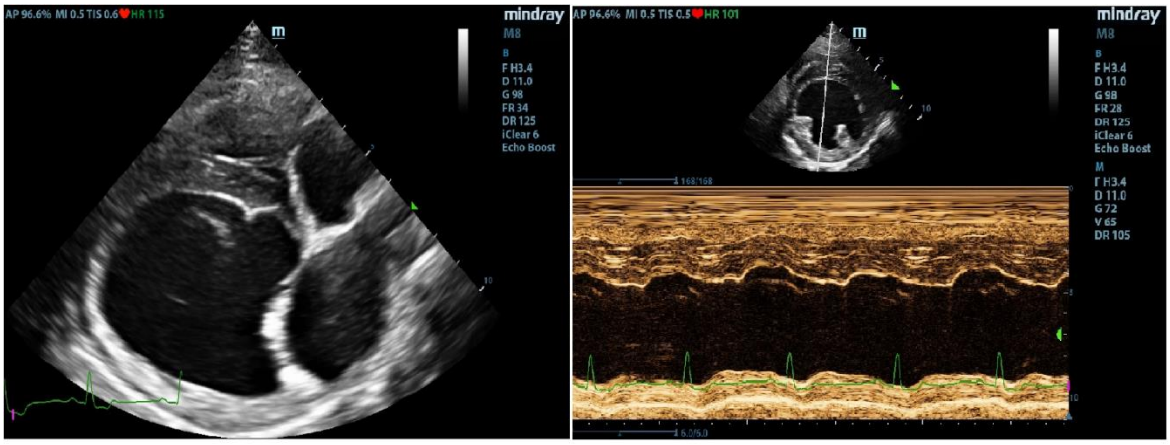

Figure 1 (a) Figure 1 (b)

Figure 1 (a): Echocardiographic exam, right parasternal 4 chambers view at diagnosis time, **(b):** Right parasternal short axis at papillary muscles M mode at diagnosis time.

No alterations were observed in the electrocardiogram.

With these findings, stage B2 canine dilated cardiomyopathy [3] was diagnosed, initiating therapy with pimobendane (0.25 mg/kg every 12 hours, orally) and spironolactone (1 mg/kg every 12 hours, orally). Primary causes of systolic ventricular dysfunction were searched. Thyroid hormones values were: T4 0.7 ug/dl (range 1-4 ug/dl) and TSH 1.68

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ng/ml (range 0.03-0.6 ng/mL). Canine hypothyroidism was diagnosed too and initiating levothyroxine therapy (10 mcg/kg every 12 hours, orally). At 6 months, a review echocardiography was performed, obtaining improvement in all echocardiographic values. Eccentric hypertrophy of the left ventricle is not observed.: LVIDNd 1.4, EDVI 94,5 ml/m², ESVI 31,24 ml/m². Left atrial dilatation not observed, with a LA/Ao ratio of 1.37. Systolic function within physiological limits, FS 36,7% y EF 66,95%.

It was decided to withdraw treatment with pimobendane and spironolactone. Treatment with levothyroxine was kept. No increase in clinical symptoms or worsening of echocardiographic values was observed.

Case 2

Canine patient, American Staffordshire terrier, 5 years old, unneutered male, with exercise intolerance, weakness, and diarrhea. On physical examination, the presence of a mitral murmur is detected, weak femoral pulse, mild abdominal distension and anormal lung auscultation. Blood analysis without relevant findings.

An abdominal ultrasound was performed finding ascitis, hepatic venous congestion, hepatomegaly, and loss of distensibility of the caudal vena cava. Echocardiography revealed left ventricle eccentric hypertrophy with: LVIDNd 2.05, EDVI de 135.34 ml/m², ESVI 153,85 ml/m². Left atrium dilatation with LA/Ao ratio of 1.85.

Right ventricle eccentric hypertrophy, RVEDAi 22.25. Left ventricle systolic dysfunction with FS de 14% y EF 22.2%, and right ventricle systolic dysfunction, RV FAC 20.33%. Concentric mitral and tricuspid regurgitation (Figure 2).

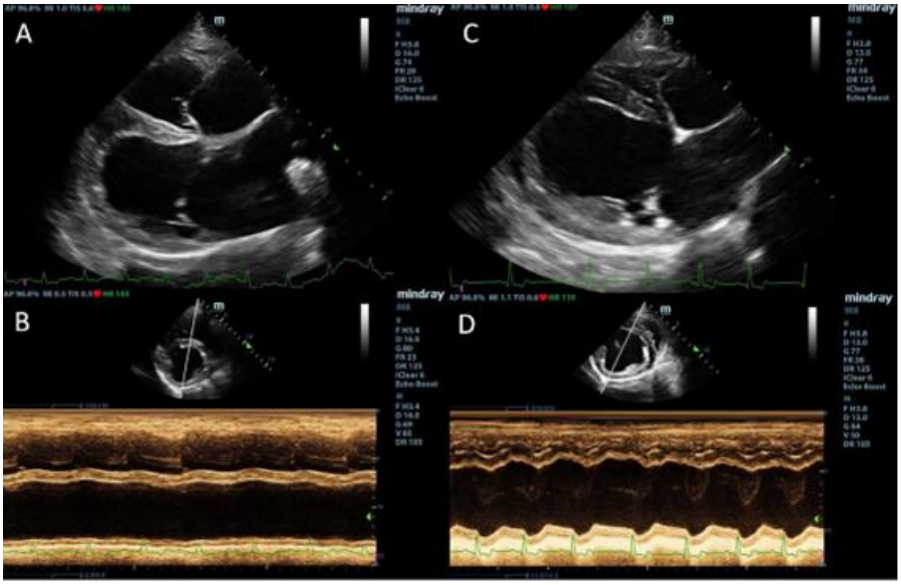

Figure 2 (a): Echocardiographic exam, right parasternal 4 chambers view at diagnosis time; (b): right parasternal short axis at papillary muscles M mode at diagnosis time; (c): right parasternal 4 chambers view 6 months after started treatment; (d): right parasternal short axis at papillary muscles M mode 6 months after started treatment.

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No alterations were observed in the electrocardiogram. Mild perihilar pulmonary interstitial pattern is reveal in chest radiographs.

Stage C canine dilated cardiomyopathy [3] was diagnosed, initiating therapy with pimobendane (0.25 mg/kg every 12 hours, orally), torsemide (0.2 mg/kg every 24 hours orally), benazepril (0.25 mg/kg every 12 hours, orally) and spironolactone (1 mg/kg every 12 hours, orally). Primary causes of systolic ventricular dysfunction were searched. Thyroid hormones values were: T4 0.6 ug/dl (range 1-4 ug/dl) and TSH 0.82 ng/ml (range 0.03-0.6 ng/mL). Canine hypothyroidism was diagnosed too and initiating levothyroxine therapy (10 mcg/kg every 12 hours, orally).

At 6 months, a review echocardiography was performed obtaining improvement in some echocardiographic values. Improvement of eccentric hypertrophy of the left ventricle was observed: LVIDNd 1.85, EDVI 103.76 ml/m^2, ESVI 63.3 ml/m^2. Right ventricle eccentric hypertrophy was disappeared, RVEDAi 8.99. Left atrial dilatation not observed, with a LA/Ao ratio of 1.55. Left ventricle systolic function below physiological limits, FS 26.7%, EF 50.2% and right ventricle systolic function within physiological limits RV FAC 55.15% (Figure 2).

No abnormalities were observed on chest radiography and abdominal ultrasound.

Pimobendane and levothyroxine treatment was maintained, the rest of the cardiac medication was withdrawn. No increase in clinical symptoms or worsening of echocardiographic values was observed.

Case 3

Canine patient, Presa Canario dog, 4 years old, unneutered male, with exercise intolerance and weakness. On physical examination, the presence of an irregular heart rate and a mitral murmur was detected, weak and irregular femoral pulse. Blood analysis without relevant findings.

Electrocardiogram showed an irregular rhythm consistent with atrial fibrillation with a mean heart rate of 180 beats per minute. Ventricular fibrillation with high ventricular penetrance was diagnosed (Figure 3).

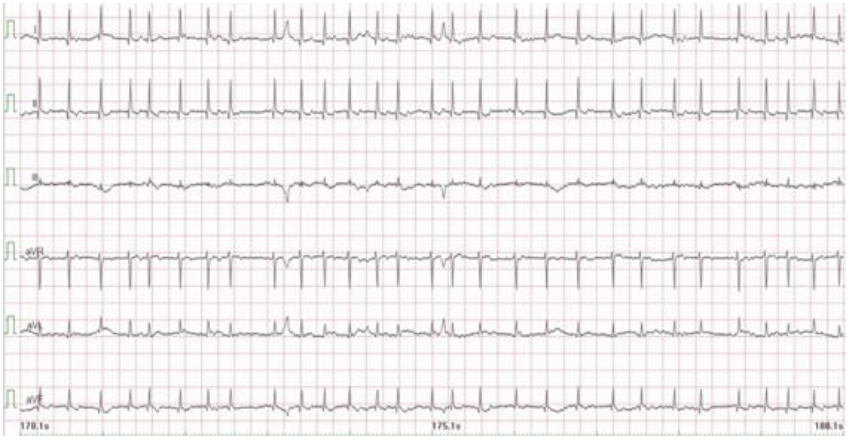

Figure 3: Electrocardiographic exam at diagnostic time. Irregular rhythm, absence of P waves, mean heart rate of 180 beats per minute. 5 mm/mv and 25 mm/s.

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Echocardiography revealed systolic dysfunction, FS 20.3%, EF 44.9%, ESVI 61.3 ml/m². Without left ventricle hypertrophy, LVIDNd de 1.5 and EDVI 76.1 ml/m². Left atrium dilatation with LA/Ao ratio of 1.81. Concentric mitral regurgitation (Figure 4).

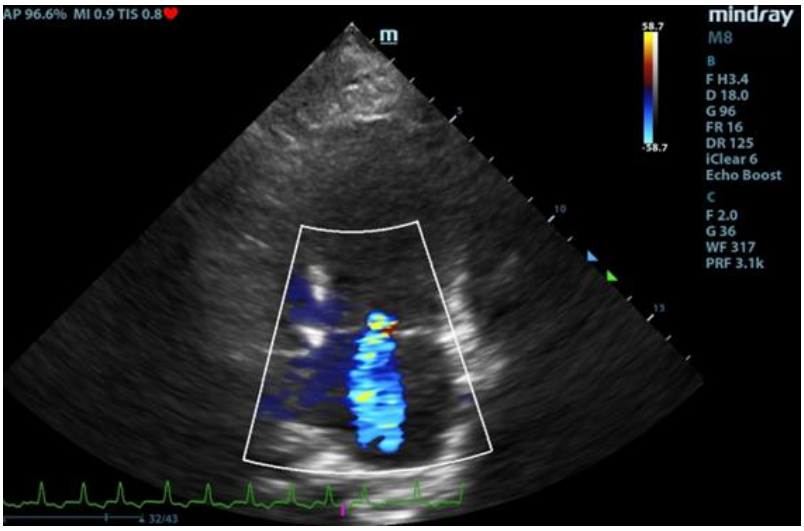

Figure 4: Concentric mitral regurgitation. Left apical 4 chambers view, mitral valve doppler color.

Stage C canine dilated cardiomyopathy [3] with atrial fibrillation was diagnosed. Pharmacological therapy with pimobendan (0.25 mg/kg every 12 hours, orally), spironolactone (1 mg/kg every 12 hours, orally), digoxin (0.003 mg/kg every 12 hours, orally) and diltiazem retard (3 mg/kg every 12 hours, orally) was initiated to decrease heart rate. Primary causes of systolic ventricular dysfunction were searched. Thyroid hormones values were: T4 0.5 ug/dl (range 1-4 ug/dl) and TSH 0.76 ng/ml (range 0.03-0.6 ng/mL). Canine hypothyroidism was diagnosed too and initiating levothyroxine therapy (10 mcg/kg every 12 hours, orally).

At 6 months, echocardiography review was performed, without improvement in left ventricle systolic function, FS 22.5%, EF 46.1% and ESVI 55.6 ml/m². Eccentric hypertrophy of the left ventricle and left atrium dilatation were not observed: LVIDNd 1.4, EDVI 76 ml/m² and LA/Ao ratio 1.75.

Electrocardiographic examination showed atrial fibrillation, with lower heart rate, 95 beats per minute.

Cardiac treatment and levothyroxine were maintained. The patient remains asymptomatic and without intolerance to exercise despite the lack of notable improvement in diagnostic tests.

Discussion

Hypothyroidism and canine dilated cardiomyopathy association is still under study in veterinary medicine. There are reports of systolic dysfunction and eccentric hypertrophy in animals with this disease [4]. This relationship is well studied in human medicine, called reversible dilated cardiomyopathy [6]. As in the canine specie,

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causes bradycardia, increases blood diastolic pressure, causes cardiac remodelling, decreases ejection fraction and cardiac output [3,4,6].

In human hypothyroidism diastolic dysfunction is common, being systolic dysfunction less common [6,7]. Veterinary medicine has observed that thyroid hormones increase sensitivity to catecholamines and beta-adrenergic receptors [8]. Experimentally, a relationship between inotropic function and thyroid hormones has been observed in canine specie [9]. Systolic dysfunction is always described, but not in human medicine, where diastolic dysfunction is most common.

The controversy is manifested in veterinary medicine, either to establish a cardiac treatment or just to maintain the treatment of hypothyroidism [9]. Pharmacological treatment used for cardiovascular alterations due to hypothyroidism can be beneficial for the patient. Quality of life is improved in these patients, although an improvement of the survival time has not been demonstrated [8,10].

Pharmacological treatment for cardiovascular alterations in hypothyroidism patients may be withdrawn due to improved systolic cardiac function, because of levothyroxine therapy [4]. Complete regression of cardiac abnormalities does not occur in every cases. Then, positive inotropic support, such as pimobendane, is needed.

These animals will present propensity to develop arrhythmias [5]. Decreased discharge rate of the sinus node, conduction disturbances through the atrioventricular node, decreased voltage of P wave and the QRS complex, polarity change of the T wave, and atrial fibrillation, are the most common alterations in these patients [5,11,12].

Thyroid hormones stimulate sarcolemma´s ion channels. Alteration in this stimulation causes arrhythmias [11]. On the other hand, atherosclerosis occurs in the coronary vessels, which can lead to formation of arrhythmias [11].

Arrhythmias or ventricular ectopies are presented in dilated cardiomyopathy patients, mainly in Doberman breed patients, even before cardiac structural changes are observed [1]. These ventricular ectopies have been observed in patients with hypothyroidism in human medicine, but not in hypothyroidism canine patients [8].

Canine hypothyroidism is not commonly causing congestive heart failure without primary heart disease [1,4,6-8]. In human medicine, it does [13], such us in case 2.

Cardiac function normalization after initiation of levothyroxine therapy in human, canine, or rodent patients has been described, allowing cardiac medication to be withdrawn [13,14], such in our cases.

In cases 1 and 2 we can see this improvement in cardiac function after implementing treatment with levothyroxine. Systolic function, systolic and diastolic ventricular volumes improved in both cases.

Stage B2 dilated cardiomyopathy was diagnosed in case 1, and treatment was initiated with pimobendane and spironolactone. Treatment´s objective was to

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prevent the progression of cardiac disorders [10,15] secondary to hypothyroidism.

In case 2, dog was diagnosed with stage C dilated cardiomyopathy secondary to hypothyroidism. Bilateral congestive heart failure signs were present and standard drug therapy was started [16]. At the same time, we started the treatment with levothyroxine.

Significant clinical and echocardiography improvement was observed, in both cases, returning to normal cardiac function values [3]. Gradually withdrawing cardiac medication.

Only hypothyroidism therapy was maintained in case 1. Pimobendane therapy was maintained to support systolic function in addition to levothyroxine treatment in case 2. Both cases have remained stable over time.

Not all hypothyroid patients who develop cardiac abnormalities return to normal function after starting treatment. Cardiac drugs couldn´t be removed in case 3because no improvement was observed in diagnostic tests. It may happen due to the presence of a negative prognostic factor such as atrial fibrillation [16,17].

Conclusion

These cases demonstrate how hypothyroidism can cause cardiac abnormalities including congestive heart failure in dogs.

Individualized evaluation of these patients is necessary, adjusting the pharmacological therapy to their needs, evaluating the appearance of negative prognostic factors such as atrial fibrillation.

Negative prognostic factors can be the difference between achieving cardiac function normalization or not.

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