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Pictorial Essay

Myocardial calcifications: Pathophysiology, etiologies, differential diagnoses, and imaging findings

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ABSTRACT

Myocardial calcifications are not uncommonly encountered by the cardiac imager and may have a range of imaging appearances, from focal calcific deposits to diffuse myocardial involvement. A number of pathological processes can both cause and result from myocardial calcification; therefore, accurate identification and characterization are important. This pictorial essay will review the mechanisms, etiologies, imaging features, and differential diagnoses of myocardial calcification with imaging examples.

1. Introduction

Myocardial calcifications can arise from a number of different etiologies. Calcium within the myocardium indicates underlying pathology associated with morbidity and mortality. It is therefore important to report and characterize myocardial calcifications when they are visible on diagnostic imaging examinations. Radiographs, CT, and echocardiography can detect myocardial calcifications. While imaging features are often nonspecific, the combination of imaging pattern and clinical history may help clinicians determine the etiology and clinical significance of myocardial calcifications when they are discovered.

2. Pathophysiology and etiologies of myocardial calcification

Pathologic calcification in any tissue represents abnormal accumulation of calcium salts. Two basic forms are recognized: dystrophic and metastatic.[1] Traditionally, the most broad classification of myocardial calcifications follows this

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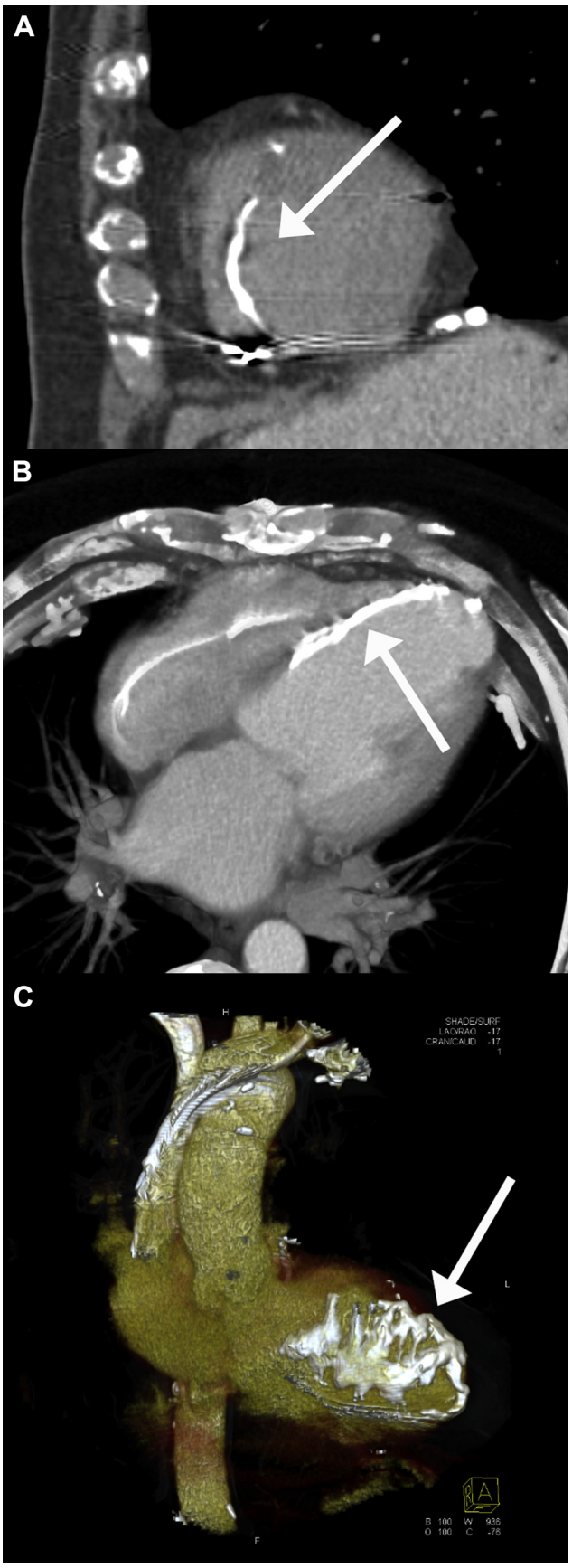

Figure 1 – Dystrophic calcifications in a 78-year-old man with a history of myocardial infarction. (A) Oblique short-axis image from an unenhanced CT shows marked thinning and calcification (*arrow*) of the left ventricular septum. (B) Oblique four-chamber maximum intensity projection image from a separate contrast-enhanced CT better demonstrates the full extent of the abnormality (*arrow*). (C) Oblique coronal volume-rendered images again show the full extent of calcification (*arrow*). This case illustrates the typical pattern of dystrophic calcification secondary to previous myocardial infarction: focal linear calcifications in a vascular distribution with associated wall thinning.

Table 1 – Specific etiologies of myocardial calcification.

Etiology
Dystrophic
Ischemic
Myocardial infarction
Ventricular aneurysm/pseudoaneurysm
Traumatic
Cardiac surgery[13]
Cardioversion[4]
Irradiation
Hemorrhage
Infectious
Myocarditis (usually fungal or viral)
Myocardial abscess
Perimyocarditis[3]
Tuberculosis[4]
Echinococcal disease[4]
Inflammatory
Rheumatic heart disease[17]
Sarcoidosis[3]
Sepsis[2,12]
Endomyocardial fibrosis[3]
Hypereosinophilic endo(myo)carditis
Cellular rejection (cardiac transplants)[12]
Neoplastic
Metastatic disease
Primary cardiac tumors
Other
Drugs, including cyclosporine, steroids,[12] calcium chloride,[13] catecholamines[19]
Caseous calcification of the mitral annulus[6]
Pulmonary hypertension[13]
Metastatic
Renal failure
Hyperparathyroidism
Oxaluria[8]
Aluminum intoxication (related to hemodialysis)
Dietary calcium and/or vitamin D deficiency[7]
Sarcoidosis (related to vitamin D hyperactivation)[1]
Idiopathic
Mimics
Valvular/annular calcification
Pericardial calcification
Coronary artery calcification
Great vessel calcification
Calcified intraluminal thrombus
Calcified intraluminal or pericardial tumors

categorization and adds “idiopathic calcification” as a third form[2]; however, the validity and clinical utility of this classification scheme is unknown.

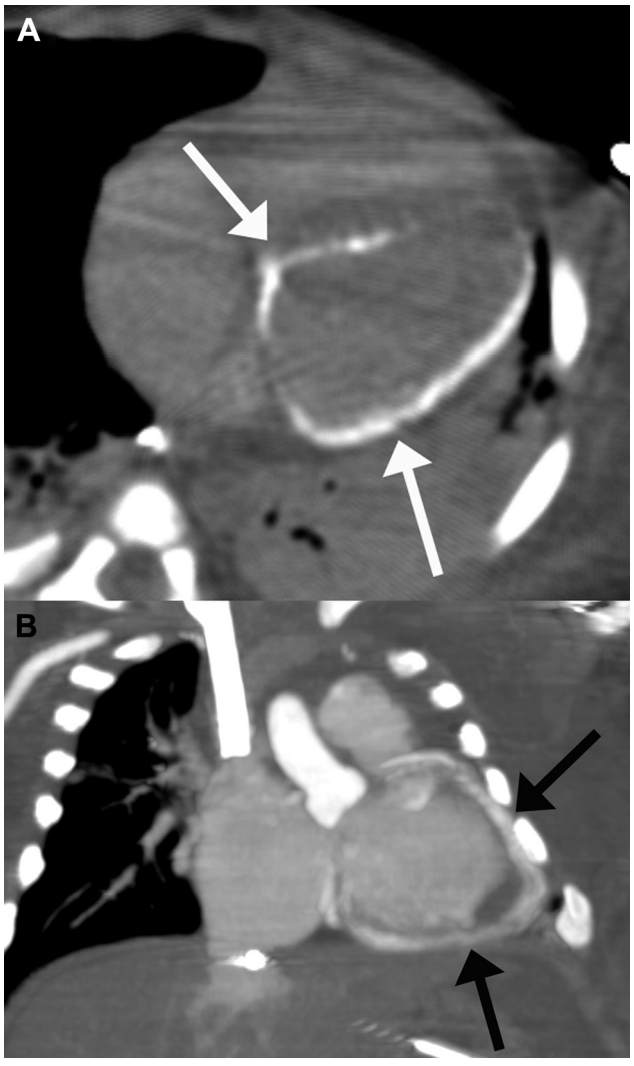

Figure 2 – Dystrophic calcification. (A and B) Unenhanced axial (A) and contrast-enhanced oblique coronal maximum intensity projection (B) CT images in a one-month-old full-term baby boy with delivery complicated by enterovirus myocarditis. Images show marked circumferential left ventricular calcifications predominantly affecting the subepicardial myocardium (*arrows*). The child expired shortly thereafter.

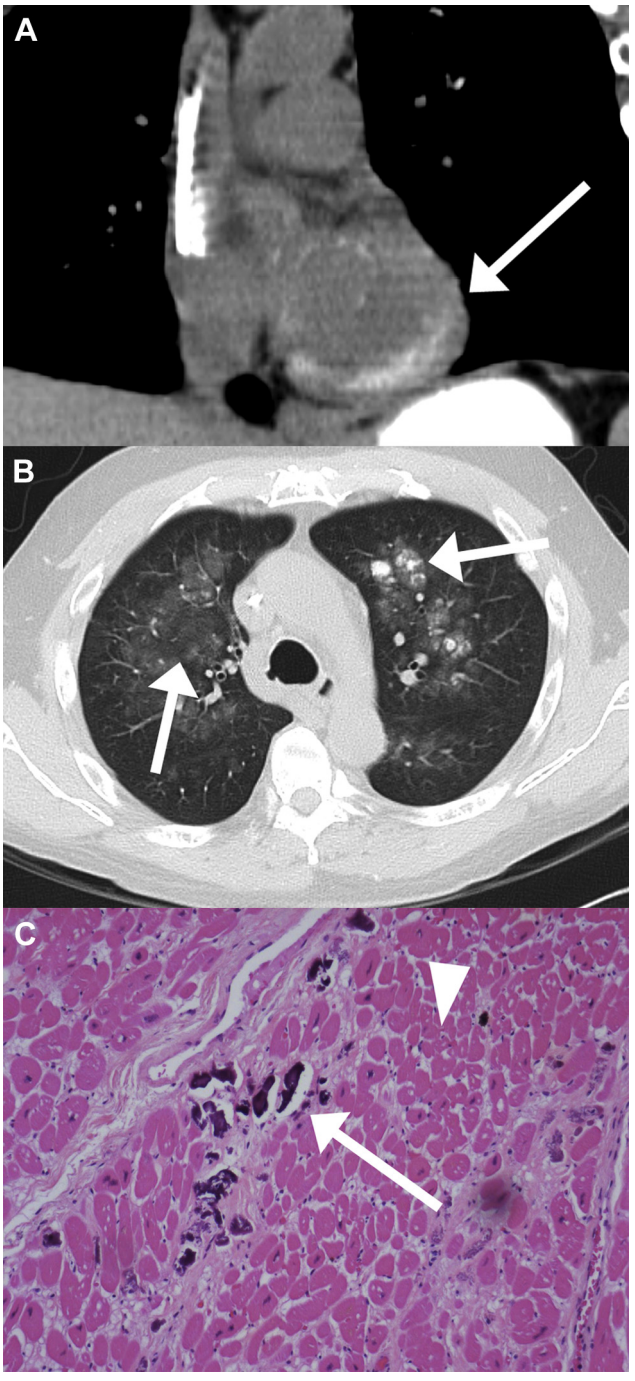

Figure 3 – Metastatic calcification in a 49-year-old man with chronic renal insufficiency on dialysis. (A) Coronal CT image shows amorphous calcifications throughout the left ventricular myocardium (*arrow*). (B) Patchy calcifications were also present throughout the lung parenchyma (*arrows*), highlighting the typical multisystemic nature of metastatic calcification. (C) At autopsy, extensive calcific foci were identified throughout the lungs, kidneys, pancreas, and heart. (C) 10× magnification image shows foci of calcification and fibrosis (*arrow*) intermixed with relatively normal myocardium (*arrowhead*).

2.1. *Dystrophic calcification*

Dystrophic calcification represents the sequelae of local tissue damage and cellular necrosis. It is not associated with abnormalities in serum calcium levels or calcium homeostasis; however, hypercalcemia will accentuate the process.[1] Coagulative, caseous, and liquefactive necrosis can all result in dystrophic calcification.[1] According to Perkins,[1] dystrophic calcification is initiated by membrane damage that leads to concentration of calcium ions within membrane-bound vesicles. Phospholipids within the vesicle membrane are hydrolyzed with the aid of phosphatases and the resulting phosphate group binds to calcium. Mineral deposits eventually accumulate near the cell membrane, where a structural change occurs and calcium phosphate microcrystals form.

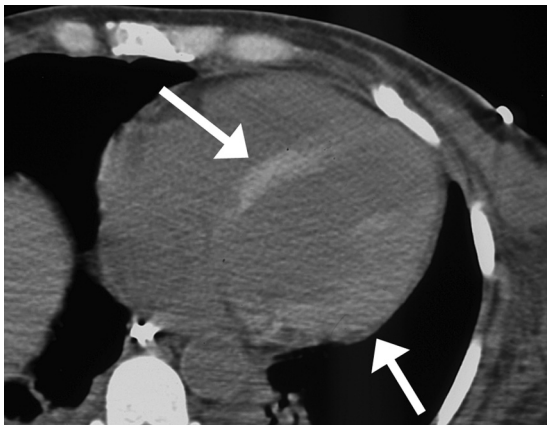

Figure 4 – Metastatic calcification in a 62-year-old woman with oxalosis. Unenhanced axial CT image shows diffuse amorphous calcifications, typical of metastatic calcification, throughout the left ventricular myocardium (*arrows*).

Progressive crystallization can result in deposits that are intracellular, extracellular, or both.[1]

Dystrophic calcification is more prevalent than metastatic calcification. The most common etiology is previous myocardial infarction leading to myocyte necrosis[2–4] (Fig. 1). Calcium deposition is accentuated by the ischemia-induced local microenvironment, including relative alkalinity, decreased calcium solubility, and carbon dioxide production,[2] with 1 study demonstrating dystrophic calcifications in 8% of myocardial infarctions older than 6 years.[5]

A number of other causes of dystrophic myocardial calcification have been reported, including traumatic, infectious and/or inflammatory, and neoplastic processes (Table 1; Fig. 2). Several cases have been reported in which the primary pathology is located outside the myocardium, for example caseous calcification of the mitral annulus[6] and calcified pericarditis[3] extending into the adjacent myocardium.

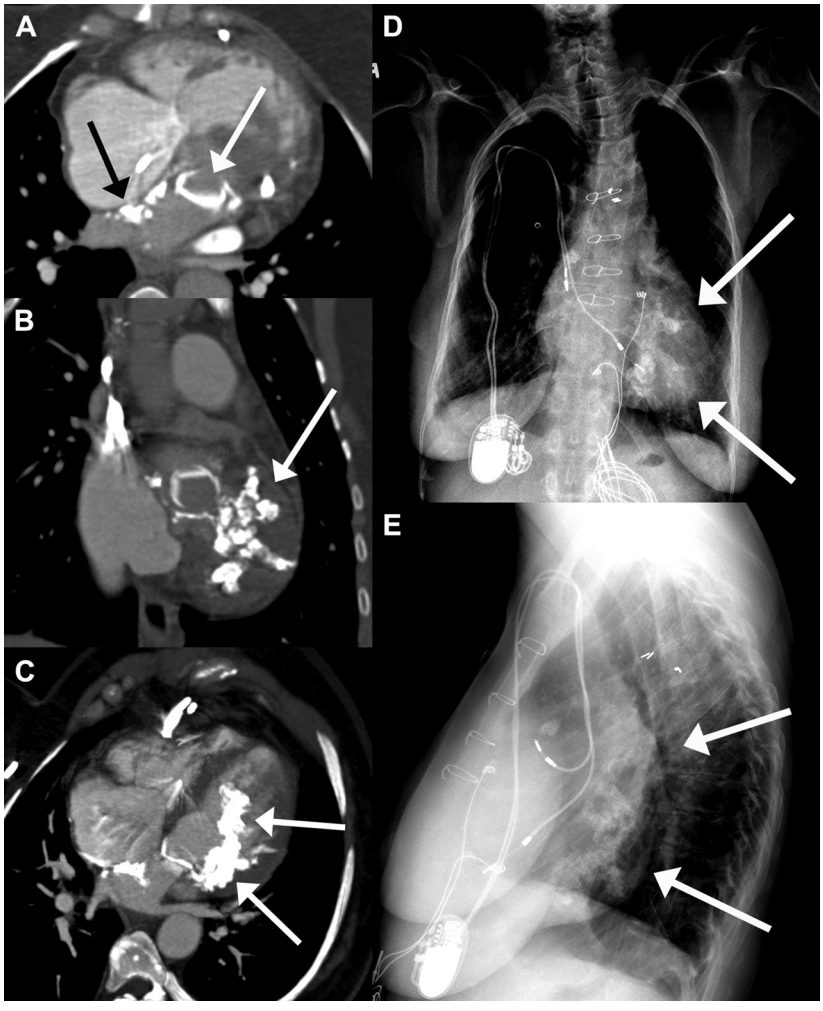

Figure 5 – Extensive cardiac calcifications in a 46-year-old man with a history of congenital heart disease. (A–C) Axial (A), coronal (B), and four-chamber maximum intensity projection (C) CT images show chunky calcifications extending from the left atrium (*arrows* in A) into the left ventricular myocardium and papillary muscles (*arrows* in B and C). (D–E) Frontal (D) and lateral (E) chest radiographs demonstrate extensive chunky calcifications in the regions of the left atrium and left ventricle (*arrows*). The patient had a history of aortic coarctation, patent ductus arteriosus, and mitral valve stenosis status post repairs in childhood, which presumably were the cause of the calcifications. There was no history of abnormal calcium homeostasis.

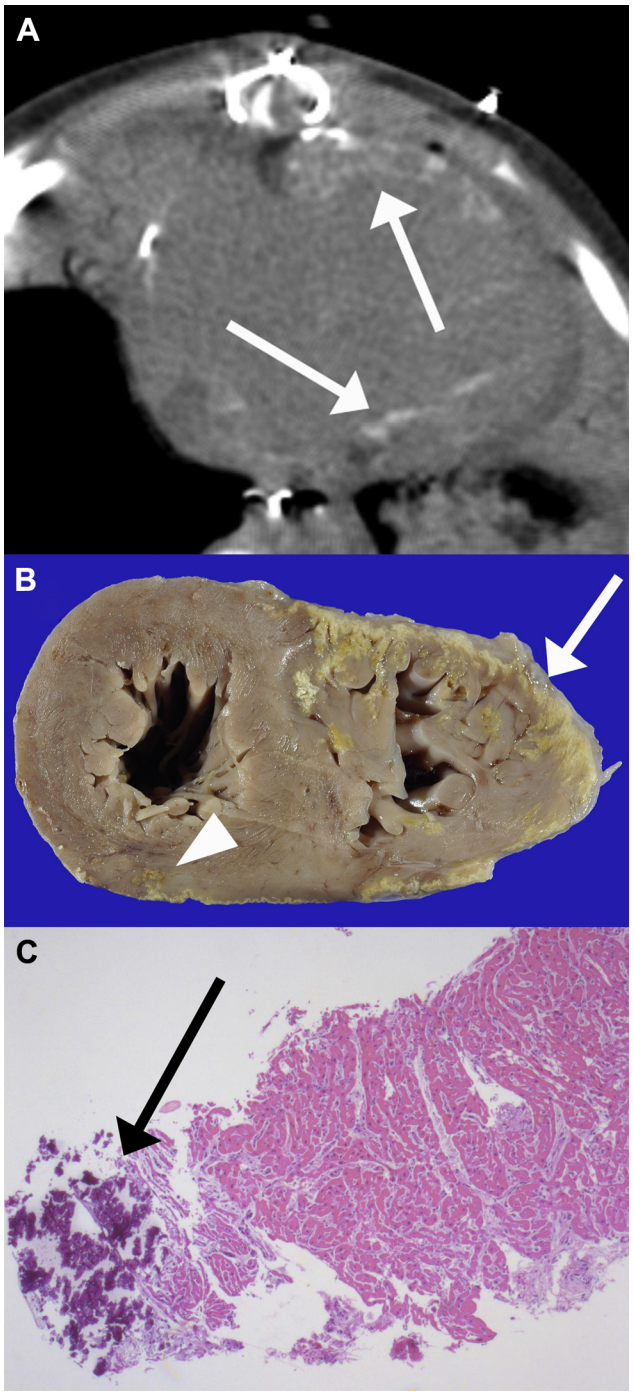

Figure 6 – Diffuse myocardial calcifications secondary to both local (ie dystrophic) and systemic (ie metastatic) processes in a 2-year-old girl status post heart transplant. (A) Axial CT image shows patchy calcifications throughout the right and left ventricular myocardium (*arrows*). (B) Gross specimen of the transplanted heart at autopsy shows extensive chalky calcifications, greater in the right ventricle (*arrow*) than the left (*arrowhead*). (C) Histopathological specimen from an earlier biopsy shows a large focus of calcification within the left ventricular myocardium (*arrow*). Biopsies also showed evidence of chronic rejection, and the combination of rejection with multiple episodes of acute-on-chronic renal failure were the likely causes of the calcifications. The patient had worsening diastolic dysfunction before death that was thought to be related to the extensive calcifications, emphasizing the clinical importance of the finding.

2.2. *Metastatic calcification*

Metastatic calcification represents the sequelae of a systemic process—hypercalcemia and/or abnormalities of calcium homeostasis—and can occur in normal or diseased tissue. Any abnormality of calcium metabolism can lead to metastatic calcification, including renal failure (results in retention of phosphate and secondary hyperparathyroidism), bone destruction or increased bone turnover, hyperparathyroidism (of any cause), and vitamin D-related disorders. Metastatic calcification can occur anywhere throughout the body but is more prevalent where there is increased alkalinity, including the gastric mucosa, kidneys, lungs, systemic arteries, and pulmonary veins. Deposits may accumulate as hydroxyapatite crystals or in a noncrystalline amorphous form.[1]

Metastatic myocardial calcification is most commonly reported in patients with chronic renal failure on hemodialysis (Fig. 3); however, it has also been reported in patients with primary hyperparathyroidism, secondary and tertiary hyperparathyroidism (from any underlying etiology),[7] oxaluria[8] (Fig. 4), and dietary deficiency of calcium and vitamin D.[7] Notably, metastatic calcification has been demonstrated in patients with hyperparathyroidism in the absence of serum calcium abnormalities, suggesting that the effects of parathyroid hormone alone may be sufficient to drive calcific deposits into myocardial tissue.[7]

2.3. *Idiopathic calcification*

The prevalence, etiology, and mechanisms of idiopathic myocardial calcification are unknown. Published data are largely limited to case reports that contain variable clinical, historical and histopathological information.[3,9–11] Presumably, idiopathic calcifications actually represent dystrophic or metastatic calcifications secondary to a clinically occult or remote pathological process. It is not currently known whether some or all these cases represent a distinct pathological entity (Fig. 5).

2.4. *Multifactorial etiologies*

It is important to remember that the etiology of myocardial calcification is often multifactorial. For instance, several cases of extensive calcification have been reported in patients after heart transplant (Fig. 6), presumably due to a combination of repeated cellular rejection, transient renal failure, cardiac trauma, steroid administration, and/or septicemia.[12,13] In addition, a number of inflammatory processes can affect both the heart and kidneys, resulting in dystrophic calcification exacerbated by abnormal calcium metabolism. We have seen myocardial calcifications develop quite rapidly in clinical scenarios in which both local (eg

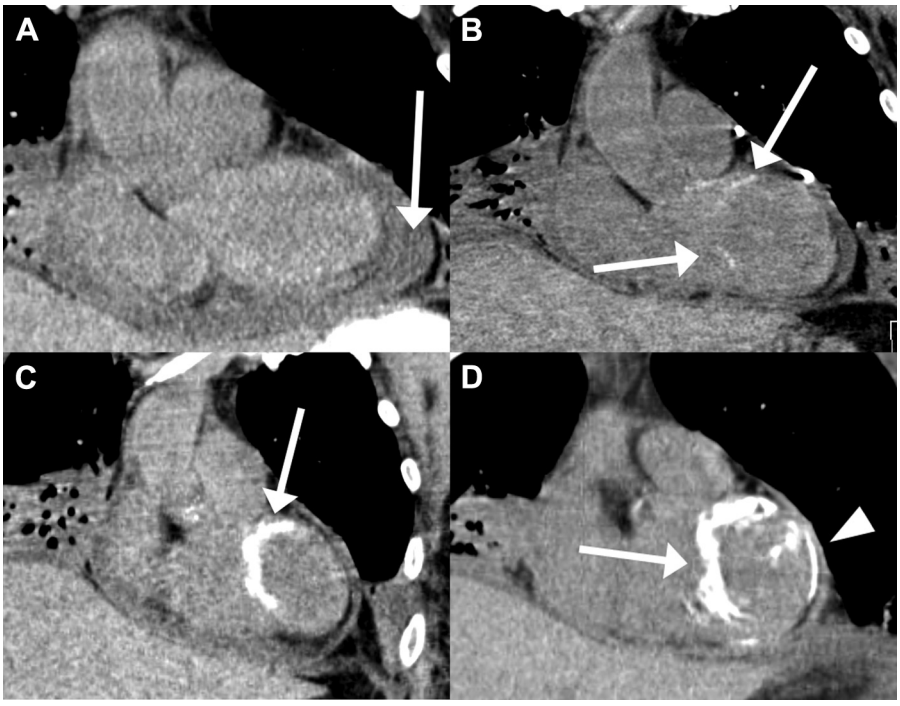

Figure 7 – Rapidly developing calcifications in a 61-year-old man with acute renal failure and myopericarditis. (A) Coronal CT image on admission shows a moderate pericardial effusion (*arrow*) but no evidence of myocardial calcification. (B) Faint amorphous calcifications (*arrow*) can be seen on a coronal CT image from follow-up examination performed 2 days later. (C) Coronal image from a follow-up CT performed 6 days after initial imaging shows that the calcifications have markedly increased in density (*arrow*). (D) The calcifications have continued to increase in extent and density 1 month after the initial study (*arrow*), and new linear epicardial calcifications are now seen (*arrowhead*).

myocarditis) and systemic (eg sepsis, acute renal failure) factors contribute (Fig. 7), emphasizing the importance of clinical history when confronted with rapidly developing myocardial calcifications.

3. Clinical implications of myocardial calcification

Myocardial calcifications are more than benign markers of pathology. Metastatic calcifications are a frequent cause of heart failure in patients on chronic hemodialysis[14] and have been reported to cause sudden cardiac death.[15] Calcifications may also cause focal wall motion abnormalities,[11] and life-threatening arrhythmias can occur if there is calcification of the conduction system.[15,16] Massive myocardial calcification often results in restrictive physiology with or without decreased systolic function.[3,6,9,17] Notably, metastatic calcifications have been shown to decrease over time with correction of the underlying abnormality[7]; however, the prognostic significance of this finding is unknown.

4. Imaging findings

Radiographs may detect dense myocardial calcifications, but precise localization is difficult (Fig. 5). Echocardiography displays myocardial calcium as echogenic foci with posterior acoustic shadowing (Fig. 8), but if extensive, shadowing may limit the examination. Calcification will be low signal on T1 and T2 weighted magnetic resonance imaging without enhancement; however, scarred myocardium surrounding calcifications can show late gadolinium enhancement.[11] CT is the optimal modality for identifying and characterizing myocardial calcifications. Although dedicated electrocardiogram-gated cardiac CT will provide the most detailed information (secondary to decreased motion artifacts), calcifications can usually be identified and localized with standard nongated chest CT.

The patterns and locations of abnormalities may reflect the underlying etiology. Dystrophic calcifications are often focal and linear, whereas metastatic calcifications are more diffuse, globular, and amorphous[8] (Fig. 9). Myocardial infarctions result in thin curvilinear calcifications at the periphery of the infarct (Fig. 1) that may be associated with aneurysm formation. Infarct size is underrepresented by the extent of calcific deposits.[2] Isolated papillary muscle calcification after myocardial infarction can also be seen[18] (Fig. 10). Calcifications in rheumatic heart disease and caseous calcification of the mitral annulus are often centered on the mitral valve, affecting the left atrium and basilar left ventricle.[6,17] Infectious and inflammatory processes can result in circumferential linear or diffuse globular deposits; involvement of the right ventricle, atria, and pericardium is variable.[19,20] Calcifications from pericarditis commonly affect the right heart and atrioventricular groove with sparing of the apex.

Metastatic calcification patterns are variable. Deposits can be faint or dense, but are usually globular or amorphous.[2,4]

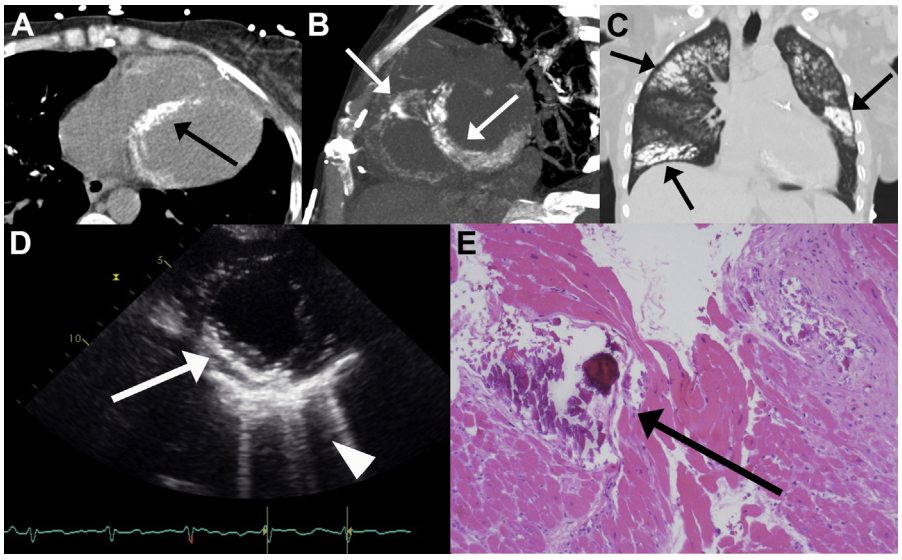

Figure 8 – Extensive calcifications in a 51-year-old woman status post heart transplant for nonischemic cardiomyopathy. The patient also had a history of chronic renal insufficiency on hemodialysis. (A) Axial image from unenhanced CT shows diffuse globular calcifications throughout the left greater than right ventricles (*arrow*). (B) The full extent of the calcifications (*arrows*) is better seen on oblique short-axis maximum intensity projection images. (C) Coronal CT image using lung window and level settings shows extensive calcifications throughout the lung parenchyma (*arrows*). (D) Short-axis transthoracic echocardiographic image reveals echogenic calcifications throughout the posterior left ventricular myocardium (*arrow*) with extensive posterior shadowing (*arrowhead*). (E) Left ventricular biopsy specimen shows chunky calcifications surrounded by fibrosis (*arrow*).

Findings can be diffuse or localized to 1 or both the ventricles (Fig. 8). Atrial involvement can be more prominent than ventricular.[2,7] When severe, metastatic calcification is rarely isolated to a single area—skin, lungs, stomach, and kidneys are commonly affected regions[1,2,14] (Fig. 3). Metastatic calcification has been shown to decrease over time with correction of the underlying abnormality[7]; however, the value of serial monitoring is unknown.

Case reports of idiopathic myocardial calcifications are often dramatic, with massive calcifications involving multiple cardiac chambers with or without involvement of the great vessels and pericardium.[3,9–11] Selection and publication bias are likely partially responsible for this trend (as more severe and visually impressive cases tend to be reported), and the incidence and patterns of less dramatic cases of idiopathic myocardial calcifications are uncertain. Furthermore and as previously noted, it is unclear how many reported cases of idiopathic calcification actually represent dystrophic or metastatic calcification with an unknown underlying etiology.

Reports should document the location, extent, and morphology of calcifications when they are detected. Associated involvement of heart valves and the pericardium can have important functional significance, and identification of extracardiac deposits (eg lung, chest wall, stomach) favors metastatic over dystrophic pathophysiology. Functional information (global and focal wall motion abnormalities, restrictive physiology, etc.) should be reported when available.

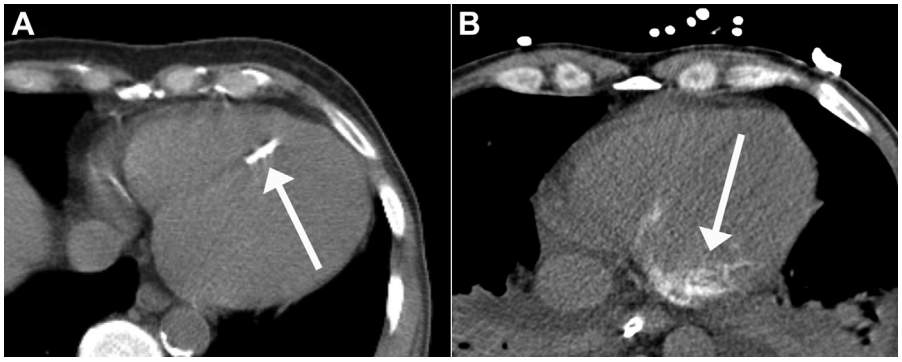

Figure 9 – Examples of dystrophic vs metastatic calcification. (A) A linear focus of calcification (*arrow*) is seen in the septum of this 76-year-old man with a history of myocardial infarction. (B) Contrast with the more diffuse, amorphous calcifications (*arrow*) in a 52-year-old man with chronic renal insufficiency secondary to lupus nephritis.

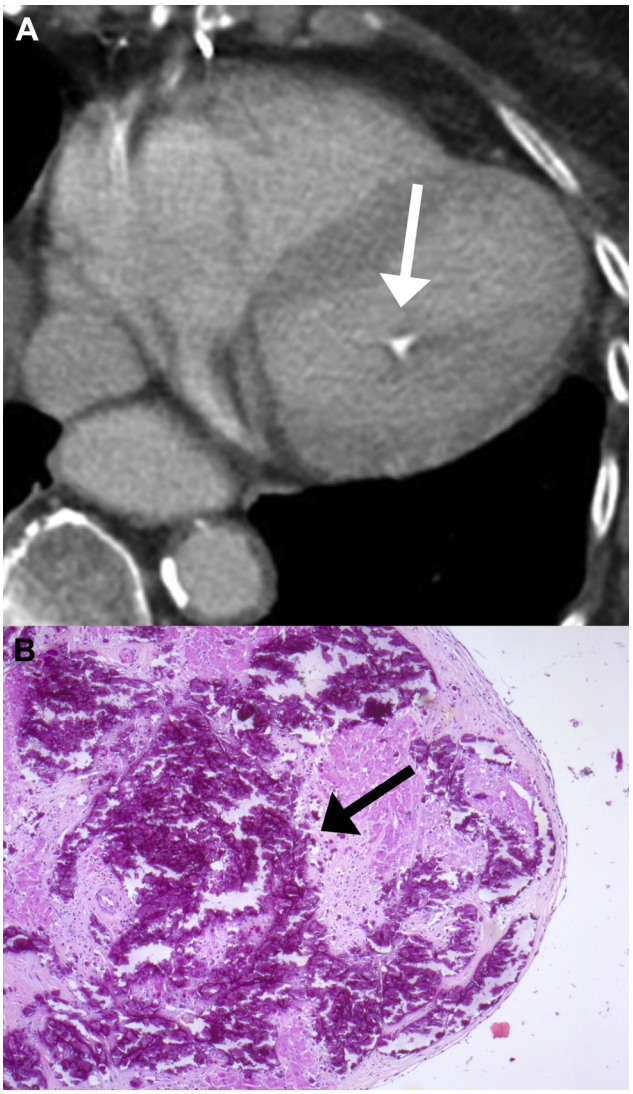

Figure 10 – Papillary muscle calcifications. (A) Isolated calcification of the left posteromedial papillary muscle in an 80-year-old woman (*arrow*). The patient had a history of coronary artery disease status post coronary artery bypass grafting, and the calcifications are presumably ischemic in etiology. (B) Calcification of a papillary muscle in a separate patient. Four year-old-girl with a history of tetralogy of Fallot status post heart transplant complicated by acute rejection. Low powered micrograph of the explant demonstrates extensive calcifications throughout a papillary muscle (*arrow*).

5. Differential considerations

Coronary artery, valvular, annular, pericardial, great vessel, and intraluminal calcifications can simulate myocardial calcification. High-quality electrocardiogram-gated cardiac CT angiography should allow precise localization of calcifications, although it may be difficult to distinguish pericardial or annular calcium from myocardial disease on standard chest CT if there is significant motion or in the absence of contrast material. Radiographs, echocardiography, and to a lesser extent magnetic resonance imaging will provide limited assessment. The morphology of calcifications can provide clues to its source in difficult cases. Coronary artery calcifications have a linear, tubular, or tram-track configuration and follow an expected anatomic course. Pericardial calcifications are usually chunky but oriented in a linear configuration and usually spare the apex[2,19] (Fig. 11). Calcifications of the mitral annulus are arranged in dense ring-like clumps (Figs. 12 and 13), whereas valvular and great vessel calcifications are thin and curvilinear and located in an expected anatomic location.[2]

6. Conclusions

Myocardial calcifications are an important marker of underlying pathology and should be thoroughly described when identified. Dystrophic calcifications are the result of local myocardial injury, the most common of which is previous myocardial infarction. Diffuse myocardial calcifications are an important sign of abnormal calcium homeostasis, and can be associated with myocardial dysfunction and abnormalities of the conduction system. Knowledge of the potential etiologies associated with myocardial calcification and their imaging patterns are important to provide a concise and accurate differential diagnosis.

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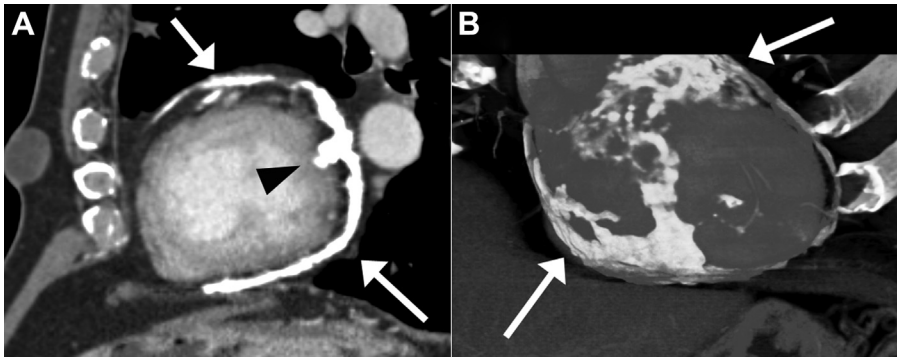

Figure 11 – Pericardial calcifications of unknown etiology in a 75-year-old man. (A) Sagittal contrast-enhanced CT image shows the typical pattern of pericardial calcifications, which are linear and largely separated from the myocardium (*arrow*). Note, however, that there is a focal area that extends into the left ventricular myocardium (*arrowhead*), which can be seen in pericardial calcifications. (B) Oblique coronal maximum intensity projection better demonstrates the full extent of pericardial calcifications (*arrows*). Note the typical apical sparing.

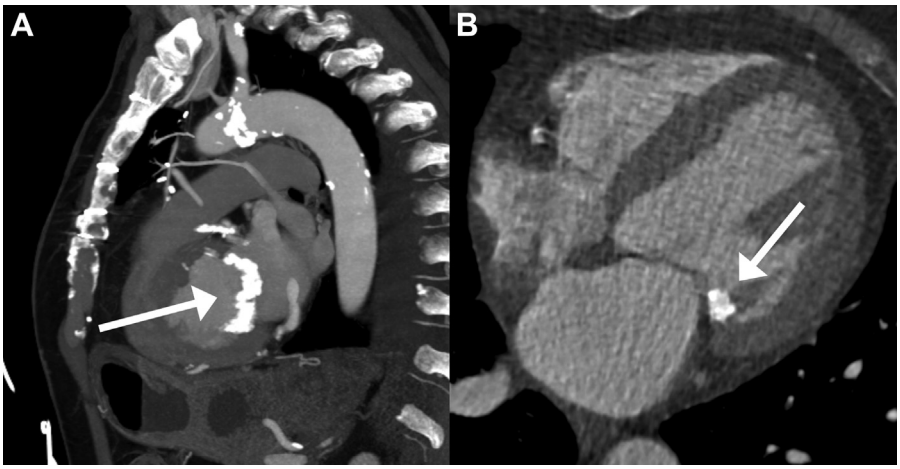

Figure 12 – Mitral annulus calcifications in a 74-year-old man. (A and B) Oblique sagittal maximum intensity projection (A) and axial (B) images shows typical dense, globular calcifications of the mitral annulus (*arrows*).

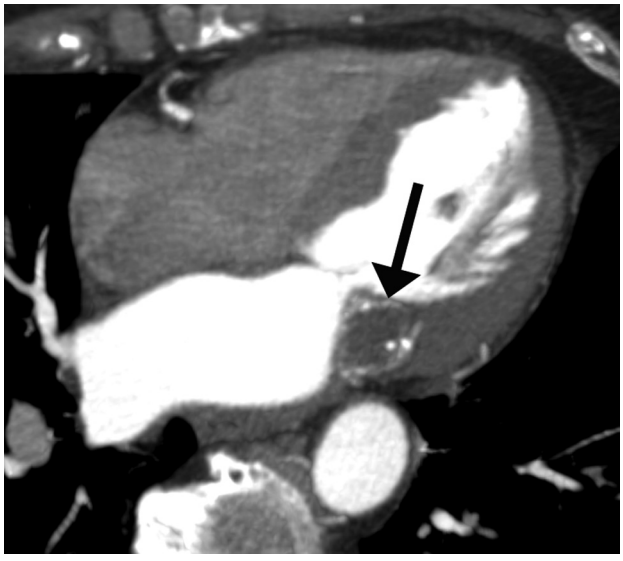

Figure 13 – A 63-year-old woman was found to have an incidental mass near the mitral annulus (*arrow*) with peripheral calcifications extending into the myocardium. The patient suffered a transient ischemic attack, and resection was performed. The imaging appearance is suggestive of caseous mitral annular calcification with liquifactive central necrosis; histopathology (not shown) showed no evidence of neoplasm and old hemorrhagic material.