

# Inversion time prolongation at late enhancement cardiac MRI in a myeloma patient

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## ABSTRACT

A patient undergoing chemotherapy for multiple myeloma had a sudden onset of heart failure. Cardiac magnetic resonance was performed after echocardiography to rule out myocardial late enhancement, which was not detected. Interestingly, the inversion time of the T1-weighted inversion recovery late enhancement sequence needed to be significantly increased (from the usual 250–300 to 490 ms) to obtain diagnostic images. This report presents the clinical case of this patient, and discusses potential implications.

**Key words:** • cardiac imaging techniques • multiple myeloma • chemotherapy • heart failure

The continuous development and improvement of anticancer treatments has led to an increase in life expectancy of oncologic patients. However, several adverse effects associated with chemotherapy drugs are known to counterbalance this favorable outcome. Among the side effects, one of the most severe, and caused by various chemotherapy drugs, is cardiotoxicity. In clinical practice, myocardial function in oncologic patients is usually monitored by serial measurements of the left ventricular ejection fraction (LVEF) with echocardiography or multiple gated acquisition scans (1).

Cardiac magnetic resonance imaging (MRI) is a reliable tool for the evaluation of cardiac function and for characterization of tissue damage in various myocardial diseases, such as cardiomyopathies (both idiopathic and associated with systemic disorders) (2, 3). Cardiac MRI has also been used in oncologic patients showing signs and symptoms of cardiotoxicity (4–9).

Several recent studies have reported the use of cardiac MRI for the assessment of LVEF in patients undergoing chemotherapy (4, 5); additionally, the late enhancement (LE) technique has been specifically employed to examine possible cardiac damage. Four recent reports focused on the use of LE imaging in chemotherapy cardiotoxicity (6–9). When describing the LE sequences, the use of a different inversion time (TI) from the usual one at 1.5 Tesla (T) (250–300 ms) has not been implemented. The TI, a fundamental parameter in LE imaging, is defined as the time between the non-selective 180° inversion pulse, used to increase the T1 weighting in the LE sequences, and the radiofrequency excitation. The TI is visually chosen with a T1-weighted scout sequence performed immediately before LE imaging to ensure that the magnetization of the normal myocardium is close to zero, so that the normal myocardium appears as dark as possible and the damaged myocardium is hyperenhanced as bright regions.

The patient described in this study underwent multiple different chemotherapy regimens and two bone marrow transplants after the diagnosis of multiple myeloma in 2002. In November 2010, he suddenly experienced symptoms of acute cardiac failure (CF) and, after echocardiography, was submitted for cardiac MRI. Interestingly, to obtain a proper nulling of the myocardial signal, we had to prolong the TI up to 490 ms.

Here we report the clinical history of this patient and our findings at cardiac MRI, and speculate towards possible explanations for the peculiar characteristics of the patient at LE imaging.

## Case report

In November 2010, a 60-year-old male patient presented with acute onset of tachycardia, hypotension, and severe dyspnea. In 2002, he had been diagnosed with IgG kappa multiple myeloma. In the following years, he underwent multiple different chemotherapy regimens, a dou-

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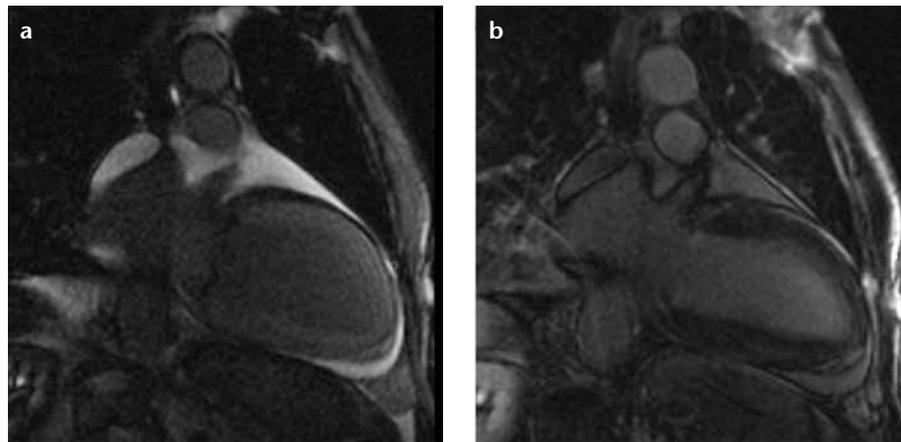
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ble bone marrow autologous transplant in 2003, and an allogenic transplant in 2008. The clinical course was characterized by several episodes of myeloma relapse, with subsequent modification of the chemotherapy course, and an acute and chronic cutaneous graft-versus-host disease following the 2008 bone marrow transplant. The most recent chemotherapy treatment was lenalidomide, which was started in March 2010. Lenalidomide is an anti-angiogenic/immunomodulator drug recently introduced for the treatment of multiple myeloma and other malignancies, such as non-Hodgkin lymphoma. Possible cardiac adverse effects of the drug include atrial fibrillation and myocarditis (10). In August 2010, the patient experienced pulmonary cryptococcosis, which was resolved with amphotericin B and fluconazole.

The patient was stable until November 2010, when he was admitted because he presented with signs and symptoms that suggested CF. The hemoculture was positive for *Streptococcus agalactiae* infection, and the patient was treated with intravenous ceftazidime. To evaluate the CF, the patient underwent echocardiography, which showed marked left ventricle (LV) hypokinesia with severe LVEF depression (20%–25%). These levels were notable, as the previous serial echocardiography studies from 2002 did not show any LVEF impairment (with LVEF always above 55%).

A cardiac MRI study with LE imaging was implemented in order to precisely quantify LV hypokinesia and to rule out myocardial damage. Cardiac MRI was performed with ECG triggering on a 1.5 T scanner (Magnetom Symphony, Siemens AG, Erlangen, Germany) using a four-element body coil (CP Body Array, Siemens AG). Cine-MRI was performed in the cardiac short-axis, vertical long-axis, and horizontal long-axis planes using a TrueFISP sequence. The short-axis images encompassed the LV from base to apex, and were used for the off-line evaluation of the ventricular functional parameters by means of Argus analytical software (Siemens AG). The LVEF was severely impaired (22%) and the LV was dilated (end-diastolic volume, 208 mL). The thickness of the left and right ventricle walls was within the limits, as well as the right ventricle and atria dimensions. Before LE imaging, a T1-weighted scout



**Figure. a, b.** Vertical long-axis phase sensitive inversion recovery late enhancement images. When using a TI of 300 ms, the myocardium is slightly diffuse and hyperintense compared to the left ventricle endocavitary blood, thus the image could not be diagnostic (a). When using a TI of 490 ms, the myocardium was hypointense compared to the left ventricle endocavitary blood; this image was considered diagnostic for absence of late enhancement (b). Note pericardial effusion in both (a) and (b).

sequence in the short-axis plane was implemented eight minutes after intravenous injection of 0.15 mmol/kg of Gd-DOTA (Dotarem, Guerbet, Roissy CdG, Cedex, France) in order to visually choose the proper TI to nullify the myocardial signal. In this patient, the best TI seemed to be 470–500 ms. This finding was confirmed when performing LE imaging in the short- and long-axis planes. The images were acquired 10 min after contrast using a two-dimensional phase-sensitive IR sequence (TE, 750 ms; TR, 1.3 ms; flip angle, 45°; slice thickness, 8 mm). When using a TI of 300 ms, the obtained images were non-diagnostic (Fig. a); with a TI of 490 ms, the images were diagnostic (Fig. b). No LE areas were detected in the LV of this patient.

The lenalidomide chemotherapy was withdrawn (with subsequent multiple myeloma relapse), and proper medical therapy for CF was initiated. The patient experienced progressive improvement of the CF symptoms, and echocardiography performed in March 2011 showed a LVEF of 40%–45%.

Unfortunately, the patient died in August 2011 due to severe streptococcal pneumonia. Therefore, we were not able to perform a follow-up cardiac MRI evaluation.

## Discussion

Four recent reports have employed the use of LE imaging in chemotherapy cardiotoxicity. Anthracycline cardiotoxicity, with evidence of subendo-

cardial LE at cardiac MRI, was reported by Perel et al. (6) in two patients following treatment for Ewing's sarcoma. This study did not mention the cardiac MRI scanner field or the TI used to null the myocardial signal in LE imaging.

Two studies by Fallah-Rad et al. in 2008 (7) and 2011 (8) used cardiac MRI (1.5 T) to study patients believed to be affected by trastuzumab-induced cardiomyopathy. This drug is usually added to conventional anthracycline chemotherapy in HER-2 positive breast cancer patients. Subepicardial LE was present in the lateral portion of the LV in all patients of both studies believed to be affected by the cardiomyopathy. As in the previous report, no mention was made of the TI used to null the myocardial signal in the LE T1-weighted inversion recovery multislice TrueFISP sequence.

In 2009, Wu et al. (9) described the case of a woman who experienced sudden onset of CF six weeks after initiation of sunitinib malate for renal cell carcinoma. Cardiac MRI was performed 45 days after diagnosis, and neither resting perfusion defects nor LE was documented. No specific data was included regarding the cardiac MRI scanner, the sequences used, or the parameters.

The review of the recent literature underlined that LE is not a constant finding in different groups of oncologic patients undergoing various chemotherapies. None of the cited articles mentioned the use of a different TI from the usual one in LE imaging.

In our patient, we had to significantly increase the TI to obtain diagnostic images. An increased TI has also been used to examine patients with amyloidosis. We are aware that cardiomyopathy in myeloma patients is usually attributed to amyloid deposition in the heart muscle, but in subjects with amyloidosis, the TI prolongation does not make myocardial suppression possible because LE is diffusely present, and myocardium is hyperintense (11). The cardiac muscle in our patient did not follow the typical cardiac MRI pattern of amyloidosis; in fact, with the TI increase, good myocardial suppression was obtained and no LE was detectable. Though not corroborated in this study by endomyocardial biopsy, we speculate that myocardial amyloid deposition was not evident, and that possibly cardiac amyloidosis was not associated with CF in this particular case. This proposed speculation shares similarities, and a few differences, with the findings of the fatal case of a patient with multiple myeloma and biopsy-proven absence of heart amyloidosis (11). Brahmbhatt et al. (11) found that subendocardial and myocardial LE was well evident in the patient, and was probably due to fibrosis. However, fibrosis was present even before any chemotherapy course, thus it was not caused by myeloma therapy. The mechanism of cardiac dysfunction in this patient remained unclear. This is also true in our case. In fact, TI prolongation has been observed during acute CF following a long and complex oncologic history and, more recently, a systemic infection and lenalidomide administration. It is difficult to conclude the cause of the cardiac damage in our patient, and many coexisting

elements should be considered. However, we observed that it was associated with TI prolongation without myocardial LE. Thus, in our opinion, another type of myocardial damage may play a role in this case, perhaps at the cellular level and undetectable with conventional LE imaging, but able to induce LV function impairment and TI prolongation.

The patient had also pericardial effusion (Fig.), but we did not believe that this condition caused the TI prolongation. In fact, through our experience with cardiac MRI since 2005, we have examined many patients with pericardial fluid accumulation but have never had to significantly prolong the TI in LE imaging to obtain diagnostic images.

One main limitation of this case report is the lack of follow-up cardiac MRI, due to the patient's death. It would have been revealing and informative to verify the possible persistence of TI prolongation upon improvement of CF.

In conclusion, the observations reported in this study suggest that significant TI prolongation could be a marker of cardiotoxicity, other than LE. Large prospective studies are needed to confirm and evaluate the real significance of this finding in oncologic populations undergoing potentially cardiotoxic chemotherapy regimens.

#### Conflict of interest disclosure

The authors declared no conflicts of interest.

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