

# Cardiac Amyloidosis Masked as Hypertrophic Cardiomyopathy: A Case Report

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## Abstract

It is well known that cardiac amyloidosis and hypertrophic cardiomyopathy (HCM) have different physiologies and pathologies. However, it might be difficult to differentiate cardiac amyloidosis from HCM in certain clinical situations.

**Keywords:** Cardiac amyloid; Hypertrophic cardiomyopathy

## Introduction

Both hypertrophic cardiomyopathy (HCM) and amyloidosis present with increased myocardial thickness and mass. The delayed enhancement patterns on cardiac magnetic resonance imaging (CMR) are thought to distinguish these two diseases. However, we report a case where the patient had patchy delayed enhancement and was thought to have HCM but then found to have amyloid pattern 5 months later. The lesson to be learned here is that in early stages of cardiac amyloid, a patient could present with less apparent delayed enhancement patterns and the imaging findings have to be correlated with the patient's clinical presentation in order to make a correct diagnosis.

## Case Report

A 64-year-old female presented with recurrent chest pain and progressive shortness of breath in April 2015. She had a history of asthma and panic attacks. The worsened symptoms triggered a cardiac workup which included cardiac catheterization which showed no obstructive lesions. The findings on

echocardiography and CMR in 2015 suggested the diagnosis of HCM (Table 1). The patient did not have a family history of HCM, but her father died suddenly at age 48. Her paternal grandfather and two paternal uncles all died suddenly before the age of 40. Genetic testing was negative for pathogenic variants. A serum protein electrophoresis and urine protein electrophoresis were unrevealing. Her breathlessness had improved with a diuretic regimen of low dose furosemide and aldactone with stable volume status. As part of the follow-up, she was re-examined in February 2016, at which time ECG showed low voltage and echocardiography demonstrated restrictive filling pattern. Repeated CMR provided the most important diagnostic information, which is the pattern of abnormal subendocardial late gadolinium enhancement (LGE) suggesting cardiac amyloidosis (Fig. 1). Based on CMR findings, a fat pad biopsy was completed, but negative. A subsequent endomyocardial biopsy was positive for amyloidosis.

## Discussion

To the authors' knowledge, such a dramatic change in CMR LGE pattern from faint patchy mid-myocardial enhancement to global subendocardial enhancement in 6-month follow-up has not been reported. This case raises an important question: could early stage of amyloidosis begin with cardiac hypertrophy without significant amyloid deposition elsewhere and thus could be confused with HCM?

Amyloidosis is a rare protein deposition disease caused by misfolding followed by tissue deposition of highly ordered aggregate proteins forming amyloid fibrils leading to progressive organ failure [1]. The definitive diagnosis should be made by endomyocardial biopsy.

The QRS amplitude on ECG is a useful discriminator in infiltrative versus HCM, since voltages are usually increased in muscular hypertrophy and diminished in the infiltrative myopathies. For our case, the voltage showed a decreasing course between the two examinations. Of note, the QRS voltage was normal on the baseline ECG, not increased, which is atypical for HCM, but certainly does not exclude HCM.

CMR is becoming the standard imaging modality for the diagnosis of cardiac amyloidosis. The goals of a comprehensive CMR evaluation of cardiac amyloidosis should include evaluation of cardiac function and myocardial characteriza-

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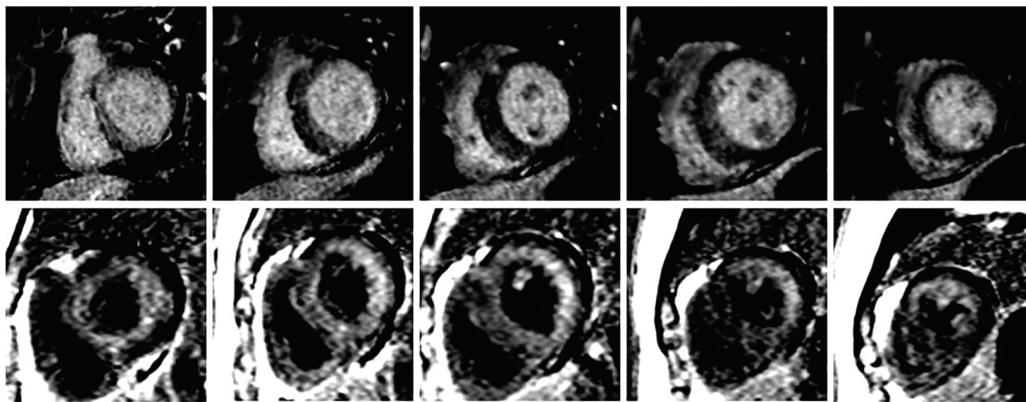
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**Table 1.** Characteristics of Examination Findings

	2015	2016
ECG	Sinus rhythm Normal QRS voltage Q waves in the inferior leads and from V1 to V4	Sinus rhythm Low QRS voltages Q waves in the inferior leads and from V1 to V4
Echocardiography	IVS thickness: 1.6 cm Normal LVEF of 61% Dilated LA Severe diastolic dysfunction	IVS thickness: 1.6 cm Normal LVEF of 55% Dilated LA Severe diastolic dysfunction
CMR	Moderate hypertrophy without obstruction (IVS thickness 1.6 cm) Normal size with mildly decreased cardiac function (LVEF 46%) Pattern of LGE: faint mid-myocardial delayed enhancement at the infero septum from base to mid-cavity	Mild hypertrophy without obstruction (IVS thickness 1.2 cm) Normal size with global hypokinesis (LVEF 41%) Pattern of LGE: subendocardial enhancement
Diagnosis	Hypertrophic cardiomyopathy	Cardiac amyloidosis

IVS: interventricular septum; LVEF: left ventricular ejection fraction; CMR: cardiac magnetic resonance; LGE: late gadolinium enhancement.



**Figure 1.** Different LGE patterns between two CMRs. The upper panel showed mid-myocardial delayed enhancement in first CMR (October 2015), and the lower panel showed global subendocardial enhancement in second CMR (March 2016).

tion. The classic CMR findings demonstrate an endocardial-epicardial signal intensity gradient typical for heart amyloidosis, with the early gadolinium clearance from the blood pool [2]. LGE patterns could be divided into no LGE, global subendocardial involvement, and transmural LGE. Transmural LGE was significantly associated with mortality (hazard ratio, 4.1; 95% confidence interval, 1.3 - 13.1;  $P < 0.05$ ) [3]. Our case showed global subendocardial enhancement on the repeat CMR, which is different from patchy mid-myocardial delayed enhancement in first CMR. Amyloid deposition essentially restructures the heart and restricts it from stretching and properly filling with blood. Our case showed the global hypokinesis and further decreased left ventricular ejection fraction in the repeat CMR, which may have reflected the progression of disease.

The findings on this case suggest that at the early stage, cardiac amyloid may demonstrate hypertrophy as the only imaging feature without significant abnormalities on LGE. It is only after the accumulation of the infiltrative substances for a period of time that the characteristics of cardiac amyloidosis on CMR begin to appear and could be detected. We have the chance to observe the progressive course in this case and place

it on the continuum of amyloid accumulation as determined by LGE pattern progressing from normal to transmural [4].

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## Disclosures

None.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

## References

- Merlini G, Bellotti V. Molecular mechanisms of amyloi-

- dosis. *N Engl J Med.* 2003;349(6):583-596.
2. Maceira AM, Joshi J, Prasad SK, Moon JC, Perugini E, Harding I, Sheppard MN, et al. Cardiovascular magnetic resonance in cardiac amyloidosis. *Circulation.* 2005;111(2):186-193.
  3. Fontana M, Pica S, Reant P, Abdel-Gadir A, Treibel TA, Banyersad SM, Maestrini V, et al. Prognostic Value of Late Gadolinium Enhancement Cardiovascular Magnetic Resonance in Cardiac Amyloidosis. *Circulation.* 2015;132(16):1570-1579.
  4. Ruberg FL, Nezafat R. Cardiovascular Magnetic Resonance Visualization of Cardiac Amyloid Infiltration: Challenges and Opportunities. *Circulation.* 2015;132(16):1525-1527.