

Caseous Calcification of the Mitral Annulus

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ABSTRACT

Soft-tissue masses or mass-like lesions involving the mitral valve include a wide range of diseases such as tumors, abscesses, vegetations, thrombus and, rarely, caseous calcifications of the mitral annulus. Caseous calcifications of the mitral annulus is a rare variant of mitral annular calcification that is usually asymptomatic and diagnosed incidentally. Echocardiography is the first-choice imaging modality. Cardiac computed tomography is an ideal tool to confirm the presence of calcifications and caseous necrosis. In cases where there is doubt, cardiac magnetic resonance imaging may be used. We present the case of a 62-year-old patient with an intra-cardiac mass diagnosed by echocardiography. Imaging modalities to achieve a correct diagnosis and avoid unnecessary surgical intervention are discussed.

CASE REPORT

CASE REPORT

A 62-year-old woman presented to our emergency department following a sudden loss of consciousness with no prodromal symptoms. Her medical history included breast cancer, hypertension and dyslipidemia. Physical examination was unremarkable. Laboratory tests were within normal limits: white-cell count 5,98 x 10⁹/L (reference range 4,00-10,00 x 10⁹/L), red-cell count 4,96 x 10¹²/L (reference range 4,20-5,40 x 10¹²/L), platelet count 176 x 10⁹/L (reference range 140-440 x 10⁹/L), creatinine 0,61 mg/dL, (reference range 0,44-0,90 mg/dL), serum calcium 9,2 mg/dL (reference range 8,5-10,1 mg/dL), cardiac troponin I <0,02 ug/L (reference level <0,09 ug/L), creatine phosphokinase 75 U/L (reference range 21-215 U/L). Computed tomography (CT) of the head was normal. A transthoracic echocardiography (TTE) revealed a large, echodense mass at the level of the mitral valve (Fig. 1). Further evaluation with transesophageal echocardiography (TEE) was performed, revealing a polylobate, echodense, non-mobile mass (6 cm in greater diameter) located at the mitral valve annulus and extending into the left atrium. Small calcifications at the posterior mitral leaflet (PML) were noted.

Reduced PML motion and mild mitral regurgitation with no outflow tract obstruction were also found. Cardiac magnetic resonance imaging (MRI) was performed for further characterization, revealing a large solid mass extending along the posterior mitral annulus (Fig. 2) with low signal intensity in both T1- and T2-weighted images. At first pass perfusion sequences the mass showed no contrast enhancement (Fig. 3). A peripheral ring of enhancement was noted on late gadolinium enhancement (LGE) sequences (Fig. 4). A presumptive diagnosis of caseous calcification of the mitral annulus (CCMA) was made based on the existing literature, and a cardiac CT scan was performed to confirm our findings. This scan revealed a hyperdense, polylobate mass with peripheral calcifications and no enhancement after contrast agent administration (Fig. 5 and 6). The syncopal event in our patient was probably caused by transient left ventricular outflow tract obstruction. Given the absence of severe valve dysfunction, arrhythmia or systemic embolization, a conservative management approach was chosen. TTE follow-up at 8 months showed no significant changes (Fig. 7).

DISCUSSION

Etiology & Demographics:

CCMA is a chronic, degenerative process usually affecting the posterior fibrous mitral annulus [1]. A rare variant of mitral annular calcification (MAC), CCMA is commonly diagnosed in elderly women with a history of hypertension and dyslipidemia [2]. It has a “toothpaste-like” texture and is surrounded by a non-collapsible calcified envelope [3, 4]. Liquefaction and caseation mechanisms are not well understood. However, a higher prevalence in patients with elevated cholesterol levels, chronic renal failure and hypercalcemic states suggests that CCMA may be associated with atherosclerosis and with an altered calcium phosphate metabolism [5-7]. Calcifications along the mitral annulus are relatively common. Studies report a prevalence of MAC ranging from 8-15%, with a higher prevalence in patients with multiple cardiovascular risk factors or chronic kidney disease [8]. The exact prevalence of CCMA is unknown. In some studies, the prevalence referred to echocardiography was 0.06-0.07% [3,4], representing 0.6% of patients with MAC. However, these data are likely underestimated due to the predominantly asymptomatic course of the condition. Mitral caseoma is unusual, aortic and tricuspid valvular localization are atypical with only two cases of tricuspid valve involvement [4, 9] and one case of left aortic cusp involvement [10] reported in the Literature.

Clinical & Imaging findings:

CCMA is usually an incidental finding presenting as an intracardiac mass. Some patients develop palpitations and dyspnea. Syncope secondary to atrioventricular blocks and systemic embolization are reported rarely [1]. Mitral valve dysfunction, stenosis and regurgitation may also be associated with this condition. Diagnosis is usually made via a multi-modality imaging approach [11]. When a great amount of calcifications are present, chest x-ray may reveal a calcified mass overlying the heart [12]. As for other intracardiac masses, echocardiography remains the first-imaging modality to investigate CCMA. At TTE, a caseoma appears as an echogenic, well-defined, avascular mass with calcified edges and central hypoechoic areas [1]. A TEE approach may be needed in patients with poor acoustic window, and can provide more information regarding the mass contents. CT and Cardiac MRI allow further characterization of the lesion [13]. On cardiac CT, CCMA appears as a well-defined, variably hyperdense mass, with peripheral calcifications and no contrast enhancement. Lesion heterogeneity is confirmed by densities varying from negative Hounsfield Unit (HU) values, reflecting the presence of fatty degeneration areas, and high HU values, which are typical of calcifications [13, 15, 16]. Cardiac MRI provides the best tissue characterization and is an excellent tool for the differential diagnosis of intracardiac masses [17]. CCMA appears as a low signal intensity mass in all sequences [18, 19], reflecting the calcium content. No contrast enhancement is detected on first pass perfusion sequences; however, a peripheral rim of enhancement in late gadolinium enhancement (LGE) sequences may be observed [18], as was the case in the instance discussed here.

Treatment & Prognosis:

The prognosis is usually benign, and the chosen management approach is generally conservative as long as the patient remains asymptomatic. However, CCMA can result in mitral valve dysfunction, conduction system abnormalities or systemic embolization [1]. Surgical excision is indicated when severe valve dysfunction is present and when the possibility of a tumor cannot be ruled out [18]. Anticoagulation therapy should be considered in patients presenting with embolic phenomena [18].

Differential Diagnosis:

CCMA is frequently misdiagnosed with other intracardiac masses such as tumors, thrombi, abscesses and vegetations.

Common differential diagnoses include:

- Benign and malignant primary cardiac tumors. Primary cardiac tumors (PCTs) are rare, with a reported incidence at autopsy varying from 0.002% to 0.3% [20, 21]. Benign lesions, with myxoma being the most common type in adults, represent 75% of PCTs [21]. Myxomas are pedunculated polypoid intracavitary lesions located more often in the left atrium. Calcifications may be present. At echocardiography, they appear as heterogeneous mobile masses with hypo-anechoic areas due to hemorrhagic, cystic and necrotic components [22]. At CT, myxomas appear as hypodense lesions with inhomogeneous contrast enhancement, reflecting the mixed composition [23]. MRI signal is heterogeneous; most myxomas are hypo-to-isointense on T1-weighted (T1W) images and hyperintense on T2-weighted (T2W) images [24]. Angiosarcoma is the most common malignant primary cardiac tumor in adults. It usually appears as a large, multilobar mass with hemorrhagic and necrotic areas. Echographic findings are non-specific [22]. Both CT and MRI show a heterogeneous mass with infiltration of adjacent structures and diffuse, inhomogeneous contrast enhancement. Areas of increased signal intensity in T1W sequences reflect the tendency of this tumor to hemorrhage. Calcifications may also be found [23, 24].
- Secondary cardiac tumors (cardiac metastases) are 20-40 times more common than primary neoplasms. Lung and breast carcinomas, melanoma and hematologic malignancies more commonly result in cardiac metastases [25]. Echocardiography may show an iso-hyperechoic mass, with pericardial effusion [22]. Cardiac metastases are usually hypo-isodense to myocardium at CT, iso-hypointense on T1W images and iso-hyperintense on T2W images. Contrast enhancement is strong and heterogeneous [23, 24]. Calcifications may be present.
- Myocardial abscess and vegetations are the common manifestations of infective endocarditis and should be considered when sepsis or infection are present. Myocardial abscesses are typically located along the mitral-aortic fibrosa. They appear as hypoechoic masses with echo-lucent areas at echocardiography and may show systolic blood flow by color doppler [26]. At CT, a myocardial abscess appears as a fluid density collection surrounded by a peripheral thick layer of inflammatory cells that enhances after contrast medium administration [23, 27]. Similarly, MRI will identify a lesion as inhomogeneously iso-hyperintense in

T1W images and inhomogeneously hyperintense in T2W images, with hyperenhancing walls on post-contrast sequences. Abscesses may also be multi-loculated with internal septa enhancing after contrast medium injection. Vegetations are soft-tissue masses made of fibrin, inflammatory cells and microorganisms [27]. They are identified at echocardiography as fluctuating hypoechoic masses attached to a valve or an endocardial structure. CT will reveal a low attenuating mass attached to the valve leaflet [28]. At MRI, vegetations show low signal intensity. Enhancement of paravalvular tissue may be present [29].

- Thrombus. Cardiac thrombus is one of the most common intracardiac masses [30]. These are identified as hyperechoic intracavitary mobile lesions at echocardiography and appear as hypodense lesions on CT, showing no contrast enhancement. MRI signal depends on the age of the thrombus. Acute thrombi have intermediate signal intensity on both T1W and T2W images. Subacute thrombi are hypointense on T1W images and hyperintense on T2W images. Chronic organized thrombi show low signal intensity on both T1W and T2W images due to water depletion [24].

In the present case, we were concerned with the possibility of cardiac metastases due to the patient's history of breast cancer. Key imaging features of the CCMA diagnosis were posterior mitral valve annulus involvement, absence of mobility, presence of calcifications on CT, tissue characteristics on MRI and lack of contrast enhancement.

TEACHING POINT

Caseous calcification of the mitral annulus is a rare, unfamiliar condition that is frequently misdiagnosed with other intracardiac masses that require surgical excision. A multimodality imaging approach including echocardiography, computed tomography and magnetic resonance imaging is essential to avoid unnecessary surgical intervention in asymptomatic cases.

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FIGURES

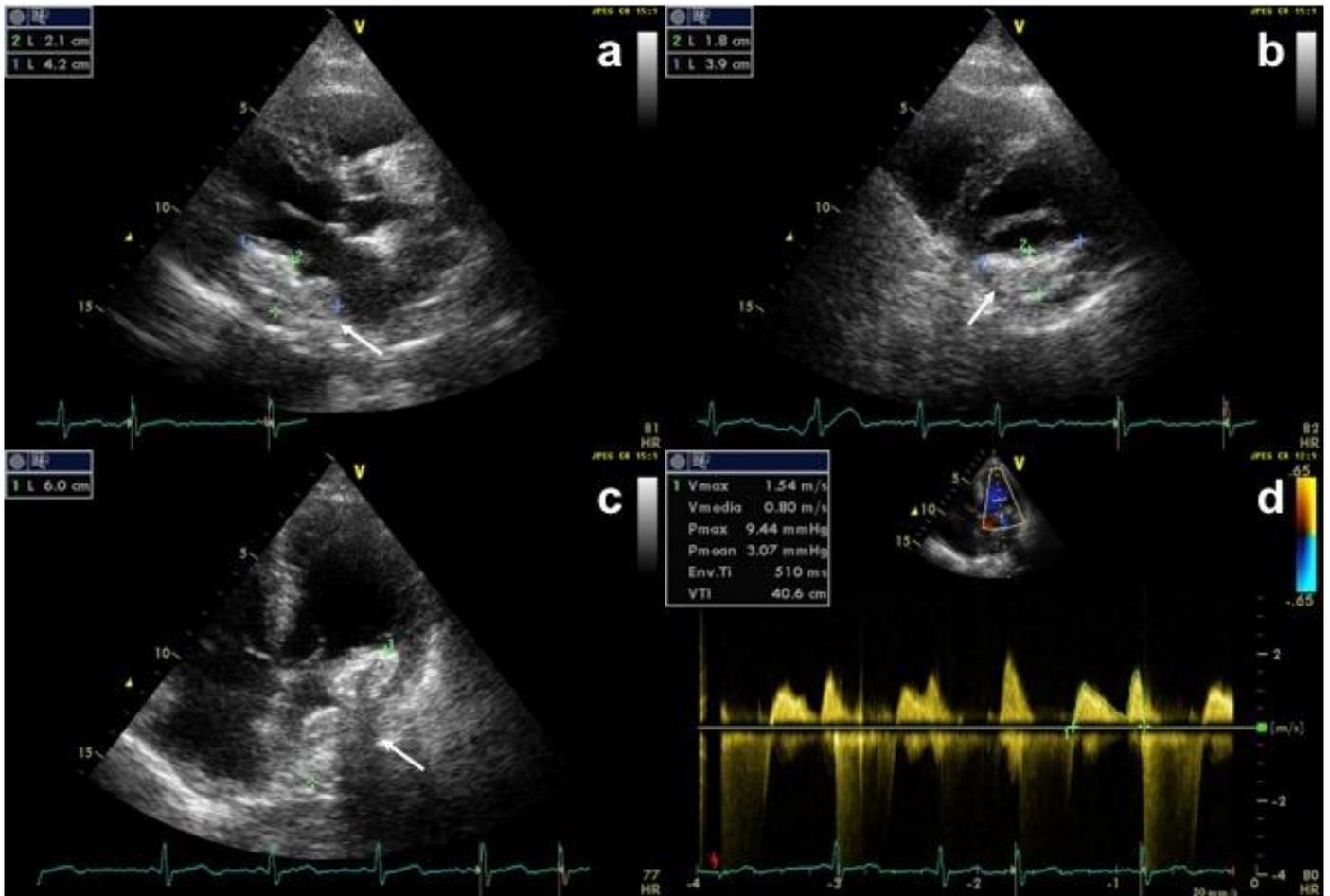


Figure 1: 62 y/o female with caseous calcification of the mitral annulus.

Technique: Transthoracic echocardiography (cardiac transducer, 2-dimensional (2D) scanning, sector phased 7-12 MHz).

Findings: Large, echodense mass (arrows) at the level of the mitral valve. Echocolor Doppler analysis revealed mild mitral regurgitation with reduced posterior mitral leaflet motion, with no outflow tract obstruction.

- a: Parasternal long-axis view
- b: Parasternal short-axis view
- c: Apical 4-chamber view
- d: Echocolor Doppler analysis

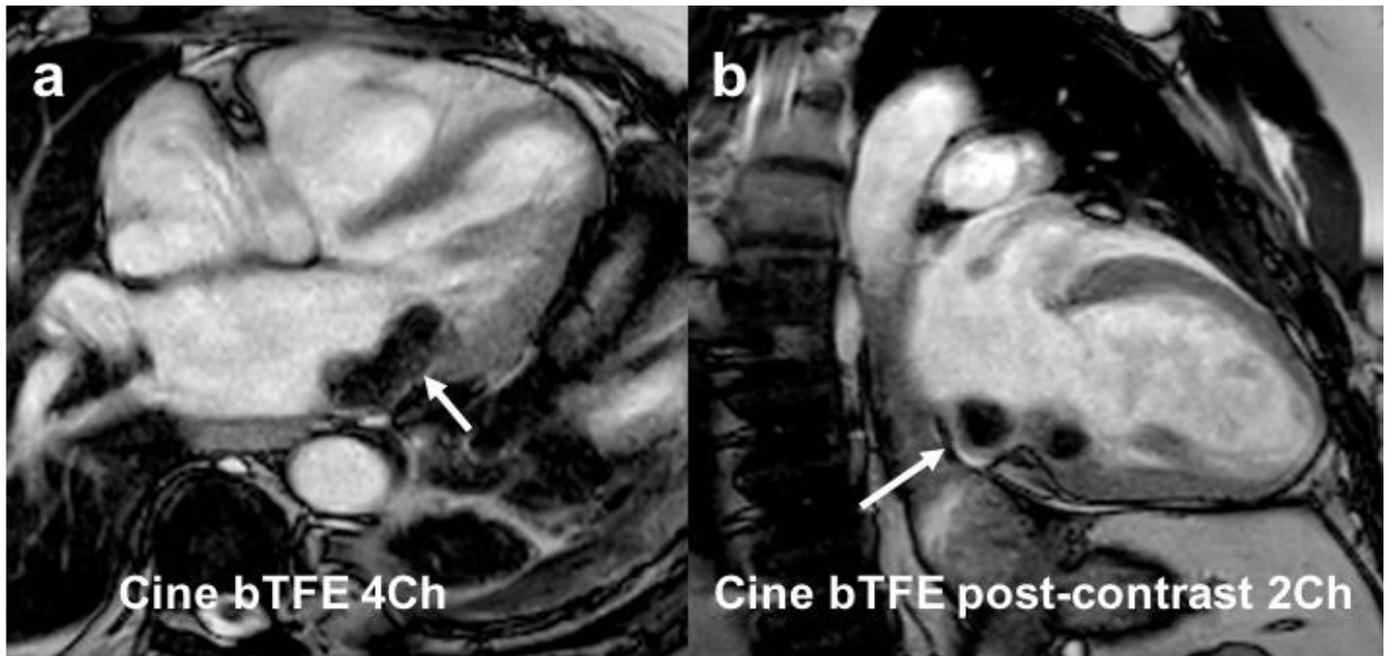


Figure 2: 62 y/o female with caseous calcification of the mitral annulus.

Technique: Cardiac MRI, Ingenia 1.5 T (Philips Healthcare, Best, The Netherlands) scanner with a SENSE torso phased-array coil. Pre and post intra-venous contrast administration (Prohance 0.15 mmol/kg, Bayer HealthCare, Germany) infused as bolus at a rate of 5 ml/s pushed by a 40 ml saline at 5 ml/s.

Findings: (a) Cine balanced turbo field echo bTFE (TR 2.5 ms, TE 1.2 ms, flip angle 60, slice thickness 6 mm) sequence in four chamber view (4Ch) and (b) Cine bTFE (TR 1.6 ms, TE 3.3 ms, flip angle 50, slice thickness 6 mm) post-contrast sequence in two chamber view (2Ch) shows a large solid mass (white arrows) extending along the posterior mitral annulus, with low signal intensity.



Figure 3 (left): 62 y/o female with caseous calcification of the mitral annulus.

Technique: Cardiac MRI, Ingenia 1.5 T (Philips Healthcare, Best, The Netherlands) scanner with a SENSE torso phased-array coil. Post intra-venous contrast administration (Prohance 0.1 mmol/kg, Bayer HealthCare, Germany) infused as bolus at a rate of 5 ml/s pushed by a 40 ml saline at 5 ml/s.

Findings: First-pass perfusion (TE 1.1, TR 2.5) sequence in short axis view shows a mitral valve mass (arrow) with no contrast enhancement.

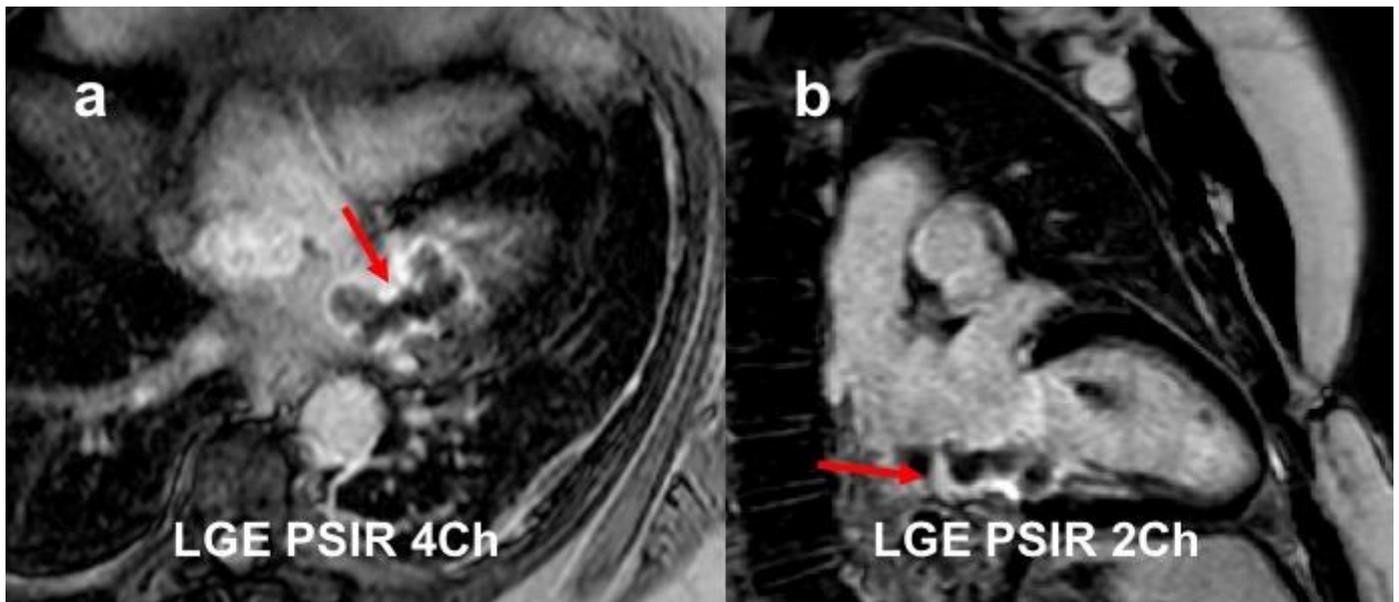


Figure 4: 62 y/o female with caseous calcification of the mitral annulus.

Technique: Cardiac MRI, Ingenia 1.5 T (Philips Healthcare, Best, The Netherlands) scanner with a SENSE torso phased-array coil. Approximately 10-15 min post-contrast, a whole heart high spatial resolution 3D gradient echo (T1 fast field echo) PSIR (phase sensitive inversion recovery) sequence was acquired after intra-venous contrast administration (Prohance 0.15 mmol/kg, Bayer HealthCare, Germany) infused as bolus at a rate of 5 ml/s pushed by a 40 ml saline at 5 ml/s.

Findings: Myocardial LGE PSIR sequence in 4Ch (a) and 2Ch (b) shows a large solid mass extending along the posterior mitral annulus with a peripheral ring of enhancement (red arrows).



Figure 5: 62 y/o female with caseous calcification of the mitral annulus.

Technique: chest computed tomography angiography (CTA) performed with Somatom Definition Flash (Siemens Healthcare, Erlangen, Germany) with ECG-gating. Pre and post-contrast agent administration (Iomeron 400 mg iodine/ml, Bracco, 100 ml at 6 ml/s); slice thickness of 0.6 mm, 100 kV, 236 mAs.

Findings: (a) axial contrast-enhanced CT in arterial phase and (b) axial non-contrast CT images show a hyperdense mass (arrows) at the level of the mitral valve annulus with peripheral calcifications and no enhancement after contrast agent administration.

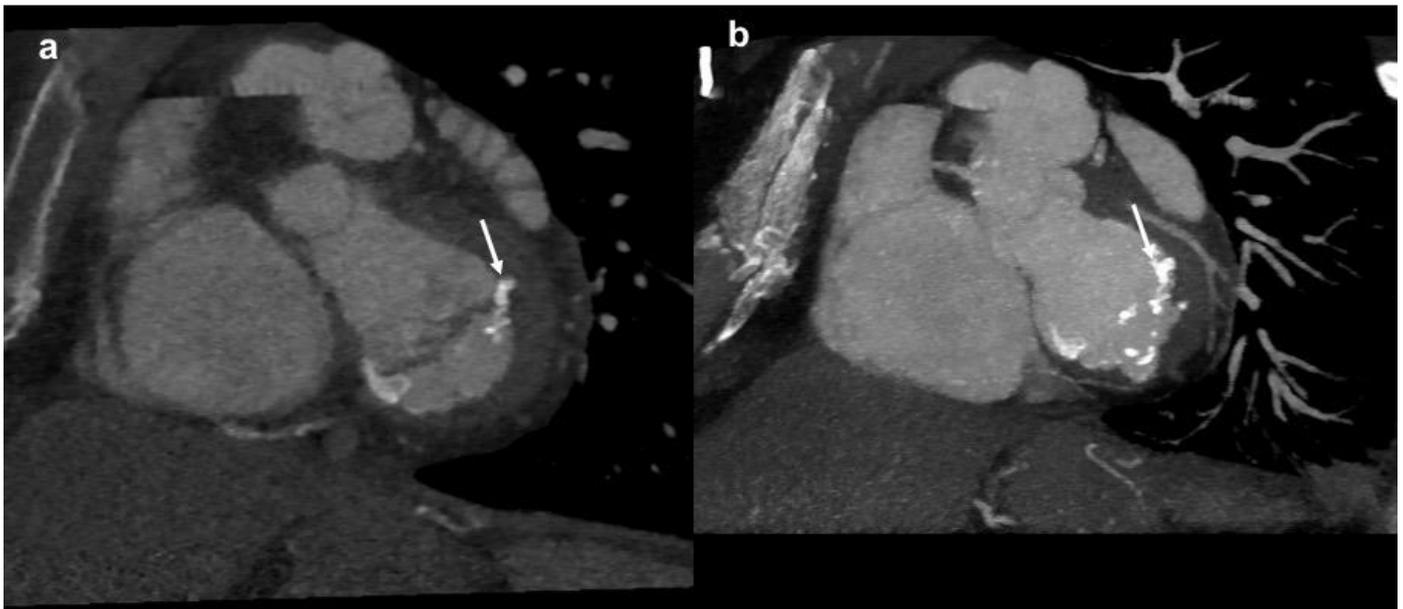


Figure 6: 62 y/o female with caseous calcification of the mitral annulus.

Technique: Chest computed tomography angiography (CTA) performed with Somatom Definition Flash (Siemens Healthcare, Erlangen, Germany) with ECG-gating. Pre and post-contrast agent administration (Iomeron 400 mg iodine/ml, Bracco, 100 ml at 6 ml/s); slice thickness of 0.6 mm, 100 kV, 236 mAs.

Findings: En face view of the mitral valve (a) multiplanar reconstruction (MPR) and (b) maximum intensity projection (MIP) images show a large hyperdense mass located at the posterior mitral valve annulus with peripheral calcifications (arrows).

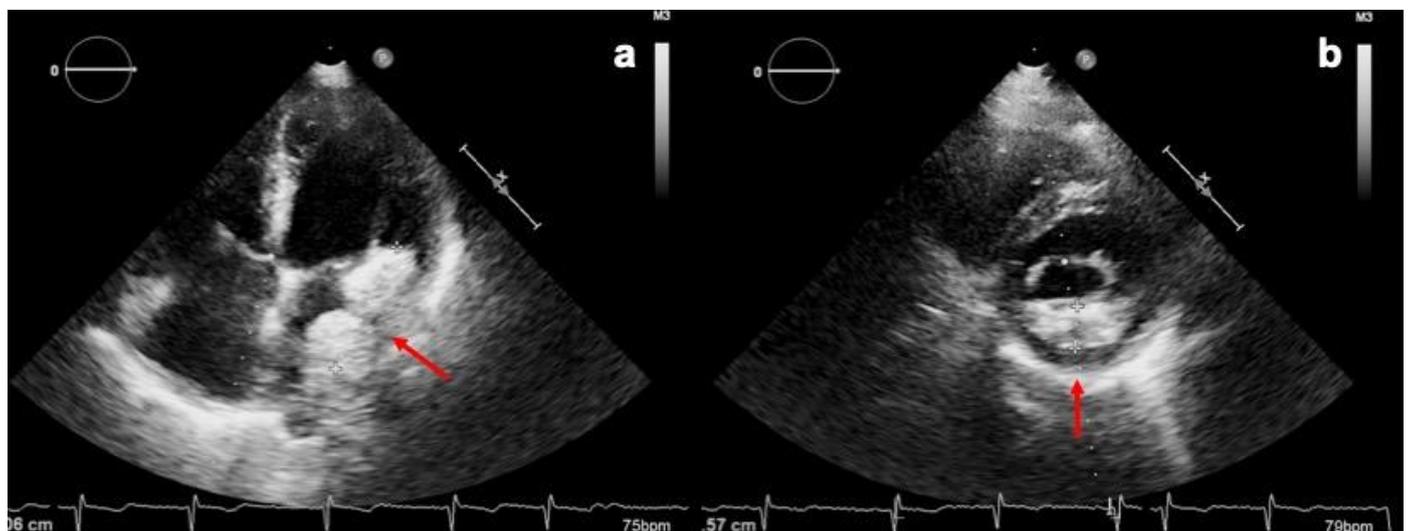


Figure 7: 62 y/o female with caseous calcification of the mitral annulus.

Technique: Transthoracic echocardiography (cardiac transducer, 2-dimensional (2D) scanning, sector phased 7-12 MHz).

Findings: Follow-up transthoracic echocardiography after 8 months confirmed the presence of a large, echodense mass (red arrows) at the level of the mitral valve; no morphological or dimensional changes were observed.

a: Apical 4-chamber view

b: Parasternal short-axis view

Etiology	Chronic degenerative process
Prevalence	0.06–0.07% in large series of patients of all ages 2.7% of cases of mitral annular calcification on a necropsy series
Gender ratio	Female predilection of approximately 10:4
Age predilection	Prevalence increases with age
Risk factors	Hypertension, dyslipidemia, altered calcium-phosphate metabolism
Treatment	Conservative medical management in asymptomatic cases Surgical excision if severe mitral valve dysfunction is present Anticoagulation therapy in case of embolic phenomena
Prognosis	Usually benign
Findings on imaging	X-ray: calcified mass overlying cardiac shadow Echocardiography: echo-dense mass with smooth borders and central hypoechoic areas CT: well-defined hyperdense mass with peripheral calcification and no contrast enhancement MRI: well-defined mass hypointense in both T1 and T2-weighted images, no enhancement on first-pass perfusion images, peripheral ring of enhancement in delayed post-contrast images

Table 1: Summary table for caseous calcification of the mitral annulus.

	Echo	CT	MRI		Contrast Enhancement
			T1W	T2W	
Caseous Calcification of the Mitral Annulus	Well-defined echo-dense mass with calcified edges and central hypoechoic areas	Well-defined, variably hyperdense mass with peripheral calcifications	Hypointense	Hypointense	NO Peripheral ring enhancement in LGE
Benign Primary Cardiac Tumor (Myxoma)	Pedunculated polypoid intracavitary mass with heterogeneous appearance	Hypodense mass with calcifications	Hypo-to-isointense	Hyperintense	YES Heterogeneous due to cystic, hemorrhagic and necrotic components
Malignant Primary Cardiac Tumor (Angiosarcoma)	Heterogeneous appearance	Large, multilobar heterogeneous mass with hemorrhagic and necrotic areas; may contain calcifications	Heterogeneous; hyperintense areas due to hemorrhage	Heterogeneous	YES Strong, diffuse, inhomogeneous
Secondary Cardiac Tumor	Iso-hyperechoic mass	Iso-hypodense mass; may contain calcifications	Hypo-to-isointense	Iso-to-hyperintense	YES Strong, inhomogeneous
Myocardial Abscess	Hypoechoic mass with anechoic areas; may show systolic blood flow by color Doppler	Fluid-density collection with peripheral thick layer of inflammatory cells	Iso-hyperintense	Inhomogeneously hyperintense	YES Rim and septa enhancement
Vegetations	Hypoechoic fluctuating mass attached to valve	Hypodense mass	Hypointense	Hypointense	YES Paravalvular tissue
Organized thrombus	Intracavitary mobile hyperechoic mass	Hypodense intracavitary mass	Hypointense	Hypointense	NO

Table 2: Differential diagnoses table for caseous calcification of the mitral annulus.

ABBREVIATIONS

2Ch = two chamber view
4Ch = four chamber view
bTFE = balanced turbo field echo
CCMA = caseous calcification of the mitral annulus
CT = computed tomography
HU = Hounsfield Unit
LGE = late gadolinium enhancement
MAC = mitral annular calcification
MIP = maximum intensity projection
MPR = multiplanar reconstruction
MRI = magnetic resonance imaging
PCTs = primary cardiac tumors
PML = posterior mitral leaflet
PSIR = phase sensitive inversion recovery
T1W = T1-weighted
T2W = T2-weighted
TEE = transesophageal echocardiography
TTE = transthoracic echocardiography

KEYWORDS

Caseous calcification of the mitral annulus; Caseoma; Cardiac masses; Cardiac MRI; Cardiac Calcifications

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