

CASE REPORT—AGOSTINO MEDURI AND RONALD RAZMI, EDITORS

## Delayed contrast-enhanced magnetic resonance imaging for the detection of autoimmune myocarditis and long-term follow-up

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MRI proved to be a valuable tool for the evaluation and monitoring of myocarditis. We report the case of a 36 year old caucasian male with an undifferentiated collagenosis who presented first four years ago with unspecific symptoms and impaired exercise capacity. On echocardiography left ventricular function was impaired as well as on MRI. In addition, after administration of Gd-DTPA an intramyocardial pathological signal enhancement was observed on TSE T1 weighted and contrast enhanced FLASH 3 D IR sequences. Based on several diagnostic tests including myocardial biopsy an autoimmune myocarditis due to an undifferentiated collagenosis was diagnosed. On long time follow up over almost 3 years with repeated MRI examinations, the delayed hyper enhancement (dHE) decreased or disappeared with successful treatment, respectively. However, in the area of recurrent inflammation, a persisting area of dHE developed with a subsequent perfusion defect. This area represents myocardial fibrosis due to recurrent inflammation.

*Key Words:* Magnetic resonance imaging; Delayed enhancement; Myocarditis

A 36-year-old Caucasian male with an undifferentiated collagenosis presented four years ago with an impaired exercise capacity and polytopic ventricular extrasystoly after a 6-month period of fever and night sweats. The medical history included recurrent arthralgia in both knee and wrist joints since the age of 15 and an episode of iritis at the age of 12. Additionally, the patient presented with Sicca syndrome with decreased lachrymal secretion, Raynaud's phenomenon, and moderate splenomegaly.

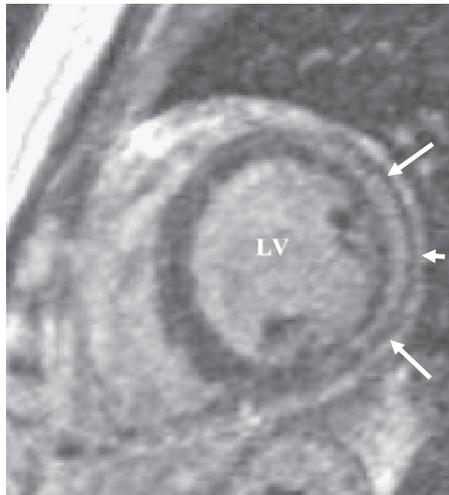
Laboratory parameters revealed a decrease of immunoglobulin G (5.5 g/L; normal range 8–18 g/L) and IgA (0.17 g/L; normal range 0.9–4.5 g/L), a significant titer for anti-nuclear antibodies (1:2560), and a positive titer for rheumatoid factor (38.6 U/mL). There was no leukocytosis or elevated C-reactive protein level present. A malignant lymphoma could be ruled out by computed tomography. Echocardiography at that time showed a moderately impaired left ventricular (LV) function with an ejection fraction (EF) of 45% and an inferior-posterior hypokinesia. In accordance with these findings, the evaluation of ejection fraction with

magnetic resonance imaging (MRI) revealed 46%. ECG-gated image acquisition using T1- and T2-weighted turbo spin echo (TSE) sequences (TE 6.7 ms, TR 700 ms, SLT 6 mm, and TE 83 ms, TR 600 ms, SLT 7 mm, respectively) in four-chamber view (CV), 2-CV, LVOT-, and short axis orientation depicted a homogeneous signal intensity of the left and right myocardium without any evidence of fatty or fibrous degeneration or inflammation at that time. Histological analysis of a right ventricular endomyocardial biopsy displayed a focal lymphocellular infiltration. Viral infection was ruled out by standard serological methods and by PCR in myocardial biopsy. An autoimmune myocarditis due to an undifferentiated collagenosis was diagnosed. With medical treatment the clinical status and EF increased in both echocardiography and MRI (50%/53%).

The status remained stable for 30 months until he presented again with an impaired exercise capacity and polytopic ventricular extrasystoly. Laboratory analysis revealed normal values for troponin I (< 0.01 ng/mL) and for creatinekinase (34 U/L; normal range < 80 U/L). Erythrocyte sedimentation rate was elevated (22/44 mm/h). Echocardiography showed an impaired LV function with a marked decrease of EF (35%) and inferolateral hypokinesia. MRI detected a lateral wall hypokinesia using steady state fast precession (SSFP) sequences (TE 1.58 ms, TR 41.08 ms, SLT 6 and 10 mm, ECG-gated) and confirmed the reduction of EF (36%). Using a contrast enhanced FLASH 3D inversion recovery sequence

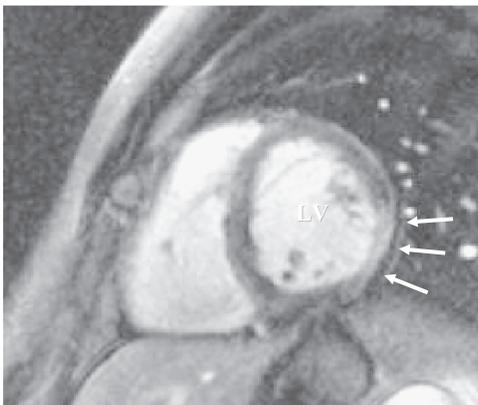
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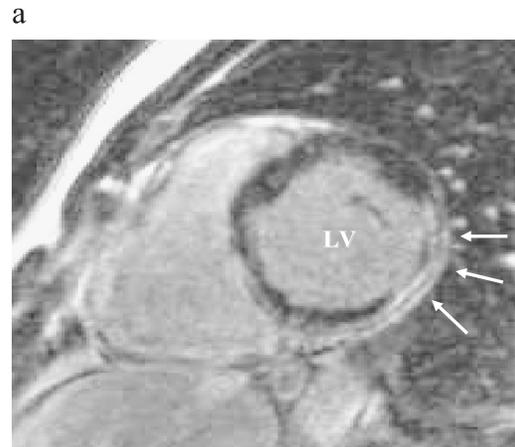


**Figure 1.** CeMRI depicted extensive intramural delayed hyperenhancement (dHE) of the antero-lateral, lateral, and infero-lateral wall. At this time, the patient presented with a reduced clinical condition, ventricular extrasystoly, and an impaired EF (36%).

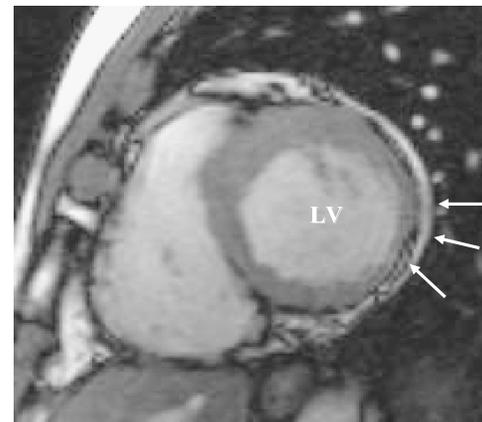
(ceMRI) (TE 1.25 ms, TR 440 ms, TI adjusted to null myocardium, TD 350 ms, SLT 5 mm, slices per slab 14, matrix  $128 \times 256$ , voxel size  $1.8 \times 1.4 \times 5.0$  mm), an extensive intramural delayed hyperenhancement (dHE) of the lateral wall could be observed 10 minutes after intravenous application of contrast agent (0.1 mmol/kg body weight, Gd-DTPA, Magnevist<sup>®</sup>, Schering, Berlin, Germany) (Fig. 1). T2-weighted TSE sequences before contrast also depicted an increased signal intensity in the lateral wall. Thus, the hyperenhanced area was interpreted as myocardial cell edema representing myocardial inflammation. The patient was treated with prednisolone and with ibuprofen. One week later, an improved EF of 46% in both echocardiography and



**Figure 2.** After a period of clinical recovery, the patient was admitted to the hospital with atrial flutter. CeMRI depicted a dHE in the inferolateral wall and myocardial thinning. EF was again reduced to 36%.



b



**Figure 3.** After recurrent episodes of myocarditis, ceMRI showed a remaining dHE in the inferolateral wall, though more sharply delineated (a). SSFP cine sequences display a thinned and akinetic myocardium in the inferolateral wall without visible systolic wall thickening (b).

MRI was documented. On repeat ceMRI and T2-weighted TSE sequences, no hyperenhancement was present.

Three weeks later, still on prednisolone, the patient was admitted to the hospital with atrial flutter (HR 159/min.). After conversion to sinus rhythm, MRI displayed the previously observed inferolateral hypokinesia and again a reduction of EF from 46% to 36%. CeMRI showed a dHE in the inferolateral wall as a correlative for a flare-up of the focal inflammation (Fig. 2). The patient was put on azathioprine for 12 weeks in combination with prednisolone. A follow up investigation was accomplished 3 weeks later. Further on, ceMRI depicted a dHE in the described area with a reasonable decrement in size while EF improved to 46%. For the first time, systolic wall thickening appeared to be diminished in the inferolateral wall.

A final follow-up was performed 4 months later. Meanwhile, the patient has remained clinically stable without any further incidence of arrhythmias. Echocardiography as

well as MRI demonstrated slightly impaired LV function (EF 51%/ EF 50%). Additionally, SSFP sequences displayed a thinned and akinetic myocardium in the inferolateral wall (wall thickness 5–6 mm) without systolic wall thickening. This area remained hyperenhanced on ceMRI, though diminished in size and more sharply delineated (Fig. 3a,b). First pass perfusion displayed a transmural perfusion defect in this area with otherwise homogeneously perfused myocardium. There was no pathologically increased signal intensity in T1- and T2-weighted TSE sequences.

Overall, the inferolateral wall motion abnormality, dHE, and a consecutive perfusion defect were interpreted as myocardial fibrosis due to recurrent inflammation. Coronary artery disease was ruled out by heart catheterization and there was no evidence of an infarction due to embolization.

## 1. Discussion

In patients with an autoimmune disease, myocarditis is a common complication (1). Several cases of myocarditis associated with systemic lupus erythematosus have been reported so far, some having led to sudden death (2). Patients commonly present with a generally impaired clinical condition like fatigue, shortness of breath due to an impaired LV function, or arrhythmias. Standard diagnostic tools include ECG, laboratory parameters (creatinine kinase, troponin), and echocardiography for evaluation of wall motion and LV function. Scintigraphic techniques for detection of leukocytic infiltrates or myocardial necrosis lack specificity and are associated with radiation exposure. Endomyocardial biopsy has been the gold standard for detection of myocarditis but displays a lack of sensitivity, especially in cases with a focal involvement of the myocardium (3).

MRI is a new, noninvasive diagnostic tool for detection of myocarditis. Several authors reported the use of T2-weighted or contrast-enhanced T1-weighted sequences, respectively, for detection of edema that is associated with acute myocardial inflammation (3–5). Another promising technique is the use of ceMRI. Intravenously given contrast agent (Gd-DTPA 0.1 mmol/kg body weight) accumulates in water-containing tissues by penetration into the extracellular but not the intracellular space (6). In the presence of injured cell membranes due to myocardial infarction or inflammation, however, contrast agent penetrates into the intracellular space as well. Furthermore, a delayed wash-out of contrast agent due to injured transport mechanisms can be observed. This has been shown in several studies for infarcted myocardium

and recently also for myocardial inflammation by Mahrholdt et al. (7).

Our case demonstrates the usefulness of ceMRI for detection and follow-up of myocarditis. CeMRI displayed a clear dHE in the inferolateral area that correlated well with a hypokinesia on wall motion analysis. There was a coherence between the patients' clinical condition, EF, and the size of dHE on ceMRI. On long time follow up over almost 3 years with repeated examinations, the dHE decreased or disappeared with successful treatment, respectively. However, in the area of recurrent inflammation, a persisting area of dHE developed with a subsequent perfusion defect. This area represents myocardial fibrosis.

MRI is a new and increasingly accepted modality for the detection of acute myocarditis (3–5). In the above described patient with recurrent episodes of acute myocarditis, we observed in close correlation to the clinical course and other technical findings varying intensities of signal enhancement intramyocardial on ceMRI with a final development of fibrotic tissue in the area of recurrent inflammation over 2 years. CeMRI should therefore be added to the MRI myocarditis protocol.

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