Clinical Case Report

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Sudden death in a patient with severe mitral annular calcification and end-stage renal disease during hemodialysis

A case report

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Abstract

Rationale: Mitral annular calcification (MAC) is a chronic, degenerative cardiac condition. Although MAC is often considered as an incidental finding in clinical and forensic practice, sudden death due to severe MAC with end-stage renal disease (ESRD) during hemodialysis is uncommon. In addition, spontaneous subepicardial hematoma due to rupture of the subepicardial vein is very rare.

Patient concerns: A 65-year-old woman had a history of hypertension, diabetes mellitus, and renal failure.

Diagnoses: Postmortem examination revealed marked MAC with cardiomegaly and ESRD. Spontaneous subepicardial hematoma due to disruption of subepicardial vein was also seen.

Interventions and outcomes: The patient became short of breath while on hemodialysis and expired en route to the hospital.

Lessons: In this case, death was attributed to the effects of the calcified mitral valve annulus. This case highlights that MAC must be considered in any patient with ESRD and fatal cardiovascular events should not be overlooked in these patients.

Abbreviations: CKD = chronic kidney disease, ESRD = end-stage renal disease, MAC = mitral annular calcification.

Keywords: end-stage renal disease, hemodialysis, mitral annular calcification, spontaneous subepicardial hematoma, sudden death

1. Introduction

Mitral annular calcification (MAC) is defined as a chronic, degenerative process characterized by calcification of the surrounding fibrous support of the mitral valve,[1] commonly seen in the olderly, especially women.[2] Since it was first described by Bonninger in 1908 in its association with complete heart block, it has been reported in association with endocarditis, coronary artery disease, and congestive heart failure.[3] Previous studies have shown that the prevalence of MAC is between 8% and 15%, but it significantly increases in women over 90 years with an incidence of 43.5%,[4] and in patients with multiple cardiovascular risk factors or chronic kidney disease (CKD).[1]

In clinical and forensic practice, though sudden death involving MAC with valve stenosis has been reported,[2,5] sudden cardiac death associated with MAC occurring during dialysis has not been extensively studied at autopsy. Subepicardial hematoma, usually as a result of coronary perforation, after or during percutaneous coronary intervention is uncommon,[6,7] spontaneous subepicardial hematoma due to rupture of the subepicardial vein is even rare. Here, we report a case of severe MAC with cardiomegaly, end-stage renal disease (ESRD) and subepicardial hematoma, occurring in a 65-year-old woman who presented as an unexpected sudden death during hemodialysis.

2. Case presentation

A 65-year-old woman, 1.66 m, 87 kg, with history of hypertension, diabetes mellitus, and renal failure became short of breath suddenly while on hemodialysis and expired en route to the hospital. Prior written and informed consent for publication of the case were obtained from the patient's family and the study was approved by the Human Ethical Commission at Medical School of Ningbo University.

At autopsy, external examination showed an obese old woman without any signs of mechanical injury and mechanical asphyxia. Internal examination revealed remarkable cardiomegaly (510 g) with normal epicardial fat. Focal subepicardial hematoma (5 × 3.5 cm) in the left posterolateral ventricle was seen. However, no significant tamponade was present. The heart presented biventricular hypertrophy and mild dilatation of left atrium: left

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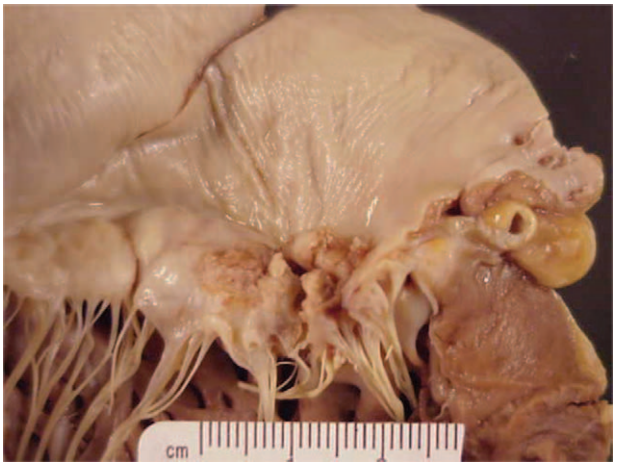

Figure 1. Severe calcification of the mitral valve annulus with focally thickened, shortened and fused chordae.

ventricular cavity diameter 30 mm, left ventricular free wall thickness 18 mm, ventricular septum thickness 20 mm, and right ventricle thickness 8 mm. Severe MAC with focally thickened, shortened, and fused chordae was seen (Fig. 1). The other valves and endocardium were unremarkable. No gross myocardial fibrosis or necrosis was seen.

Histological examination showed biventricular myocyte hypertrophy with subendocardial and perivascular interstitial fibrosis and patchy small foci of replacement fibrosis. Epicardial and subepicardial hemorrhage in the left posterolateral ventricle, with focally disrupted subepicardial vein showing adherent platelet-rich thrombus were observed (Fig. 2). Sections of mitral valve showed fibrosis, neovascularization, nodular calcification and chronic inflammation of valve annulus with extension into the underlying myocardium. Focal moderate atherosclerosis with 70% narrowing of proximal and 35% narrowing of mid left anterior descending artery were seen. In addition, ESRD with severe arterial and arteriolar sclerosis, global glomerulosclerosis, and thyroidization of tubules were also observed. In the other organs, no lethal diseases were present that could have contributed to the death.

3. Discussion

MAC is a relatively common degenerative condition in the elderly, even so, macroscopically evident disease is uncommon in those under 70 years of age.[2] Though MAC is usually considered an incidental finding clinically and at autopsy, severe MAC may play an important role in the development of potentially fatal complications or sudden death.

The pathogenesis contributing to the formation of MAC is still not fully understood. Studies have found that female sex is a risk factor of MAC and the possible reason is the severe bone loss caused by postmenopausal osteoporosis.[1,8] Although MAC was first considered a passive, degenerative, age-related process, accumulating evidence now suggest that it can also result from a tightly regulated, active atherosclerotic process.[1] Though MAC has been shown to be associated with atherosclerosis, the exact mechanism linking these 2 processes remains elusive.[9] Studies have shown a strong association between MAC and cardiovascular risk factors such as age, hypertension, hyperlipidemia, diabetes mellitus, and obesity.[1,3,10,11] Patients with MAC have been shown to have higher prevalences of different forms of atherosclerotic cardiovascular disease including carotid stenosis, coronary artery disease, peripheral artery stenosis and aortic atheroma.[3,12,13]

MAC is a common finding in patients with CKD. Vascular and valvular calcifications are common and severe in the adult hemodialysis population and had a more higher prevalence compared with the general population.[14,15] Studies showed that coronary artery calcification is common in patients with ESRD undergoing dialysis,[16] and MAC is common in patients with ESRD.[17] The possible reason is an increased prevalence and severity of cardiovascular risk factors in these patients.[18] Abnormal calcium-phosphorous metabolism in patients with chronic renal failure or ESRD may also contributes to the pathogenesis of MAC.[1] In addition, increased mitral valve stress caused by hypertension or by hypertrophic cardiomyopathy may also contribute to the development of MAC.[1]

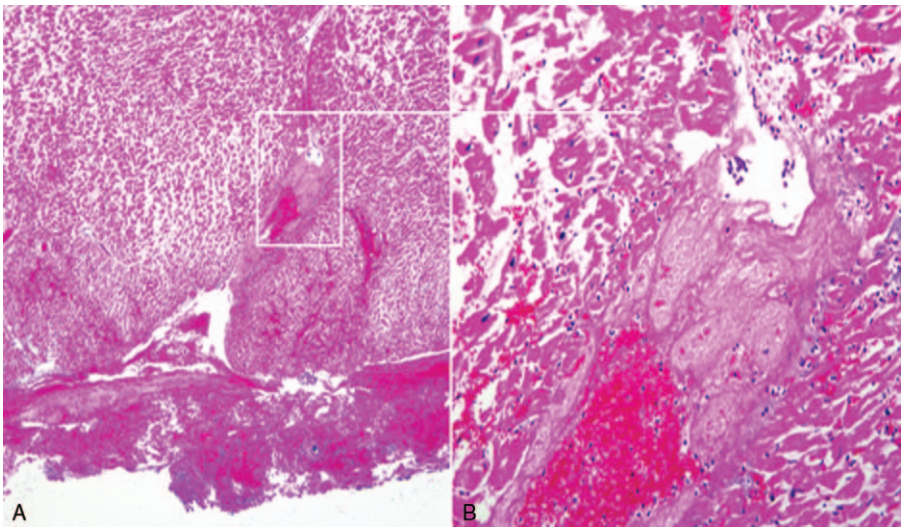

Figure 2. Histological examination of the focal subepicardial hematoma in the left posterolateral ventricle. (A) Epicardial hemorrhage, focal subepicardial hematoma and a disrupted subepicardial vein were observed. (B) Higher magnification of the disrupted subepicardial vein showing adherent platelet-rich thrombus. (H–E staining, A ×10 magnification; B ×40 magnification).

Patients with MAC have higher prevalence of atrioventricular block, bundle branch block, and intraventricular conduction delay.[1] Prospective studies found that MAC was independently associated with stroke,[19] as well as incident cardiovascular disease, cardiovascular death, and all-cause death after adjusting for traditional cardiovascular risk factors.[3] Though MAC generally has little or no effect on left ventricular inflow or mitral valve function, severe MAC may cause mitral regurgitation or mitral stenosis.[1] In addition, studies also observed a strong association between the presence of MAC and hypertension, left atrial enlargement, and atrial fibrillation.[1,20] The above findings suggest that MAC is a marker of increased cardiovascular risk.

In this case, the patient had several risk factors, including female sex, obesity, hypertension, diabetes mellitus, and ESRD undergoing hemodialysis, which might contribute to the development of cardiomegaly, coronary atherosclerosis and severe MAC. The hypertension and vascular damage caused by the diabetes mellitus[21] might caused the spontaneous rupture of the subepicardial vein, resulting in subepicardial hematoma but not cardiac tamponade. Arrhythmias, such as atrial fibrillation and cardiac conduction defects, caused by severe MAC, might contributed to the final sudden death. Hemodialysis was the inducement and hastened her death.

In summary, we report a sudden death in a femal patient with severe MAC, ESRD and spontaneous rupture of the subepicardial vein resulting in subepicardial hematoma during hemodialysis. This case highlights that MAC must be considered in any patient with ESRD and fatal cardiovascular events should not be overlooked in these patients.

Author contributions

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