CASE REPORTS

Elevation of troponin T in mechanical ventilated patient with amyotrophic lateral sclerosis

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Abstract

Troponin T is a specific structural protein to the heart and its detection in blood is determined by cardiomyocyte damage. It has also been reported that some non-cardiac disease can increase the circulating level of troponin T. Here we reported a case of Amyotrophic Lateral Sclerosis (ALS) patient with acute thoracic pain and a longstanding increase of troponin t blood levels.

Keywords

Amyotrophic lateral sclerosis, Mechanical ventilation, Troponin T, Thoracic pain

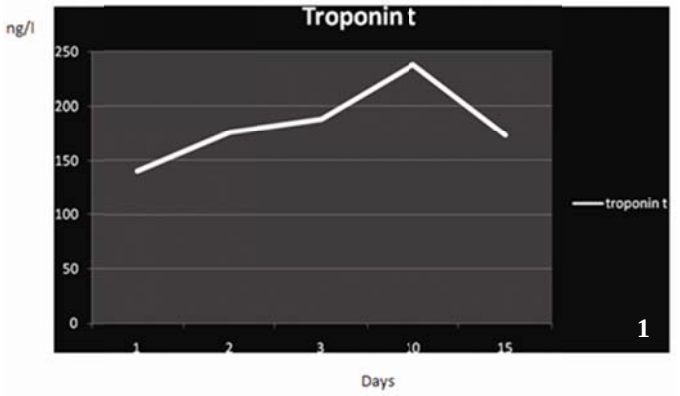
1 Background

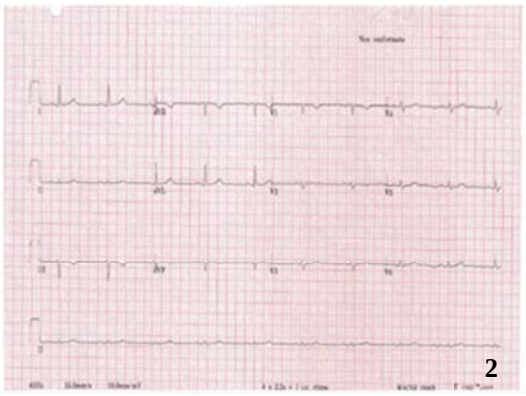
Amyotrophic Lateral Sclerosis (ALS) is a selected degeneration of somatic motor neurons, extending from upper motor cortical pyramidal neurons to lower motor neurons of the brainstem and spinal cord that lead to a non-inflammatory muscle degeneration [1]. It usually progresses toward a complete disability with a high mortality rate: only 20% of patients survive more than five years, but ten percent survive more than ten years. Awaji criteria, a composite clinical-electrophysiologic evaluation, has been recently adopted for the diagnosis of the disease [2]. During the course of the disease, patients have a progressive respiratory failure and non-invasive mechanical ventilation represent the first step of the respiratory therapy. In an advanced stage patients need a definitive tracheal tube to protect the airways from fluid inhalation [3]. Nevertheless respiratory failure remains the main cause of death. Some authors described elevated plasma levels of cardiac troponin (cTn) in ALS patients with chest pain that could determine a wrong diagnosis of Acute Coronary Syndrome (ACS). The cause of this phenomenon it's not well understood, but in some cases it could be due to a secondary hypoxic damage of myocardium in patients with advanced disease.

2 Case report

A 65-year-old male with limb-ons*et al*S, and invasive mechanical ventilation, was referred to our hospital due to acute chest pain. Past medical history was significant for Inferior Acute Miocardial Infarction (AMI) on this occasion he

underwent Percutaneous Coronary Intervention (PCI). ALS was diagnosed two years before, following Awaji Criteria. Since then, the patient's respiratory conditions progressively got worse requiring tracheostomy and continuous invasive mechanical ventilation. At his arrival in the Emergency Department he complained of oppressive, left anterior chest pain radiated to the left arm. He had stable hemodynamic values and Electrocardiogram (EKG) similar to previous EKGs showing signs of an old AMI. The patient's laboratory data revealed normal values of electrolytes level, complete blood cell, C reactive protein (CRP), creatinine and myocardial specific creatinine kinase (CK-MB). We observed an isolate increase in circulating high-sensitivity cardiac troponinT (hs-cTnT: 140 ng/l-normal value < 15.99 percentile) without significative changes from the baseline after serial testing. Arterial Blood Gas (ABG) analysis taken at this time revealed a good ventilator setting: pH 7.39, PCO_2 38 mmHg, PO_2: 92 mmHg, SaO_2: 100%, HCO_3 24 mmol/l. Chest X-Ray was unremarkable with normal mediastinal vascular imagine and a CT angiography of the chest excluded an aortic dissection. Patient was admitted to the Internal Medical Department and was subjected to continuous poly-parametric monitoring. During his hospital stay thoracic pain was controlled by the administration of non-steroidal anti-inflammatory drugs. EKG didn't demonstrate any significant alteration in spite of unchanged high levels of hs-cTnT (see Figures 1 and 2). 2D-echocardiogram showed a left ventricular ejection fraction of 60%-65%, normal valvular apparatus and minimal left inferior hypocinesia sign of previous AMI. The patient underwent to a Single-Photon Emission Computed Tomography (SPECT) with technetium-99m (99mTC) to exclude a coronary disease. The investigation didn't show any defect of the myocardial perfusion at the basal state and after a maximal pharmacological vasodilatation induced by intravenous dipiridamol (see Figure 3). The patient was discharged home asymptomatic, hemodinamically stable with a value of hs-cTnT that remained persistently high.





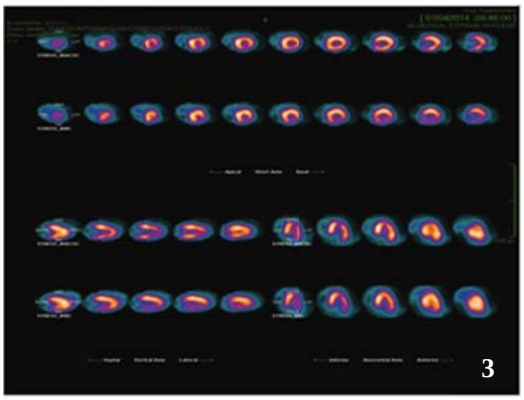


Figure 1. hs-cTnT values during hospitalization
Figure 2. EKG
Figure 3. SPECT with technetium-99m

3 Discussion

Cardiac troponin T and I (cTnT; cTnI) have been the mainstay for diagnosing AMI and stratification of the risk for future adverse cardiac events. Actually high sensivity troponin assays (hs-cTn) are an important advance with added sensitivity

for myocardial necrosis detecting lower concentration of circulating proteins. Compared to the previous assays, hsTns are extremely sensitive making the first low-level elevation of troponin measurable within 90 to 180 minutes of the event. For the diagnosis of myocardial damage, the current clinical guidelines recommend a cutoff value greater than the 99th percentile of a healthy population with a coefficient of variance (CV) of 10% [4, 5]. Unfortunately, as the former assays, hs-cTns can result increased in a wide range of non ischemic cardiac conditions, acute and chronic, cardiac and extra-cardiac, such as heart failure, pulmonary embolism, renal failure, acute neurological diseases, sepsis. The current guidelines recommended that is necessary to observe a "rise and fall" pattern for a diagnosis of AMI, while patients with renal failure or chronic systolic or diastolic heart failure can have a persistently elevated cTn [6]. Some authors observed high levels of cTn in blood in patients with skeletal muscles disease in absence of myocardial ischemia [7, 8]. Aggarwal, *et al*. reported high levels of cTnT and CK in blood, but not cTnI, in a group of patients with idiopathic inflammatory myopathies [9]. Several studies reported a closed correlation between elevated cTnT and skeletal tissue muscle regeneration as demonstrated in biopsies from patients with myositis [10, 11]. Hughes, *et al*. identifies patients with inflammatory myopathies and systemic sclerosis-spectrum disorders where only cTnT but no cTnI was increased. They concluded that cTnT is re-expressed in regenerating skeletal tissue muscle while cTnI is considered to be more specific to cardiac muscle tissue [12]. Recently some authors reported a persistent increase of cTnT levels in ALS patients without any acute cardiac disease. In particular Von Lueder, *et al*. [13] described a patient admitted to the hospital for progressive dyspnea, minor ST-segment depression and elevated cTnT levels. After the exclusion of cardiac and respiratory diseases the diagnosis of ALS was done and the authors hypothesized that the raise of cTnT circulating level was determined by myocardial damage induced by hypoxemia. They demonstrated a correlation between the worse Arterial Blood Gas parameters and the higher cTnT values. Moreover Hof, *et al*. [14] reported an ALS patient with chest discomfort and nocturnal dyspnea; despite a slight elevation of myocardial markers (CK-MB, Myoglobin, cTnT) EKG was unremarkable, cTnI and SPECT were normal; interestingly chest discomfort and dyspnea improved after starting nocturnal ventilation. The authors failed to demonstrate a clear correlation with hypoxemia and suggested a possible cTnT isoform expression in non-cardiac cells, as observed in some patients with skeletal muscle myophathies. They concluded that cTnT should be measured at defined time-intervals to identify the rise and/or fall suggestive of ACS. We report a case of a mechanical ventilated ALS patient with thoracic pain and increased value of circulating cTnT. Arterial Blood Gas values at the admission to the Hospital were normal confirming correct ventilator settings, so hypoxemia could be excluded as a cause of myocardial damage. Differently from the other cases report, cTnT was the only elevated muscular myocardial markers, because either CK or CK-MB was in the normal range. The persistence of high hs-cTnT value after two months from the discharge in absence of cardiac symptoms and EKG alteration suggest a cause probably correlated with skeletal muscles damages in ALS disease. This condition could be evident in patients with an advanced stage of the disease as recently reported by some Autors [15]. Beyond the obvious conclusion that invite to have caution in AMI diagnosis by means of cTnT in subjects affected by to skeletal muscle injury a positive conclusion could be attempted: the high sensibility of cTnT, the conceivable cause of the impaired specificity for AMI diagnosis, might candidate cTnT as an marker of progressive impairment in ALS patients.

References

[1] Kiernan MC, Vucic S, Cheah BC, *et al*. Amyotrophic Lateral Sclerosis. Lancet. 2011; 377: 942-55. http://dx.doi.org/10.1016/S0140-6736(10)61156-7

[2] Costa AJ, Swash M, de Carvalho M. Awaji Criteria for the Diagnosis of Amyotrophic Lateral Sclerosis. A Systematic Review Arch Neurol. 2012; 69(11): 1410-16. PMid:22892641 http://dx.doi.org/10.1001/archneurol.2012.254

[3] Andersen PM, Abrahams S, BorasioGD, *et al*. EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force The EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis. European Journal of Neurology. 2012; 19: 360-75. PMid:21914052 http://dx.doi.org/10.1111/j.1468-1331.2011.03501.x

[4] Thygesen K, Alpert JS, White HD, *et al*. Universal definition of myocardial infarction. J Am CollCardiol. 2007; 50: 2173-95 http://dx.doi.org/10.1093/eurheartj/ehm355

[5] Mair J. High-sensitivity cardiac troponins in everyday clinical practice. World J Cardiol. 2014; 26: 175-82. PMid:24772257 http://dx.doi.org/10.4330/wjc.v6.i4.175

[6] Trerenbold R, Jaffe AS, Reichlin T, *et al*. High-sensitive troponin T measurements: what do we gain and what are the challenges? European Heart Journal. 2012; 1: 2-8. http://dx.doi.org/10.1093/eurheartj/ehr492

[7] Agewall S, Giannitsis E, Jernberg T, *et al*. Troponin elevation in coronary vs non coronary disease. European Heart Journal. 2011; 32: 404-11. http://dx.doi.org/10.1093/eurheartj/ehq456

[8] Tanindi A, Cemri M. Troponin elevation in condiction other than coronary syndromes. Vascular Health and Risk Management. 2011; 7: 597-603. PMid:22102783 http://dx.doi.org/10.2147%2FVHRM.S24509

[9] Aggarwal A, Lebieddz-Odrobina D, Sinha A, *et al*. Serum cardiac troponin T, but not troponin I, is elevated in idiopathic inflammatory myopathies. J Rheum. 2009; 36: 2711-14. PMid:19833747 http://dx.doi.org/10.3899/jrheum.090562

[10] Bodor GS, Survant L, Voss M, *et al*. Cardiac troponin t composition in normal and regenerating human skeletal muscle. Clin Chem. 1997; 43: 476-84. PMid:9068591

[11] Jaffe AS, Vasile VC, Milone M, *et al*. Diseased skeletal muscle: a non-cardiac source of increased circulating concentrations of cardiac troponin. J Am Coll Cardiol. 2011; 58: 1819-24. PMid:21962825 http://dx.doi.org/10.1016/j.jacc.2011.08.026

[12] Hughes M, Lilleker JB, Herrick AL, *et al*. Cardiac troponin testing in idiopathic inflammatory myopathies and systemic sclerosis-spectrum disorders: biomarkers to distinguish between primary cardiac involvement and low-grade skeletal muscle disease activity. Ann Rheum Dis. 2015 March.

[13] Von Lueder, Melsom NM, Atar D, *et al*. Amyotrophic lateral sclerosis (ALS), a novel rare cause of elevated plasma troponin T levels. Clin Lab. 2011; 57(7-8): 615-8. PMid:21888026

[14] Hof D, Jung H, Bloch KE. Troponin T elevation in amyotrophic lateral sclerosis without cardiac damage. Amyotrophic Lateral Sclerosis and Fronto Temporal Degeneration. 2013; 14 (1): 75-77. PMid:22734916 http://dx.doi.org/10.3109/17482968.2012.696659

[15] Mack L, Konecny T, Jaffe AS, *et al*. Can amyotrophic lateral sclerosis chronically elevate troponin T Cor et Vasa (in press). http://dx.doi.org/10.1016/j.crvasa.2014.12.006