Serial Measurement of High-Sensitivity Cardiac Troponin I and N-Terminal proB-Type Natriuretic Peptide in a Patient Presenting with Cardiac Sarcoidosis

Yohei Tanada, Yukihito Sato, Takuma Sawa, Hisayoshi Fujiwara and Yoshiki Takatsu

Abstract

A 65-year-old woman presenting with cardiac sarcoidosis underwent serial measurement of her serum high-sensitivity cardiac troponin I (Hs-cTnI) and N-terminal proB-type natriuretic peptide (NT-proBNP) concentrations. She was treated with 1,000 mg/day methylprednisolone for 2 days, which was subsequently replaced by 30 mg/day prednisolone, and decreased to 20 mg/day at the time of discharge, 2 months later. Her echocardiogram showed improvements in the left ventricular systolic and diastolic function, along with a decrease in the concentration of Hs-cTnI and NT-proBNP. This is the first report suggesting that Hs-cTnI might be a reliable means of assessing the effects of treatment of cardiac sarcoidosis.

Key words: cardiac sarcoidosis, high-sensitivity cardiac troponin I


Introduction

Corticosteroids are considered to be effective in the treatment of cardiac sarcoidosis, though not based on evidence (1). The efficacy of treatment has usually been ascertained based on the alleviation of symptoms and changes in radiographic or echocardiographic images. However, the interpretation of these serial changes may be challenging. Furthermore, while the concentration of cardiac troponin (cTn) is a reliable marker of myocyte injury, its level in cardiac sarcoidosis, using the early assays, was below the sensitivity of the method (2). A high-sensitivity (Hs) assay of cTn has recently been developed (Siemens Medical Solutions), allowing accurate measurements of low concentrations. This report presents the first case of the measurement of Hs-cTnI in advanced cardiac sarcoidosis, and documents a correlation between the clinical course and the Hs-cTnI concentration.

Case Report

A 65-year-old woman was admitted to the hospital with a primary complaint of palpitation and dyspnea on exertion. She had a history of uveitis, and pulmonary sarcoidosis, with bilateral hilar lymphadenopathy which had been detected 2 years earlier on chest roentgenograms. She also had a history of a single syncopal episode, and frequent, multifocal premature ventricular complexes and non-sustained ventricular tachycardia on 24-h ambulatory electrocardiogram (ECG). She began experiencing palpitation and dyspnea 4 months prior to her admission to the hospital. She had no family history of sarcoidosis.

A physical examination revealed that the patient was alert, her heart rate was 85 bpm, blood pressure 150/80 mmHg, respiratory rate 16 breath per min, arterial oxygen saturation 99% on room air, and her cardio-pulmonary examination was normal. The ECG showed normal sinus rhythm, a complete right bundle branch block, right axis deviation, and frequent premature atrial contraction. No congestion was observed the chest radiographs. Blood counts, coagulation studies and biochemical laboratory screening tests were normal, though the angiotensin-converting enzyme was elevated at to 26 IU/L (normal range = 8.3-21.4 IU/L).

The patient underwent cardiac catheterization and coronary angiography, which confirmed the presence of normal coronary arteries. The left ventriculography, however, re-
Table. Measurements of NT-proBNP, Hs-cTnI and Echocardiographic Indices of LV Function between Baseline and 360 Days of Treatment with Corticosteroids

<table>
<thead>
<tr>
<th>Follow-up (days)</th>
<th>Baseline</th>
<th>3</th>
<th>7</th>
<th>21</th>
<th>56*</th>
<th>150</th>
<th>360</th>
</tr>
</thead>
<tbody>
<tr>
<td>N-terminal proB-type natriuretic peptide†, pg/mL</td>
<td>2.345</td>
<td>3.022</td>
<td>2.438</td>
<td>1.440</td>
<td>1.518</td>
<td>1.758</td>
<td>1.331</td>
</tr>
<tr>
<td>High-sensitivity cardiac troponin ††, ng/mL</td>
<td>0.319</td>
<td>0.077</td>
<td>0.041</td>
<td>0.025</td>
<td>0.030</td>
<td>0.028</td>
<td>0.016</td>
</tr>
<tr>
<td>Echocardiographic measurements</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left ventricular</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>32</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>52</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Diameter, mm</td>
<td>35</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>27</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>End systolic</td>
<td>45</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>39</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>End diastolic</td>
<td>1.15</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1.05</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>E/A</td>
<td>18.2</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>14.3</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

*before discharge from the hospital
normal concentrations: †< 125 pg/mL; †† < 0.04 ng/mL

Figure. Prominent decreases in NT-ProBNP and Hs-cTnI concentrations after the initiation of corticosteroid therapy. mPSL: methylprednisolone, PSL 5: prednisolone

revealed the presence of severe left ventricular (LV) anterior wall hypokinesia and inferior wall dyskinesia, a 131.3 mL LV end diastolic volume and 30% ejection fraction. Epithelioid cell granulomas, lymphocytic infiltration and interstitial fibrosis were found on an endomyocardial biopsy of the right interventricular septum, where cardiac magnetic resonance imaging revealed the presence of a late enhancement of gadolinium contrast, which is consistent with a diagnosis of cardiac sarcoidosis.

The patient was placed on a regimen of 1,000 mg/day methylprednisolone, i.v. for 2 days, replaced by 30 mg/day prednisolone, p.o. The prednisolone dosage was lowered to 25 mg/day on day 39, and 20 mg/day on day 59, when she was discharged from the hospital. The transthoracic echocardiographic measurements made between before treatment with corticosteroids and her discharge from the hospital showed of improvements in LV systolic and diastolic functions (Table).

The cardiac biomarkers N-terminal proB-type natriuretic peptide (NT-proBNP; Roche Diagnostics) and Hs-cTnI were measured serially to assess the effects of treatment. Both NT-proBNP and cTnI were elevated at baseline, though they decreased in parallel after the initiation of corticosteroid therapy (Table and Figure). The patient underwent implantation of a cardiac resynchronization therapy system with a defibrillator on day 75 of follow-up. The concentrations of NT-proBNP remained stable at 5 and 12 month of follow-up, though still elevated, while the level of Hs-cTnI had normalized (Table).

Discussion

Sarcoidosis is characterized by the formation of epithelioid, non-caseating granulomas without necrosis in the lungs, lymph nodes, skin, eyes, heart, striated muscles and other organs. Cardiac sarcoidosis causes life-threatening arrhythmias, severe heart failure, and sudden death, and involvement of the heart is responsible for nearly 60% of the deaths from sarcoidosis in Japan (1).

Patients with cardiac sarcoidosis present with a variety of symptoms, recently described in the “Diagnostic Standard and Guideline for Sarcoidosis, 2006”, which was of diagnostic assistance in this case (3). The main criterion in the current patient was LV wall dysfunction. A right bundle branch block and ventricular arrhythmias on the electrocardiogram, and lymphocyte infiltration and interstitial fibrosis endomyocardial biopsy were the minor diagnostic criteria.

The effects of corticosteroids in cardiac sarcoidosis have not yet been studied in large, randomized trials. However, several reports have observed improvements in the cardiac function, and the abatement of arrhythmias with corticosteroids, typically administered initially as prednisone, 30 mg/ day, tapered to 5 to 15 mg/day and continued for 6 to 12 months (1, 4). The efficacy of treatment is based on; a) the
alleviation vs. progression of symptoms, b) imaging studies, thus including the evolution of bilateral hilar lymphadenopathy on roentgenogram, and echocardiographic or cardiac magnetic resonance imaging studies of LV function, and c) measurement of serum angiotensin-converting enzyme and lysozyme. The current patient was initially treated with methylprednisolone, which was replaced by prednisolone on the long-term. The treatment resulted in marked improvements in echocardiographic LV systolic and diastolic function.

The concentration of cTnT measured by the standard assay is below the lowest detectable limit in patients with cardiac sarcoidosis, while measurement of BNP seem useful (2). The current study found that the concentration of cTnT measured by the standard assay was also consistently below the measurable limit (data not shown). A 10% coefficient of variation was reached at a concentration of 0.03 to 0.04 ng/mL by using Hs-cTnI, and the 99th percentile of normal references was 0.04 ng/mL (5). The current patient showed a serum concentration of Hs-cTnI above the normal limit before the initiation of corticosteroids, and the concentration fell prominently and normalized during treatment. This change occurred in parallel with improvements in echocardiographic LV function. However, the improvement of LV function did not occur in a few days after the administration of corticosteroids, though NT-proBNP and Hs-cTnI were decreased on day 3 and day 2. This means that the decrease of NT-proBNP and Hs-cTnI did not depend on LV function. In addition, the concentration of NT-proBNP rose on day 3, reflecting the fluid retention induced by the corticosteroids, a change which was not observed with Hs-cTnI. Therefore, Hs-cTnI could become a useful biomarker of therapeutic process in cardiac sarcoidosis.

Although NT-proBNP was still elevated after the decrease of Hs-cTnI to the normal level, this discrepancy might be due to their different implications as biomarkers. Theoretically, NT-proBNP is a marker of myocardial load and Hs-cTnI is a marker of myocyte injury. Therefore, combined measurement of cardiac troponin and BNP can identify high risk patients and sometimes a discrepancy is seen between the two markers during the treatment period (6-8).

A limitation of this study is the stage of sarcoidosis. The current patient presented with advanced cardiac sarcoidosis. Although Hs-cTnI has yet not been studied in early cardiac sarcoidosis, it might be capable of detecting small amounts of cardiac injury and could be used as a biomarker of therapeutic monitoring. However, Hs-cTnI may not be used as a biomarker of therapeutic monitoring at the end stage of cardiac sarcoidosis, where the effect of corticosteroid is limited. The current patient was not followed up until the end stage, so further studies are necessary to evaluate the long-term efficacy of Hs-cTnI as a biomarker. Studies are warranted to examine its value in patients presenting with sarcoidosis at various stages in terms of 1) detection of myocyte injury and 2) therapeutic monitoring.

The authors state that they have no Conflict of Interest (COI).

References