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Research Article

Fibrosing Cardiomyopathy within a Population of Managed Primates at a Single Zoological Facility 2000 - 2015

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Abstract

Gross and histopathological review of 74 cases of primate mortality from a single zoological facility from January 2000-December 2015 revealed that the cause of death (COD) in approximately 27% of the cases was cardiovascular disease (CVD). Among the most common CVD diagnoses were fibrosing cardiomyopathy (FCM). Fibrosing cardiomyopathy has been well documented in the great ape species but only on occasion in other primate species. Cardiomyopathy was diagnosed in 11 genera of primates within this collection during the study period including chimpanzees *(Pan troglodytes)* and Bornean orangutans *(Pongo pygmaeus).*

Keywords: *Fibrosing Cardiomyopathy; Myocardial Fibrosis; Renal Disease; Primates; Zoo; Nutrition*

Abbreviations

AZA: American Zoo Association; ACM: Animal Care Manuals; ZT: ZooTampa; COD: Cause of Death; FCM: Fibrosing Cardiomyopathy; CVD: Cardiovascular Disease; SDMA: Symmetric Dimethylarginine

Introduction

Reviews of primate mortality have generally focused on a single species [1-3] or similar taxonomic groups [4-7]. This review examines all primate mortalities in a single facility. Clinical findings prior to death in several of these cases involving non-great ape species suggested that cardiac disease was more common than expected as the example in Figure 1 demonstrates. This clinical impression was what prompted a more detailed retrospective evaluation of the mortality within this collection.

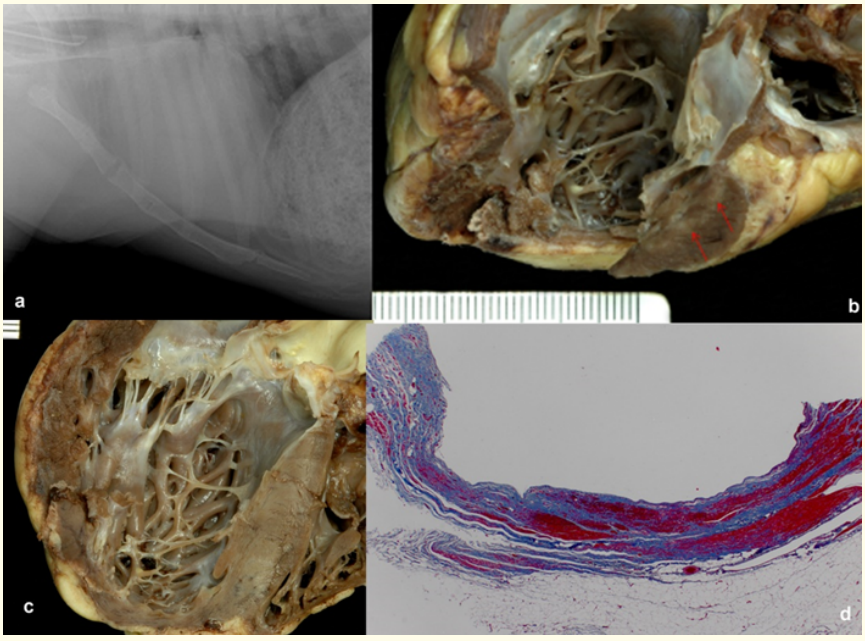

Figure 1: *1a. Lateral radiograph of 8 yr. 1 month old male Angola colobus (Colobus angolensis) found laterally recumbent and weakly responsive. Cardiomegaly is clearly seen with tracheal elevation and increased sternal contact. This colobus expired during this evaluation. 1b. Posterior left ventricle showing discoloration in the posterior wall (basally). This area corresponded with fibrosis seen microscopically. 1c. 4-chamber view (anterior half) of X-year old Silvery langur (Trachypithecus cristatus) that suffered cardiac arrest during pre-shipment exam, showing enlarged, dilated left ventricle with marked apical thinning and discrete gray discoloration in the septum and apex. 1d. Trichrome stain of the apical left ventricle, demonstrates both interstitial fibrosis (blue) and areas with replacement of myocytes (red) by fibrosis.*

Materials and Methods

All primates at ZooTampa at Lowry Park (ZT) are cared for utilizing the best practices currently known as detailed in the American Zoo Associations (AZA) Animal Care Standards (ACMs). An ACM is finalized for chimpanzees (*Pan troglodytes*), Bornean orangutans (*Pongo pygmaeus*), *lowland gorillas* (*Gorilla gorilla gorilla*) and the genus Eulemur. Ethical approval was not required because no animals were used for research in this study. Primate deaths were reviewed at ZT from January 1, 2000 until December 15, 2015. A subset of these records that included both gross necropsy and comprehensive histopathological findings were then evaluated. Cause of death or other significant histological findings as defined by the consulting pathologist were tabulated. Several veterinary and a human pathologist were utilized in case evaluations over this period. Cause of death or significant histological findings were then reviewed based on sex, age, infectious vs. non-infectious, and organ system. Organ systems were defined as respiratory, reproductive, renal, neurological, hepatic, gastrointestinal, cardiovascular, neoplasia, and miscellaneous. Stillbirths were not included in this review nor were neonates that had apparently been cannibalized. Miscellaneous category included anything not categorized in the preceding groups and included sepsis, disseminated amyloidosis and trauma.

Results and Discussion

108 primate deaths were recorded during this study period with 74 meeting the inclusion criteria (Table 1). Eleven different genera were represented, including two great ape species. When all species deaths were summated, 36/74 (48.6%) were male, 28/74 (37.8%) female and 10/74 (13.5%) unknown sex. Primates of unknown sex were always neonates and sex was not recorded in some instances. Neonates comprised 17/74 (23%), juveniles and adults together accounted for 40/74 (55%), and geriatric 17/74 (23%) of all primate deaths. Infectious causes were noted as COD or a significant feature in 31/74 deaths (41.9%) and non-infectious deaths were seen in 43/74 cases (58.1%). Four cases of neoplasia as COD (5.4%) were also seen and counted as non-infectious deaths. The cardiovascular system was the most commonly implicated organ system in terms of COD or predominant pathological feature (20/74, 27%), followed by miscellaneous (14/74, 18.9%), hepatic and respiratory equally (11/74, 14.9%), renal (7/74, 9.5%), gastrointestinal (6/74, 8.1%), neurological (3/74, 4%), and reproductive (2/74, 2.7%). Within the cardiovascular category, five of the 20 cases (25%) were due to infectious causes, four of these were due to encephalomyocarditis virus infection and one case of toxoplasmosis myocarditis. The vast majority of cardiovascular deaths were due to cardiomyopathy (15/20, 75%). A single case of dilated cardiomyopathy was noted as well as 3 cases of hypertrophic cardiomyopathy with significant fibrosing. Fibrosing cardiomyopathy (FCM) was determined to be COD in 11/20 (55%) of the cardiovascular deaths (Figure 1). Cardiac fibrosis as a histological finding was significant in 14/20 (70%) of the cardiovascular related deaths with 10 of them (71.4%) also having significant renal lesions. Six of seven cases with renal disease as the COD had cardiac fibrosis (85.7%). Significant histopathological lesions, typically chronic nephritis or glomerulonephritis were noted in 37/74 (50%) of all the cases even if the renal lesions were not implicated as COD.

Genus	No. Individuals	Myocardial fibrosis	Renal pathology
Alouatta	1		
Calicebus	5		X
Callithrix	12		X
Colobus	7	X	X
Erythrocebus	3	X	X
Eulemur	2		
Lemur	3	X	X
Leontopithecus	10	X	X
Mandrillus	3	X	X
Otolemur	1		
Pan	4	X	X
Pongo	1	X	X
Saimiri	13	X	X
Symphalangus	2	X	X
Trachypithecus	2	X	X
Varecia	5	X	X

Table 1: *Genera of primates included in the final analysis of mortality review from 2000-2015. Myocardial fibrosis category includes fibrosing cardiomyopathy (FCM) and hypertrophic cardiomyopathy (HCM) with significant reported cardiac fibrosis. Renal pathology category includes renal disease as cause of death as well as notable renal pathology.*

While this review is descriptive in nature and statistical comparisons were not attempted, there are notable findings that were unexpected. Reviews of this nature have limitations due to the small number of individuals but can provide a general database to detect the presence of any trends or common features that may exist. The age distribution of deaths shows the juvenile and adults group together with the most mortality. This is in contrast to the expectation that mortalities would be expected to be highest in neonates or geriatric within a given population [4]. Infectious causes have also been reported to be significant COD in primates [1,7], but non-infectious causes found were found more often in this review. Cardiovascular events, particularly myocardial fibrosis, was a leading contributor to primate deaths in this facility. While myocardial fibrosis is well documented in great apes [8,9], it has not received much attention in other primates until recently [10]. An interesting association made in this review is the one between myocardial fibrosis and renal pathology. While renal pathology has been noted previously [5,9], this association between the two organ systems has not been examined until recently [11]. Uremic cardiomyopathy or cardiorenal syndrome warrants closer examination both from an etiological perspective and for interventions. The myocardial fibrosis across numerous genera of primates at a single facility strongly suggests a common environmental cause and nutrition is the suspected cause in all these species. High calorie, low fiber, and especially high sodium diets are all potential contributing factors to compromised renal and cardiovascular health. Sodium is extraordinarily low when measured in wild mountain gorilla diets [12] and easily exceeded in captivity. Monitoring blood pressure and echocardiology evaluations in trained primates may not be a sensitive enough indicator of impending cardiovascular disease as changes in pressure and volume load occur later in the course of the disease [13]. Myocardial fibrosis can be seen in early chronic kidney disease in humans without elevations in serum creatinine [14]. Utilizing symmetric dimethylarginine (SDMA) in primates may be useful in monitoring renal health but also a potential biomarker for cardiac fibrosis in all primate species.

Conclusion

The associations shown in this review suggest that all primate species managed in captivity and fed typical diets consisting of a predominance of commercial primate biscuit should be considered at risk for developing renal disease and potentially FCM. Sodium intake warrants further investigation as a possible cause for the renal and ultimately cardiac pathology seen in such a wide array of species. Monitoring blood pressure and echocardiology in primates may only be useful in managing primates that have already developed pathology but because it is not sensitive has limitations in helping determine etiologies and providing preventative care measures. It is suspected that renal pathology precedes most of the cardiac changes seen in myocardial fibrosis in all primate species. Monitoring renal function may be a more sensitive indicator of both renal and potentially cardiac health. A deviation from a completely forage based diet in most of these species to one that consist of commercial primate biscuits may need more evaluation as well. The potential for enhanced sodium uptake in tropical herbivores may also need to be considered in the face of sodium provided in rations of managed primates.

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Conflict of Interest

No financial interest or any conflict of interest exists.

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