

## CASE REPORT

# Detection of Anderson-Fabry Cardiomyopathy with CMR in a Patient with Chest Pain and Elevated Cardiac Biomarkers

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## ABSTRACT

**This case illustrates the utility of CMR in evaluating a patient with undiagnosed Anderson-Fabry disease who presented with chest pain, elevated cardiac biomarkers, normal coronary arteries, and an abnormal echocardiogram.**

## INTRODUCTION

The large field of view and 3 dimensional aspect of cardiac MRI render it uniquely capable of accurately assessing the left ventricle for regional wall motion abnormalities. In addition, assessing tissue characteristics with or without gadolinium contrast enhancement may elucidate the etiology of various myocardial abnormalities. The following case illustrates the value of cardiac MRI in a patient with conflicting findings on other imaging tests.

## CASE REPORT

A 61-year-old hypertensive female was transferred for management of chest pain and elevated cardiac biomarkers. Her past history was significant for the development of dyspnea and light-headedness over the preceding 6 months. The patient worked as a paper carrier and noticed that she was unable to walk her full route as before. She also described “pins and needles” involving her right shoulder and both upper arms. Her only medical problem was well-controlled hypertension.

The patient's current episode of chest pain was quite severe, substernal, radiated to the left lateral chest, and was associated with mild dyspnea. Inverted T-waves were present in the inferior and precordial leads. Serial CPK's were normal at 83 and 69 (normal 25–145 IU/L), albeit with slightly elevated MB bands of 9.0 and 6.8 (normal 0–5 ng/mL), respectively. Two corresponding troponin I's were normal. An echocardiogram revealed concentric LVH, normal systolic function, and hypokinesia of the inferobasilar wall. Diagnostic heart catheterization was performed with the findings of normal coronary arteries and normal left ventricular wall motion in the RAO projection.

A cardiac MRI scan was performed to better answer the question of whether or not a wall motion abnormality actually existed. The patient was scanned in a 1.5 Tesla Siemen's Symphony magnet. Steady-state free precession (SSFP) imaging in left ventricular long and short axis planes was performed and demonstrated biventricular hypertrophy and normal wall motion (Fig. 1). The maximal left ventricular end diastolic diameter was 16 mm. Left ventricular mass was increased at 120 gm/m<sup>2</sup> (normal 63–95 gm/m<sup>2</sup>) and RV mass was increased at 56 g/m<sup>2</sup> (normal 18–33 g/m<sup>2</sup>). Gadolinium was administered at a dose of 0.10 mmol/kg IV and 10 minutes later an inversion recovery segmented gradient echo sequence was used to assess for possible infarction. Midwall hyperenhancement was seen involving the inferolateral aspect of the LV (Fig. 2). Subendocardial involvement to suggest an ischemic mechanism was not present.

The unique pattern of hyperenhancement observed, in combination with concentric biventricular hypertrophy, is suggestive of Anderson-Fabry disease. A leukocyte  $\alpha$ -galactosidase level was obtained and was confirmatory at 0.51 (normal 0.60–3.63).

*Keywords: Anderson-Fabry Disease, CMR, Cardiomyopathy.*

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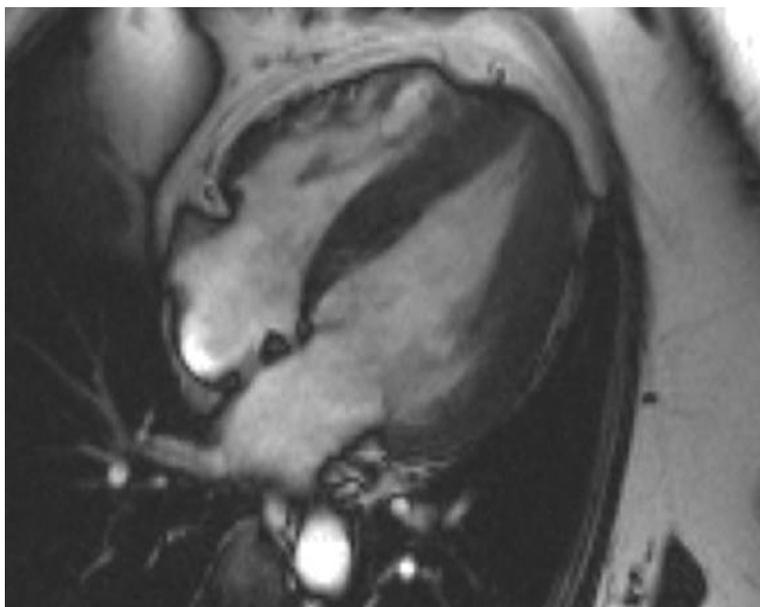
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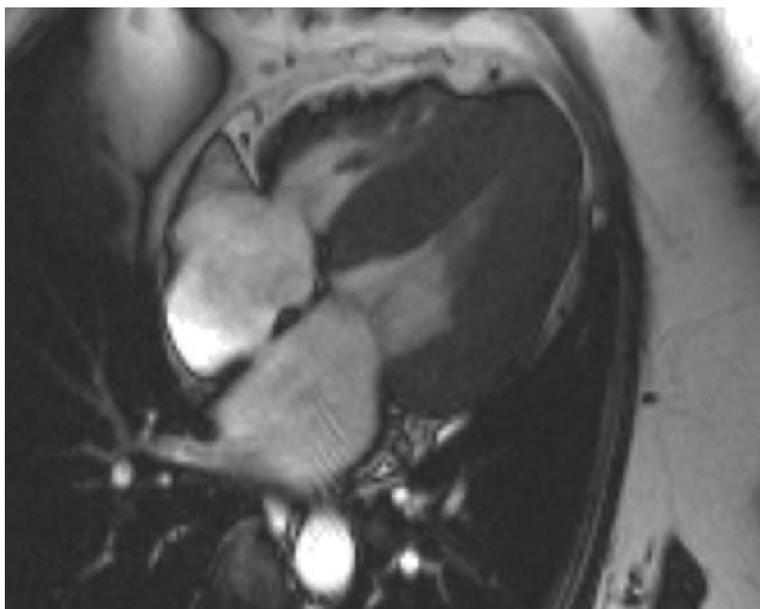
Interestingly, the patient was seen two months following her hospitalization and her total CPK was still normal at 82 with a persistently elevated MB band of 11.7. Her chest pain remained but was slightly improved on empiric therapy with metoprolol and an ACE inhibitor. Genetic testing was ultimately performed and was also diagnostic of Anderson-Fabry disease (D92N mutation). Enzyme replacement (Fabrazyme) has been initiated to hopefully improve the patient's symptoms.

## DISCUSSION

This case highlights the important role of CMR in patients with conflicting results from other imaging modalities. CMR has become the accepted standard for measurement of LV volumes and mass (1). It is an excellent arbitrator for questionable wall motion abnormalities, due to its excellent spatial and temporal resolution and the fact that all segments of the heart are included in the field of view. The wall motion



(A1)



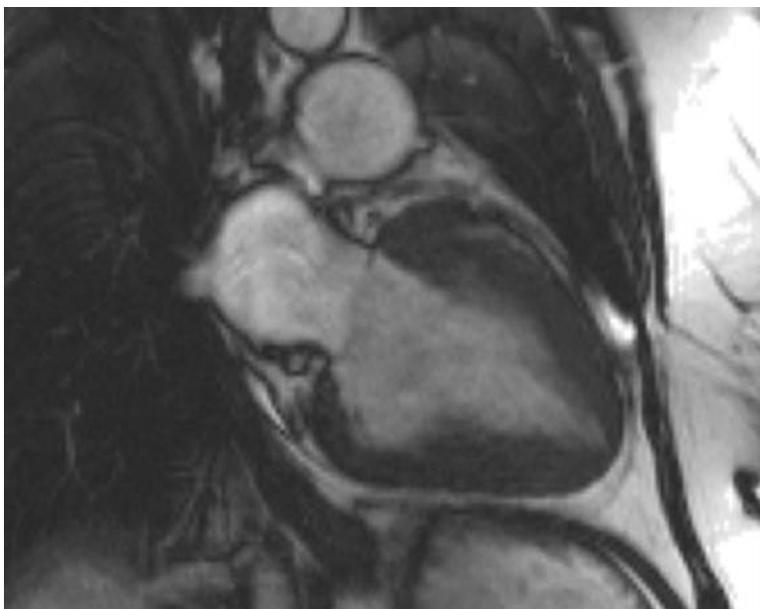
(A2)

**Figure 1.** End diastolic (A1, B1, C1) and end systolic (A2, B2, C2) frames of apical 4 and 2 chamber and basal short axis cines demonstrating a concentrically hypertrophied left ventricle with normal wall motion. (Continued)

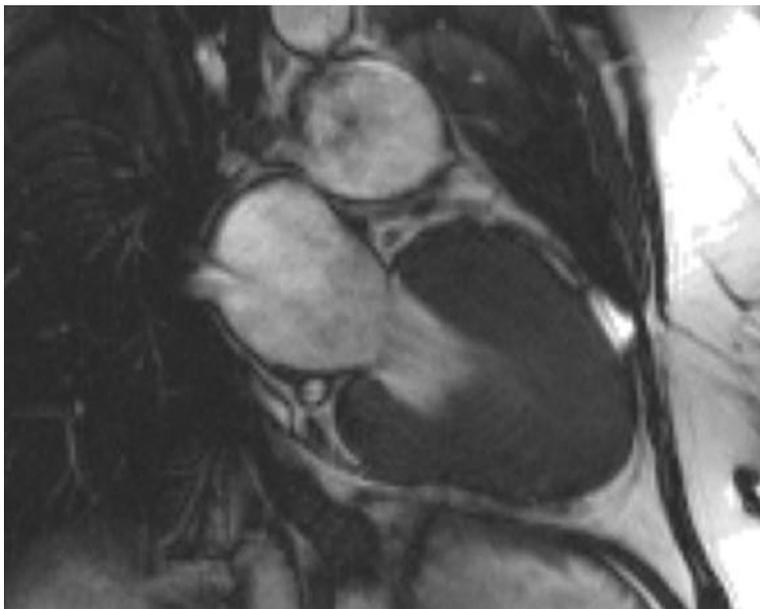
abnormality noted on this patient's echocardiogram was most likely due to echo dropout, as the base of the inferior wall contacted normally on both the CMR images and the invasive left ventriculogram.

Information regarding the etiology of cardiomyopathies can be obtained with CMR. Prior studies have described the ability of CMR to distinguish ischemic from nonischemic etiologies (2). The current case demonstrates the importance of contrast enhancement in patients with hypertrophic cardiomyopathies. Interstitial expansion and variable degrees of

fibrosis can lead to the finding of midwall hyperenhancement in patients with myocardial hypertrophy. One previous report has documented the presence of midwall hyperenhancement in the basal infero-lateral wall of patients with Anderson-Fabry cardiomyopathy (3). In that study, 50% of the patients with Anderson-Fabry cardiomyopathy demonstrated hyperenhancement with gadolinium. In those with abnormal uptake, 92% demonstrated midwall hyperenhancement involving the basal inferolateral region of the LV. The majority of these patients also had normal wall motion. The cause of the

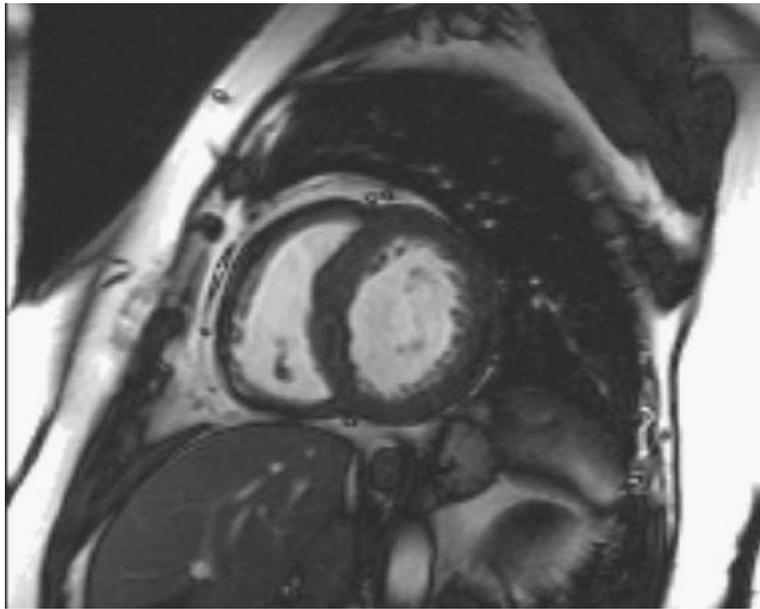


(B1)

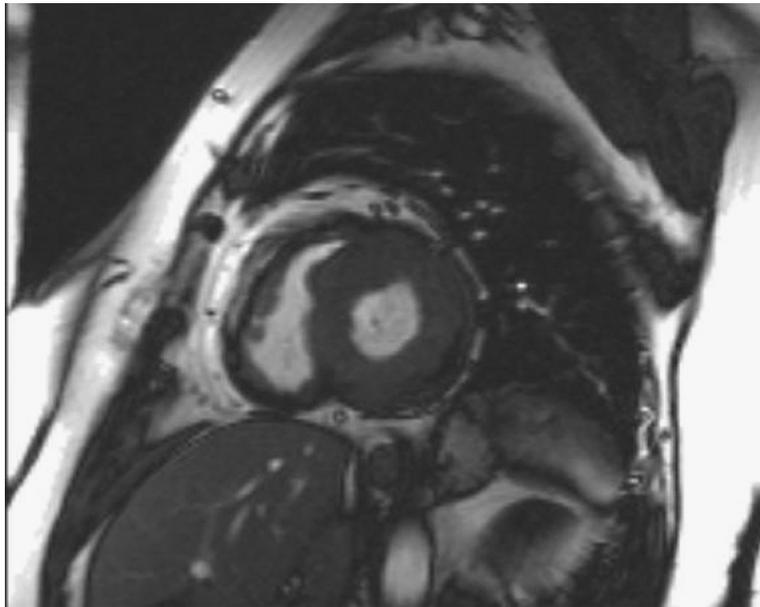


(B2)

**Figure 1.** (Continued)



(C1)



(C2)

**Figure 1.** (Continued)

abnormal uptake was speculated to be secondary to myocardial fibrosis.

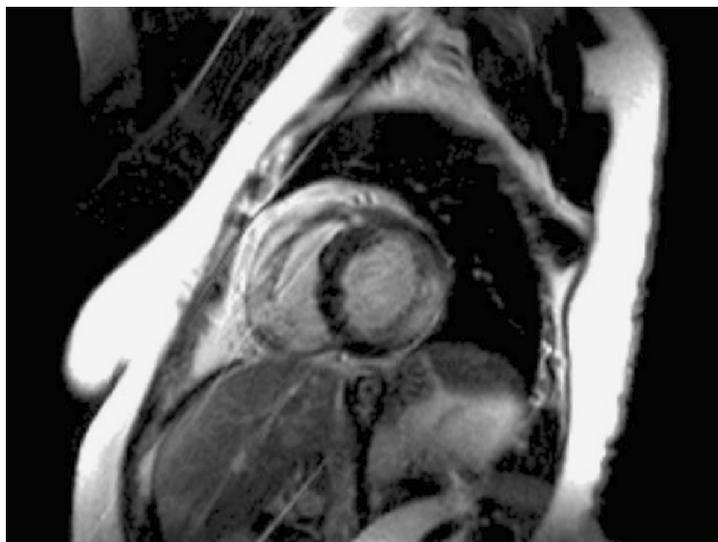
Anderson-Fabry disease is an x-linked disorder of glycosphingolipid metabolism leading to an accumulation of globotriaosylceramide throughout the body. These deposits result in the characteristic angiokeratomas, acroparesthesias, hypohidrosis, and corneal opacities of Anderson-Fabry disease. Deposition of undegraded glycosphingolipids in the vascular endothelium

also leads to renal, cardiac, and CNS disease, which can result in death in early adulthood. A cardiac variant of the disease exists where patients have a gene mutation that results in sufficient enzyme activity to prevent the classic phenotype from developing. Such patients typically present in their 5th decade or later with concentric LVH. The diagnosis of Anderson-Fabry disease is confirmed by low or absent  $\alpha$ -galactosidase activity in plasma or serum, leukocytes, tears, or biopsied tissue.

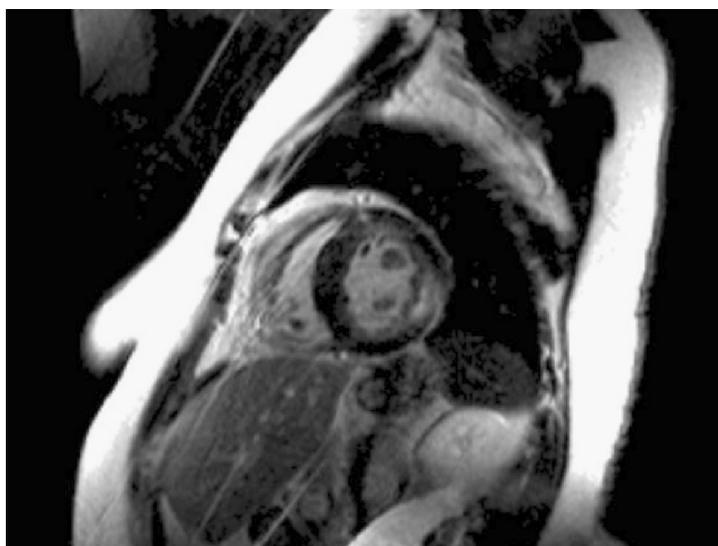
The unique predilection of the infero-lateral wall to manifest delayed hyperenhancement is an important clue to the presence of Anderson-Fabry disease. This diagnosis should be considered in patients with LVH, as 10.3% of patients without a secondary cause for concentric LVH were found to have Anderson-Fabry disease in one study (4). Treatment with recombinant  $\alpha$ -galactosidase A replacement therapy is available, and in one study, this treatment cleared microvascular endothelial deposits of globotriasylceramide from the heart, kidney, and skin of patients with Fabry's disease (5). One case has been reported where intravenous infusions of galactose were

able to improve systolic performance and reduce LV mass in a 55-year-old patient with the cardiac variant of Anderson-Fabry disease (6).

The patient in this case report suffered from chest pain and dyspnea, the etiology of which was undoubtedly a cardiomyopathy from Anderson-Fabry disease. CMR accurately depicted wall motion and the unusual pattern of delayed hyperenhancement with gadolinium led to the correct diagnosis. This is the only report we are aware of in the literature of a persistently elevated CPK-MB band in a patient with Anderson-Fabry disease.

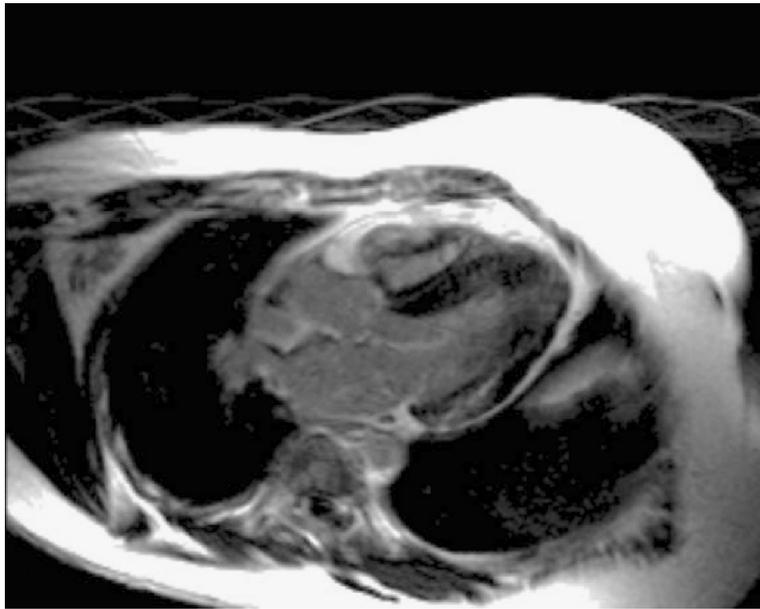


(D1)



(D2)

**Figure 2.** Midwall hyperenhancement of the basal infero-lateral wall demonstrated in two basal short axis (D1, D2) views and an apical 3 chamber (E1) view. (Continued)



(E1)

Figure 2. (Continued)

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