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CASE REPORT
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Hypertrophic Phenotypic Cardiomyopathy in an Ocelot (*Leopardus pardalis*)

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ABSTRACT

***Background*:** Hypertrophic cardiomyopathy phenotype (HCM) is the most common cardiac disease in domestic cats but is rarely described in wild species. This phenotype is characterized by concentric hypertrophy of the left ventricle and may be of familial inheritance or secondary to other diseases such as hyperthyroidism, chronic kidney disease, systemic arterial hypertension, and hyperaldosteronism. HCM can cause diastolic and systolic dysfunction and may cause congestive heart failure in affected animals. The present work aims to describe the first report of cardiomyopathy of the hypertrophic phenotype in a specimen of *Leopardus pardalis*, kept under human care.

***Case*:** A 11-year-old female ocelot *(Leopardus pardalis)* kept under human care, during a preventive care visit, had hypertrophic cardiomyopathy phenotype detected by cardiological evaluation with echocardiogram and a murmur grade III/VI could be detected on cardiac auscultation. This preventive care occurred under chemical restraint with ketamine [6 mg/kg, i.m] associates with midazolam [0.5 mg/kg, i.m] and other evaluations have been done like complete blood count (CBC), biochemistry (alanine aminotransferase, aspartate aminotransferase, total proteins, albumin, albumin:globulin ratio, creatinine, urea, sodium, potassium, calcium, phosphorus, and globulin) and tyroid hormones [free tyroxine (T4) and thyroid-stimulating hormone (TSH)]. Medical management based on clopidogrel, and atenolol was administered for 3 months until the patient showed manifestations of congestive heart failure (CHF) 80 days later the initial evaluation. In this moment the patient presented with dyspnea, so a cardiological and laboratory evaluation was requested. On pulmonary auscultation crackling was identified, suggesting pulmonary edema and, on echocardiographic examination, some parameters had worsened. The CBC and biochemistry were all within reference ranges. Then, the beta-blocker was discontinued and replaced by pimobendan combined with furosemide as treatment of CHF, and the condition stabilized. After one year, the patient was re-evaluated and showed a slight improvement in the condition but still remained stable. Also, feline proBNP levels was tested (SNAP Feline proBNP® IDEXX) in this moment and it was increased.

***Discussion*:** The findings on echocardiography associated with the subjective evaluation associated with progressive worsening and clinical manifestation of CHF, as well as the response to treatment, even though there are no reference values for the species, reinforce the diagnosis. There is no evidence to suggest diseases that may contribute to secondary left ventricular hypertrophy. It is believed that pimobendan plays a key role in maintaining hemodynamic balance, since this has already been observed in other mammalian species. The use of beta blockers is commonly employed in domestic cats with HCM, and they have been prescribed in an attempt to promote greater ventricular relaxation, decrease left ventricular outflow obstruction, thus improving ventricular filling for maintenance of cardiac output. In view of the atrial enlargement and possible risk of thrombus formation, clopidogrel was prescribed, extrapolating what is known from domestic cats. It is reasonable to conclude that in this case, the cardiomyopathy behaved similarly to what is observed in domestic cats, both in its clinical evolution and in the means of diagnosis, and in its response to the therapy instituted.

Keywords: Felidae, feline, cardiovascular disease, heart disease, echocardiogram, echocardiography.

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INTRODUCTION

Hypertrophic cardiomyopathy (HCM) is the most common heart disease in domestic cats and affects the mainly left ventricular myocardium [9,11]. The disease is known to present an autosomal dominant inheritance of incomplete penetrance; thus, different phenotypes of hypertrophy can be identified in affected animals [18,19]. Concentric left ventricular hypertrophy (LVH) may be secondary to systemic diseases, manifesting with the same phenotype and complications as HCM. The most frequent causes of LVH in domestic cats are hyperthyroidism, chronic kidney disease, systemic arterial hypertension, and hyperaldosteronism [1,11]. As consequence of LVH, diastolic dysfunction, increased diastolic filling pressures and congestive heart failure (CHF) are common [5].

Animals with hypertrophic cardiomyopathy can be asymptomatic or show similar manifestations as animals with CHF [1,5]. The diagnosis is made by echocardiography, and other complementary examinations are still important to evaluate possible complications. Thoracic radiographs and electrocardiogram (ECG) can help in the diagnosis of congestive heart failure (CHF) and arrhythmias, respectively [7].

The treatment of asymptomatic animals is still widely discussed, since different studies have shown that there is no increase in survival [3,15,21]. For symptomatic animals' treatment consists of improving ventricular diastolic performance, decreasing congestion, minimizing ischemia, and preventing thromboembolism [5,7,11].

The present work aims to describe the first report of cardiomyopathy of the hypertrophic phenotype in a specimen of *Leopardus pardalis*, kept under human care.

CASE

A 11-year-old female intact *Leopardus pardalis*, weighing 11 kg, negative for feline immunodeficiency virus infections and leukemia, arrived at Rio de Janeiro Zoo (current name Bioparque do Rio). The patient was chemically restrained for preventive care, with ketamine[1] [Vetnil® - 6 mg/kg, i.m] and midazolam[2] [Dorminid® - 0.5 mg/kg, i.m], requiring ketamine rescue [2 mg/kg, i.m] 30 min after the first dose. Blood samples were collected, and a physical examination was performed. Cardiac auscultation revealed a grade III/VI sternal border murmur, normokinetic pulse, and systemic systolic blood pressure of 120 mmHg. Electrocardiographic tracing showed a normal sinus rhythm with no changes in the morphology of the electrocardiographic deflections. Echocardiogram showed concentric hypertrophy of the left ventricle [diastolic septum interventricular: 8.2 mm; diastolic posterior wall of the left ventricle: 8.7 mm; left ventricle systolic diameter: 11.1 mm; left ventricular diastolic diameter: 17.9 mm; left atrium: 23. 2 mm; aorta: 11.2 mm; LA:AO: 2.05; shortening fraction: 38%; ejection fraction: 71%] (Table 1) with outflow tract obstruction, consistent with cardiomyopathy of the hypertrophic phenotype. Treatment was initiated with clopidogrel[3] [clopidogrel hydrogen sulfate® 25 mg - 1.7 mg/kg p.o,

Table 1. Evolution of echocardiographic measurements of the left ventricle and atrium over time in the treatment follow-up of a *Leopardus pardalis* with hypertrophic phenotypic cardiomyopathy.

Parameter	First exam	Second exam	Third exam
LA	23.2 mm	27.5 mm	30.0mm
AO	11.2 mm	10.6 mm	13 mm
LA:AO	2.05	2.58	2.30
dSIV	8.2 mm	8.7 mm	0.9 mm
dVED	17.9 mm	16 mm	1.71 mm
sDVE	11.1 mm	9.1 mm	0.97 mm
dPW	8.7 mm	8.4 mm	0.93 mm
Fenc%	38%	43%	43%
Fej%	71%	78%	78%

LA: Left atrium. Ao: Aorta. LA:AO Left atrium aorta ratio. dSIV: Diastolic Septum interventricular. dVED: Diastolic ventricular diameter. sDVE: Sitolic Ventricular Diameter. dPW: Diastolic posterior wall.

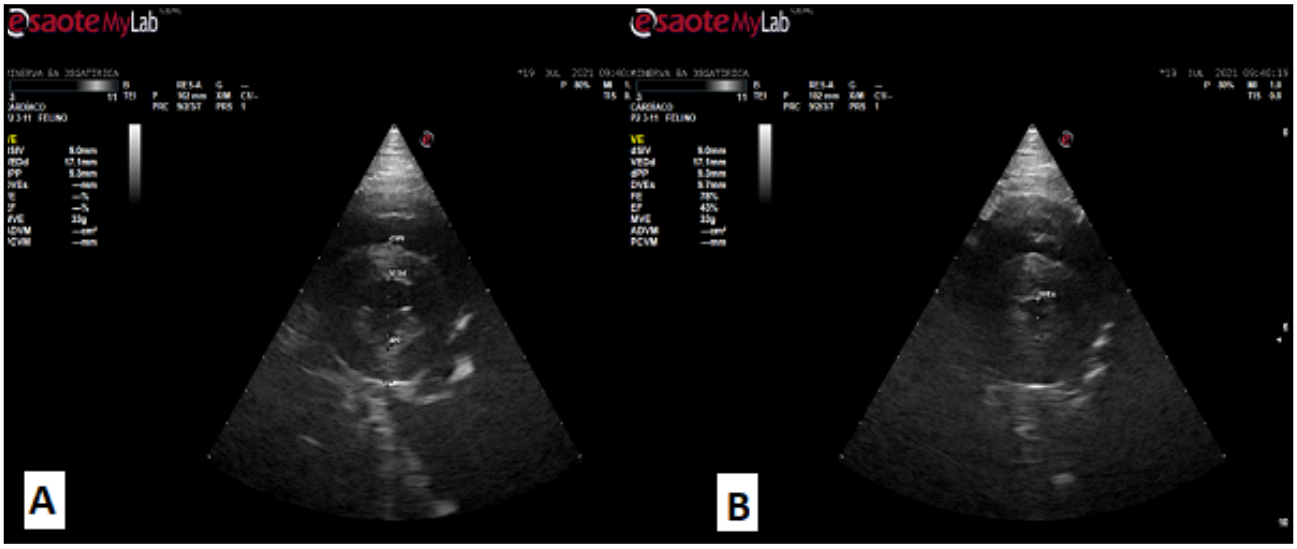

Figure 1. Echocardiographic image of the left ventricle in the short axis in two-dimensional mode, at the level of the papillary muscles in diastole (A) and systole (B) showing hypertrophy of the interventricular septum and of the left ventricle free wall.

SID] and atenolol[4] [atenolol® - 12.5 mg/animal p.o, SID] for 90 days until reevaluation.

For the differential diagnosis of LVH, a thyroid panel was submitted. The thyroid stimulating hormone (TSH) was 0.09 ng/dL (reference: 0.01 to 0.60 ng/mL) free thyroxine (T4) 1.9 ng/dL (reference: 1.6 to 4.0 ng/dL), total T4 18.2 ng/dL (reference: 15.0 to 30.0 ng/mL). The references used were from domestic cats.

Approximately 80 days after the initial evaluation, the patient presented with dyspnea, and a cardiological and laboratory evaluation was requested. The examination was performed again under chemical restraint, with ketamine[1] [2.5 mg/kg, i.m] and midazolam[2] [0.7 mg/kg, i.m] needed to perform the exams. On pulmonary auscultation crackling was identified, suggesting pulmonary edema and, on echocardiographic examination, some parameters had worsened (Table 1). Mitral insufficiency, dynamic obstruction of the left ventricular outflow tract (LVOTO), and signs of congestion were identified (left atrium-to-aorta ratio, 2.58; isovolumetric relaxation time, 12 ms; left atrial flow velocity, 0.29).

The CBC and biochemistry (alanine aminotransferase, aspartate aminotransferase, total proteins, albumin, albumin:globulin ratio, creatinine, urea, sodium, potassium, calcium, phosphorus, and globulin) were all within reference ranges. The electrocardiogram and the measurement of systemic blood pressure revealed no changes.

In light of the appearance of cardiac insufficiency, the beta- blocker was discontinued and furosemide[5] [furosemide® 40 mg - 1.8 mg/kg, p.o., BID] and pimobendan[6] [pimobendan® 2.3 mg - 0.2 mg/kg, p.o., BID] were prescribed, and clopidogrel was continued.

Approximately one year after the diagnosis, the patient was re-evaluated in a follow-up procedure. At that time, the patient was chemically restrained with ketamine[1] [6 mg/kg, i.m.], pethidine[7] [4 mg/kg, i.m.], and midazolam[2] [0.3 mg/kg, i.m.]. After sedation, no electrocardiographic changes or variations in blood pressure were observed. Echocardiography showed concentric hypertrophy of the left ventricle (Figure 1), dynamic obstruction of the left ventricular outflow tract (Figure 2), enlargement of the left atrium (Figure 3),

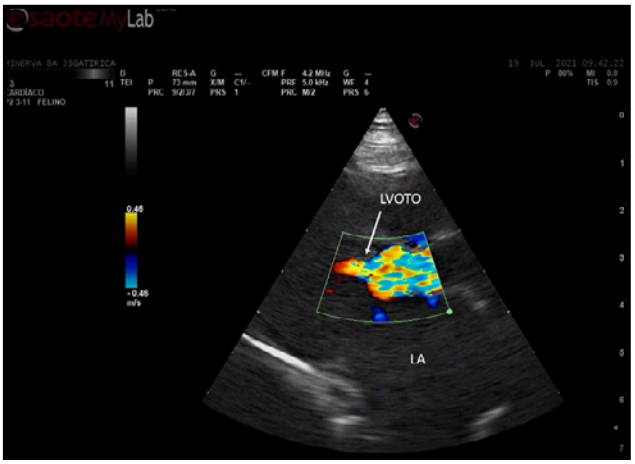

Figure 2. B-mode echocardiographic image in the left ventricular outflow tract, showing the presence of dynamic obstruction of the left ventricular outflow tract (LVOTO). [LA= left atrium].

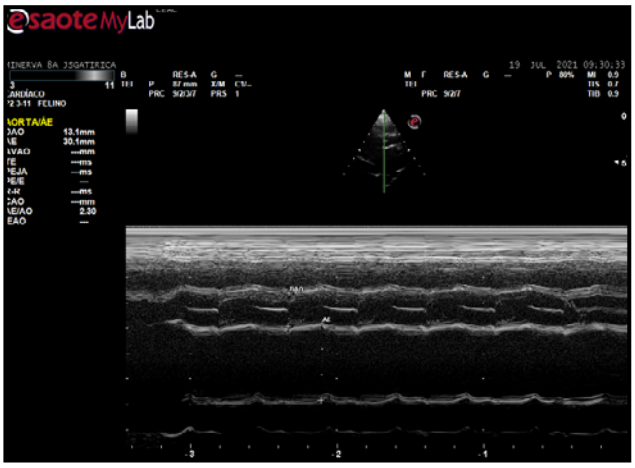

Figure 3. M-mode echocardiographic image of the left atrium and the aorta ratio, by the left longitudinal parasternal section showing severe increase.

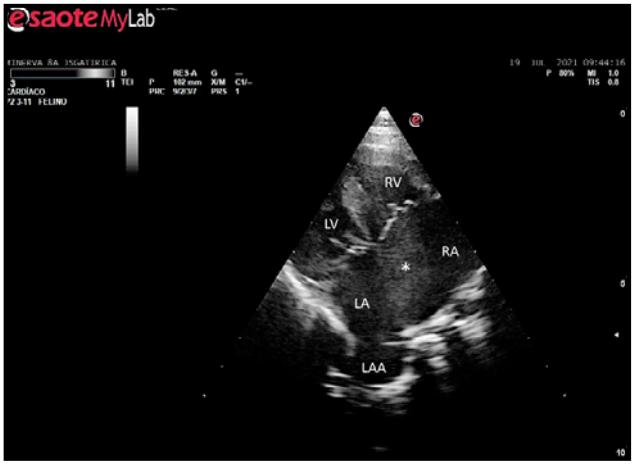

Figure 4. Echocardiographic image in apical 4-chamber view showing left atrial enlargement (LA) and right atrial enlargement (RA) and presence of spontaneous contrast (*). [RV= right ventricle; LV= Left Ventricle; LAA= Left Auricular Appendage].

and atrial appendage. Right atrial enlargement and the presence of spontaneous contrast was also observed (Figure 4).

Blood samples were collected for evaluation of biological and biochemical parameters and feline proBNP[8] levels (SNAP Feline proBNP® IDEXX). The hematological and biochemical tests (alanine aminotransferase, total proteins, albumin, albumin:globulin ratio, creatinine, sodium, potassium, calcium, phosphorus, globulin, alkaline phosphatase, and glucose) were within reference values. The plasma levels of ProBNP increased (Figure 5).

DISCUSSION

Considering the findings on echocardiography, it appears that the anesthetic protocol did not interfere with the diagnosis. Even though there are no reference

Figure 5. Feline proBNP Test showing positive result for increased ProBNP levels.

values for the species, the subjective evaluation associated with progressive worsening and clinical manifestation of CHF, as well as the response to treatment, reinforce the diagnosis [1,5,7,11].

The use of beta blockers is commonly employed in domestic cats with HCM, and they have been prescribed in an attempt to promote greater ventricular relaxation, decrease LVOTO thus improving ventricular filling for maintenance of cardiac output [4,7]. In view of the atrial enlargement and possible risk of thrombus formation, clopidogrel was prescribed, extrapolating what is known from domestic cats [10,13,14].

Although there are no studies that determine thyroid hormone reference values for *Leopardus pardalis*, when considering the clinical history of the patient and the observed results, there is no evidence to suggest diseases that may contribute to secondary left ventricular hypertrophy [1,4,23].

With the development of the venous congestion and pulmonary edema, atenolol was discontinued due to its negative inotropic effects that may worsen the congestive state [12]. In view of the CHF, furosemide was added to decrease preload and treat pulmonary edema [5,12]. In addition, pimobendan was added,

which has positive inotropic and vasodilatory effects [6], which are known to be beneficial in domestic cats with congestive cardiomyopathy [12,16,24].

After approximately 1 year, the patient was stable and showed no clinical manifestations related to cardiomyopathy, thus demonstrating the effectiveness of the established protocol. The patient then underwent a new cardiological evaluation where, despite the slight worsening of some echocardiographic measurements, contractility indexes showed no worsening, showing that the patient was hemodynamically stable. It is believed that pimobendan plays a key role in maintaining hemodynamic balance, since this has already been observed in other mammalian species [2,20]. Although a study did not observe the benefits of the use of pimobendan in cats with obstructive cardiomyopathy after 180 days of use [22] it is interesting to highlight that in the present report, even in the presence of LVOTO, there was clinical improvement in the patient, indicating that further studies of pimobendan in different species are needed.

By detecting increased levels of pro-BNP, it is possible to suggest that screening for cardiomyopathies in wild cats can be performed by point-of-care tests, especially in more severe cases [8,17]. Thus, further studies on its sensitivity and specificity in other species are needed before their use in clinical practice.

It is reasonable to conclude that in this case, the cardiomyopathy behaved similarly to what is observed in domestic cats, both in its clinical evolution, means of diagnosis, and response to the therapy instituted.

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