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Case Study

First Report of Massive Myocardial Calcifications in a Vervet Monkey (*Chlorocebus pygerythrus)*

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Abstract

A 13-years-old male vervet monkey that was kept in a primates breeding and research facility at Razi Vaccine and Serum Research Institute, Karaj, Iran (RVSRI) died suddenly. Massively scattered grayish-yellow mottling on both ventricles were the most significant gross necropsy findings. There was a gritty feeling on palpation and sectioning of the yellow areas. Microscopically, the lesions demonstrated scattered degeneration and necrosis of myocardial cells. Inside the affected areas, large calcium deposit plaques were detected using the Von kossa staining method. The development of myocardial calcification in the present case can be attributed to the dystrophic calcification following spontaneous myocardial necrosis or an undetected infection/inflammatory process. Persistent anxiety might trigger spontaneous biventricular necrosis in vervet monkeys. In conclusion, due to similarities between the clinical and histological presentation of the current case with sudden death syndrome associated with myocardial calcification in humans, it was suggested that vervet monkeys might be a relevant animal model for research on the pathophysiological processes of this complication.

Keywords: Calcification, Myocardium, Non-human primate, Vervet monkey

1. Introduction

Myocardial calcification (MC) is one of the rare complications in severely ill patients and has various etiologies whose pathophysiology is not fully understood. This complication can result in sudden death, heart failure, restrictive diseases, abnormalities in ventricular wall movement, and arrhythmias. Moreover, MC could be involved in the mechanism of metastatic calcification which is the result of abnormal calcium homeostasis in such cases as chronic renal failure infections, primary parathyroidism, bone disturbances, and neoplasms. Furthermore, the MC process can be trigged through dystrophic calcification that represents the outcome of local tissue damage and necrosis, particularly in cases of myocardial ischemia, infections, inflammatory processes, and myocarditis (1-2). Pohle (3), using electron-beam tomography (EBCT), reported MC in 95.1% of young patients with acute myocardial infarction. Based on the evidence, necrotic tissue in the myocardium of some infants with congenital heart disease tends to become calcified rather than be removed and scarred as occurs in the adult. It also confirms that prenatal cardiac disease and trauma, such as surgery, might account for the presence of myocardial calcification (4). It has been well documented that cardiovascular calcifications, particularly in patients with chronic kidney disease (CKD), are more prevalent, progressive, extensive, and severe compared with the non-CKD people (5). Nevertheless, there are unusual reports of idiopathic massive MC in humans (6).

In animals, some diseases show characteristic myocardial alteration, such as calcification in calcinosis

of mice (7). In fact, calcification of myocardial necrosis is a common complication in mice (8). Chondro-osteogenic differentiation can take place in infarcted rat hearts (9). Focal areas of calcification have been frequently reported in rat myocardium, 30 and 60 days after administration of dihydrotachysterol (10). Although the spontaneous occurrence of myocardial cell necrosis has been reported in some monkey species (11), such alterations as myocardial mineralization has a low incidence in primates (12-13). In an exceptional report, Kent, Vawter (14) have described extensive calcification and degeneration in the myocardium of rhesus monkeys that apparently died due to hypervitaminosis D.

2. Case Presentation

A 13-year-old, 5.5 kg, male vervet monkey (*Chlorocebus pygerythrus*) was housed and maintained in a facility at the Razi Vaccine and Serum Research Institute (RVSRI), Karaj, Iran.

This monkey was kept in an indoor large-caged breeding colony consisting of four females and one male. One day, while performing the experimental procedure on another group of monkeys in an adjacent colony, the animal suddenly collapsed and died, despite the best efforts of veterinarians. Three months before death, the animal had a history of weakness and depression for a few days that was treated symptomatically with an injection of a combination of antibiotics and vitamins. A systematic necropsy was performed to determine the cause of death. Massively scattered grayish-yellow mottling on both left and right ventricles were the most significant findings of gross necropsy (Figure 1). These areas are projected slightly above the adjacent muscle. There was a tenacious and gritty feeling on palpation and sectioning of the yellow areas. Microscopically, the lesions demonstrated degeneration and necrosis of myocardial cells (Figure 2). Large plaques of deposits of calcium were detected inside necrotic areas through the application of the Von Kossa staining procedure. Although the deposits consisted of irregular plaques along with the muscle fibers (Figure 3, 4), the inflammatory reaction was not so obvious. However, occasionally, there was an infiltration of lymphocytes and histiocytes at the periphery of the large areas. Capillaries, veins, and arterioles in both the necrotic and intact myocardium were not involved. There was no perivascular reaction. However, foci of hemorrhages were observed in the areas with necrotic muscles. In the remaining organs, foci of consolidation and acute tubular necrosis (ATN) were observed in the lung and the kidney, respectively.

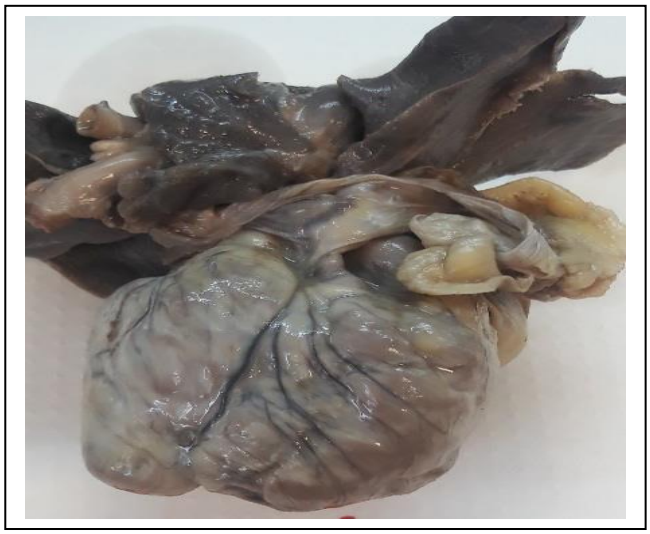

Figure 1. Mottled shape of the myocardium is observed due to calcification in the heart of the vervet monkey

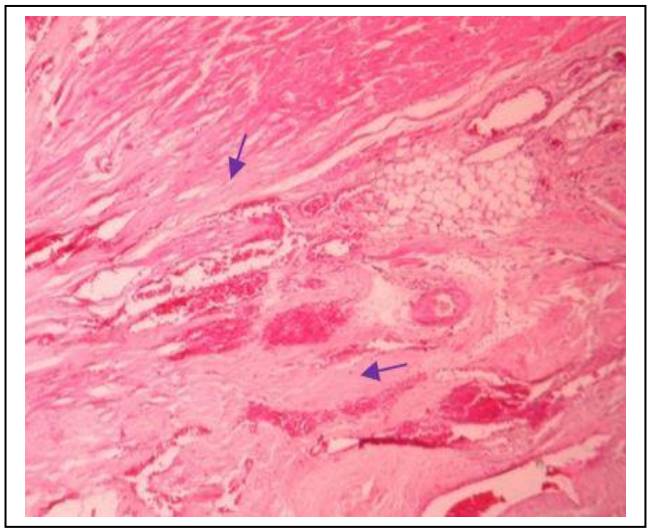

Figure 2. Diffuse myocardial cell necrosis (arrows) with hemorrhage in the heart of vervet monkey. The cells on top of the image are nearly intact. H&E ×100

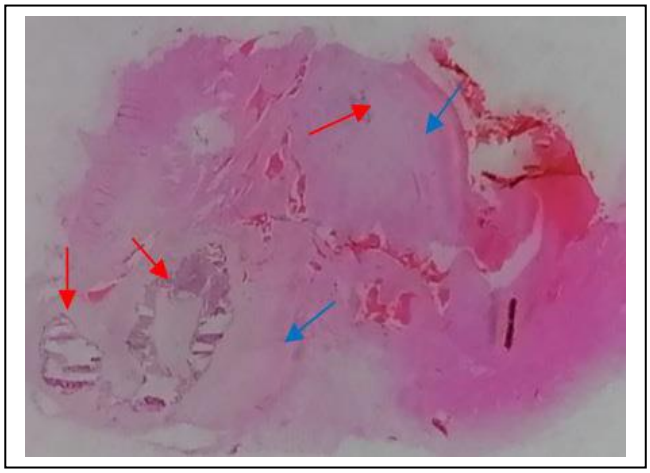

Figure 3. Extensive calcium deposits (red arrows) observed inside the necrotic myocardial cells (blue arrows) in the heart of the vervet monkey (H&E ×5).

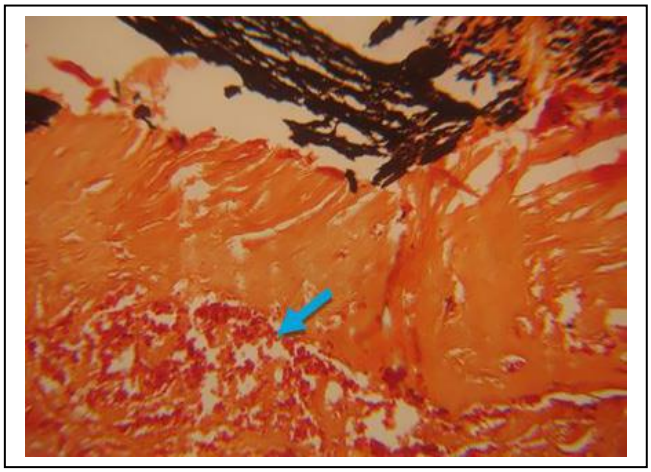

Figure 4. Myocardial calcification, a large plaque of black calcium deposit, is observed on top of the picture taken from the heart of the vervet monkey. The adjacent myocardial cells are degenerated and necrotic. There was a focal area of hemorrhage at the bottom of the picture (arrow). Von Kossa ×200.

4. Discussion

In humans, diffuse myocardial calcification is a very rare condition that is associated with very poor cardiac function and high mortality (15). Previous myocardial infarction, chronic renal failure, endomyocardial fibrosis, and such infections as tuberculosis have been reported as the inducers of MC (16). However, according Tu, Hu (17), diffuse biventricular calcification, such as that in the present case, may be associated with multiple factors. Increased myocardial calcium content resulting from poor calcium and phosphorus control, which may be enhanced by parathyroid hormone hyperactivity, could be an important pathophysiologic mechanism for initiation of MC (18). Vitamin D is a stimulant for osteocalcin biosynthesis that is closely linked to the process of physiological and pathological calcification (19). Higher plasma concentrations of 25(OH)D3 have been reported to be associated with more favorable cardiovascular risk factors in female non-human primates (NHPs) (20). It has been reported that high-dose inotropic support is likely a contributing cause of calcification due to cardiomyopathy (15). Although sepsis-related MCs are a rare phenomenon in patients with septic cardiomyopathy, there are reports of the rapid appearance of MC following septic cardiomyopathy (21). Therefore, in cases of incidental findings of myocardial calcification, it is recommended that the physicians must be alert and think beyond the heart (22).

To the best of our knowledge, reports of myocardial calcification in NHPs are very rare, and the present case is the first report of massive myocardial necrosis and calcification in a captive vervet monkey. Nonetheless, mineralization of the myocardium and heart vessel wall has been described as spontaneous heart finding in some species of macaques (13, 23). From the authors' point of view, the development of MC in the present case could be attributed to dystrophic calcification following spontaneous myocardial necrosis or an undetected infection/inflammatory process. Actually, stress, anger, and depressed mood can act as acute triggers of major cardiac events (24). In a study on spontaneous cardiomyopathy in cynomolgus monkeys, morphologic changes were detected in multifocal areas of myocardial necrosis. The presence of acute and chronic necrosis lesions implied that the pathogenic process was either continuous or involved multiple components. This type of lesion might be induced by the stress-associated release of catecholamines that can occur with routine handling of

the monkeys during the experimental procedures (25-26). The authors believe that persistent anxiety might be a trigger of spontaneous biventricular necrosis and calcification in vervet monkeys, which in turn could develop to arrhythmia, sustained ventricular tachycardia, heart failure, and death. In conclusion, due to similarities in clinical and histological presentation of this case with sudden death syndrome associated with myocardial calcification in humans, it is suggested that vervet monkeys can be a relevant animal model for research on pathophysiological processes of this complication.

Authors' Contribution

Study concept and design: M. H. H.
Acquisition of data: M. H. H.
Analysis and interpretation of data: M. E.
Drafting of the manuscript: M. E.
Critical revision of the manuscript for important intellectual content: M. E.
Statistical analysis: M. H. H
Administrative, technical, and material support: M. H. H

Ethics

The monkey was housed and maintained in a facility at the Razi Vaccine and Serum Research Institute (RVSRI), Karaj, Iran, according to the animal welfare committee of the research deputy in RVSRI and National Ethical Framework for Animal Research in Iran, the Ministry of Health and Medical Education (TUMS, reference code: 91-01-159-18022).

Conflict of Interest

The authors declare that they have no conflict of interest.

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