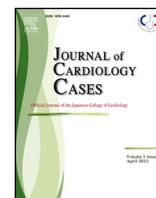




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## Case report

## Development of caseous calcification of mitral annulus after initiation of hemodialysis therapy



Hiroki Usuku (MD PhD)<sup>a,b</sup>, Eiichiro Yamamoto (MD PhD)<sup>b,\*</sup>, Fumi Oike (MD)<sup>b</sup>, Ryusuke Tsunoda (MD PhD)<sup>c</sup>, Kazuhiro Nishigami (MD PhD)<sup>d</sup>, Takeshi Sakaguchi (MD PhD)<sup>e</sup>, Ryusuke Suzuki (MD PhD)<sup>e</sup>, Soichi Uekihara (MD PhD)<sup>f</sup>, Hiroataka Matsui (MD PhD)<sup>a,g</sup>, Kenichi Tsujita (MD PhD FJCC)<sup>b</sup>

<sup>a</sup> Department of Laboratory Medicine, Kumamoto University Hospital, Kumamoto, Japan

<sup>b</sup> Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan

<sup>c</sup> Department of Cardiovascular Medicine, Japanese Red Cross Kumamoto Hospital, Kumamoto, Japan

<sup>d</sup> Department of Cardiovascular Medicine, Miyuki Hospital, Kumamoto, Japan

<sup>e</sup> Department of Cardiovascular Surgery, Japanese Red Cross Kumamoto Hospital, Kumamoto, Japan

<sup>f</sup> Department of General Internal Medicine, Japanese Red Cross Kumamoto Hospital, Kumamoto, Japan

<sup>g</sup> Department of Molecular Laboratory Medicine, Faculty of Life Sciences, Kumamoto University, Kumamoto, Japan

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## ABSTRACT

We here present a 59-year-old man who had undergone peritoneal dialysis (PD) for 7 years and hemodialysis for the following 6 years in the Japanese Red Cross Kumamoto Hospital. Six years after commencing PD, transthoracic echocardiography showed a highly echogenic mass with a transverse diameter of almost 15 mm in the posterior mitral leaflet. Because the mass increased from 2 years after initiation of hemodialysis, reaching over 25 mm by 6 years after commencing hemodialysis, tumor resection and mitral valve replacement were performed. When the surface of the mass was incised, white opalescent liquid drained out of the mass and histological examination showed multiple calcified nodules and granulation tissue, resulting in diagnosis of a caseous calcification of mitral annulus.

<Learning Objective: Caseous calcification of mitral annulus (CCMA) is usually associated with end-stage renal disease. In the present case, a 59-year-old man had undergone peritoneal dialysis for 7 years, after which he had undergone hemodialysis for 6 years. The development of CCMA was seen after initiation of hemodialysis therapy. Routine echocardiography is useful for early diagnosis of CCMA, especially in patients whose type of dialysis changed from PD to hemodialysis.>

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## Introduction

Mitral annular calcification (MAC) is defined as chronic degeneration of the mitral valve fibrous ring involving the posterior annulus. MAC is very common in patients with chronic kidney disease [1]. While caseous calcification of mitral annulus (CCMA) is a rare variant of MAC due to caseous transformation of the inner material and prevalence of CCMA is about 0.63% of all MAC cases and has a prevalence of 0.067% in the general

population [2]. There were few reports which described time-dependent changes in these lesions. We herein report a patient who developed a CCMA after initiation of hemodialysis therapy.

## Case report

A 59-year-old man attended the Japanese Red Cross Kumamoto Hospital regularly to undergo hemodialysis. He had a history of acute nephritis at age of 15 years. The detailed cause of acute nephritis was unclear because it happened in the too distant past. After that, his renal function gradually got worse and he was introduced to peritoneal dialysis (PD) at 46-years-old. Then, he had undergone PD for 7 years, after which he had undergone hemodialysis for another 6 years.

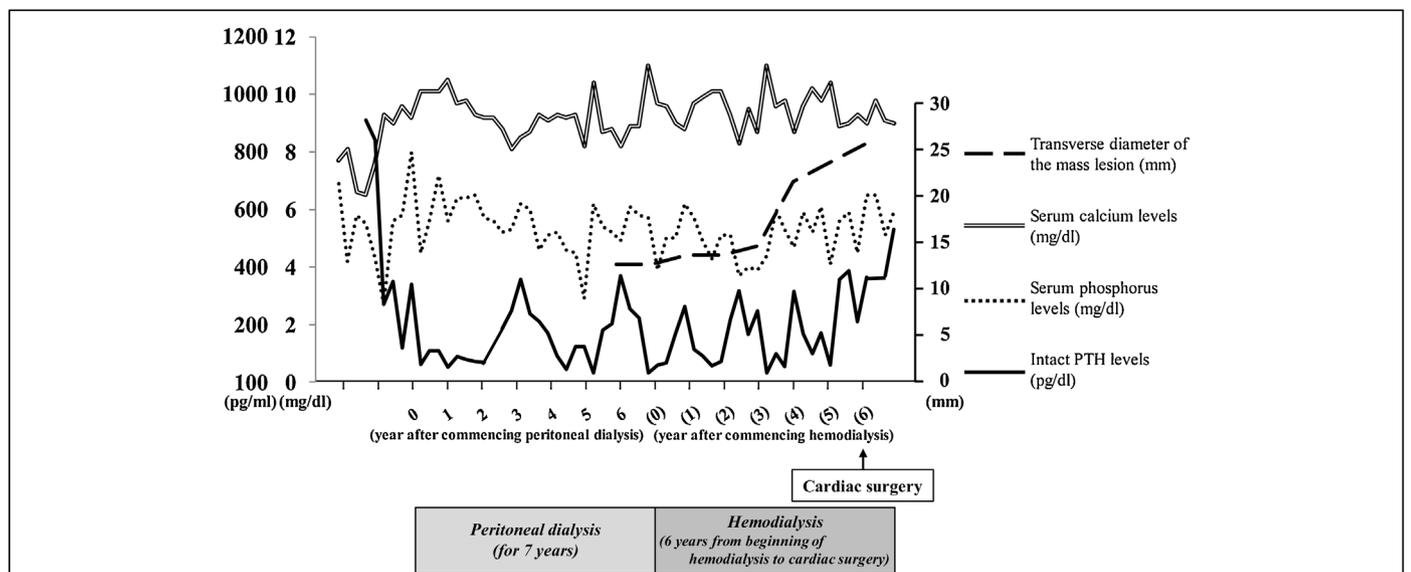
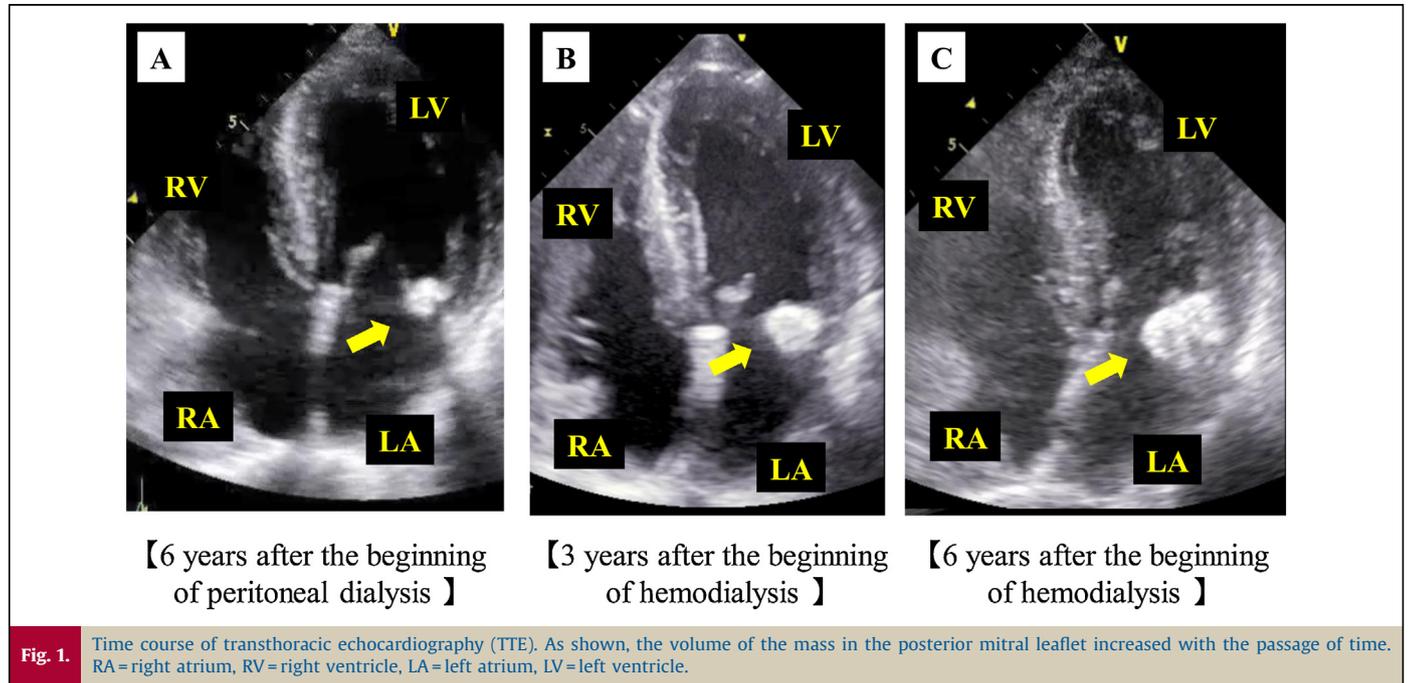
\* Corresponding author at: Department of Cardiovascular Medicine, Graduate School of Medical Sciences, Kumamoto University, 1-1-1 Honjo, Chuo-ku, Kumamoto, Japan.

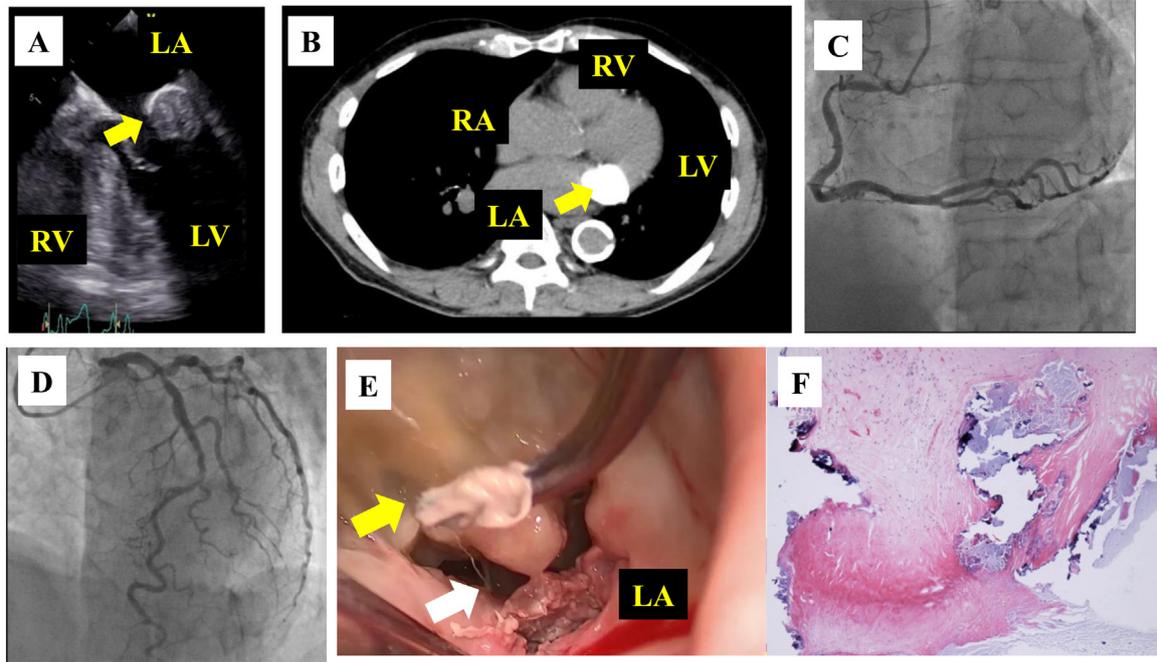
E-mail address: [eyamamo@kumamoto-u.ac.jp](mailto:eyamamo@kumamoto-u.ac.jp) (E. Yamamoto).

Routine transthoracic echocardiography (TTE) had been performed annually from six years after the beginning of PD therapy. TTE examination showed a highly echoic mass with a transverse diameter of almost 15 mm in the posterior mitral leaflet (Fig. 1A). Because, he did not have mitral stenosis and his left ventricular ejection fraction was acceptable, he was managed simply by follow-up. The transverse diameters of the mass and indexes of phosphate and calcium metabolism are shown in Fig. 2. Although control of phosphate and calcium metabolism was similar during PD and hemodialysis, the mass gradually increased in size from 2 years after initiation of hemodialysis, reaching over 25 mm 6 years after commencing hemodialysis (Fig. 1B and C, Fig. 2). Additionally, mild mitral

stenosis was diagnosed (mitral valve area 1.62 cm<sup>2</sup> measured by the planimetry method on TTE) 6 years after commencing hemodialysis. Transesophageal echocardiography (TEE) also showed a mass in the posterior mitral leaflet with a surface of high density, and low internal density (Fig. 3A). Computed tomography (CT) showed a highly dense shadow in the posterior mitral leaflet (Fig. 3B). And he had severe calcification of aortic roof, descending aorta, and coronary artery, but not of ascending aorta. However, coronary arteriography revealed no coronary artery stenosis (Fig. 3C, D). According to these results of imaging modalities, we thought this mass lesion as CCMA.

Although the patient was asymptomatic and no thrombotic embolism had occurred, cardiac surgery was performed to prevent





**Fig. 3.** Transesophageal echocardiography showing a mass in the posterior mitral leaflet with a surface of high density and low internal density (A). Computed tomography image showing a highly dense shadow in the posterior mitral leaflet (B). Coronary arteriography revealed no coronary stenosis or occlusion (C, D). (E) Intraoperative photograph. White opalescent liquid came out of the mass when its surface was incised. Histological examination showed multiple calcified nodules and granulation tissue with chronic inflammatory cell infiltration (F). RA = right atrium, RV = right ventricle, LA = left atrium, LV = left ventricle.

serious potential complications. After median sternotomy, a cannula was inserted into the ascending aorta and another two cannulae into the superior and inferior vena cava via the right atrium. After the right atrium had been opened, soft mass was found on the posterior mitral annulus. White opalescent liquid drained out of the mass when its surface was incised (Fig. 3E). After most of this liquid had been squeezed out, the mitral valve was replaced with a mechanical valve because he was relatively young. Histological examination of the resected specimen showed multiple calcified nodules and granulation tissue with chronic inflammatory cell infiltration (Fig. 3F). Therefore, we diagnosed this mass lesion as CCMA. Three days after cardiac surgery, he developed a cerebral infarction that caused incomplete left-sided paralysis. However, his condition improved with medical treatment and he was discharged from our hospital on the 21st postoperative day.

## Discussion

MAC is a well-known degenerative process and common finding on TTE, whereas CCMA is a rare variant of MAC. It is sometimes difficult to distinguish CCMA from other types of mass lesion. In this present case, various types of tumor, abscess, and calcified amorphous tumor (CAT) could be stated as differential diagnosis (Table 1) [3–6]. This mass lesion was a large, round, and echodense mass with smooth borders; no acoustic shadowing artifacts; and central areas of echolucencies resembling liquefaction which was typical for CCMA [2,3]. There were no stalks, pedicles, pericardial effusion, or direct invasion into the myocardium. Thus, benign and malignant tumor were excluded from diagnosis. In addition, there were no infection signs. Thus, we thought this mass lesion was CCMA. However, we could not exclude the possibility of CAT by echocardiographic findings. Finally, we diagnosed this mass lesion as CCMA because we could see caseous material exuded from this mass and histological

examination showed calcified nodules and granulation tissue with chronic inflammatory cell infiltration. Although CCMA tends to occur in older patients and be associated with hypertension [2], the precise mechanism involved in liquefaction and caseation of CCMA is not well understood. As the prevalence of CCMA is higher in patients with end-stage renal disease, especially those on hemodialysis, an altered calcium phosphate metabolism is thought to be implicated in its pathogenesis [7]. Given that the transverse diameter of the mass increased dramatically after initiation of hemodialysis, we thought it likely that this development had occurred after initiation of hemodialysis. The usual mechanism underlying development of CCMA is thought to be impairment of phosphate and calcium metabolism. However, in our patient, control of phosphate and calcium metabolism was similar during PD and hemodialysis, making it unlikely that impaired phosphate and calcium metabolism was the reason for CCMA developing in this patient. The fact that there are few reports of CCMA developing in patients undergoing PD, the change from PD to hemodialysis

**Table 1** Typical echocardiographic features for each cardiac mass lesion.

Type of mass lesion	Typical echocardiographic features
Caseous calcification of the mitral annulus (CCMA)	Round, echo-dense structure. No acoustic shadowing could be detected behind the mass.
Abscess	Irregularly shaped, inhomogeneous paravalvular masses within periannular region, myocardium or pericardium.
Calcified amorphous tumor (CAT)	Calcified intracardiac mass lesion. It is often difficult to distinguish CAT from other cardiac mass including CCMA.
Tumor	
Myxoma	Narrow stalk and tumor mobility and distensibility.
Papillary fibroelastoma	Small, mobile masses attached to valves by a short pedicle.
Malignant tumor	Pericardial effusion and direct invasion into the myocardium.

may have contributed via some unidentified mechanism to our patient developing CCMA.

Although CCMA is usually a benign, asymptomatic condition, it can cause hemodynamic or embolic complications [8,9]. To our knowledge, there is no consensus regarding the optimal timing of operation for CCMA. However, surgery for CCMA is generally performed for severe mitral valve dysfunction or/and for embolic complications. The present case was asymptomatic, and had no thrombotic embolism and severe mitral valve stenosis. However, he was a young hemodialysis patient, and his mass lesion in mitral valve gradually increased in the relatively short time. Raggi et al. previously reported the case of a young hemodialysis patient demonstrating a rapid progression of a MAC that resulted in embolic events and mitral valve replacement [10]. Thus, we were concerned that the operative and postoperative risk such as atrioventricular dissociation, periprosthetic leakage, and embolic events would increase if his mass lesion got even bigger, and decided to perform the operation in this timing. In our patient, development of CCMA was identified after initiation of hemodialysis. Routine echocardiography is useful for screening, making an early diagnosis, and following CCMA, especially in patients whose type of dialysis changed from PD to hemodialysis.

#### Conflict of interest

The authors declare that there is no conflict of interest.

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