Case Report

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# Demystifying Cardiac Amyloidosis with Cardiac MRI: A case report

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## Abstract

Amyloidosis refers to the accumulation of amyloid fibrils in different organs of the body that may result in the dysfunction of the organ systems. Cardiac amyloidosis (CA) is an accumulation of amyloid fibrils in cardiac tissue that leads to an increase in the thickness and mass of the ventricular wall inducing progressive and restrictive infiltrative cardiomyopathy. We present here a case of 62-year-old male with complaints of shortness of breath on exertion, abdominal distention, and leg edema, had elevated jugular venous pressure, pedal edema, and ascites. Echo findings showed biventricular wall thickening, restrictive left ventricular inflow pattern in pulse wave Doppler, and strain pattern characteristic of an infiltrative process. He was thus referred for a cardiac MRI for further evaluation with the suspicion of restrictive cardiomyopathy. Based on the CMR findings and the clinical scenario, the patient underwent a rectal mucosal biopsy that was confirmative of systemic amyloidosis.

**Keywords:** Cardiac amyloidosis, Cardiac MRI, Cine cardiac imaging, Myocardial T1 and T2 mapping

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## Introduction

Amyloidosis, in general, refers to the accumulation of amyloid fibrils that may involve the dysfunction of multiple different organ systems.[1] Cardiac involvement, although rare, is not an infrequent finding that is associated with poor prognosis. Cardiac amyloidosis (CA) is an accumulation of amyloid fibrils in cardiac tissue that leads to an increase in the thickness and mass of the ventricular wall inducing progressive and restrictive infiltrative cardiomyopathy. It may cause conduction diseases such as atrioventricular block with faintness, syncope, and occasional ischemia, eventually resulting in progressive diastolic and systolic dysfunction, congestive heart failure, and sudden death. However, the deposition of amyloid fibril does not only affect the myocardial tissue and may manifest in any region of the heart, including valves, vessels, endocardium, epicardium, and parietal pericardium.[1] CA is recognized as a heterogeneous and difficult-to-diagnose disease with a poor prognosis which is often misdiagnosed as hypertensive heart disease and hypertrophic cardiomyopathy. The cases of underdiagnosed and misdiagnosed CA, however, may be reduced by the recent advancement in imaging technologies such as cardiac MRI and its updated sequences. CMR has significantly improved the timing and accuracy of CA diagnoses, contributing to the appropriate management of this ailment. We hereby present and discuss a case report of a 62-year-old male who had a CMR done with the suspicion of restrictive cardiomyopathy and demonstrated spectrum of CMR findings associated with cardiac amyloidosis. We report this case because, in our opinion, every clinician dealing with cardiac amyloidosis should be aware of the imaging findings related to it. This work has been reported in line with CARE criteria.[2]

## Clinical History

A 62-year-old male patient presented to our emergency department with complaints of shortness of breath on exertion, abdominal distention, and leg edema. He had complaints of occasional light-headedness and syncopal attacks in the past with brief episodes of palpitations. He had baseline investigations done such as electrocardiography (ECG), echocardiography (ECHO), and cardiac biomarkers to rule out the possibility of acute myocardial infarction and the reports were negative. On physical examination, he had elevated jugular venous pressure, pedal edema, and ascites. On auscultation, heart sounds were regular and no murmurs were heard. No other comorbidities were present. The echo findings showed biventricular wall thickening, restrictive left ventricular inflow pattern in pulse wave Doppler, and strain pattern characteristic of an infiltrative process. He was thus referred for a CMR for further evaluation with the suspicion of restrictive cardiomyopathy. Based on the CMR findings and the clinical scenario, the patient underwent a rectal mucosal biopsy that was confirmative of systemic amyloidosis.

## Imaging findings

Cardiac MRI was performed for the patient on a 3 Tesla platform. The CMR sequences of transverse black blood images and bright blood vertical long axis, four-chamber, short-axis cine images, left ventricular outflow tract (LVOT) views along with three-chamber images were obtained. Phase contrast imaging of the aorta and pulmonary artery was obtained for flow quantification. T1, and T2 mapping and the time of inversion scout (TIS) sequence or Look-Locker (LL) technique were obtained before delayed gadolinium enhancement (DGE) imaging which allowed choosing the null time of myocardium. Delayed gadolinium enhancement phase-sensitive inversion recovery (PSIR) sequences in short-axis, four-chamber, and vertical long-axis views were obtained. The imaging findings showed diffuse symmetrical thickening of the left ventricular wall with mild thickening of the right ventricular wall as well. Associated thickening of the interatrial septum and the bilateral atrial wall was also evident (Figure 1). Bilateral atria were dilated. During the look locker sequence, it was very difficult to null the myocardium showing a reverse nulling pattern (RNP) where nulling of the myocardium occurred before the blood pool (normally the nulling of blood appears before the myocardium).On early and delayed GAD images there was diffuse subendocardial and transmural myocardial enhancement noted involving the basal cavity, mid-cavity as well as the apical cavity. There was also diffuse enhancement of the right ventricular wall and the bilateral atrial wall (Figure 2). The enhancement pattern was diffuse and was not pertaining or limited to the vascular territories. Pre-contrast T1 mapping or native T1 showed an increased T1 value of 1468 ms (Figure 3). Minimal pericardial effusion was present. Gross right and minimal left pleural effusion was also noted.

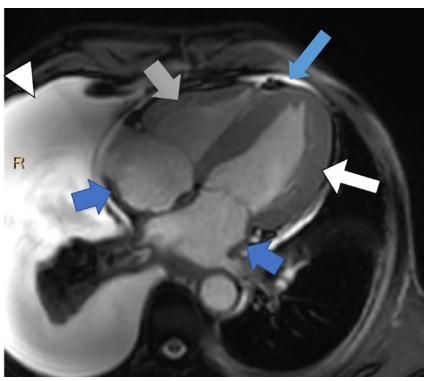


*Figure 1. Cardiac MR bright blood image four-chamber view showing diffuse symmetrical thickening of the left ventricular wall (white arrow) associated with mild symmetrical thickening of the right ventricular wall (short grey arrow), and the bilateral atrial wall (short blue arrows). Minimal pericardial effusion was present (long blue arrow) with gross right pleural effusion (arrowhead).*

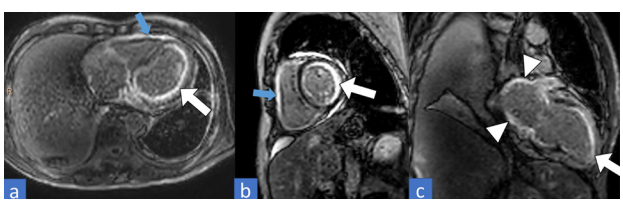


*Figure 2. LGE MR images four-chamber view (a), short axis view (b), and vertical long axis two-chamber view showing diffuse subendocardial and transmural myocardial enhancement involving the basal cavity, mid-cavity and apical cavity (white arrow). There was also diffuse enhancement of the right ventricular wall (blue arrows in a and b) and the bilateral atrial wall (arrowheads in c). The contrast enhancement was diffuse and was not pertaining or limited to the vascular territories.*

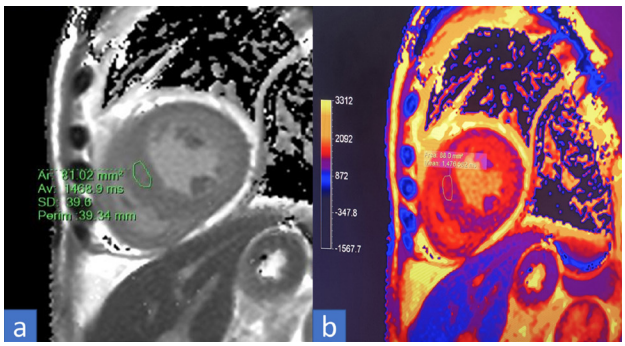


*Figure 3. Pre-contrast T1 mapping (native T1) short axis view (a) and (b) showing significantly increased T1 value of 1468 ms shown by region of interest (ROI) drawn in the septal segment of mid-cavity of the left ventricular wall with the depiction of the corresponding color map (b).*

## Discussion

The hallmark of cardiac amyloidosis is cardiomyocytes with extracellular, insoluble deposits of amorphous protein complex. According to the fibrillar protein involved, there are primarily three types of amyloidosis that are recognized: amyloidosis light-chain (AL), transthyretin-related amyloidosis (TTRA), and amyloid A (AA).3 Cardiac amyloidosis may not be immediately apparent in its early presentation, because its clinical presentation might mimic those of other heart diseases. However, recent advancements in cardiac imaging have helped to reduce the underdiagnosed and misdiagnosed cases of CA. Although endomyocardial biopsy (EMB) is considered a gold standard method of assessing CA, its invasive nature makes it less of an option in day-to-day practice. Hence, CMR is an imaging modality of choice where cine images and LGE sequences,and myocardial T1 and T2 mapping are the mandatory sequences in the assessment of CA.1 The typical CMR findings in CA include extensive amyloid infiltration causing difficulty in nullifying the myocardium, concentric, symmetric, or asymmetric thickening of the ventricular wall, elevated native T1 time and extracellular volume (ECV), diffuse subendocardial, or patchy enhancement patterns in LGE sequences. Many of these typical findings were present in our case making it suitable for a case report (as it is difficult to see all the typical findings in a single case).

## CMR features

**1. Cine cardiac imaging**

The myocardial anatomy along with both global and regional cardiac function can be easily evaluated through cine cardiac images. These sequences define CA on the basis of either concentric, symmetric, or asymmetric LV wall thickening, which might be misdiagnosed as hypertrophic cardiomyopathy (HCM) at times. Therefore, the other imaging features of HCM need to be familiarized such as the systolic anterior motion of the mitral valve (SAM), and LVOT obstruction which is not evident in CA.1,4 The involvement and thickening of the right ventricular and atrial walls and interatrial septum are also frequently evident in amyloidosis. Extracardiac findings such as pericardial effusion, pleural effusion, and ascites may be observed in patients with CA.[1,3]

**2. LGE sequence**

LGE sequence possesses both higher sensitivity and specificity in identifying cardiac involvement in amyloidosis.1,5 The usual LGE pattern observed in CA involves global subendocardial LGE distributed in a non–coronary artery territory.[1,6] The LGE signal corresponds to interstitial amyloid deposition and subendocardial fibrosis driven by ischemia, which occurs due to capillary obstruction as a consequence of the amyloid deposit itself.[6,7] However, LGE findings may alter over time and may show variable patterns including focal patchy, diffuse patchy, subepicardial,and

diffuse transmural LGE depending on the progression of CA.[1,8] Additionally, it is believed that amyloid accumulations develop in three stages: (a) absence of LGE, (b) appearance of typical subendocardial LGE pattern, and (c) progression to transmural LGE, which denotes a bad prognosis in CA patients.[9]

**3.T1 mapping**

Myocardial T1 mapping allows noninvasive detection and quantification of tissue characterization associated with myocardial edema, fibrosis, and material deposition. Non-enhanced T1 mapping, also known as native T1 mapping is obtained without the use of gadolinium-based contrast agents that reveals myocardial diseases involving the myocyte and interstitium. While using a contrast-enhanced T1 mapping, the ECV fraction can be calculated from the ratio of pre and post-contrast T1 in conjunction with the patient's hematocrit level.10 Hence, either T1 mapping pre-contrast as native T1 or post-contrast as ECV may be utilized in the detection and quantification of amyloidosis infiltration with high accuracy. However, native T1 is proven to be useful not only for the diagnosis but also for quantification of the amyloidosis burden and assessment of the degree of progression in myocardial damage.[11] In the post-contrast T1 image, an exceptionally short T1 signal in more than 50% of the myocardium leads to difficulty in nulling the myocardium and is suggestive of increased fatality associated with amyloidosis.[1]

**4. T2 mapping**

The myocardial T2 signal increases in the presence of edema that is commonly used to assess myocardial inflammation. Myocardial T2 mapping provides the potential for a more sensitive assessment of the estimation of myocardial edema compared to the standard black-blood T2 and short-tau inversion recovery (STIR) images. In patients with CA, myocardial T2 values are found to be increased due to amyloid accumulation and its toxic effect on cardiomyocytes.12 However, it may be lower or normal as it was in our instance.[13]

All the mentioned CMR features in the corresponding sequences were observed in our case, thus confirming the diagnosis of cardiac amyloidosis.

## Conclusion

In conclusion, Cardiac MRI is a non-invasive sensitive and reliable imaging modality that aids in identifying as well as in prognosticating cardiac amyloidosis by distinguishing it from other probable causes of heart failure. The benefits of tissue characterization along with the detailed analysis of cardiac function and the degree of involvement make CMR an essential tool for imaging patients with cardiac amyloidosis. Furthermore, CMR can be utilized to follow the progression or the regression of the disease post-initiation of therapies in the management of cardiac amyloidosis.

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**Conflicts of interest**

All of the authors declare that they have no conflicts of interest.

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**Ethics approval and consent to participate**

Ethical approval is not required in our institution for the publication of anonymous case reports.

**Consent for publication**

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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