

The “MAC” Attack: When Mitral Annular Calcification Goes Rogue! A Case Series of Mobile Mitral Annular Calcifications



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INTRODUCTION

Calcified amorphous tumor (CAT) is a rare non-neoplastic tumor that can affect multiple structures of the left and right heart.¹ Mitral annular calcification (MAC)-related CAT represents a subgroup of CAT that may have a mobile component. Although often perceived as a chronic, slowly progressing disease, it is becoming more apparent that mobile MAC-related CAT can not only present over short periods of time but can also cause acute pathology (MAC attack). In this case series, we report three cases that highlight the various clinical manifestations and associated pathologies in an effort to better understand this rare disease.

CASE PRESENTATIONS

We present three cases demonstrating the many faces of mobile MAC.

Embolic Stroke

The first patient was a 65-year-old woman with a history of arterial hypertension and gout. She also underwent a remote partial nephrectomy for a right renal mass. She presented with 6 months of periodic right arm weakness and unsteady gait. Brain magnetic resonance imaging/magnetic resonance angiography confirmed the presence of small subacute cerebellar infarcts. Transthoracic echocardiography showed a nonobstructing mobile echodensity measuring 1.5 × 0.6 cm attached to the medial aspect of the left ventricular outflow tract (LVOT), adjacent to the mitral annulus (Figures 1A-1C). These findings were confirmed by transesophageal echocardiography (Figures 1D and 1E, Video 1). An extended infectious workup was initiated, including empiric antibiotics despite persistently negative blood cultures. Cardiac magnetic resonance imaging demonstrated a small filamentous mass on the basal aspect of the septum at the proximal LVOT, too small to characterize (Figure 1F). In the setting of multiple cerebral ischemic events, cardiac surgery was consulted. Preoperative chest computed

tomography (Figure 1G) and cardiac angiography were significant only for MAC. Intraoperatively, the surgeon resected a mobile mass, which was confirmed by pathology to be fibrous tissue with nodules of calcium surrounded by mixed inflammatory cell infiltrates suggestive of CAT.

Heart Failure

The second patient was a 77-year-old woman with a history of coronary artery disease, who presented with new-onset dyspnea (New York Heart Association functional class III). Transthoracic and transesophageal echocardiography showed normal biventricular function and severe calcific mitral stenosis (1.02 cm² by three-dimensional planimetry; Figures 2A-2C). There was also an incidental finding of a highly mobile echodensity attached to the calcified posterior mitral annulus (Figures 2A and 2D, Videos 2 and 3). Cardiac surgery was consulted for symptomatic severe calcific mitral stenosis. After preoperative chest computed tomography and cardiac angiography (Figures 2E and 2F), the surgeon excised the anterior mitral leaflet and the subvalvular connections and debrided the posterior leaflet of calcium, leaving a 25-mm Carpentier-Edwards Magna mitral valve (Edwards Lifesciences, Irvine, CA) in place. The samples resected demonstrated moderately fibrotic material with myxoid changes along the edge. The valve was markedly calcified, without vegetation or perforation. There was, however, an irregular segment of thrombus.

ST-Segment Elevation Myocardial Infarction

The third patient was a 59-year-old woman with a history of hypothyroidism, hemochromatosis, and gastric bypass surgery. Emergency medical services were called for substernal chest pain. She was transported to the catheterization laboratory for suspicion of ST-segment elevation myocardial infarction. The initial angiogram demonstrated a complete occlusion of the distal right coronary artery (Figure 3A). Aspiration thrombectomy without stenting was performed. Upon admission to the coronary unit, transthoracic and subsequent transesophageal echocardiography demonstrated a mobile pedunculated mass (1.6 × 0.5 cm) attached to ventricular aspect of the anterior mitral valve leaflet (Figure 3B). The echodensity was prolapsing into the LVOT without causing obstruction (Figures 3C-3E, Videos 4 and 5). Initial suspicion was for a symptomatic fibroelastoma or vegetation, prompting a cardiac surgery consult and eventual cardiac surgery. During the operation, the mass was visualized on the anterolateral commissure of the mitral valve, just underneath the attachment of the anterior mitral leaflet. It was excised and sent for pathology and ultimately demonstrated a calcified thrombus (Figures 3F and 3G).

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VIDEO HIGHLIGHTS

Video 1: Midesophageal long-axis transthoracic view of the LVOT demonstrating a mobile echodensity on the ventricular aspect of the mitral valve and prolapsing into the LVOT.

Video 2: Midesophageal four-chamber transthoracic view demonstrating a hyperechoic echodensity with independent motion on the atrial aspect of the mitral valve.

Video 3: Three-dimensional rendering demonstrating mitral stenosis and a hyperechoic echodensity with independent motion on the atrial aspect of the mitral valve.

Video 4: Midesophageal four-chamber two-dimensional transthoracic view demonstrating a hyperechoic echodensity with independent motion on the ventricular aspect of the mitral valve, prolapsing into the LVOT.

Video 5: Midesophageal four-chamber three-dimensional transthoracic view demonstrating a hyperechoic echodensity with independent motion on the ventricular aspect of the mitral valve, prolapsing into the LVOT.

View the video content online at www.cvcasejournal.com.

DISCUSSION

CAT is a rare non-neoplastic tumor of the heart first described by Reynolds *et al.* in 1997.¹⁻³ CAT presents in middle-aged patients (mean age, 58 ± 17 years), spanning a range of 16 to 85 years.² There is a female predominance, and it has been associated with end-stage renal disease, MAC, valvular disease, and diabetes mellitus.² CATs have been described within the left-sided cardiac structures (71%), including the left ventricle, left atrium, papillary muscles, and mitral valve. They have also been described within

the right-sided structures (31%), including the superior vena cava, right atrium, right ventricle, and tricuspid valve. In a small subset, multiple attachment sites within the same heart have been described (18%).⁴

MAC-related CAT constitutes a subgroup of CAT, often associated with end-stage renal disease.^{2,5,6} MAC is classically felt to be benign other than causing impedance to transvalvular flow. Interestingly, in a series of 182 patients who had documented arterial thromboembolic events, 10 patients had MAC as the only abnormality identified.⁷ Three of those patients (1.46% of the cohort) had documented pedunculated vegetation-like masses attached to the very heavily calcified mitral annulus and labeled as “swinging CAT.” Alternative names have also been suggested, including “MAC with associated CAT and a mobile component” or more commonly “mobile MAC.”^{2,7,8} The addition of a mobile component conveys a high risk for embolization and rapid growth characteristics, which have been documented in past cases and demonstrated in our three cases.⁸

The physiopathology of CAT remains unclear, more so for MAC-related CAT with a mobile component. Some reports suggest that it is caused by abnormalities of calcium phosphorus metabolism, while others have reflected on Virchow’s triad to explain the formation of thrombus followed by calcification.⁹

Mobile MAC is best identified on echocardiography as a hyperechoic lesion around the mitral annulus with an associated hypermobile echodensity. This echodensity is commonly described as homogenous and linear with a maximum length > 1 cm (Table 1). Although it may present near the mitral commissures or posterior mitral annulus. Those near the anterior mitral leaflet can prolapse into the LVOT or aortic valve, typically without obstruction. The differential diagnosis includes caseous calcification of the mitral annulus, thrombus, vegetation, or a cardiac mass such as papillary fibroelastoma.^{11,12} However, definitive diagnosis is made with histopathology. Reynolds *et al.*,¹ in their initial description of CAT, described nodular deposits or flecks of calcium within a background of eosinophils and amorphous, sometimes fibrillary material. Included in their initial discussion was the suggestion that CAT may represent the remnants of a

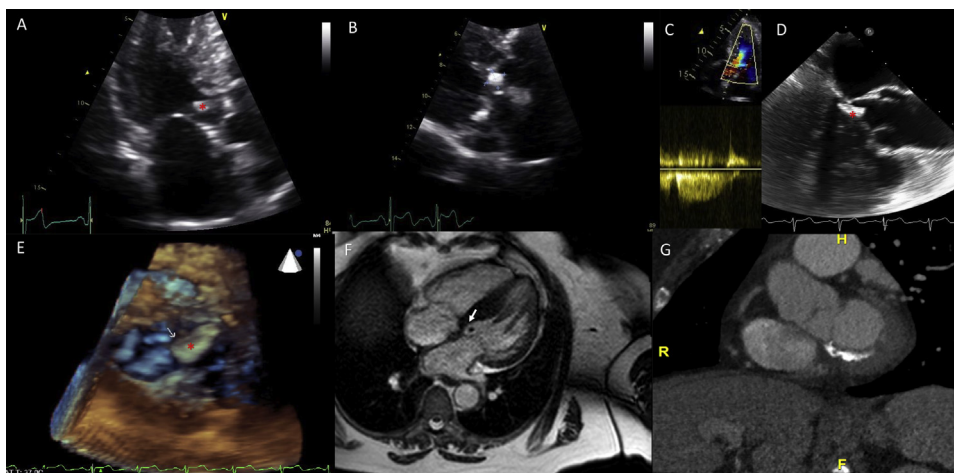


Figure 1 (A) Apical long-axis view on transthoracic echocardiography demonstrating an echodensity within the LVOT (asterisk). (B) Parasternal long-axis view of the mitral valve with a hyperechoic mass adjacent to the anterior mitral leaflet. (C) Absence of LVOT obstruction noted on spectral Doppler. (D) Long-axis midesophageal view on transesophageal echocardiography showing the hyperechoic mass within the LVOT (asterisk) and the (E) corresponding three-dimensional image. (F) Preoperative cardiac magnetic resonance imaging demonstrating signal void within the ventricle/LVOT likely reflecting the calcified mobile mass (arrow). (G) Preoperative computed tomography demonstrating significant posterior MAC.

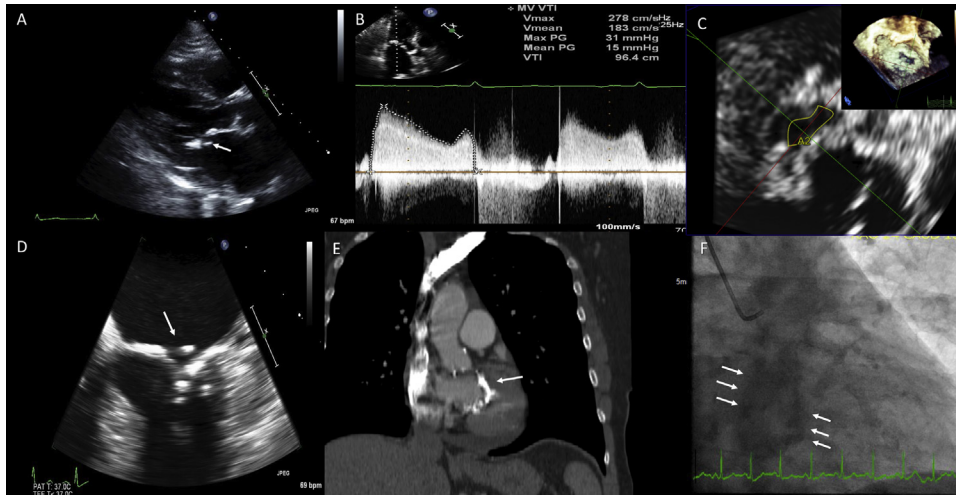


Figure 2 Parasternal long-axis view on transthoracic echocardiography showing significant MAC and a small linear hyperechoic lesion prolapsing into the left atrium (arrow). (B) Spectral Doppler across the mitral valve demonstrating a mean gradient of 15 mm Hg at a heart rate of 70 beats/min. (C, D) Transesophageal echocardiographic midesophageal view of the calcified mitral valve with a mobile component (arrow) and the associated three-dimensional multiplanar reconstruction with planimetry confirming severe stenosis. (E) Preoperative computed tomography showing significant MAC (arrow). (F) Preoperative angiogram demonstrating significant MAC preinjection (arrows).

mummified thrombus. This hypothesis was supported by the presence of degenerating fibrin in all tumors and the presence of hypercoagulable risk factors in several cases reported in their series. However, they concluded that CAT is likely its own entity, with calcified thrombus remaining in the differential.¹

The hypothesis of calcified thrombus is further supported by Kubota *et al.*⁸ and Fealey *et al.*¹³ They described mobile MAC as thrombus in its late phase of chronological changes. Of the cases

reported with mobile MAC, pathologic specimens revealed either calcium deposits or fibrin or, similar to our case, the presence of red thrombus covered with calcium and fibrin deposits (Table 1). Interestingly, histological appraisal of two reported cases of mobile MAC did demonstrate the classic nodular appearance and calcium deposits characteristic of CAT (Table 1).¹⁰ This constellation of findings suggests that calcified thrombus and CAT may not be mutually exclusive but rather exist on a spectrum, with thrombus

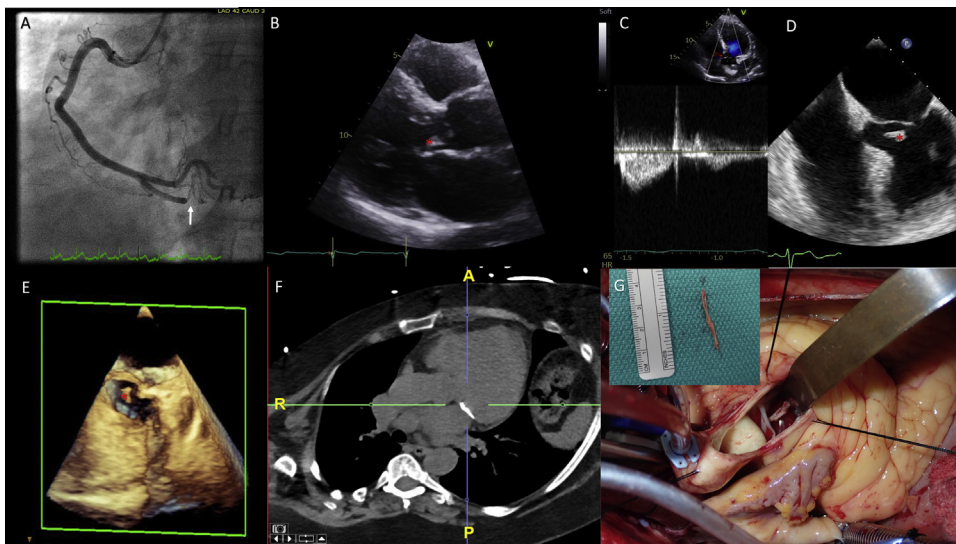


Figure 3 (A) Initial angiogram of the right coronary artery demonstrating a complete occlusion (arrow) of the posterior descending artery within an otherwise healthy artery. (B) Parasternal long-axis view on transthoracic echocardiography showing a small mobile echodensity within the LVOT (asterisk). (C) No dynamic obstruction was noted on spectral Doppler. (D, E) Midesophageal two-dimensional and three-dimensional transesophageal echocardiographic views also demonstrating the mobile echodensity (asterisk). (F) Preoperative computed tomography confirming the presence of MAC and (G) intraoperative images showing the filamentous mobile mass that was excised.

Table 1 Cases of MAC-related CAT with a mobile component

Author (year)	Presentation	Symptoms	Echocardiography	Imaging characteristics	Risk factors	Pathology
de Hemptinne <i>et al.</i> (2015) ²	67-year-old man with hypertension and dyslipidemia	TIA and evidence of emboli on MRI	Highly mobile mass (9 × 7 mm) attached to the ventricular aspect of the calcified mitral annulus (close to the posterior commissure)	Size: <1 cm Characteristics: hyperechoic circular, mobile, homogenous echodensity Location: ventricular side of mitral valve adjacent to the LVOT, near the posterior commissure Associated with: MAC	Normal creatinine	Heterogeneous calcium deposits with surrounding amorphous eosinophilic and fibrinous material
Kubota <i>et al.</i> (2010) ⁸	64-year-old woman with diabetes and ESRD	Thought to be endocarditis	Pedunculated crotchet-shaped mobile tumor (3 × 27 mm) originating from the annulus of the anterior commissure of the mitral valve	Size: >1 cm Characteristics: hyperechoic, linear mobile homogenous echodensity Location: ventricular side, anterior commissure of the mitral valve and prolapses in the LVOT Associated with: moderate MR/AR	Hemodialysis	Fibrin and calcium deposits
Kubota <i>et al.</i> (2010) ⁸	44-year-old Male	Incidental	Hyperechoic mass (5 × 18 mm) at the base of the anterior papillary muscle that grew to 5 × 28 mm	Size: >1 cm Characteristics: hyperechoic and mobile echodensity Location: ventricular side, on a papillary muscle Associated with: anterior MAC	Hemodialysis, lupus erythematosus	Red thrombus covered with fibrin and calcium deposits
Kawata <i>et al.</i> (2013) ⁹	59-year-old man with diabetes and ESRD	Incidental	Cudgel-shaped, hyperechoic mobile echodensity (6 × 28 mm) on the ventricular side of the mitral valve and likely originating from the annulus of the anterior commissure	Size: >1 cm Characteristics: hyperechoic, homogenous, linear and mobile Location: ventricular side of the mitral annulus and prolapsing into the aortic valve Associated with: MAC	Hemodialysis	Multiple calcified nodules surrounded by collagenous fibers, amorphous fibrin, and inflammatory cells suggestive of CAT
Tsuchihashi <i>et al.</i> (1999) ¹⁰	70-year-old woman with interstitial nephritis due to recurrent pyelonephritis	Incidental	Crotchet-shaped mobile interventricular mass	Size: >1 cm Characteristics: hyperechoic, homogenous, linear and mobile Location: attached to the membranous septum Associated with: MAC	Hemodialysis	Tumor calcinosis and calcification of the mitral annulus and the aortic root, which was partially connected to the interventricular septum where the tumor was attached

Author	Case Description	Imaging Findings	Pathology	Associated Conditions
Tsuchihashi et al. (1999) ¹⁰	62-year-old woman with ESRD from renal tuberculosis	Giant mobile left atrial mass attached to the base of the posterior mitral leaflet	White mass attached to the mitral leaflet with superficial red thrombus; microscopic examination also showed calcinosis with fibrous sequestration and thrombi formation	Cerebrovascular accident
Tsuchihashi et al. (1999) ¹⁰	55-year-old woman with DM, diabetic nephropathy	Mobile left atrial mass attached to the base of the posterior left atrial wall	No pathology reported	Incidental
Tsuchihashi et al. (1999) ¹⁰	71-year-old man with chronic glomerulonephritis requiring dialysis	Mitral annular calcinosis with left atrial mobile tumors attached to the base of the AML	No pathology reported	Incidental

AML, Anterior mitral leaflet; AR, aortic regurgitation; DM, diabetes mellitus; ESRD, end-stage renal disease; MR, mitral regurgitation; MRI, magnetic resonance imaging; TIA, transient ischemic attack.

forming in the more acute phase and calcifications representing a more chronic phase of CAT. This hypothesis is supported by our three cases of mobile MAC, the first with findings consistent of CAT on histology in a patient with risk for hypercoagulability (renal mass), and cases 2 and 3 with clear thrombus detected.

Symptomatic mobile MAC is a clear indication for surgical resection of the tumor to prevent any further embolization. However, preventive surgery remains controversial and is an area of future research given the risk associated with a heavily calcified mitral valve. On the basis of limited available data, the prognosis is good after complete removal of the mass, with only one documented recurrence in a patient who underwent incomplete resection of the tumor.^{2,13,14}

CONCLUSION

CAT is a rare non-neoplastic tumor that may be associated with MAC and have a mobile component. Mobile MAC has a high risk for embolization resulting in acute pathology (MAC attack) and can be safely resected surgically. Echocardiography remains the most widely used noninvasive tool for identification of mobile MAC, while histology is necessary for a definitive diagnosis.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2020.07.004>.

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