Asymptomatic Caseous Calcification of the Mitral Annulus in a 66-Year-Old Woman with 3-Year Imaging Follow-Up

Objective: Rare disease

Background: Caseous calcification of the mitral annulus (CCMA) is an uncommon form of mitral annular calcification and can be misdiagnosed as heart abscess, neoplasm, or other lesions occupying the atrioventricular groove. Data regarding imaging follow-up of patients with CCMA are limited. This report presents a case of CCMA with a 3-year imaging follow-up.

Case Report: A 66-year-old asymptomatic woman was referred to our cardiology department for further evaluation of a rapidly expanding intracardiac mass observed using transthoracic echocardiography (TTE) in an outpatient setting. A neoplasm was suspected. Echocardiographic examination was normal 5 years ago, and 2 years later, TTE revealed an echodense structure (10×10 mm) occupying the atrioventricular groove. Three years later, TTE revealed an increase in the size of the lesion (21×18 mm) and a mild acoustic shadow. Cardiac magnetic resonance imaging revealed a pathological mass (20×20×37 mm) in the posterior portion of the mitral annulus that extended into the left ventricle. Using computed tomography, a round mass (20×19×39 mm) with a demarcated area of calcification was revealed in the posterior portion of the mitral annulus. Thus, the intracardiac mass was diagnosed as CCMA. Although there was a considerable increase in lesion size (doubling of lesion size within 3 years), normal intracardiac flow and asymptomatic course of the disease remained. Therefore, this patient underwent conservative management with imaging follow-up.

Conclusions: In cases of atypical presentation of CCMA, multimodal imaging may provide an accurate diagnosis and important information regarding the course of the disease.

Keywords: Cardiac Imaging Techniques • Case Reports • Echocardiography • Heart Neoplasms • Mitral Valve

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**Background**

Caseous calcification of the mitral annulus (CCMA) is an uncommon form of mitral annular calcification (MAC). This pathologic state is a result of liquefaction and caseous degeneration of calcified areas of the mitral valve annulus; however, the exact mechanism of pathogenesis is unknown [1,2]. CCMA primarily affects older patients (mean age, 69 years), particularly women, and is associated with hypertension [3,4] and chronic renal failure, especially due to advanced renal disease or abnormalities in phosphorus and calcium metabolism [5]. The true prevalence of CCMA remains unknown. Using echocardiography, 2 clinical trials have revealed that CCMA occurs in 0.067-0.068% of the general population and 0.63-0.64% of patients with MAC [3,6]; however, CCMA on post-mortem examination was found to account for 2.7% of cases of MAC [4]. The difference between echocardiographic and pathologic prevalence rates suggests that this condition is underdiagnosed using imaging techniques, probably due to lack of symptoms, prompting evaluation using imaging, or lack of knowledge or experience in assessment of CCMA using echocardiography.

CCMA requires differentiation from other cardiac masses such as tumors (including myxoma, lipoma, hemangioma, or leiomyosarcoma), vegetations, and abscesses [2,7]. The clinical context is relevant to make the correct diagnosis. In the case of infective endocarditis, in addition to changes discovered by imaging, such as vegetations or abscesses, a clinical history or bacteriological tests are equally important. With an echocardiogram, the vegetation presents as an oscillating or non-oscillating cardiac lesion on a valve or other endocardial structures, or on implanted intracardiac material. The abscess appears as a thickened, non-homogeneous perivalvular structure with echoluent or echodense manifestation, usually without the calcified areas, and may show systolic blood flow by color Doppler [2,8]. In the case of myxoma, it may have quite variable shape (including round, oval, amorphous, or polyploid). Myxoma is usually mobile, pedunculated, and attached to the interatrial septum in the area of fossa ovalis. In contrast to CMMA, myxoma is highly vascular (blood flow may be visualized by color Doppler) and has not calcified at the edge of the mass [2]. Myxoma and other tumors such as fat-containing neoplasms (included liposarcomas and lipomas) can be easily detected and characterized by multimodality imaging approaches. On computed tomography (CT) scans, lipomas are homogeneous masses with well-characterized margins and attenuation values ranging between -30 and -100 HU, with no contrast-enhanced areas. On magnetic resonance imaging (MRI), lipomas are homogenous masses with hyperintense signal intensity on both T1- and T2-weighted images [7]. Other cardiac neoplasms have characteristic imaging features as well, but the detailed description of these is beyond the scope of this case report.

CCMA is usually an indolent and benign disease with an asymptomatic course, and the diagnosis is generally established using imaging modalities performed for other objectives. However, in some patients, this condition may be complicated by conduction abnormalities [9,10], systemic embolization [11-16], or mitral valve dysfunction, both stenosis and regurgitation [1,17,18], and cause symptoms such as palpitation, fainting, or dyspnea [2].

Transesophageal echocardiography (TEE) and transthoracic echocardiography (TTE) are useful diagnostic tools for the detection of CCMA and assessment of valvular function. Specific imaging features and typical location are usually adequate to confirm the diagnosis of CCMA on echocardiography. However, for some lesions, it is necessary to use a multimodal imaging approach to distinguish between CCMA and other intracardiac masses [19]. On echocardiography, CCMA can be recognized as a round or semilunar echodense mass with well-defined edges and a relatively hypoechoic central area of echolucency that represents the area of liquefactive necrosis, surrounded by a calcified margin. In the case of CCMA, no acoustic shadowing artifacts and no flow are noted on color Doppler. CCMA is attached to the mitral annulus and is typically located in the posterior portion of the mitral annulus, but rarely in the anterior portion of the mitral annulus or both parts of the mitral annulus [3,5,6,20-22]. On CT without contrast, CCMA appears as a hyperdense round or semilunar mass with a calcified envelope, placed in the perianular territory of the mitral valve. After contrast agent administration, CCMA appears as a hypodense, isodense, or hyperdense mass with no enhancement of the lesion. Features of CCMA on CT, especially unenhanced scans, are characteristic and can confirm the diagnosis [19]. MRI is useful for identifying pericardial and myocardial lesions, including CCMA [23]. On T1-weighted MRI, CCMA has a low signal intensity in relation to the myocardium and is dark. On T2-weighted short inversion time inversion recovery (STIR) scans, CCMA shows no signal in the central part (black area) and higher signal intensity in the capsule compared with the surrounding myocardium [2,24]. In balanced steady-state free precession (bSSFP) scans, the territory of caseous calcification appears only slightly darker than the myocardium [24]. On postcontrast MRI studies, no enhancement of the CCMA lesion with contrast agent administration is observed on first-pass scans; however, late gadolinium enhancement may be revealed at the edge of the mass [22,24].

There are limited data regarding long-term imaging follow-up in patients with CCMA. This report describes a case of CCMA in an asymptomatic woman who underwent a 3-year imaging follow-up.
Case Report

Herein, we present the case of a 66-year-old woman with untreated dyslipidemia (total cholesterol, 276 mg/dL; low-density lipoprotein, 197 mg/dL) and arterial hypertension well-controlled with drug therapy (lisinopril 20 mg orally once a day), without history of chronic or acute kidney disease, and without a history of smoking or alcoholism, who was referred to our hospital for further diagnostic evaluation of a rapidly expanding intracardiac mass revealed on TTE in the outpatient setting. The first TTE was performed 5 years ago and was unremarkable. Two years later, an echodense structure, measuring 10×10 mm and occupying the atrioventricular groove, was revealed on TTE. Follow-up TTE performed after 3 years revealed that the lesion had increased to 21×18 mm in size and had a mild acoustic shadow, and a heart neoplasm was suspected. However, no image is available. The patient was asymptomatic, without clinical features suggestive of infective endocarditis. The results of clinical examination, including physical examination and laboratory tests for inflammatory markers (CRP, procalcitonin), troponin level, blood urea, serum creatinine, and blood counts were normal. All serial blood cultures were negative. A normal sinus rhythm and a left anterior fascicular block were observed on a 12-lead electrocardiogram.

After admission, the first-line imaging modality was TTE, which was followed by TEE. These imaging techniques confirmed the echogenic round lesion measuring 21×18 mm with smooth border in the posterior region of the mitral annulus and the basal segment of the posterior wall of the left ventricle. No typical morphological characteristics of CCMA, including a central area of echolucency, were revealed on TTE and TEE. These techniques revealed the acoustic shadow behind this calcified mass (Figures 1, 2). Moreover, mild mitral regurgitation and preserved left ventricular ejection fraction were observed.

MRI was performed to obtain further information regarding this lesion. The MRI confirmed the presence of the mass in the posterior territory of the mitral annulus and the basal segment of the posterior wall of the left ventricle. The size of the lesion was 20×20×37 mm. On T1-weighted MRI, the mass had a low signal intensity in comparison with the surrounding myocardium (Figure 3). On the T2-weighted STIR scan, the mass revealed no signal in the central area and had a high signal intensity at the edge (Figure 4). On postcontrast MRI, the lesion showed no contrast uptake on first-pass scans; however, late gadolinium enhancement images showed a non-enhanced central area surrounded by a hyper-enhanced envelope (Figure 5). The size of the lesion was 20×20×37 mm.

CT without contrast was performed to confirm CCMA. CT revealed a hyperdense, well-defined, round mass measuring 20×19×39 mm and having a couple of internal calcification areas and a partly calcified border (Figures 6, 7). The attenuation value range of the central area of the lesion was from 410 HU to 650 HU. The edge of the mass had attenuation values ranging from 723 HU to 1245 HU. The internal calcification areas of the lesion had attenuation values ranging from 1124 HU to 1169 HU.

Based on the findings of multimodal imaging, CCMA was diagnosed. The patient was consulted by the Heart Team, and
Figure 3. Cardiac magnetic resonance imaging in T1-weighted sequence showing caseous calcification of the mitral annulus (CCMA). CCMA (arrow) is localized in the posterior area of the mitral annulus and the basal segment of the left ventricle, and it is homogeneous and hypointense (dark area).

Figure 4. Cardiac magnetic resonance imaging in T2-weighted short inversion time inversion recovery (T2w-STIR) sequence demonstrating caseous calcification of the mitral annulus (CCMA). CCMA (arrow) is localized in the posterior region of the mitral annulus and the basal segment of the left ventricle. CCMA has no signal in the central part (black area) and high signal intensity in the envelope of the lesion compared with the surrounding myocardium.

Figure 5. Late gadolinium enhancement cardiac magnetic resonance imaging demonstrating caseous calcification of the mitral annulus (CCMA). CCMA (arrow) is localized in the posterior area of the mitral annulus and the basal segment of the left ventricle. The CCMA has a hypointense area without late gadolinium enhancement surrounded by a hyperintense envelope with late gadolinium enhancement.

Figure 6. Non-contrast-enhanced computed tomography (CT) with axial reconstruction showing caseous calcification of the mitral annulus (CCMA). CCMA (arrow) is situated in the atrioventricular groove, and it is a hyperdense, well-defined, round mass, measuring 20×19×39 mm and having a couple of internal calcification areas and a partly calcified border. The attenuation value range of the central area of the lesion was from 410 HU to 650 HU. The edge of the mass had the attenuation value range from 723 HU to 1245 HU. The internal calcification areas of the lesion had attenuation values ranging from 1124 HU to 1169 HU.
because of the asymptomatic course of CCMA and lack of significant valvular dysfunction, a conservative approach with regular clinical and imaging assessments was adopted. Six months after the diagnosis, the patient was found to be asymptomatic.

Informed consent was obtained from the patient for the anonymous use of their clinical and imaging data.

**Discussion**

Because CCMA is rare, its characteristics are not well-known and can be confusing, especially when it has an atypical presentation. Imaging plays a significant role in the differential diagnosis and active surveillance of intracardiac masses. Although a heart neoplasm was suspected primarily, surgery was avoided in our patient. CCMA is usually a benign disease with a chronic and asymptomatic course. However, rarely, it can cause cardiovascular complications such as conduction abnormalities, systemic embolization, or mitral valve dysfunction. Typically, an echocardiographic examination is diagnostic for CCMA. The echocardiographic examination was not conclusive in our patient; therefore, other imaging techniques were performed. Multimodal imaging revealed features consistent with CCMA. Conservative treatment and further follow-up were proposed for our patient owing to the asymptomatic course of CCMA, preserved valvular function, and uncertainty regarding the effects of surgery.

Most reported cases of CCMA were those of asymptomatic incidental CCMA. The other described cases were those of complicated CCMA, or details regarding invasive therapies for this condition. For example, Pala et al [18] described a case of a symptomatic patient with severe mitral regurgitation and CCMA, Pozsonyi et al described a case of a symptomatic patient with severe mitral regurgitation and CCMA who underwent surgery [17], Thomas et al described a case of CCMA with symptomatic conduction abnormality [9], and Goldberg et al described a case of stroke and CCMA [12]. However, data regarding long-term imaging follow-up of patients with CCMA and conservative management of CCMA are limited. Mayr et al described a case of the detection of CCMA with CT scanning in a patient with previous biological aortic valve replacement and bypass surgery with long-term CT imaging surveillance. The imaging observation lasted for 19 years and revealed dynamic evolution of CCMA with an increase and decrease in the size of the lesion [25]. Abuarqoub et al described a case of asymptomatic CCMA lesion with a sustained size during a 2-year observation period. They used echocardiography for the confirmation of CCMA and imaging follow-up [26]. Deluca et al observed that CCMA can be dynamic, based on observational data that showed progression of MAC to CCMA in 3 participants and reversion of CCMA to MAC in 3 participants during the study period. However, in 8 patients with CCMA, no changes in the characteristics of the lesion in comparison with baseline evaluation were revealed. In this study, the diagnosis of CCMA was based on echocardiographic features consistent with CCMA. During a mean observation period of 3.4±1.2 years, all patients with CCMA underwent repeated TTE and sometimes TEE [3].

The present report describes a case of CCMA in an asymptomatic woman who underwent a 3-year imaging follow-up. A considerable increase in the size of the lesion was confirmed using TTE, but the patient remained asymptomatic and had no complications. The patient remains under observation. Long-term imaging follow-up is a key element in understanding the natural history of CCMA.

Our report has a few limitations. First, the imaging follow-up period was quite short (3 years). Second, as lucid identification of the mass was established, a diagnostic biopsy was not performed.
Conclusions

Multimodal imaging techniques may be necessary for differentiating intracardiac masses. Moreover, these techniques provide information on the natural history of cardiac masses on long-term imaging follow-up.

References:

1. Curl E, Riemer E. Caseous calcification of the mitral annulus: Case report and brief review. Eur Heart J Case Rep. 2018;2(4):fyy124
2. Elgendy IY, Conti CR. Caseous calcification of the mitral annulus: A review. Clin Cardiol. 2013;36(10):E27-31
3. Deluca G, Correale M, Ieva R, et al. The incidence and clinical course of caseous calcification of the mitral annulus: A prospective echocardiographic study. J Am Soc Echocardiogr. 2008;21(7):828-33
4. Pomerance A. Pathological and clinical study of calcification of the mitral valve ring. J Clin Pathol. 1970;23(4):354-61
5. Akram M, Hasanin AM. Caseous mitral annular calcification: Is it a benign condition? J Saudi Heart Assoc. 2012;24(3):205-8
6. Harpaz D, Auerbach I, Vered Z, et al. Caseous calcification of the mitral annulus: A neglected, unrecognized diagnosis. J Am Soc Echocardiogr. 2001;14(8):825-31
7. Turek Ł, Sadowski M, Kurzawski J, Andrychowski J. A 64-year-old woman with imaging features consistent with a posterior intrapericardial lipoma and 5-year imaging follow-up. Am J Case Rep. 2021;22:e934500
8. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC Guidelines for the management of infective endocarditis: The Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J. 2015;36(44):3075-128
9. Thomas B, Danda N, John B. Caseous calcification of the mitral annulus presenting with symptomatic complete heart block. HeartRhythm Case Rep. 2021;7(10):655-58
10. García-Barrondo N, Lang RM. [Caseous calcification of the mitral annulus, a rare echocardiographic finding.] Rev Esp Cardiol. 2011;64(9):828-31 [in Spanish]
11. Chevalier B, Reant P, Laffite S, Barandon L. Spontaneous fistulization of a caseous calcification of the mitral annulus: A rare echocardiographic finding. Rev Esp Cardiol. 2011;64(9):e184-85
12. Goldberg A, Singh G, Tracy M. Multiple cardioembolic strokes caused by caseous calcification of the mitral annulus. CASE (Phil). 2017;1(1):34-36
13. Fong LS, McLaughlin AJ, Okiwelu NL, et al. Surgical management of caseous calcification of the mitral annulus. Ann Thorac Surg. 2017;104(3):e291-93
14. Tan JL, Finkel J, Geller C. Caseous calcifications of mitral annulus as an unusual cause of cardioembolic stroke in a 40-year-old man. Cureus. 2018;10(7):e3015
15. Durao D, Pitta Mda L, Alves M, et al. Myocardial infarction as the first probable manifestation of caseous calcification of the mitral annulus. Rev Port Cardiol. 2009;28(11):1271-75
16. Motwani M, Fairbairn TA, Logija R, et al. Caseous calcification of the mitral valve complicated by embolization, mitral regurgitation, and pericardial constriction. Eur Heart J Cardiovasc Imaging. 2012;13(9):792
17. Pozonzi Z, Toth A, Vago H, et al. Severe mitral regurgitation and heart failure due to caseous calcification of the mitral annulus. Cardiology. 2011;118(2):79-82
18. Pala AA, Iner H, Ercisli MA. Approach to an unusual cardiac mass: Mitral annulus caseoma. Braz J Cardiovasc Surg. 2020;35(1):120-22
19. Michalowska L, Szymanski P, Kwiatek P, et al. Caseous calcification of the mitral annulus – the complementary role of computed tomography and transthoracic echocardiogram. Pol J Radiol. 2018;83:e621-26
20. Stamou SC, Braverman AC, Kouchoukos NT. Caseous calcification of the anterior mitral valve annulus presenting as intracardiac mass. J Thorac Cardiovasc Surg. 2010;140(1):e9-10
21. Mazzucco A, Abbasciano R, Onorati F, et al. Anterior mitral annulus caseoma: As benign as posterior counterparts? Cardiovasc Pathol. 2016;25(4):336-38
22. Balci S, Akkaya S, Ardali S, Hazirolan T. Caseous necrosis of mitral annulus. Case Rep Radiol. 2015;2015:561329
23. Gravina M, Casavecchia G, Manuppelli V, et al. Mitral annular calcification: Can CMR be useful in identifying caseous necrosis? Inter Med Appl Sci. 2019;11(1):71-73
24. Monti L, Renifilo E, Profili M, Balzarini L. Cardiovascular magnetic resonance features of caseous calcification of the mitral annulus. J Cardiovasc Magn Reson. 2008;10(1):25
25. Mayr A, Muller S, Feuchtner G. The spectrum of caseous mitral annulus calcifications. JACC Case Rep. 2021;3(1):104-8
26. Abuamro A, Kumar V, Atoot A, et al. Caseous calcification of posterior mitral annulus: A forgotten benign condition mimicking atrial mass. Ann Transl Med. 2019;7(22):697

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