

Anasarca Associated with Restrictive Cardiomyopathy in Cats

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ABSTRACT

Background: Cardiomyopathies are a primary heart disorder and are one of the most causes of heart failure and sudden death in cats. Restrictive cardiomyopathy is a diastolic dysfunction resulting from endomyocardial fibrosis, with filling restriction and ventricular distention. In these cases, a poor outcome is expected. Anasarca in animals is often associated with dystocia secondary to congenital changes. In adults, this is a rare condition, since subcutaneous edema in animals with congestive heart failure is an uncommon finding. Therefore, this report describes clinical and pathological findings in an unusual presentation of anasarca in two adult cats with restrictive cardiomyopathy.

Cases: A 12-year-old female mixed breed cat (case 1) and a 6-year-old male mixed-breed cat (case 2) were present on an emergent basis at the veterinary hospital with a history of respiratory distress. Case 1 showed on physical examination intense restrictive mixed dyspnea and lethargy, with muffled heart sounds and respiratory noises in cardiorespiratory auscultation. The cat exhibited abdominal distension resulting from ascites. Generalized subcutaneous edema was evident mainly in the abdominal and submandibular areas and the thoracic and pelvic limbs. In these regions, a positive Godet signal was observed. Thoracic radiography revealed pleural effusion, and the cat underwent fluid drainage on both sides of the thoracic cavity. Drainage material was sent to the laboratory for clinical analysis, which indicated that it was a modified transudate. The clinical signs worsened, and the cat was euthanized. In case 2, physical examination showed severe restrictive mixed dyspnea, lethargy, and low body temperature (< 32°C). Abdominal distension resulting from ascites and generalized edema in the subcutaneous tissue with a positive Godet sign was observed. On cardiorespiratory auscultation, cardiac sounds and breathing noises were muffled. Thoracic radiography revealed pleural effusion. The cat was immediately placed in an incubator for clinical stabilization with oxygen therapy and warm-up. After 2 h of hospitalization, thoracentesis and drainage of cavity fluids were performed, which were classified as modified transudate. The patient remained in critical condition during hospitalization, evolving to death. The two cats were referred for a complete *post mortem* examination. Grossly, both cats showed distension of the abdomen and marked edema of subcutaneous tissue, mainly in the abdominal, ventral cervical, and thoracic and pelvic members. In the abdominal and thoracic cavities, a moderate amount of serous-free liquid, slightly reddish was observed. The heart of both cats was enlarged, with a globose appearance and a slightly whitish epicardium. The left ventricular endocardium was mild and diffusely thick and whitish, in addition to moderate dilation of the left atrium. Histological analyses of the heart showed in both cats moderate and diffuse proliferation of fibrous connective tissue in the endocardial region.

Discussion: Restrictive cardiomyopathy has major importance in feline medicine due to its severity and poor outcome. Pleural effusion, pulmonary edema, and ascites are common findings in cats with congestive heart failure; however, generalized subcutaneous edema is uncommon. To the author's knowledge, there are no published cases in the literature of anasarca in adult cats with restrictive cardiomyopathy. In human cardiology, this presentation is commonly related to congestive heart failure, and it is reported under several conditions, such as restrictive cardiomyopathy and constrictive pericarditis. The present study suggests that anasarca should be included in the list of associated clinical signs suggestive of severe congestive heart failure, mainly related to restrictive cardiomyopathy.

Keywords: cardiomyopathy, endomyocardial fibrosis, feline, generalized edema.

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INTRODUCTION

Cardiomyopathies are a primary heart disorder of the heart and are one of the most important causes of heart failure and sudden death in cats [8,19]. Restrictive cardiomyopathy (RCM) is a diastolic dysfunction resulting from endomyocardial fibrosis, which causes filling restriction and ventricular distention [12]. In veterinary medicine, anasarca is usually associated with dystocia secondary to congenital changes [1]. In adults with heart disease, this condition is considered rare, since subcutaneous edema in patients with congestive heart failure (CHF) is an uncommon finding [22].

RCM is a severe disease and has an unfavorable outcome [17]; therefore, studies involving the feline population are needed to provide data that can assist clinical diagnosis. To our knowledge, there are no published reports of anasarca associated with RCM in cats. Therefore, the present study aimed to characterize the clinical and pathological characteristics of two adult cats with anasarca caused by RCM.

CASES

Case 1. A 12-year-old female mixed breed cat was presented on an emergent basis to the veterinary hospital with a 7-day history of respiratory distress. Physical examination revealed intense restrictive mixed dyspnea and lethargy. Muffled heart sounds and respiratory noises were observed in cardiorespiratory auscultation. Systemic blood pressure and body temperature were within normal limits for the species. The cat exhibited abdominal distension resulting from ascites. Generalized subcutaneous edema was evident mainly in the abdominal and submandibular areas and the thoracic and pelvic limbs. In these regions, a positive Godet signal was observed. Laboratory investigations were normal, and the rapid diagnostic test for feline immunodeficiency virus¹ (FIV) and feline leukemia virus (FeLV)¹ was negative for both. After thoracic radiography, which revealed pleural effusion, the patient underwent fluid drainage on both sides of the thoracic cavity. Drainage material was sent to the laboratory for clinical analysis, which indicated that it was a modified transudate. The cat remained in hospital for 10 h and, during this period, underwent oxygen therapy and administration of furosemide² [4 mg/kg - IV, every 2 h, during the period of hospitalization]. The clinical signs worsened, and the cat was euthanized.

Case 2. A 6-year-old male mixed-breed cat was presented to the veterinary hospital on an emergent basis with a 2-day history of respiratory distress. On physical examination, the cat exhibited severe restrictive mixed dyspnea, lethargy, low body temperature (< 32°C), systemic blood pressure 50 mmHg, abdominal distension resulting from ascites, and generalized edema in the subcutaneous tissue with a positive Godet sign. On cardiorespiratory auscultation, cardiac sounds and breathing noises were muffled. No significant changes in blood count and biochemical tests were identified, and the rapid test for the diagnosis of FIV¹ and FeLV¹ was negative. Thoracic radiography revealed pleural effusion. The cat was immediately placed in an incubator for clinical stabilization with oxygen therapy and warm-up. After 2 h of hospitalization, thoracentesis and drainage of cavity fluids were performed, which were classified as modified transudate according to laboratory analysis. The patient's treatment consisted of oxygen therapy, tramadol³ [2 mg/kg - SC, BID], furosemide² [2 mg/kg - IV, BID], benazepril⁴ [Fortekor flavour[®] - 0.2 mg/kg, VO, SID], and clopidogrel⁵ [18.75 mg/cat - VO, single dose], during the period of hospitalization. The patient remained in critical condition during hospitalization but, after 18 h, experienced cardiorespiratory arrest and, without responding to attempts at resuscitation, died.

The 2 cats were referred for a complete *post mortem* examination. On external examination, both exhibited distention of the abdomen and, on inspection of subcutaneous tissue, marked edema was identified, characterized by deposition of translucent to slightly yellowish serous to gelatinous material (Figure 1), mainly in the abdominal, ventral cervical, and thoracic and pelvic members. In the abdominal and thoracic cavities, a moderate amount of serous-free and reddish liquid (approximately 300 mL) was observed. Both livers were firm on palpation, congested, and with an accentuated lobular pattern ("nutmeg liver"). The lungs were bright and exhibited multifocal to coalescent reddish areas, which when cut, discharged a large amount of translucent to slightly red foamy liquid. The heart of both cats was enlarged, with a globose appearance and a slightly whitish epicardium. The left ventricular endocardium was mild and diffusely thick and whitish, in addition to moderate dilation of the left atrium (Figure 2). In case 1, discrete thrombi adhering to the left atrium and moderate myocardial thickening of the left ventricle were identified.

Multiple tissue samples were collected, fixed in 10% neutral buffered formalin for 48 h, routinely processed for histopathology, and stained with hematoxylin⁶ and eosin⁷ (HE). Heart histological sections, including the interventricular septum and left ventricle, were also stained with Masson's trichrome (MT) for connective tissue analysis.

Histological examination showed, in both cases, a moderate proliferation of fibrous connective tissue, diffuse in the endocardial region (Figure 3), which extended to the adjacent myocardium. In case 1, mild hypertrophy of cardiomyocytes was evident, with multifocal areas of disarray characterized by interwoven myofibers. In case 2, mild multifocal vacuolar degeneration of cardiomyocytes and moderate multifocal cardiomyocyte macrocariosis were also evident, characterized by enlarged and irregularly shaped nuclei (Figure 3). Endomyocardial fibrosis appeared intensely blue on MT staining (Figure 4). Pulmonary edema and congestion and hepatic congestion were also observed in both cats.

DISCUSSION

Cardiomyopathies represent the main cardiovascular diseases and are important causes of mortality in cats [8]. Cats with cardiomyopathies vary widely in age; however, researchers have reported a mean age of 7 to 10.7 years [5,8,10,13,15,17,21] which is similar to the age of the cats described in the present study. Mixed breeds are the most frequently diagnosed [13,15,21]; however, these data may be related to the fact that they represent most of the feline population in the analyzed region [21].

RCM may vary in clinical manifestation; however, dyspnea and changes in cardiorespiratory auscultation are the main clinical signs [8,10,15], which corroborate findings in the present study. Restrictive dyspnea is caused predominantly by obliteration of alveolar spaces by edema and pleural effusion, with a consequent decrease in lung volume and inability to fully expand the lungs [14]. The muffling of cardiac sounds and respiratory sounds is mainly related to a pleural effusion [8,13]. Abdominal distention due to ascites, lethargy, hypothermia, and hypotension resulting from a significant reduction in cardiac output, although less frequent, are also described in cats with cardiomyopathies [8,10,15,17]. Clinical signs resulting from CHF are an indicator of an unfavorable prognosis [9]. The cats described in the present stu-

dy showed minimal survival after the onset of CHF signs [13]. The tutors reported not observing signs or behavioral changes related to cardiomyopathy before



Figure 1. Anasarca in a cat with restrictive cardiomyopathy. *Case 2.* Abdominal distention resulting from edema. In detail, deposition of translucent yellow gelatinous material is apparent in the subcutaneous tissue of the abdominal region.

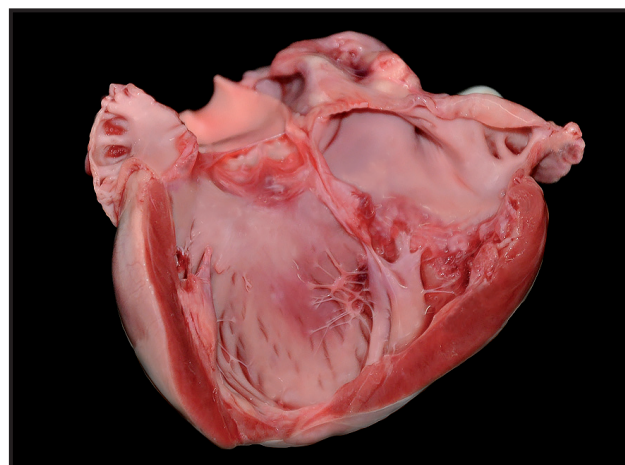


Figure 2. Gross aspect of restrictive cardiomyopathy. *Case 2.* Heart with slightly whitish and thick endocardium and dilated left atrium.

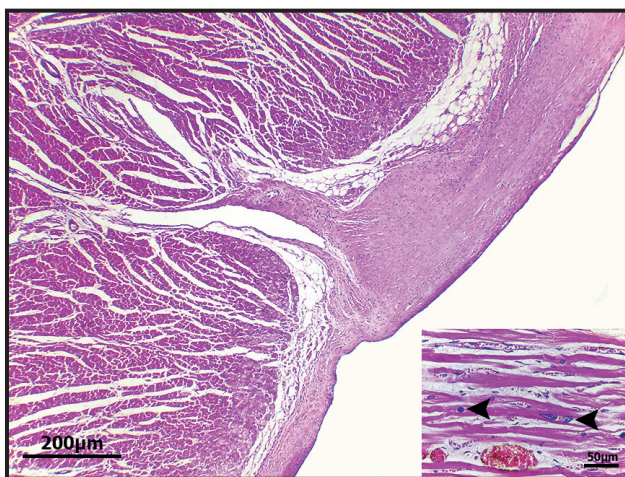


Figure 3. Microscopic characteristics of restrictive cardiomyopathy. *Case 1.* Heart with fibrous connective tissue proliferation in the endocardial region [HE; 100x]. In detail, multifocal cardiomyocyte macrocariosis (arrowhead).

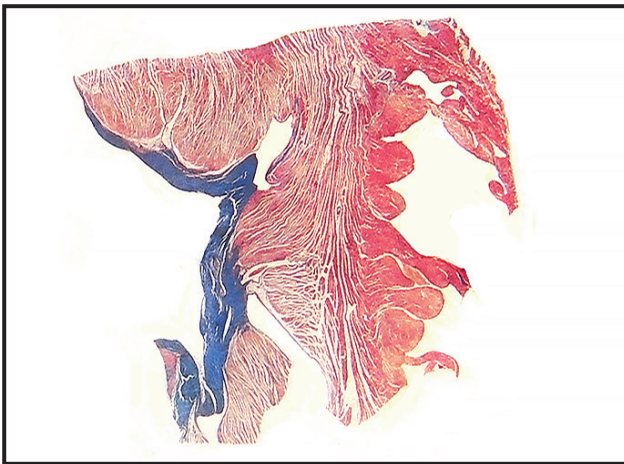


Figure 4. Submacroscopic characteristics of restrictive cardiomyopathy. Case 1. Heart with endomyocardial fibrosis intensely stained blue.

CHF and emergency care; however, this assessment is relative and according to the perception and contact of the tutors with their animals, in addition to the cats' ability to mask signs of weakness, pain, or disease [7]. Radiographic examination often reveals varying degrees of cardiomegaly, pleural effusion, and pulmonary edema [13,15]; however, the clinical diagnosis and classification of cardiomyopathies are performed during echocardiography [9,10]. In the present study, this test was not performed because cats are high-risk patients, was referred for emergency care, and died within hours of hospitalization.

Grossly, the heart exhibited increased size, atrial dilation, and a whitish and thick endocardium resulting from fibrosis [12,13]. Endomyocardial fibrosis has two morphological patterns, diffuse and trabecular, involving the interventricular septum and the free wall of the left ventricle. In the present study, the diffuse pattern was identified; however, the trabecular pattern is the most common presentation [12,15]. The myocardium is often thicker and thrombi in the atrial wall can be observed in RCM [12,13,15]; these data corroborate those from the present study.

Pleural effusion, pulmonary edema, and ascites are common findings in cats with CHF [12,13,15]; however, generalized subcutaneous edema is uncommon [22]. The development of edema occurred mainly due to the increase in hydrostatic pressure resulting from blood stasis caused by bilateral heart failure. The activation of the renin-angiotensin-aldosterone system contributes to the formation of edema and worsening of clinical signs [19]. Subcutaneous edema occurs mainly in the abdominal, ventral, submandibular, and limb regions, which may be related to the effects of gravity.

In the present study, edema was evaluated according to the presence of the Godet signal, in which digital pressure on the skin causes depression as the interstitial fluid is displaced. Other factors can cause edema, including low vascular oncotic pressure, changes in vascular permeability, or lymphatic obstruction [22]; however, these changes were not identified in the blood count, serum biochemistry, and anatomopathological findings of the present study. In the veterinary field, anasarca is commonly associated with dystocia secondary to congenital changes, and neonatal mortality [1]. To our knowledge, there are no published cases of anasarca in adult cats with RCM in the literature. In human cardiology, this presentation is reported under several conditions, such as RCM and constrictive pericarditis, and is related to CHF [2,23].

Fibrosis is histologically subdivided into 2 forms: endomyocardial and myocardial [12,15]. The endomyocardial form is the most found in cats and was identified in the felines described in this study. Cardiomyocyte hypertrophy and myofiber disarray, although uncommon, have been described in RCM [10,12,15]. Cardiomyocyte macrocariosis has been reported in monkeys with hypertrophic cardiomyopathy (HCM) and cats with a final phase of HCM similarly to RCM [4,16]. This alteration may be related to the hypertrophy of myofibers, which present histologically as large cardiomyocytes, enlarged and pleomorphic nuclei, and prominent nucleoli [3,11].

In cats, the etiology of RCM is not completely understood; however, it has been suggested that a lesion in the endomyocardium with consequent reparative fibrosis may be associated with viral, immune-mediated, or bacterial endomyocarditis [6,12]. However, researchers report that the occurrence of RCM is not significantly related to a virus-induced inflammatory response [15,18]. There is also the possibility that RCM is a consequence of the final stage of HCM [4,17]. Hypereosinophilic syndrome is related to endocardial fibrosis in humans, but there is no evidence to associate it with RCM in cats [20]. In addition, eosinophils are rarely observed in the myocardium of cats with cardiomyopathy [13] and were not observed in the cases analyzed.

RCM has major importance in feline medicine due to its severity and poor outcome, especially when associated with CHF. The present study described the unusual clinical presentation of anasarca in 2 adult

cats and suggests that it should be included in the list of associated clinical signs suggestive of severe CHF, mainly related to RCM.

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