Published in final edited form as:

J Heart Lung Transplant. 2010 July ; 29(7): 820–822. doi:10.1016/j.healun.2010.03.006.

Serial Troponin-I Measurement as a Diagnostic and Therapeutic Tool in Chronic Myocarditis

Rene Quiroz, MD MPH^{*}, Lija Joseph, MD[†], and Flora Sam, MD^{*,‡}

^{*}Cardiovascular Section and Evans Department of Medicine, Boston Medical Center, Boston MA

[‡]Whitaker Cardiovascular Institute, Boston Medical Center, Boston MA

[†]Department of Pathology, Boston Medical Center, Boston MA

A 40-year old African-American female with non-ischemic cardiomyopathy and a left ventricular ejection fraction (LVEF) of 28% was admitted to our institution with a chief complaint of lightheadedness. The patient was a disabled bus driver who denied tobacco, alcohol or illicit drug use. Home medications were valsartan 80mgs daily, furosemide 20mgs daily, carvedilol 12.5mgs twice daily, trazodone 50mgs daily and citalopram 20mgs daily.

One year prior to her current admission, she had presented with 4 days of exertional chest pain and shortness of breath. Admission labs are shown in Table 1. A trans-thoracic echocardiogram (TTE) showed a normal LV cavity size and wall thickness, with a LVEF of 28% and regional variation. Left heart catheterization demonstrated no evidence of coronary disease. Right-sided filling pressures were obtained (Table 1), along with a right heart biopsy (RVB; Figure 1A). Histologic evaluation demonstrated focal areas of inflammation with lymphocytes and eosinophils, without evidence of amyloid or granulomas. Immunohistochemical staining showed primarily T-lymphocyte infiltration, and overall pathology consistent with acute myocarditis. She was discharged and managed supportively.

On physical exam, her blood pressure was 113/76 mmHg and her heart rate was 88 bpm. She had no jugular venous distention, her lungs were clear and there was no S₃ gallop. Labs are shown in Table 1. A TTE showed severely reduced LV function with LVEF of 28% and 1-2+ mitral regurgitation. Because troponin-I (cTnI) was elevated at 10.4ng/ml, the clinical suspicion for subacute myocarditis was entertained, she underwent right heart catheterization (Table 1) and RVB (Figure 1B). Compared to the previous biopsy, the current biopsy showed resolution of inflammation and absent eosinophils. Given the evidence of indolent myocardial injury (in the absence of inflammatory cells), the diagnosis of chronic myocarditis was made.

Our patient was started on prednisone 40mgs daily and, after 30-days, was subsequently tapered to 5mgs daily. cTnI decreased from 8.783ng/ml to 0.489ng/ml (Figure 1C). However, when prednisone was stopped, cTnI levels increased to 12.221ng/ml (Figure 1C). As seen in Figure 1C, cTnI levels did not correlate with BNP levels. In addition, both intra-cavitary dimensions and LVEF were similar between her index admission and initial presentation (Table 1). Her LVEF remained 28% until she was readmitted with HF symptoms and a BNP of 722pg/ml and

Corresponding Author: Flora Sam, MD, Whitaker Cardiovascular Institute, Evans Department of Medicine; Cardiovascular Medicine Section, Boston University School of Medicine, 715 Albany Street, W507, Boston, MA, 02118, Phone: (617) 638-8072, Fax: (617) 638-4066.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

a cTnI of 1.731ng/ml. Her LVEF had declined to 23%, and she was now found to have a moderately dilated intra-cavitary diameter. She was restarted on prednisone 40mgs daily. Three weeks after discharge, her symptoms had improved, she was euvolemic and her cardiac biomarkers had trended down to a cTnI of 0.475ng/ml and a BNP of 307pg/ml. She is currently stable with NYHA class II symptoms on standard HF therapy and will remain on prednisone 40 mgs for at least 3-4 months before being tapered.

Chronic myocarditis is defined as evidence of indolent myocardial injury (in the absence of inflammatory cells), where at an earlier time point there was evidence of active myocarditis, and may lead to an inflammatory cardiomyopathy¹. Although cellular and humoral autoimmunity are implicated in the pathogenesis of chronic myocarditis^{1, 2}, there is no consensus regarding immunosuppression as a therapeutic option. We describe persistent increases in cTnI after the remission of initial myocardial injury from presumed acute viral myocarditis, suggestive of continued, chronic myocardial damage.

Increased cTn levels are prognostic in myocarditis patients and are important for assessing the presence of myocardial necrosis¹ and thus the diagnosis of myocarditis¹. However, detectable troponin levels may represent *reversible* cardiac injury. Mechanical alterations of the cardiomyocyte sarcolemma results in release of cTnI from the cytosol, even in the absence of necrosis³. Additionally acute cardiomyocyte stress (from increased preload) can cause proteolysis and release of troponin⁴.

It is unknown how much troponin can be released before there is a decline in LVEF. Persistent troponin release has been associated with LV dilation² and as a tool for identifying high risk ambulatory patients with systolic heart failure⁵. Increased cTnI in myocarditis patients are significantly correlated with <1-months duration of HF symptoms, suggesting myocyte necrosis occurs early⁶.

Despite the persistently elevated cTnI levels in our patient, there was minimal change in LV function over 18-months. The presence of cTnI levels may not indicate ongoing cardiomyocyte necrosis, but rather imply a poor prognosis. Thus, immunosuppression and standard HF therapy were initiated and continued for chronic myocarditis. Potential future directions in myocarditis would be to explore, in at least experimental models, the relationship of troponin to other cardiac biomarkers, such as BNP, that are synthesized in cardiomyocytes.

References

1. Cooper LT Jr. Myocarditis. N Engl J Med 2009 April 9;360(15):1526–38. [PubMed: 19357408]
2. Kadota S, Takeuchi Y, Izuhara M, et al. The importance of serial cardiac troponin measurement for evaluating the response to immunosuppressive therapy for myocarditis. J Cardiol 2008 October;52(2): 154–8. [PubMed: 18922390]
3. Giannoni A, Giovannini S, Clerico A. Measurement of circulating concentrations of cardiac troponin I and T in healthy subjects: a tool for monitoring myocardial tissue renewal? Clin Chem Lab Med 2009;47(10):1167–77. [PubMed: 19803806]
4. Feng J, Schaus BJ, Fallavollita JA, Lee TC, Canty JM Jr. Preload Induces Troponin I Degradation Independently of Myocardial Ischemia. Circulation 2001 April 24;103(16):2035–7. [PubMed: 11319190]
5. Perna ER, Macin SM, Canella JPC, et al. Ongoing Myocardial Injury in Stable Severe Heart Failure: Value of Cardiac Troponin T Monitoring for High-Risk Patient Identification. Circulation 2004 October 19;110(16):2376–82. [PubMed: 15477403]
6. Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of Cardiac Troponin I Associated With Myocarditis: Experimental and Clinical Correlates. Circulation 1997 January 7;95(1):163–8. [PubMed: 8994432]

Figure 1.

Hematoxylin and Eosin stain of myocardial biopsies showing: (A). lymphocytic and eosinophilic infiltrate and (B). resolution of inflammation with interstitial fibrosis (during index admission). (C). Serial Cardiac Troponin I and corresponding BNP levels.

Table 1

<i>Hospital Admissions</i>	<i>Index (5/2009)</i>	<i>5/2008</i>
Laboratory Values		
White Blood Cell Count (1000 / μ L)	5.1	
Hematocrit (%)	42	
Platelets (100 000 / μ L)	146	
Sodium (mmol/L)	140	
Potassium (mmol/L)	4.1	
Blood Urea Nitrogen (mg/dL)	16	
Creatinine (mg/dL)		
Troponin-I (ng/mL)	10.4	29
Brain Natriuretic Peptide (pg/mL)	>300	
Creatine Kinase (U/L)	125	139
D-dimer (mg/L)		742
Hemodynamics		
Right atrium *	10	4
Right ventricle (mean) *	54/5 (11)	41/1 (7)
Pulmonary Artery (mean) *	50/25 (36)	41/26 (27)
Pulmonary Capillary Wedge Pressure *	21	15
Cardiac output (L/min)	2.94	
Pulmonary Vascular Resistance (dynes/sec $\times$ cm ⁻⁵)	382	
Echocardiography parameters		
Left atrium (mm)	34	37
Interventricular septal thickness (mm)	10	8
Posterior wall (mm)	11	9
Left ventricular end-diastolic diameter (mm)	55	57
Left ventricular end-systolic diameter (mm)	49	49
Left ventricular ejection fraction (%)	28	28

* Expressed in mmHg