Case report

Can amyotrophic lateral sclerosis chronically elevate troponin T?

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**Abstract**

A 57-year-old woman with progressive amyotrophic lateral sclerosis (ALS) presented repeatedly with atypical chest pain over a period of 4 years. Her initially normal cardiac troponin T (cTnT) value became progressively elevated during subsequent visits in the absence of clinically overt heart disease, and in the absence of alternative explanations for cTnT elevation. In this one patient there appeared to be a relationship between her rising levels of cTnT and increasing severity of ALS.

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**Keywords:**
Troponin T
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**Background**

Cardiac troponin T (cTnT), a highly specific marker of myocardial injury, must be interpreted in an individualized clinical context as elevations of cTnT in the absence of coronary artery disease are common [1]. Increased cTnT has been described in patients with immune-mediated skeletal myopathies [2], but whether amyotrophic lateral sclerosis (ALS), the most common motor neuron disease, can elevate cTnT remains unclear [3,4]. If this is the case, then knowledge that cTnT may gradually increase in patients with ALS may improve our understanding of the pathophysiologic interactions in this devastating neuropathy, and it may help facilitate appropriate evaluation of these patients who can on occasion also present with chest pain and thus consideration of an acute coronary syndrome (ACS).

**Case report**

A 57-year-old woman with medical history significant for controlled hypertension and diabetes, paroxysmal atrial
fibrillation in the remote past, and treated obstructive sleep apnea, presented with gradual increase in atypical chest pain and dysarthria. Her serial cTnT values obtained to rule out ACS were normal (Table 1 and Fig. 1), and her ECG as well as stress echocardiography was unremarkable for ischemia. Four months later she presented with dyspnea secondary to food aspiration and with some atypical chest pain. While the resting ECG remained unchanged, serial cTnT values during this evaluation reached detectable levels at 3 and 6 h and exceeded local criteria for a rising pattern (Table 1 and Fig. 1). Her chest pain subsided and dyspnea resolved with non-invasive respiratory support. With respect to patient’s wishes and recent negative echocardiography finding no further cardiovascular testing was performed. At this time, progression of dysarthria and the occurrence of dysphagia led to a comprehensive neurological evaluation, which established the diagnosis of ALS. Gradually increasing dyspnea in the following 3 years ultimately necessitated ventilator for respiratory support.

At age 61, the patient again presented with atypical chest pain, and serial cTnT were elevated (Table 1 and Fig. 1). Three subsequent episodes of atypical chest pain occurring in the following 10 months revealed similar cTnT findings with a rising pattern of values, while her repeated ECG and wall motion on an echocardiogram remained negative for ischemic changes. Given her underlying comorbidities and the lack of evidence for ACS, coronary angiography and treatment with dual long term anti-platelet therapy were not pursued. Repeated assessments of B-type natriuretic peptide, creatinine, white blood cell count, and D-dimer were not suggestive of other possible causes of cTnT elevations such as renal insufficiency, heart failure, sepsis, or pulmonary embolism [5]. Atrial fibrillation or other arrhythmias were not recorded at any of the hospital admissions despite extensive ECG monitoring in the emergency room.

<table>
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<th>ALS symptoms</th>
<th>Dysarthria</th>
<th>Dysphagia</th>
<th>Dyspnea</th>
<th>Ventilator dependent, s/p tracheostomy</th>
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**Table 1 - cTnT levels at each presentation and correlating ALS symptoms. The cut-off value for cTnT was set on 99th percentile of normal reference population which was 0.01 ng/mL.**

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**Fig. 1** - Temporal evolution of cTnT levels over the period of 4 years. The cut-off value for cTnT was set on 99th percentile of normal reference population which was 0.01 ng/mL.
Discussion

This report identifies a possible connection between chronic elevations in cTnT levels and the evolution of ALS symptoms in a patient without overt clinical evidence of cardiovascular disease, and it raises the need to further investigate this phenomenon in other patients with progressive ALS. Although there was little clinical information to suggest concomitant cardiovascular disease, we cannot exclude the possibility that this patient had clinically occult cardiac involvement either due to ALS or due to some other cardiovascular abnormality and she certainly had risk factors for the latter which would provide the most parsimonious explanation for the cTnT elevations [6]. However, because it has now been shown that elevations in the cTnT assay can occur due to proteins that exist in skeletal muscle after injury [7], it may be that the elevations we observed were due to ALS alone. Unfortunately, we did not obtain a measurement of cardiac troponin I (cTnI) to help with this analysis and the patient’s status precluded additional investigations. Thus, these findings are hypothesis generating at best. However, if these elevations were indeed due to skeletal muscle disease, it would represent one of the few times where an increasing pattern of values was observed. If such a phenomenon can occur, it will need to be taken into account in the care of patients with ALS who may require evaluation with cardiac troponin I assays which seem to avoid this problem [7].

Conclusion

This case highlights the novel observation that patients with ALS may present with gradually elevated cTnT without clinically overt heart disease. Further studies are needed to provide a clearer understanding of whether this is a unique case, a case where cardiac disease was missed or an important caveat concerning the use of cTnT.

Conflict of interest

Dr. Allan S. Jaffe has or presently consults for most of the major diagnostic companies. The other authors have no conflicts of interest to disclose.

Funding body

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Ethical statement and informed consent

This project was approved by Institutional Review Board of Mayo Clinic, Rochester, MN, USA (IRB Number: 12-004350) which waived the requirement for patient informed consent for retrospective review of patient data. The patient discussed in this report passed away 2 years before the manuscript was drafted. No information that could reveal the identity of the patient is included in the manuscript.

REFERENCES