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CASE REPORT

Caseous calcification of the mitral annulus: case report and brief review

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Background Caseous calcification of the mitral annulus (CCMA) is a very rare variant of mitral annular calcification, which is typically asymptomatic but can manifest as a cardiac tumour, abscess, or in the form of mitral valve dysfunction.

Case summary We present a patient who developed shortness of breath and was initially thought to have an intracardiac tumour, but ultimately was recognized as massive calcification of the mitral valve by computed tomography angiogram. This finding was unfortunately made only shortly before the patient's clinical deterioration, and the specific diagnosis of CCMA was made on post-mortem findings, precluding any directed treatment for this entity.

Discussion Caseous calcification of the mitral annulus can lead to significant pathology, including mitral regurgitation, stenosis, or systemic embolization of caseous material. Due to its relative scarcity and tendency to be asymptomatic, a diagnosis of CCMA is often difficult to make or easily overlooked. Early recognition and appropriate treatment is crucial for avoiding these potential complications.

Keywords Case report • Caseous calcification • Mitral annulus • Calcinosis

Learning points

- Rare forms of mitral annular calcification (MAC) such as caseous calcification of the mitral annulus are often overlooked and initially misdiagnosed.
- Caseous calcification of the mitral annulus appears to share an aetiology with the classic form of MAC, with an added component of atherosclerotic cardiovascular disease leading to caseous necrosis.

Introduction

The mitral valve annulus is the C-shaped portion of fibrous tissue at the junction of the left atrium and left ventricle, where the leaflets of the mitral valve are attached to provide structural support. Mitral annular calcification (MAC) is a relatively common degenerative condition of the mitral valve, in some series affecting 8.5% of the general population.[1] Mitral annular calcification occurs when there is progressive deposition of calcium within the annulus, which may cause significant mitral regurgitation, or less commonly, mitral stenosis.

A rare variant of MAC named caseous calcification of the mitral annulus (CCMA) occurs where there is caseous degeneration of these calcified areas. The condition most commonly affects elderly patients and women in particular.[2] Due to its relative scarcity and tendency to be asymptomatic, the true incidence of caseous calcification is unknown, but several studies estimate that it affects just 0.06% of the general population and only 0.6% of all cases of MAC.[2–4] An autopsy series found CCMA comprised 2.7% of MAC cases,[1] a finding which suggests this condition is underdiagnosed on imaging, most likely due to unfamiliarity with the condition and lack of symptoms prompting evaluation by imaging.

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Although CCMA is generally a benign and asymptomatic condition, it is often misconstrued as a cardiac tumour (benign or malignant), abscess, or calcified vegetation based on imaging.[5,6] This condition can also manifest with conduction abnormalities or sometimes with systemic embolization of caseous material.[7] Caseous calcification of the mitral annulus is nearly always described as involving the posterior portion of the mitral annulus, but uncommonly involves the anterior portion alone or the entire annulus.[8]

Timeline

18 June 2015	• Patient developed bilateral leg oedema
24 June 2015	• Presented to primary care with atypical right-sided chest pain and worsening leg oedema • Developed shortness of breath and perspiration while in clinic • Admitted to hospital with elevated troponins and chest pain
25 June 2015	• Electrocardiography revealed first degree heart block and non-specific intraventricular conduction delay without ST changes; patient diagnosed with non-ST elevation myocardial infarction • Echocardiography showed moderate aortic stenosis, moderate mitral regurgitation, and a calcified intracardiac mass at the base of the interventricular septum • Cardiac-gated computed tomography angiography revealed a massively calcified mitral valve with extension into the interventricular septum
26 June 2015	• Cardiac catheterization performed, revealing severe stenosis of left circumflex (CFX) coronary artery and suggestion of acute plaque rupture; stent placed in CFX • High creatinine continued to rise • Patient diagnosed with post-contrast nephropathy causing oliguric renal failure
27 June 2015	• Episode of hypoxic respiratory failure, required Bilevel Positive Airway Pressure (BiPAP) • After 2 h of BiPAP, hypoxaemia improved and patient weaned to his baseline 2L O_2 requirement
28 June 2015	• As creatinine continues to rise, clinical team monitors potassium and pH levels; plans made for renal replacement therapy or dialysis in the near future • Patient became suddenly pulseless and unresponsive during a second breathing treatment with BiPAP • Sinus bradycardia noted on telemetry; code was called for pulseless electrical activity • Received 5–6 cycles of chest compressions and defibrillation once with return of spontaneous circulation
29 June 2015	• Patient remains intubated and sedated • Neurology consulted and intracranial process ruled out via computed tomography of the head; unable to give family specific prognosis regarding neurological recovery
30 June 2015	• Family elects for palliative extubation after discussion regarding patient's wishes and his poor prognosis • Time of death called at 14:40
1 July 2015	• Medical autopsy performed

Case summary

Our case involves a 77-year-old man with a history of severe coronary artery disease requiring stenting of the proximal left anterior descending coronary artery (LAD) 6 years prior, left cerebral stroke with subsequent patent foramen ovale closure 2 years prior, chronic obstructive pulmonary disease requiring 2 L of oxygen support, and chronic kidney disease (CKD) who was admitted to our institution for shortness of breath, chest pain, and elevated troponin levels at 3.16 ng/mL (normal <0.03 ng/mL). On initial physical examination, the patient had a temperature of 36.6° Celsius, heart rate of 72 b.p.m., blood pressure of 132/57 mmHg, oxygen saturation of 95%, and respiratory rate of 18 b.p.m.. At the time of admission, no specific abnormalities were heard on cardiac or pulmonary auscultation.

Electrocardiography revealed first degree heart block and non-specific intraventricular conduction delay without ST changes, thus the patient was diagnosed with non-ST elevation myocardial infarction. Echocardiography was technically difficult with suboptimal views, revealing an ejection fraction of 69%, moderate aortic stenosis (mean gradient across aortic valve of 23 mmHg), moderate mitral regurgitation, and a calcified intracardiac mass at the base of the interventricular septum. The left atrial volume index was severely dilated, but no regional wall abnormalities were ascribed to the left or right ventricles. The aortic valve was tri-leaflet and no aortic regurgitation was appreciated.

Further imaging with computed tomography angiography revealed advanced three vessel coronary atherosclerosis, a calcified aortic valve with aortic stenosis, and a massively calcified mitral valve with extension of calcification into the interventricular septum (*Figure 1*).

He underwent cardiac catheterization the following day which revealed a patent stent in place within the LAD, a left circumflex coronary artery (CFX) with severe stenosis and suggestion of acute

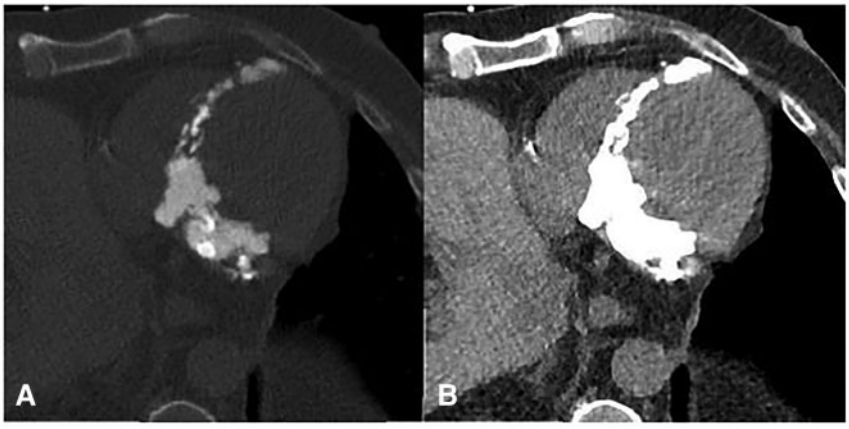

Figure 1 Non-contrast (*A*) and post-contrast (*B*) axial images from computed tomography angiogram of the heart revealed massive calcification of the mitral valve annulus which also expanded the intraventricular septum and extended into the moderator band of the right ventricle.

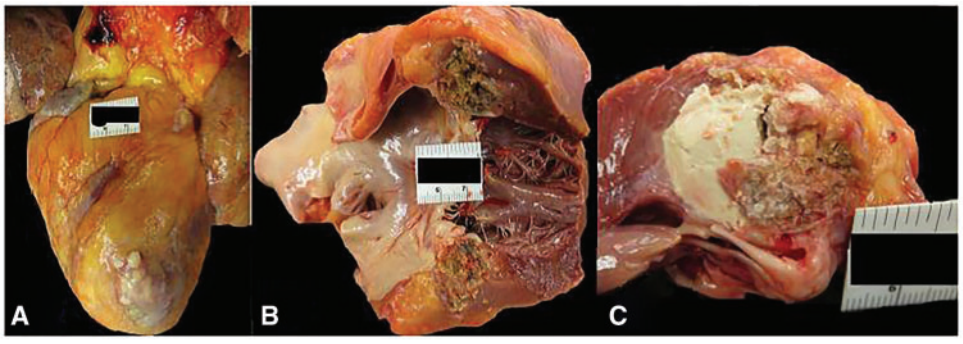

Figure 2 Gross findings from autopsy. An irregular 2.6 × 2 cm yellow-tan plaque was present at the cardiac apex (*A*). On cut surface, the mass measured 3 × 1.9 cm along the posterior portion of the mitral annulus and was overlying the mitral valve (*B*), with diffuse tan-brown calcification and abundant tan-yellow, friable and caseous material (*C*).

plaque rupture, and a calcified right coronary artery (RCA) with severe stenosis in the mid vessel. A stent was placed within the CFX with plans for percutaneous coronary intervention of the RCA in the future. Following catheterization, the patient developed oliguria and rising creatinine levels. The patient's creatinine at admission was 2 mg/dL, improved to 1.6 mg/dL over the first 2 days of hospitalization and had risen to 3.9 mg/dL at the time nephrology was consulted on hospital day four. The suspected aetiology was CKD with superimposed acute kidney injury as a result of IV contrast use without pre-hydration; in fact, the patient was receiving diuretics at that time for symptoms of congestive heart failure. Concurrently with the oliguric acute renal failure, he developed hypoxic respiratory failure and required treatment with Bilevel Positive Airway Pressure (BiPAP).

Nephrology planned to closely monitor the patient's potassium and pH levels, and schedule renal replacement therapy or dialysis soon thereafter. The same afternoon, the patient became unresponsive and pulseless. After receiving defibrillation and 5–6 cycles of chest compressions, return of spontaneous circulation was achieved, but the patient remained unresponsive and intubated. Neurology evaluated the patient and was unable to give a specific prognosis for neurological recovery. In the setting of suspected cardiorenal syndrome, both cardiac and renal function rapidly declined. With the patient's neurological status in question and due to concerns regarding quality of life, his family made a joint decision for palliative extubation on hospital day seven, and the patient expired shortly afterwards. A medical autopsy was requested by the family.

At autopsy, cardiomegaly (cardiac weight of 640 g; normal 233–383 g) and evidence of heart failure were observed, including pericardial effusion (20 mL of serous fluid), bilateral serous pleural effusions (500 mL right; 250 mL left), and passive congestion of the liver in the form of nutmeg discoloration of the liver parenchyma. In addition to severe calcific atherosclerosis involving all coronary arteries, a calcified 3 × 1.9 cm mass was present along the posterior portion of the mitral annulus, overlying the mitral valve. It extended to involve the

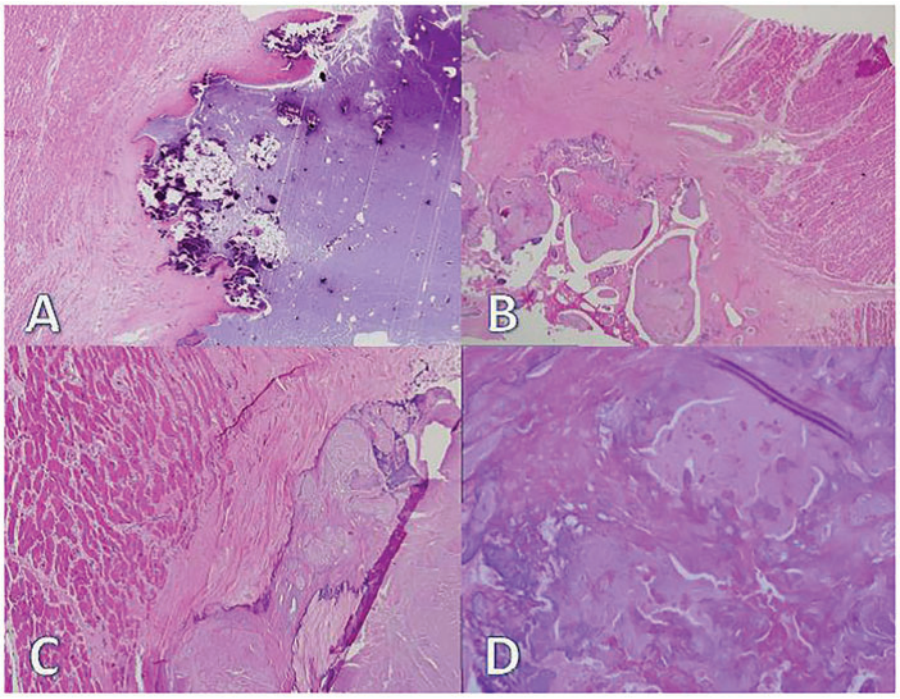

Figure 3 Histopathological findings. The epicardial plaque at 4× (*A*) displayed diffuse calcification with admixed necrotic, eosinophilic material. Sections of the intracardiac mass (B-2×, C-10×, and D-40×) demonstrate similar dense calcification with areas of amorphous, necrotic material, and sparse chronic inflammation including lymphocytes and histiocytes. The adjacent myocardium contained myocyte hypertrophy and perivascular fibrosis.

majority of the interventricular septum, a large portion of the left ventricular wall, and a portion of the right ventricular wall. There was also extension through the myocardium and onto the epicardium, forming an irregular 2.6 × 2 cm yellow-tan plaque at the apex (*Figure 2A*). On cut surface, the mass contained diffuse tan-brown calcification and abundant tan-yellow, friable and caseous material (*Figure 2B* and *C*).

In addition to routine sections of lung, heart, and kidney, multiple sections of epicardial plaque and both calcified and caseous areas of the mass were submitted for microscopic examination. Sections of epicardial plaque revealed necrotic eosinophilic material, diffuse calcification, and fat necrosis with a surrounding mixed inflammatory infiltrate composed of histiocytes and lymphocytes (*Figure 3A*).

Following post-mortem examination, the cause of death was determined to be complications of CCMA, with cardiomegaly and severe atherosclerotic cardiovascular disease listed as contributory. Given the patient's preserved ejection fraction on echocardiography, the mechanism of heart failure was thought to be diastolic in nature with progressive renal impairment contributing to cardiorenal syndrome. On post-mortem examination, evidence of venous congestion such as congestive hepatopathy supported the clinical impression of congestive heart failure. Caseous calcification of the mitral annulus can predispose to arrhythmia, especially when extensively involving the myocardium as seen in this case; therefore CCMA was believed, in combination with renal impairment, to play a direct role in the patient's cardiac arrest and subsequent clinical decline.

Discussion

Diagnosis of CCMA is most commonly made by typical imaging findings; for example, on echocardiogram CCMA is typically located within the posterior portion of the mitral annulus, has echolucency centrally with a surrounding hyperechogenic rim, and does not show flow or acoustic shadow.[9] Cardiac magnetic resonance and computed tomography are similarly characteristic and can be used for diagnosis.[10]

Caseous calcification of the mitral annulus is thought to share an aetiology with mitral annular calcification, where calcium is deposited within the heart leading to a chronic degenerative process. This is commonly seen in elderly women and patients with calcium metabolism abnormalities or renal failure, suggesting that a high turnover of calcium contributes to the development of MAC.[11] The aetiology of caseous necrosis in CCMA is still debated, but similarities to atheromas seen in atherosclerotic cardiovascular disease have been

suggested.[8,11] Findings such as severe calcific atherosclerosis of the coronary arteries and hypertension, both present in our case, are commonly described in patients with CCMA, further supporting this theory.

No standard treatment protocol for CCMA exists, but surgery is generally indicated for severe mitral valve dysfunction related to other conditions and surgical management has been implemented in cases of CCMA with severe symptomatic mitral regurgitation, stenosis, or systemic embolization of caseous material, with considerable success.[2,7] While most patients are instead treated conservatively and spontaneous resolution or transformation back to typical MAC has been described, there are also cases where CCMA recurred even after surgical excision.[2,12,13]

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 image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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