Takotsubo-like Cardiomyopathy Associated with Capture Myopathy in a Zoo-Kept, Red-Necked Wallaby (*Macropus Rufogriseus*)

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ABSTRACT

A 2-year-old, male intact, zoo-kept red-necked wallaby (*Macropus rufogriseus*) presented for an annual examination. Complications occurred during routine anesthesia and recovery was prolonged after administration of reversal agents. On echocardiogram, there was left ventricular concentric hypertrophy noted and serum cardiac troponin was significantly elevated. The wallaby developed biochemical changes compatible with capture myopathy and progressed into cardiac arrest. Post-mortem findings were supportive of capture myopathy of both skeletal and cardiac muscle. The cardiac findings were partially reminiscent of disease processes like feline transient myocardial thickening (TMT) and Takotsubo cardiomyopathy (TC). As this case demonstrated, hypertrophic cardiomyopathy phenotype can be associated with suspected capture myopathy and may have underlying pathophysiological processes similar to TMT and/or TC.

Keywords: Red-Necked Wallaby; *Macropus Rufogriseus;* Myocardial Necrosis; Stress-Induced Cardiomyopathy; Takotsubo Cardiomyopathy; Transient Myocardial Thickening.

INTRODUCTION

Hypertrophic cardiomyopathy phenotype is defined by concentric hypertrophy of the left ventricle. Hypertrophic cardiomyopathy phenotype can be classified as primary (genetic) or secondary (hyperthyroidism, systemic arterial hypertension, acromegaly, infiltrative disease, pseudohypertrophy, and transient idiopathic) (1). With the exception of pseudohypertrophy, this phenotype results in diastolic dysfunction that can progress to atrial dilation, congestive heart failure, arrhythmia and thromboembolism in some species (2). Here, we report a wallaby which presented with hypertrophic cardiomyopathy phenotype associated with suspected capture myopathy.

CASE REPORT

A 2-year-old, male, intact red-necked wallaby (*Macropus rufogriseus*) presented to the Kansas State University Zoological Medicine Service for annual wellness examination. According to the zoo staff, he was doing well overall with no known pertinent medical history. The wallaby was manually restrained and hand-injected with dexmedetomidine (Orion, Espoo, Finland; Distributed by Zoetis, Kalamazoo, Michigan, USA) (0.07mg/kg) and ketamine (VETone, MWI Animal Health, Boise, Idaho, USA) (3mg/kg) intramuscularly and the patient was maintained on isoflurane (Akorn, Lake Forest, Illinois, USA) (1-2% via facemask). Atipamezole (Orion, Espoo, Finland; Distributed by Zoetis, Kalamazoo,

Michigan, USA) (0.15 mg/kg) was administered intramuscularly once the patient was sufficiently anesthetized. Salient features on examination were hyperthermia (temperature 107°F, or 41.7°C) and hypotension (systolic blood pressure=40 mmHg). The heart rate was 113 beats per minute with no appreciable murmur although an intermittent gallop sound was noted on auscultation. The respiratory rate was 48 breaths per minute with clear lung sounds bilaterally. Samples for complete blood count, chemistry profile and urinalysis were obtained within 30 minutes and a second dose of atipamezole (0.15 mg/kg) was administered subcutaneously during recovery. The patient experienced a prolonged recovery, bradycardia (26 bpm), and hypothermia (98 F, or 36.7 C). Atropine (VETone, MWI Animal Health, Boise, Idaho, USA) (0.03mg/kg intravenously), atipamezole (0.15mg subcutaneously), and epinephrine (PAR Pharm, Chestnut Ridge, New York, USA) (0.02mg/kg intravascular) were administered to improve vital parameters.

Pertinent hematologic and biochemical findings obtained during the sedated wellness examination include hemoconcentration (PCV 61%; reference range: 40-56%), hyperphosphatemia (8.9 mg/dl; reference range: 1.61-3.17 mg/dl), hyperkalemia (7.1 mmol/L; reference range: 3.6-6 mmol/L), mild hypochloridemia (86 mmol/L; reference range: 92-102 mmol/L), low bicarbonate (11 mmol/L; reference range: 15.6-28.6 mmol/L) and an increased anion gap (46) (3). Urinalysis revealed alkaline urine (pH>9) and 3+ heme, consistent with hemoglobinuria based on a follow-up ammonium sulfate assay. The blood gas analysis revealed a base deficit of 11.7 mmol/L and lactate of 9.6 mmol/L.

Due to the prolonged anesthesia recovery, an echocardiographic examination was performed using a 6 MHz transducer (Vivid-q Cardiovascular Ultrasound System, GE Healthcare, Chicago, Illinois, USA). On two-dimensional echocardiogram, the left ventricular posterior wall and interventricular septum at end diastole measured 14 mm and 17 mm, respectively, and there was subjective moderate left ventricular concentric hypertrophy with the subendocardial layer of the myocardium appearing significantly hyperechoic. The entirety of the caudal papillary muscle was hyperechoic. Fractional shortening measured 38% and the left atrium appeared normal in size. In the right parasternal, long-axis view, the pulmonary arteries and coronary sinus appeared dilated (Figure 1). Five milliliters of agitated saline were injected into the left cephalic vein, ruling out a persistent left cranial cava. No additional evidence of right-sided heart disease (i.e. tricuspid regurgitation, right atrial dilation, right ventricular hypertrophy) was appreciated. Cardiac troponin I (Gastrointestinal Laboratory, Department of Small Animal Clinical Sciences, Texas A&M University, College Station, Texas, USA) was elevated at >50 ŋg/mL consistent with severe myocardial damage such as myocarditis or necrosis, though normal values for this species are not known. The echocardiographic findings were consistent with a hypertrophic cardiomyopathy phenotype. Given the lack of right-sided disease, the dilation of the coronary sinus and pulmonary artery were presumed not to be a significant part of the patient's clinical status at presentation.

Thoracic radiographs revealed pulmonary artery distension and a moderately gas-distended esophagus. The cardiac silhouette, pleural space, and pulmonary parenchyma did not reveal any significant abnormalities.

The patient was treated for suspected capture myopathy with calcium gluconate 10%[b] (6mls intravenously), fentanyl (Hospira, Lake Forest, Illinois USA) (4 µg/kg/hr intravenously), thermal support, and intravenous fluid therapy (lactated ringer solution; 60 ml/kg/day). Serum potassium was rechecked 4 hours later and revealed progressive hyperkalemia (15.1 mmol/L). The patient was treated with simultaneous insulin and dextrose constant rate infusion, adjusted on a sliding scale according to his blood glucose (5). Unfortunately, five hours later, the patient experienced apnea followed by cardiac arrest, and the body was submitted for a full necropsy.

On post-mortem examination, areas of locally extensive hemorrhage of the medial left thigh extended from the stifle to the hip. Multiple muscle groups including the biceps femoris, gracilis, semimembranosus, and sartorius muscles of both hindlimbs had irregular areas of streaky pallor extending through the muscle bodies. Despite the lack of radiographic findings consistent with left-sided congestive heart failure, pulmonary edema, mild pleural effusion (50 mL) and abdominal effusion (150 mL) were also noted.

In the heart, large areas of pallor were appreciated in the subendocardial left ventricle. Both papillary muscles had areas of dark red hemorrhage at the site of chordae tendineae attachment, with marked diffuse pallor of the entire papillary muscle. The left ventricular free wall and the interventricular septum measured 1.4 cm with both being subjectively thickened. The heart weighed 103 g (0.68% of

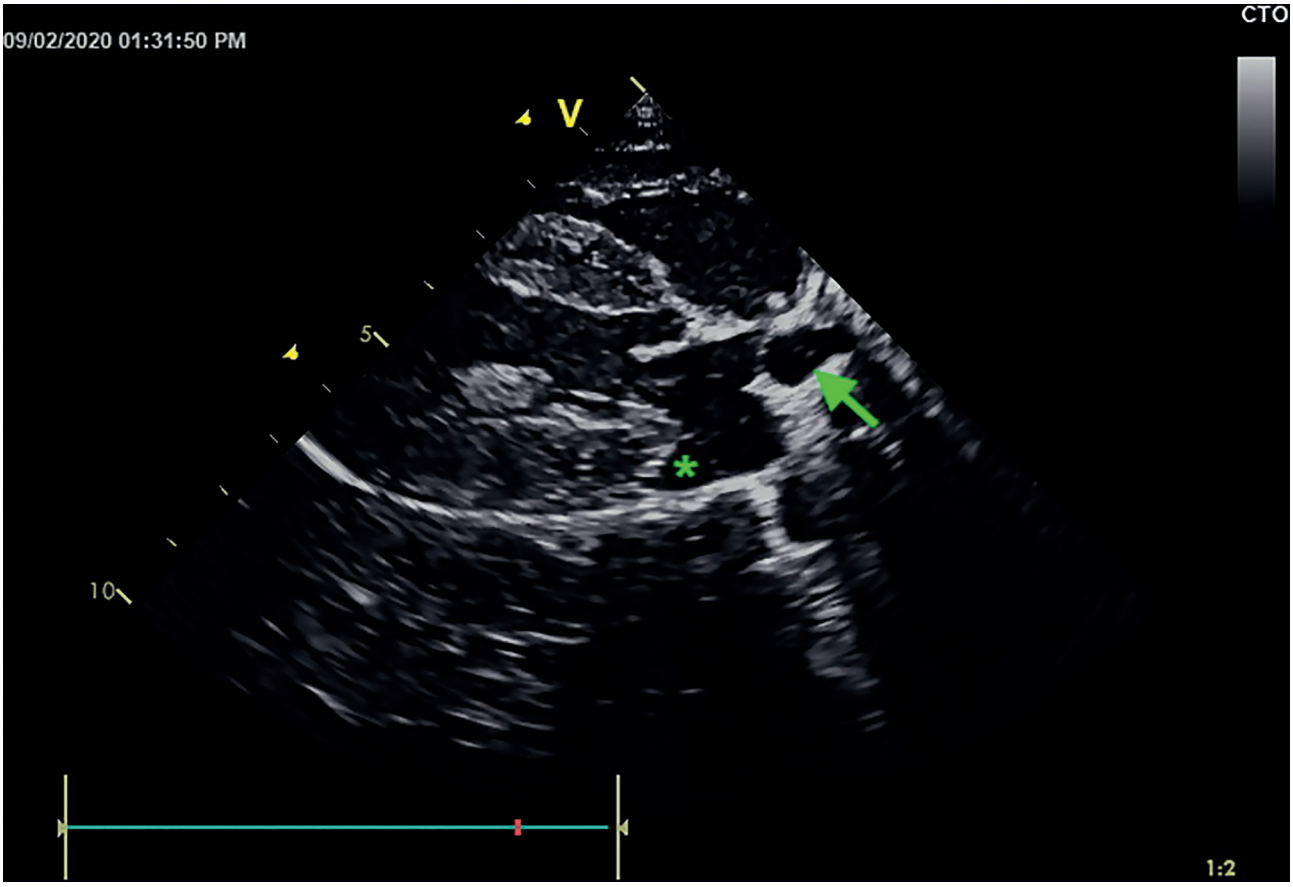

Figure 1. A right parasternal long-axis echocardiographic view during mid-diastole in a zoo-kept wallaby with suspected hypertrophic cardiomyopathy phenotype associated with capture cardiomyopathy (partially mimicking Takotsubo-like cardiomyopathy). No overt right-sided cardiomegaly was appreciated. Dilation of the right pulmonary artery (arrow) and coronary sinus (asterisk) was suspected at the lateral aspect of the left atrium. There was subendocardial and caudal papillary muscle hyperechogenicity visualized. Mild apical dilation was suspected within the left ventricle.

body weight). Histopathology of the muscles and cardiac tissue confirmed that areas of pallor coincided with acute, monophasic necrosis and degeneration with sarcoplasmic vacuolation and interstitial edema frequently appreciated (Figure 2). Additionally, histology confirmed pulmonary edema and mild hepatic necrosis.

DISCUSSION

This case presents a zoo-kept wallaby with hypertrophic cardiomyopathy phenotype associated with capture cardiomyopathy (Takotsubo-like cardiomyopathy).

Takotsubo cardiomyopathy (TC), also known as apical ballooning syndrome or stress cardiomyopathy, is a human phenomenon that mimics myocardial infarction and is precipitated by acute emotional or physiological stress. TC is characterized by reversible, left ventricular concentric hypertrophy (5). While the underlying cause of the left ventricular dysfunction and ventricular wall dyskinesis is unknown, it is postulated that the disease is linked to exaggerated sympathetic stimulation (6). It is documented that Sprague-Dawley rats, once administered beta-adrenergic agonist isoproterenol, develop similar TC-like dysfunction from activation of Gi-protein pathways. This mechanism is hypothesized to decrease myocardial lipid and glucose metabolism as a protective measure from Gs-cAMP-PKA overstimulation, leading to increased myocardial lipid accumulation (7). Significant myocardial edema is also a characteristic finding of TC and can contribute to left ventricular concentric hypertrophy (8). Similarly, the wallaby presented here had myocardial edema on histopathology, which could have been responsible for the concentric hypertrophy noted on echocardiography.

A similar disease process, transient myocardial thicken-

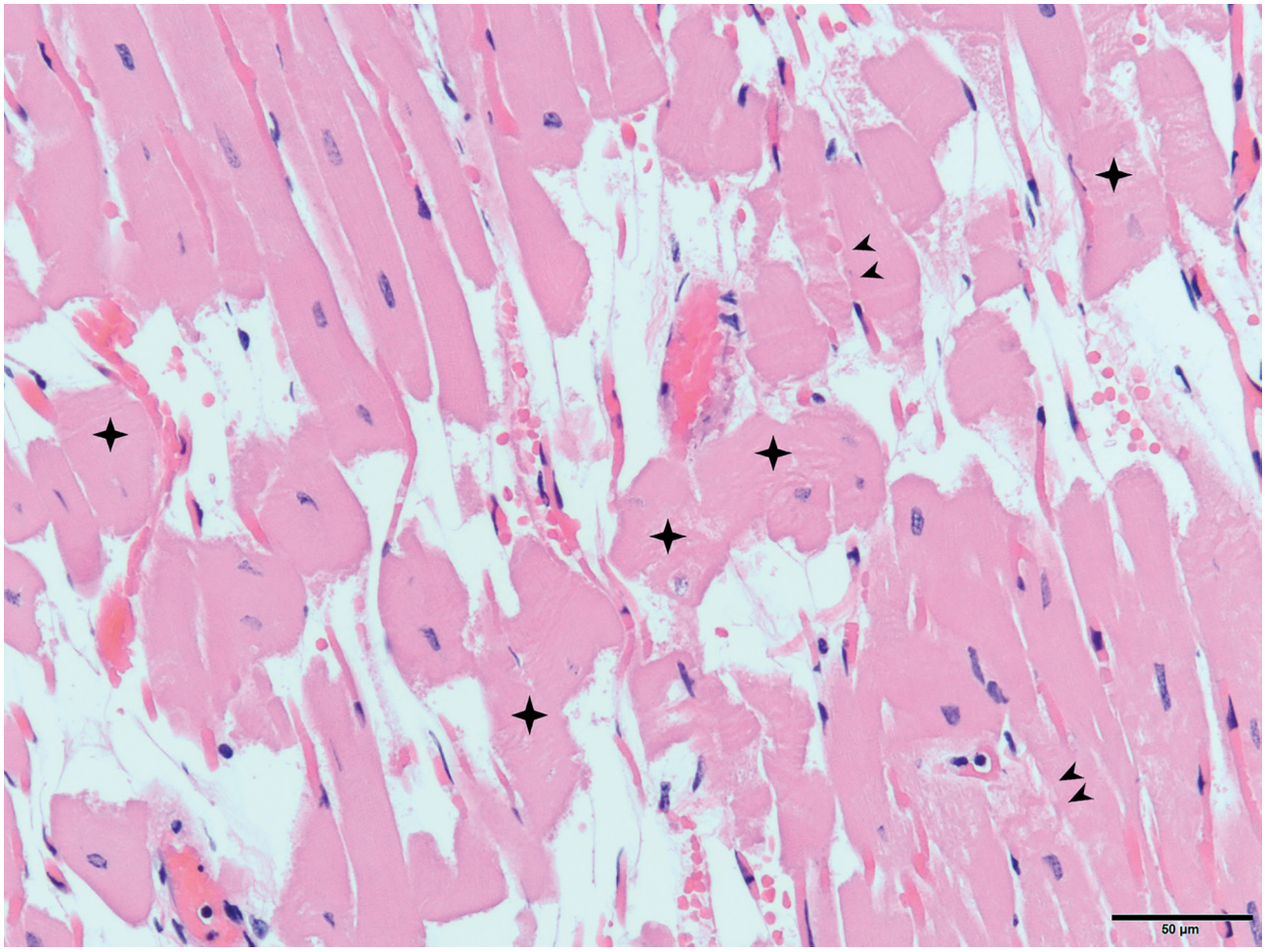

Figure 2. A histopathological preparation from a wallaby left ventricular free wall myocardium is presented. In affected areas, cardiomyocytes (large pink cells) were acutely necrotic with contraction band necrosis (arrowheads), cytoplasmic fragmentation and nuclear karyorrhexis (stars), and drop out of cells with interstitial edema (clear spaces). H&E 20x magnification.

ing, has also been documented in the feline species. Often, there have been noted stressors in the cats' lives, and they present in acute respiratory distress secondary to left-sided congestive heart failure. Echocardiographic findings are consistent with a hypertrophic cardiomyopathy phenotype, and overtime, the cardiac changes reverse to normal left ventricular wall thickness. The underlying pathophysiology is unknown, but with the rapid rate of resolution, it is considered that myocardial edema or a transient myocardial infiltration might be the cause. Cats with transient myocardial thickening also frequently have marked elevations in circulating cardiac troponin concentrations, suggesting an underlying acute, severe disease process like myocarditis or necrosis (9). The extreme elevations in circulating cardiac troponin levels in the case presented here were also suggestive of acute, severe myocardial damage. Given the absence of inflammatory infiltration on histopathology, myocarditis was considered unlikely. Myocardial necrosis was confirmed on histopathology.

Prey animals, like the red-necked wallaby, are prone to the development of capture myopathy. This disease process, also known as exertional myopathy, is defined as an acute, peracute, or chronic disease state found in prey species that can present with variable clinical signs. Classically, skeletal muscle necrosis, severe electrolyte abnormalities, and acid-base derangements are noted. Although it is known that cardiac necrosis and congestive heart failure can occur with capture myopathy, the specific cardiac disease phenotype and pathophysiology are poorly described (10). The wallaby in this report succumbed to capture myopathy, and the cardiac changes noted on echocardiogram and histopathology might have been consistent with a capture cardiomyopathy that

shares underlying pathological features similar to TC. In addition, the hyperthermia documented upon presentation might be compatible with malignant hyperthermia reported in some porcine and bovine blood-lines and in some other wild life species when experiencing severe, acute stress such as capture or general anesthesia (11).

There are several limitations to this case report. An electrocardiographic recording was not documented during case evaluation, so the authors cannot comment on the typical ST segment elevation that is commonly documented in humans with TC (5). Additionally, normal echocardiographic measurements for the red-necked wallaby have never been documented.

In conclusion, when presented with a red-necked wallaby or other prey animal with suspected capture myopathy, hypertrophic cardiomyopathy phenotype (capture cardiomyopathy or TC-like) should also be considered.

CONFLICTS OF INTEREST STATEMENT:

The authors report no actual or potential conflicts of interest relative to this paper.

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