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CASE REPORT

Acute / Subacute Development of Diffuse Left Ventricular Myocardial Calcification in Sepsis Associated with High Mortality

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ABSTRACT

Diffuse myocardial calcification is very rare and can be either dystrophic or metastatic. Acute / subacute development of diffuse myocardial calcification of the left ventricle in an acute setting has been rarely reported but is found in a septic patient in our case. We believe that the cause of myocardial calcification is likely multifactorial. In particular, high-dose inotropic support is likely a contributing cause of calcification due to cardiomyopathy. More importantly, it is associated with very poor cardiac function and high mortality.

Key Words: *Calcinosis; Catecholamines; Sepsis*

中文摘要

敗血症中具高死亡率的瀰漫性左室心肌鈣化的急性/亞急性發展

陳煥章、曾佩琪、韓予偉、王耀忠

瀰漫性心肌鈣化非常罕見，可能是萎縮性病變或轉移瘤引致。急性/亞急性瀰漫性左室心肌鈣化鮮有報導，作者在一個膿毒症患者中發現此症。特別是使用大劑量強心劑時有很多因素可以造成心肌鈣化。此病與心功能差相關並死亡率高。

INTRODUCTION

Diffuse myocardial calcification is very rare and only a few cases have been reported in the literature. In general terms, pathogenesis of calcification can be dystrophic or metastatic.[1] Dystrophic calcification occurs due to calcium deposition in tissue that is necrotic and in turn can be caused by any sort of insult to the myocardium, most commonly an ischaemic cause. Metastatic calcification occurs in normal tissue due to elevated calcium levels associated with renal failure. In a clinical context of sepsis, many factors come into play as causes of these calcifications.

The case presented here is a middle-aged male who was admitted for elective resection of colonic carcinoma but developed postoperative complications and sepsis and thus required intensive care unit (ICU) admission. A postoperative computed tomographic (CT) scan showed diffuse calcification of the left ventricular (LV) myocardium that was absent 6 weeks previously and the patient soon succumbed to multiorgan failure. A review of the literature of similar cases and an analysis of the

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possible causes were performed.

CASE REPORT

Our patient was a 56 year-old male who was a chronic smoker. He had a 1-year history of hypertension requiring medication. He was admitted for elective laparoscopic lower anterior resection in February 2014. Anastomotic leakage was suspected 3 days postoperatively and the patient returned to operating theatre for drainage and formation of a defunctioning loop ileostomy. Intraoperative finding of a grossly contaminated peritoneal cavity was reported. The patient developed hypovolaemic shock after the second operation and a clinical diagnosis of abdominal compartment syndrome was made. Thus the patient was once again sent back to theatre for decompression. Postoperatively, the patient was treated in the ICU. He required extremely high dose of inotropic support, with noradrenaline 30 ml per hour (840 μg/ml), which was approximately 8 times the usual dose. He also developed acute renal failure and required haemodialysis. Calcium and phosphorus levels were within normal limits. He had metabolic acidosis. He had elevated troponin I to 6.3 ng/ml but electrocardiogram (ECG) did not show ST elevation and he was assumed to have acute coronary syndrome. Thrombolytics or antiplatelet agents were not administered as they were contraindicated in the postoperative period. He had multiple bacterial infections including pseudomonas, enterococcus, and methicillin-resistant *Staphylococcus aureus* cultured from blood, the drains, and the respiratory tract. He was treated with broad-spectrum antibiotics.

The patient had a downhill course with persistent sepsis. CT was performed in early April 2014 (around postoperative 6 weeks; Figure 1) to look for residual intra-abdominal collections. There were no signs of persistent intra-abdominal sepsis but an incidental finding of diffuse calcification of the myocardium of the left ventricle. The calcification was thick and linear

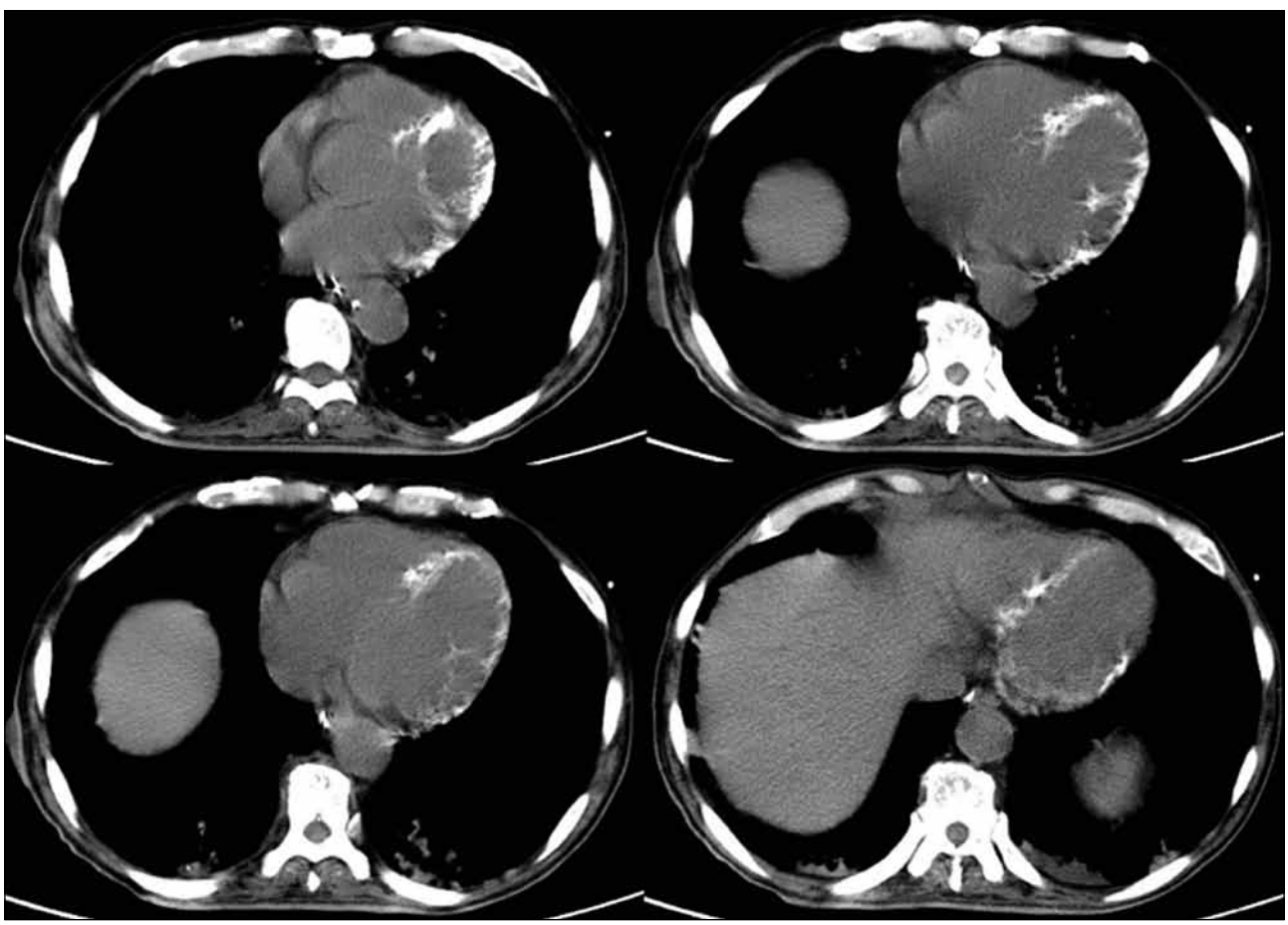

Figure 1. Postoperative non-contrast computed tomography: serial axial slices through the left ventricle of the heart showing thick, linear calcification in the myocardium of the left ventricle.

in appearance involving the basal, mid, and apical segments of the left ventricle. It did not extend to the pericardial surface. The other chambers were not involved and the heart did not appear dilated. Some mild vascular calcification was seen in the rest of the systemic vasculature but no calcification was seen in the lungs or soft tissue. The calcification, however, was not dense enough to be appreciated on chest radiograph.

The patient succumbed around 1 week after the CT scan. The cause of death was considered to be postoperative sepsis. No autopsy was performed.

With regard to cardiac imaging, the preoperative CT scan for tumour staging 6 weeks previously showed normal appearance and size of the heart (Figure 2). An echocardiogram (ECHO) during his ICU stay showed severe LV hypokinesia with an ejection fraction of 20%. There was no mention of any abnormalities in the thickness or increase in reflectivity of the myocardium.

DISCUSSION

The development of diffuse calcification of the myocardium is very rare and not many cases have been reported in the literature. A review of the literature

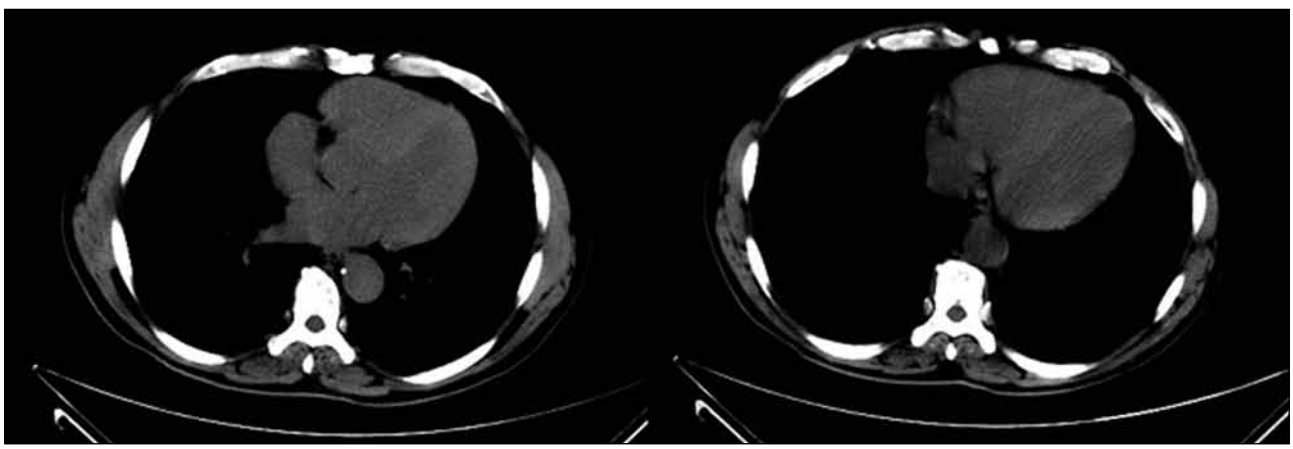

Figure 2. Preoperative non-contrast computed tomography 6 weeks previously: axial slices through the left ventricle of the heart showing that the calcification of the left ventricle was absent at that time.

Table. Summary of reported cases in the literature with myocardial calcification with sepsis.[2-5]

	van Kruijsdijk et al[2]	Schellhammer et al[3]	Simonson et al[4]	Lapatto-Reiniluoto et al[5]	Our patient
Age (years) / gender	56/M	20/F	58/F	34/M	56/M
Past heath	Good	Aplastic anaemia	Leukaemia	Good	Hypertension for 1 year
Acute problem	Sepsis*				
Distribution of calcification	Diffuse myocardial calcification of left ventricle*				
Duration of development (days)	N/A	30	24	42	42
Evidence of myocardial injury	ECG: diffuse ST elevation; troponin 5.72 ng/ml	N/A	Troponin 50 ng/ml	ECG: diffuse ST elevation; troponin 13.9 ng/ml	ECG: unremarkable; troponin 6.3 ng/ml
ECHO cardiac function	LV dysfunction	N/A	Global LV dysfunction; EF 20%	Global LV dysfunction; EF 35%	Severe LV dyskinesia; EF 20%
Inotropes (catecholamines)	N/A	High dose	High dose	10-times dose	8-times dose
Calcium-phosphate product	Normal	N/A	Normal	Normal	Normal
Outcome	N/A	Clinical improvement	Clinical improvement. Residual EF 55%	Died at day 50 after admission	Died around 7 weeks after admission; around 1 week after identification of myocardial calcification

Abbreviations: ECG = electrocardiography; ECHO = echocardiogram; EF = ejection fraction; LV = left ventricular; N/A = not available.
* Same for all five patients.

found four cases of acute development of myocardial calcification of the left ventricle in the presence of sepsis. A summary of the findings is shown in the Table.[2-5] The development of calcification can occur over a period of 30 to 42 days. None of these patients had any relevant medical history of cardiac disease. Most reported associated poor ejective fractions of the left ventricle on ECHO and evidence of myocardial injury on ECG with elevated troponins. Interestingly high-dose inotropic medications were given in three of the four cases up to 10 times the normal dose.

Myocardial infarction is a common cause of calcification, but it usually affects the myocardium in a more focal distribution and in a particular vascular territory. Ischaemia was suspected to be present in our patient as evidenced by the presence of elevated cardiac enzymes. Nonetheless, the calcification appeared very diffuse and did not follow a vascular territory. The patient did have risk factors for atherosclerosis including smoking and a short history (1 year) of hypertension, but he did not complain of any angina and neither were there ischaemic changes on the preoperative ECG. The elevated cardiac enzyme could just be a reflection of myocardial damage and not necessarily ischaemia. Thus we believe that the calcification is not fully explained by ischaemia. Lapatto-Reiniluoto et al[5] performed a coronary angiogram in their patient and found no signs of atherosclerotic disease.

Our patient had acute renal failure and required haemodialysis. Metastatic calcification related to renal failure is a possible mechanism but is unlikely due to three reasons. First, calcium and phosphorus levels were normal, as they were in all the reported cases. Second, metastatic calcification usually occurs in patients with a longer history of renal failure. Third, calcification was not seen in other organs that are more prone to calcification due to this mechanism, such as soft tissue or the lungs.

Both Schellhammer et al[3] and Lapatto-Reiniluoto et al[5] proposed that the calcification could be related to the use of high-dose catecholamines in the process of resuscitation leading to cardiomyopathy. This mechanism was also suggested by previous studies[6] and the pathogenesis was proposed to be due to myofibrillary degeneration and cellular necrosis.[7] Our patient was prescribed around 8 times the usual dose of noradrenalin during the postoperative period. We believe that this was also a likely possibility in our case with very high–dose inotropes given.

Viral myocarditis can also cause myocardial calcification. Cytomegalovirus has been reported to induce perimyocarditis and eventually dilated cardiomyopathy. Such calcification, however, usually involves the pericardium and also affects the right heart.

Other cases of extensive myocardial calcification such as sarcoidosis, fungal infection, and endomyocardial fibrosis are not relevant in this clinical scenario.

The extensive calcification of the myocardium is associated with the diffusely hypokinetic heart and poor ejection fraction as demonstrated by the ECHO and as seen in the reported cases as well as in ours. The prognosis of this condition is very poor with one of the reported cases recovering approximately 50% of cardiac function and one reporting death. Our patient also succumbed 1 week after identification of myocardial calcification and is similar to the clinical course described by Lapatto-Reiniluoto et al.[5]

We believe that the cause in our patient was multifactorial. Catecholamine-induced cardiomyopathy and ischaemia are very probable contributors. The high mortality associated with this finding highlights its clinical significance. Further reports of similar cases are required before a conclusion can be made with regard to its relationship with the level of catecholamines.

CONCLUSION

Acute / subacute development of diffuse myocardial calcification of the left ventricle is associated with poor cardiac function and high mortality. The cause cannot be fully explained by more common pathologies such as ischaemia. We postulate that the calcification is related to the use of high-dose inotropes that cause myocardial damage and calcification.

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