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CASE REPORT
Cardiac imaging

Big mitral annular calcification: a case report of a dynamic liquefaction necrosis as a potential source of embolism

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Background Mitral annular calcification (MAC) is a degenerative, mostly asymptomatic abnormality usually in elderly patients. Caseous MAC (cMAC) is a rare form with central liquefaction necrosis, which typically involves the posterior annulus of the mitral valve and can cause serious sequelae. However, optimal management of patients with cMAC is not clearly defined.

Case summary In a 71-year-old female patient, MAC was incidentally detected. Tissue characterization with cardiac magnetic resonance (CMR) revealed a cMAC and a conservative approach was chosen. Six months after cMAC diagnosis, the patient developed an acute hemi-occlusion of a retinal artery with cholesterol embolism. At this time, CMR showed a liquefied cavity of the cMAC. Except for atherosclerotic plaques in the aorta and carotid arteries, further stroke work-up was negative. Therefore, the conservative approach was continued. During follow-up, the liquefied cavity regressed completely after another 6 months and the patient was free from further events (total follow-up 3 years since diagnosis of cMAC).

Discussion A clear diagnosis and quantitative assessment of dynamic processes, such as cMAC, are made possible by performing CMR with multi-parametric tissue characterization. Dynamic changes in cMAC may have serious clinical implications, such as mitral regurgitation or systemic embolization. Among cardiac tumours, thrombus and abscess, cMAC should be included in the differential diagnosis of an intracardiac mass of the posterior mitral annulus in order to avoid further inappropriate diagnostic interventions.

Keywords Caseous mitral annular calcification • Cardiac magnetic resonance • Multi-parametric tissue characterization • Dynamic liquefaction of mitral annular calcification • Cardiac mass • Case report

Learning points

- Caseous mitral annular calcification (cMAC) is a dynamic condition and underestimated as a source of potentially serious complications, such as mitral regurgitation and systemic embolization.
- Cardiac magnetic resonance with multi-parametric tissue characterization can help to diagnose and quantitatively assess the process of liquefaction of MAC.

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Introduction

Mitral annular calcification (MAC) is a degenerative abnormality in mostly elderly patients without specific symptoms caused by peri-annular calcium deposits on the fibrous skeleton of the heart. It constitutes one of the most common findings in autopsy series.[1] Caseous calcification of the mitral annulus (cMAC) is a rare form of MAC with central liquefaction necrosis. Its aetiology is not completely understood which can lead to an erroneous diagnosis of intracardiac primary tumour, myxoma, fibroelastoma, abscess, thrombus, or vegetation and could result in unnecessary surgery.[2] cMAC typically involves the posterior annulus of the mitral valve and represent only 0.6% of MACs detected in echocardiography[3,4] and only 0.06–0.07% of patients referred for echocardiography.[4] The prevalence in necropsy of patients with MAC having a caseous variant has been shown to be 2.7% suggesting that cMAC is still underdiagnosed.[1]

We report a case of a patient with dynamic changes of a large MAC to cMAC, who experienced a stroke during follow-up.

Timeline

4 weeks prior	Hypertensive urgency at referral centre. Exclusion of acute coronary syndrome. Detection of a mass at postero-lateral mitral annulus.
Initial presentation	Referral for lesion evaluation with transthoracic echocardiogram, transoesophageal echocardiogram, and cardiac magnetic resonance. Diagnosis of cMAC established. Decision for conservative treatment by heart team (aspirin 100 mg, atorvastatin 40 mg).
6 months	Acute retinal artery occlusion with a small cholesterol. Enlarging mass with near-total liquefaction of cMAC. Continuation of conservative approach (switch to clopidogrel 75 mg, atorvastatin 40 mg).
12 months	Disappearance of centrally liquid-filled cavity.
>36 months	No further events occurred.

Case presentation

A 71-year-old Caucasian female patient initially presented with chest tightness, malaise, and elevated blood pressure values. Except for treated arterial hypertension (without end-organ damage, such as hypertensive heart disease), dyslipidaemia, moderate non-alcoholic fatty liver disease, and gallstone disease, the patient's medical history was unremarkable. The physical examination was normal. An acute coronary syndrome was ruled-out by electrocardiogram, and laboratory work-up and treatment for hypertension were optimized. In transthoracic echocardiography, an echolucent, partially calcified lesion (28 mm × 24 mm × 21 mm) was identified at the posterolateral mitral annulus without mitral valve dysfunction (*Figure 1*).

Due to typical location, asymptomatic course and female sex, MAC was suspected. Irregular borders warranted further evaluation to exclude a possible malignant cause.

Cardiac magnetic resonance (CMR) demonstrated an 18 mm × 23 mm × 31 mm non-invasive heterogeneous mass near the posterior mitral valve annulus (*Figure 2A*). Further tissue characterization (*Figure 3A*) led to the diagnosis of a caseous calcification of the posterior mitral valve annulus (cMAC). Mobile vegetations were excluded by transoesophageal echocardiography, but an atherosclerotic lesion (6 mm) in the aortic arch was detected.

Due to lack of symptoms, mobile vegetations or significant mitral valve dysfunction, an expectative approach was chosen and primary prevention was established regarding the aortic plaque (aspirin 100 mg, atorvastatin 40 mg).

Six months later, the patient presented with blurry vision for 4 days in the right lower visual field. Ophthalmologists detected an acute right-sided hemi-central retinal artery occlusion with a small cholesterol embolism on the right papilla. A duplex-sonography of both internal carotid arteries and vertebral arteries in the V2-segment did not show any haemodynamically relevant atherosclerosis. Cranial computer tomography revealed mild atherosclerosis of the internal carotid arteries without relevant stenosis, cranial bleeding, or ischaemia. Further stroke follow-up including electrocardiogram (ECG), two Holter-ECG, and basic haemostatic laboratory tests was normal.

A follow-up CMR (*Figures 2B and 3B*) demonstrated an enlarging mass (42 mm × 22 mm × 32 mm) in proximity to the posterior mitral valve annulus and new evidence of mitral regurgitation. Tissue characterization showed near-total liquefaction of cMAC as quantified by elevated native T1 and T2 values inside the cardiac mass (*Figures 2B and 3B*). Similar to the initial CMR examination, first-pass perfusion (FFP) revealed no perfusion of the mass, suggesting continuous encapsulation (*Figure 3B*).

While the blurry vision in the right visual field still persisted in a milder form 6 months after the embolic event, the centrally liquid-filled cavity of the cMAC had completely disappeared, as revealed in second follow-up CMR (12 months after cMAC diagnosis). Cine sequences showed a hyperintense well-defined small c-shaped mass at the endo- and epicardial myocardium lateral of the mitral valve and mild persisting mitral valve regurgitation (*Figure 2C*). Again, similar to the initial CMR, first pass perfusion revealed no perfusion and late gadolinium enhancement showed enhancement of the residual mass (*Figure 3C*). Tissue characterization findings suggested a residual calcification of the mitral valve annulus (MAC) which—12 months after the initial CMR—, again, revealed no sign of a centrally liquid cavity. Dynamic changes are illustrated in *Video 1*.

As the patient experienced one embolic event only, aspirin has been switched to clopidogrel 75 mg at the time of retinal infarction and atorvastatin 40 mg continued. Since mitral valve function was not restricted and only mild regurgitation was present, a conservative approach was chosen after a second interdisciplinary heart team discussion. During the total follow-up of 3 years since initial presentation, no further embolic events occurred.

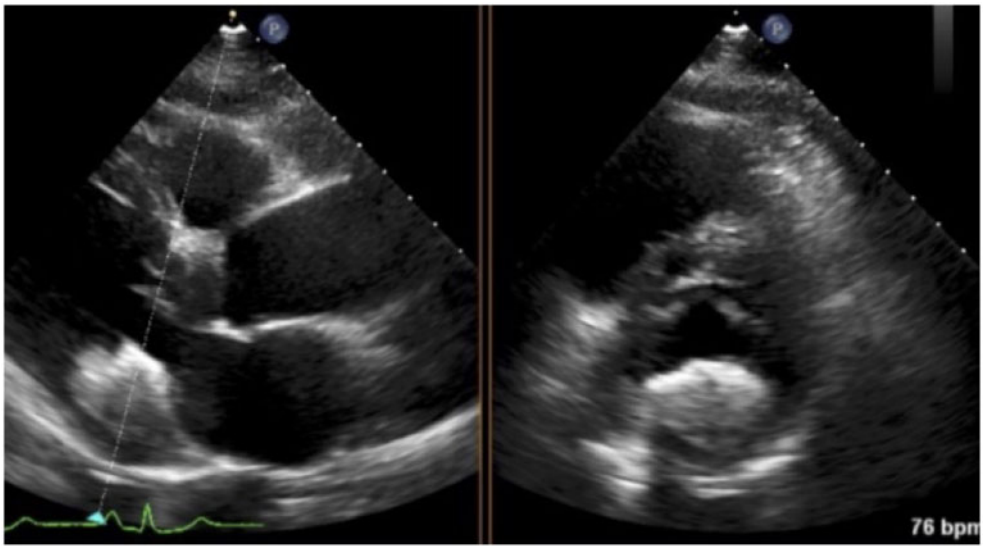


Figure 1 Initial echocardiography. Initial transthoracic echocardiography at first presentation. The parasternal long axis is shown on the left, whereas the basal short axis is shown on the right. Transthoracic echocardiogram reveals an echo-lucent, sclerotic structure of 28 mm × 24 mm × 21 mm at the posterior mitral annulus with a posterior echo shadow. There were no signs of mitral valve regurgitation or stenosis and normal biventricular function.

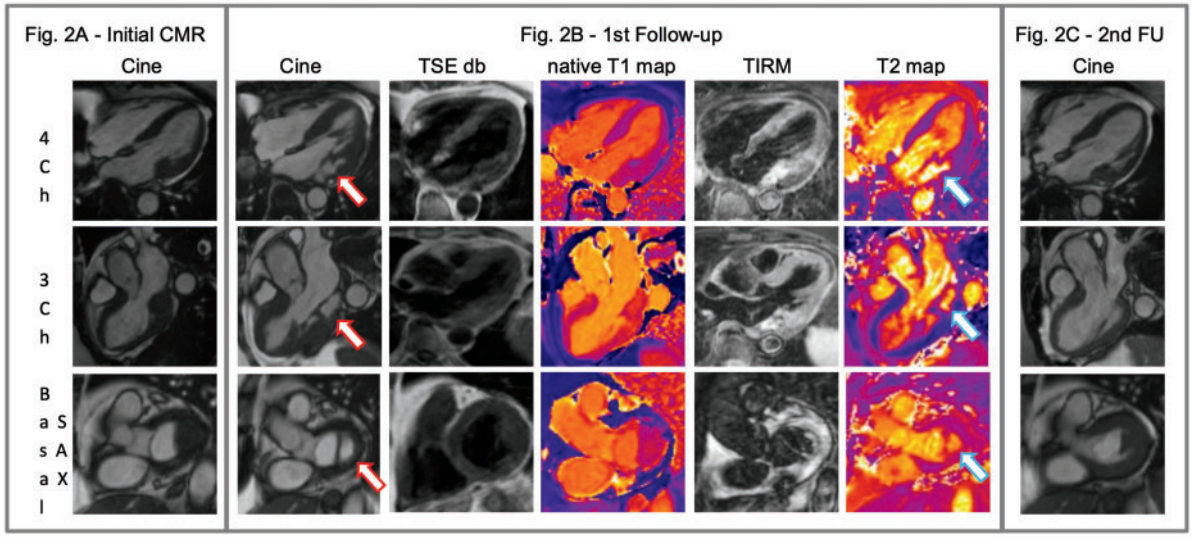


Figure 2 Native cardiac magnetic resonance of the dynamic changes of the caseous calcification of the posterior mitral annulus. Dynamic changes in native cardiac magnetic resonance in caseous calcification of the posterior mitral annulus in a 71-year-old woman. (*A*) Cine balanced steady-state free precession sequences demonstrated an 18 mm × 23 mm × 31 mm non-invasive heterogeneous mass in the left atrium in proximity to the posterior mitral valve annulus. (*B*) First follow-up cardiac magnetic resonance after 6 months. Cine balanced steady-state free precession showed an enlarging, centrally hyperintense mass (42 mm × 22 mm × 32 mm) (red arrow), further protruding into the lateral wall of the myocardium and new evidence of mitral regurgitation. In T1 Turbo Spin Echo dark blood (TSEdb) and Turbo Inversion Recovery Magnitude (TIRM), the central part of the mass presented as hyperintense with elevated values of 1138 ms (1.5 T) in quantitative tissue characterization by native T1 mapping and 225 ms by T2 mapping (blue arrow). The elevated T1 values implicate a dyshomogeneous content (liquid, calcification, and cell infiltrates) with values lower than blood pool (1551 ms). T1 relaxation time was 965 ms for myocardium (septal). (*C*) Second follow-up cardiac magnetic resonance after 12 months. Cine balanced steady-state free precession sequences showed an iso-/hypointense, well-defined, c-shaped rim at the endo- and epicardial myocardium lateral of the mitral valve and mild persisting mitral valve regurgitation. The liquid core was not detectable anymore. Cardiac magnetic resonance has been performed on a dedicated 1.5-T scanner (Magnetom Avanto fit; Siemens Healthcare) equipped with multi-channel phased-array surface receiver coils (up to 32 channels). Native T1 mapping was done using an electrocardiogram triggered 5-3 Modified Look-Locker Inversion Recovery balanced steady-state free precession sequence.

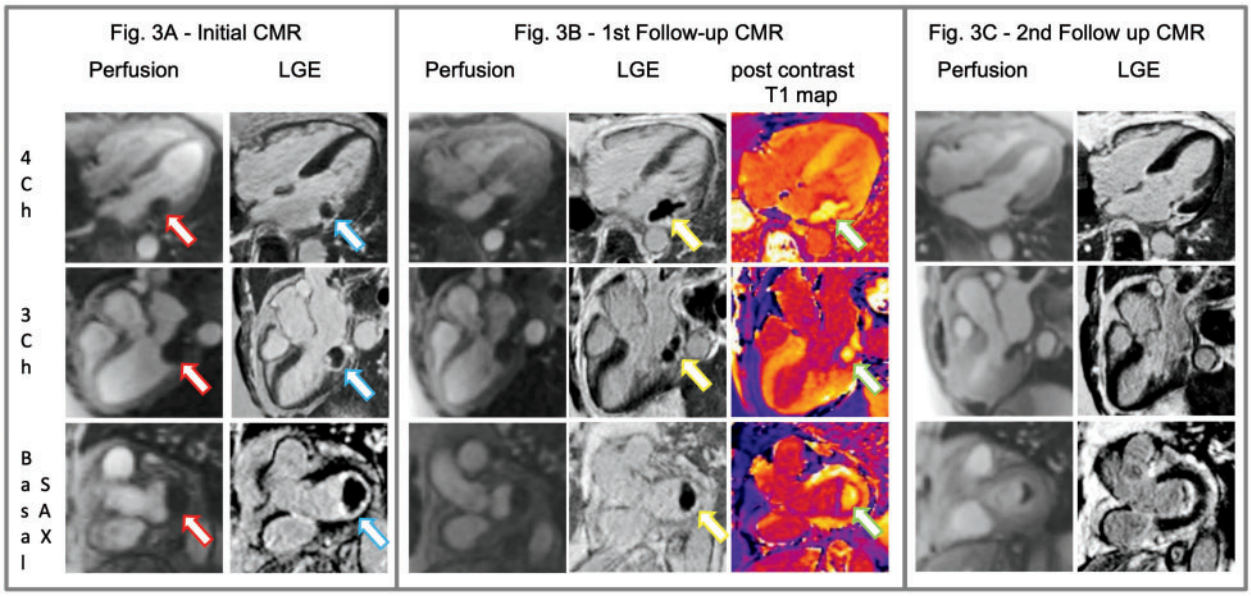


Figure 3 Post-contrast cardiac magnetic resonance of the dynamic changes of the caseous calcification of the posterior mitral annulus. Dynamic changes in post-contrast cardiac magnetic resonance of the caseous calcification of the posterior mitral annulus. (*A*) Initial cardiac magnetic resonance showing a non-invasive nodular mass in the left atrium in proximity to the posterior mitral valve annulus. First pass perfusion (FFP) revealed no perfusion of the mass (red arrow) and late gadolinium enhancement showed enhancement along the periphery of cMAC with only minimal peripheral contrast-uptake of the mass (blue arrow). (*B*) Cardiac magnetic resonance 6 months later showed again no perfusion of the grown mass. Similarly to the initial scan, late gadolinium enhancement revealed enhancement along with the periphery of cMAC (yellow arrow) with only minimal contrast-uptake of the mass [lower post-contrast T1 values compared to native T1 values (green arrow)]. (*C*) Follow-up cardiac magnetic resonance 12 months after diagnosis showed a residual mass at the lateral mitral valve still without perfusion in the FFPs and no contrast-uptake in the late gadolinium enhancement.

Discussion

We report a case with dynamic changes of MAC in a patient who developed cholesterol embolism of the retinal artery. Between the initial presentation and the stroke, liquefaction of MAC was documented. Although the patient had other potential sources of stroke (known atherosclerotic lesions at the aortic arch and the internal carotid arteries), MAC as potential cause is highly likely, especially given the detection of cholesterol embolism and a demonstration of evacuation of cMAC during follow-up.

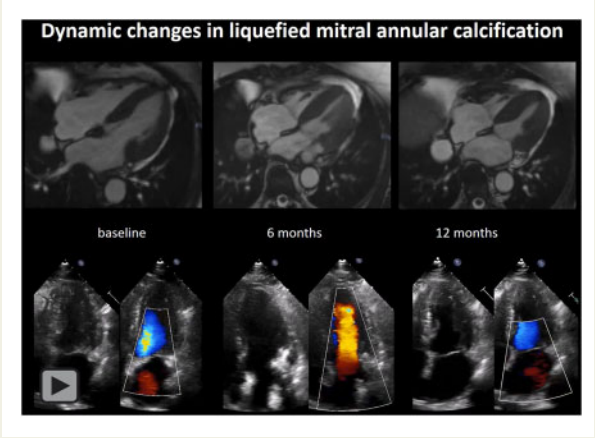
cMAC is usually first detected by echocardiography and can be characterized as a large echogenic mass with a central echo-lucent area and usually—in contrast to MAC—without acoustic shadowing artefacts.[3] Whereas MAC is usually low in signal on all CMR sequences (calcium), the calcium salts and proteinaceous fluid in cMAC may generate high signal on T1-weighted images. Furthermore, cMAC appears to be more tumefactive than MAC. The central 'toothpaste-like' texture histologically is a composition of calcium, fatty acids, and cholesterol.[5] The dynamic nature of cMAC has been demonstrated in a large echocardiography patient series[6] where both, development of MAC to cMAC as well as reversion from cMAC to MAC, have been documented, similar to our case. Spontaneous resolution of cMAC has also been described.[7] Quantitative tissue characterization with novel mapping techniques enables direct visualization of these processes.

CMR tissue characterization helps clinicians to precisely describe the lesions' size, localization, borders, tissue properties, and perfusion. Being able to discriminate fat and water content, fibrosis, vascularity, and perfusion patterns at different time points along with the high spatial and temporal resolution, many differentials can be distinguished.[8]

Currently, the optimal treatment of cMAC remains to be established.[9] The usually benign mass may cause sequelae, such as significant mitral stenosis or regurgitation, left ventricular outflow obstruction, or (recurrent) systemic embolization. A conservative approach can be chosen if the diagnosis is certain and haemodynamic is not compromised. Surgical resection can be necessary in cases of severe mitral valve dysfunction, embolic events, or uncertainty of the diagnosis (e.g. tumour).[9]

Conclusions

In summary, clear diagnosis of the dynamic process of liquefaction of MAC is made possible by performing CMR with quantitative multiparametric tissue characterization such as T1 and T2 mapping. A near-total liquefaction of MAC to cMAC and resolution from cMAC to MAC can be demonstrated with CMR suggesting that MAC is a dynamic condition with clinical implications such as mitral regurgitation and potential systemic embolization as demonstrated in the current



Video 1 Dynamic changes in liquefied mitral annular calcification. Cine balanced steady-state free precession sequences (four-chamber view) and echocardiographic loops (four-chamber view with colour Doppler on mitral valve) demonstrated an 18 mm × 23 mm × 31 mm (cardiac magnetic resonance) non-invasive mass of the posterior mitral valve at initial diagnosis. 6 months later, an enlarging and central liquefaction of the described mass and new evidence of mitral regurgitation can be appreciated. A second follow-up cardiac magnetic resonance 12 months after the initial cardiac magnetic resonance diagnosis, revealed a residual, well-defined, small, c-shaped mass in proximity to the lateral mitral valve with no sign of a centrally liquid cavity and mild persisting mitral valve regurgitation. The mitral regurgitation was still detectable. These findings describe the dynamic process of a near total liquefaction of the initial calcification of the mitral valve annulus to a caseous mitral annular calcification and again resolution from cMAC to a residual mitral annular calcification.

case. The differential diagnosis of an intracardiac mass of the posterior mitral annulus should include cMAC, not least to avoid further inappropriate diagnostic interventions.

Lead author biography

Simon Frey studied medicine at the University of Basel, Switzerland, where he graduated in 2014 and received his MD in 2015. After residency in Internal Medicine (Baden, Switzerland), he is currently specializing in non-invasive cardiology at the University Hospital Basel. Dr Frey participated actively in many research projects in different fields of cardiology (cardiac resynchronization therapy, implantable cardioverter defibrillator, nuclear imaging, and biomarkers). His special interest lies in multimodality imaging.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

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