AMERICAN JOURNAL OF MEDICAL CASE REPORTS

ISSN 2374-216X

Serum cardiac troponin T in patients with amyotrophic lateral sclerosis without miocardial damage: case reports

Alessandro Graziani*; Mario Casmiro; Martina Zaninotto; Federica Mirici Cappa; Ilaria Lazzari; Stefania Valenti; Giuseppe Francesco Stefanini

***Alessandro Graziani**

Medicina Interna, Ospedale Infermi Faenza, 48018 Faenza Italy

Abstract

Cardiac Troponins (cTn) and more recently high sensibility troponins (hsTns) are used in clinical practice for the diagnosis of acute myocardial infarction (AMI) and for risk stratification of patients with acute coronary symptoms Many clinical conditions, as some skeletal muscle diseases, cause an elevation of cTn in the absence of myocardial ischaemia. Recently Authors described patients with Amyotrophic Lateral Sclerosis (ALS) and elevated levels of troponin T (TnT) thought not to be of myocardial origin. Here we report a case reports of ALS limb onset patients with advanced disease and persistently high levels of TnT in the blood in the absence of any other markers of myocardial disease. For this reason clinician needs to keep this in mind when evaluating ALS patients for potential cardiovascular disease.

Keywords

amyotrophic lateral sclerosis; troponin T; troponin I; myocardial damage

Introduction

Cardiac Troponins (cTn) are used in clinical practice for the diagnosis of acute myocardial infarction (AMI) and for risk stratification of patients with acute coronary symptoms [1]. Unfortunately, many clinical conditions cause troponin elevation in the absence of myocardial ischemia [2]. As in some skeletal muscle diseases, recently Authors described patients with Amyotrophic Lateral Sclerosis (ALS) and elevated levels of cTn T thought not to be of myocardial origin [3-5]. Here we report a brief series of ALS patients with persistently high levels of circulating cTn T in the absence of any other markers of myocardial disease.

Case 1

A 65 year old male with limb-onset ALS and invasive mechanical ventilation. In terms of past medical history, ten years earlier he experienced Inferior Acute Myocardial Infarction (AMI) which was treated with Percutaneous Coronary Intervention (PCI). At the age of 62, he was diagnosed with ALS and two years later he was intubated for pneumonia and acute respiratory failure. Six months earlier, he suffered from prolonged left anterior thoracic pain that increased with the pressure of the ribs. Electrocardiogram (ECG) measurements were unchanged compared to the previous ones, but there was an elevation of high sensitive cTn T (hs-TnT-Roche®) 140 ng/ml; normal value < 15 ng/ml and normal

value of Creatine Kinase Myocardial Band (CK-MB). He underwent a thoracic Computed Tomography that excluded aortic dissection and Single Photon Emission Computed Tomography with Technetium 99 that excluded coronary disease. He was discharged from hospital with no symptoms but with a persistently stable high value of hs-TnT. The patient was then re-admitted to hospital for replacement of his Percutaneous Endoscopic Gastrostomy (PEG) tube. He was haemodynamically stable and was asymptomatic for chest pain but the value of hs-TnT remained constantly high (305 ng/ml). In this occasion we determined Troponin I (cTnI- Abbott®; cTnI- Siemens®), Creatine Kinase (CK), CK-MB and N-terminal pro Brain Natriuretic Peptide (NT-proBNP) levels to be within their normal ranges (Table 1).

Case 2

A 74 year old male with limb-onset ALS diagnosed two years earlier, was evaluated to start non-invasive mechanical ventilation. He had a Vital Capacity (VC)of below 50%, mild orthopnoea and ALS Functional Rating Scale (ALS-FRS) of 21.At the time of hospital admission the patient was haemodynamically stable, asymptomatic at rest with moderate exertional dyspnoea. Laboratory workup revealed the following results: Arterial Blood Gas (ABG), glucose, liver function, electrolytes and renal function were within their normal ranges; hs-TnT (hs-TnT-Roche®) levels were markedly and persistently high (190ng/ml) without a typical "rise and fall" pattern. ECG tests did not demonstrate any signs of myocardial ischemia. To try to better understand these results we also tested TnI (cTnI- Abbott®; cTnI- Siemens®), CK-MB, NT-proBNP and, as shown in Table 1, all of which were within their normal ranges.

Case 3

A 72 year old male with limb-onset ALS diagnosed three years earlier, was transferred to our institution from another hospital where the individual experienced tracheal intubation for pneumonia and acute respiratory failure. At the time of hospital admission, the patient was mechanically ventilated in pressure support ventilation, with a correct setting of ventilation as shown by ABG (PH 7, 42, pCO2 38 mmHg, pO2 89 mmHg, HCO3 24 mmol/l). ECG show a sinus rhythm without any pathological manifestation. Abnormal laboratory test results included a WBC count of 13,200/mm^3, C-Reactive Protein 45 mg/dl, albumin level of 3,2 g/dL and hs-TnT 71 ng/ml (hs-TnT-Roche®). Results from other cardiac biomarker tests are shown in Table 1.

Discussion

Troponin (Tn) is composed of three subunits that interact strongly with one another: the Ca2+-binding troponin C (TnC), the inhibitory troponin I (TnI) and the Tm-binding troponin T (TnT) subunits [7]. They are present in all muscle cells but cTns are specific for myocardium and released in the blood from damaged myocardial cells. In 2012, a Task Force of the European Society of Cardiology, American Heart Association, American College of Cardiology and World Heart Federation re-defined the diagnosis of AMI. The Third Universal Definition of AMI, distinct five types and promote the use of 99th percentile of a normal healthy population as the decision level (coefficient of variance (CV) of<10%) for the dosage of TnI and TnT in peripheral blood [8]. More recently highly sensitive assays (hs-TnI and hs-TnT) have been introduced which are extremely sensitive and allow an earlier and faster diagnosis of AMI, detecting cTns derived from minimal myocyte necrosis. Compared to less sensitive assays, highly sensitive troponin

assays (hsTns) have higher diagnostic accuracy at time of presentation for the diagnosis of AMI mainly in patients presenting early after chest pain onset [9-11]. Unfortunately, similar to the former, hs-cTns are increased in a wide range of non-ischemic, acute, chronic, cardiac and extra-cardiac conditions such as Left Ventricular Hypertrophy (LVH), Heart Failure (HF), Pulmonary Embolism (PE), Renal Failure (RF), and this condition is associated with a worse prognosis [12].

Troponins and muscular damages

In the last decade, some authors have reported high levels of cTnT in patients with skeletal muscle disease in the absence of myocardial damage. In a retrospective series of patients with Idiopathic Inflammatory Myopathies (IIM), elevation of cTnT was observed, but no cTnI, which strongly correlated with CK levels despite the absence of myocardial ischemia [13]. Hughes, et al. have reported high levels of cTnT in patients, without known cardiac disease, with inflammatory myopathies and systemic sclerosis-spectrum as an effect of skeletal muscle disease activity. For these patients they proposed two clinical pathways to screen those with subclinical cardiac involvement and/or low-grade skeleton muscle activity. In one case, they measured cTnT and used cTnI as a confirmatory test to exclude cardiac involvement; whereas in an alternative institution where cTnI is available it should be measured at first examination [14]. Jaffe and coll. described a series of patients with myopathies (inflammatory or congenital) that express proteins in diseased skeletal muscle recognised by an antibody used in fourth generation and in hs-TnT, but not by TnI. Despite the limitations arising from the low number of muscular biopsies and skeletal muscle biochemical profiles, they concluded that cTnT is re-expressed in regenerating skeletal muscle whilst cTnI is considered more specific to cardiac muscle [15-16].

Troponins and ALS

More recently some authors have reported a persistent increase of cTnT levels in ALS patients without known cardiac disease. Von Lueder et al. [3] have described a patient frequently hospitalised for progressive dyspnoea and elevated cTnT levels who received the correct diagnosis of ALS after the exclusion of cardiac and respiratory diseases; these authors demonstrated a correlation between the worse Arterial Blood Gas parameters and the higher cTnT values and hypothesised that myocardial damage induced by hypoxemia .Hof, et al. [4] reported an ALS patient with chest discomfort and nocturnal dyspnoea; despite a slight elevation of myocardial markers (CK-MB, Myoglobin, cTnT), ECG tests were unremarkable and normal SPECT and cTnI levels. After starting nocturnal non-invasive ventilation chest discomfort and dyspnoea disappeared. They did not demonstrate a clear correlation with hypoxemia, but instead suggested possible cTnT isoform re-expression in skeletal muscular cells as observed in some patients with myopathies. For practical purposes, they recommended repeat measurements in order to identify the“rise and fall” pattern suggestive for AMI.

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 [17-19]. Here we report three patients with advanced limb-onset ALS and persistently high blood levels of hs-TnT. The patients did not demonstrate any cardiac diseases, were haemodynamically stable and despite the different clinical condition had normal values of TnI, NT-Pro BNP and CK-MB, whereas myoglobin level was increased. This data suggests the hypothesis that, in different stages of the disease [20], non-inflammatory skeletal muscle degeneration could be the cause

of re-expressed cTnT in diseased skeletal muscle and therefore the source of circulating cTnT. Unfortunately we could not perform a muscle biochemical profile in order to better explain this condition. Our observation indicates that hs-TnT suffers from the same limitations of fourth generation TnT. For this reason, the clinician needs to keep this in mind when evaluating ALS patients for potential cardiovascular disease.

Table

Table 1: Laboratory data

	hs-TnT-Roche® 0-15 ng/L	Mioglobin 12-70 µg/L	CK 30-240 U/L	CK-mb 0-5 µg/L	cTnI-Siemens® 0.000-0.045µg/L	cTnI-Abbott® 0.0-26.2ng/L	NT-proBNP 0.0-26.2ng/L
Case 1	305	129.1	88	5.91	<0.017	14.5	694
Case 2	190	210	106	16.3	<0.017	1.6	13
Case 3	71	179.2	152	3.55	<0.017	4	386

References

1. Giugliano RP, Braunwald E. The year in Acute Coronary Syndrome. J Am CollCardiol. 2014; 63: 201-14.

2. Agewall S, Giannitsis E, Jernberg T, et al. Troponin elevation in coronary vs non coronary disease. European Heart Journal. 2011; 32: 404-11.

3. 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.

4. 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.

5. Graziani A, Del Giudice E, Casmiro M et al.Elevation of troponin T in mechanical ventilated patient with amyotrophic lateral sclerosis. Case Reports in Internal Medicine 2015; Vol. 2 (3); 22-25.

6. Mack L, Konecny T, Jaffe AS, et al. Can amyotrophic lateral sclerosis chronically elevate troponin T Coret Vasa (in press).

7. Gomes AV, Potter JD, Szczesna-Cordary D The Role of Troponins in Muscle Contraction Life 2002; 54: 323–333.

8. Steg PG, James SK, Atar D et al ESC guidelines for the management of acute myocardial infarction in patients presenting with ST segment elevation. EurHeart J 2012;33:2569-619.

9. Sherwood MW, Newby LK High Sensitivity Troponin Assays: Evidence, Indications and Reasonable Use. J AmHeartAssoc. 2014;3:1-10.

10. Mair J. High-sensitivity cardiac troponins in everyday clinical practice. World J Cardiol. 2014; 26: 175-82.

11. 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.

12. Tanindi A, Cemri M. Troponin elevation in condiction other than coronary syndromes. Vascular Health and Risk Management. 2011; 7: 597-603.