Misleading elevated levels of troponin-T in a patient with inflammatory myopathy

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Introduction

Elevations in levels of enzymes such as creatine kinase and troponin-T are used as serum biomarkers for myocardial injury (Mair et al, 2018). However, levels of these biomarkers can also be elevated in processes that are not related to cardiac disease (Long et al, 2020). This case highlights the importance of correct interpretation of levels of such biomarkers, especially in patients with underlying rheumatological diseases.

Case report

A 53-year-old woman presented with a 2-week history of chest pain, dyspnoea, lethargy and fatigue. She had a medical history of Sjögren's syndrome, discoid lupus and fibromyalgia. Her medications included fexofenadine 180 mg, hydroxychloroquine 400 mg and lansoprazole 15 mg. She did not smoke and drank 4 units of alcohol per week. Sjögren's syndrome was diagnosed at a different hospital, based on positive antibodies which included positive rheumatoid factor, Ro and La.

The chest pain was central and pleuritic, but was not pericardial in nature. There were no accompanying features, but she had complained of mild weakness in her limbs over the last few months. Clinical examination was normal apart from a heart rate of 110 beats per minute (bpm). 12-lead electrocardiogram showed sinus tachycardia but no ischaemic changes. Blood tests were normal apart from levels of troponin-T which was elevated at 355 ng/litre (normal <14 ng/litre) with a repeat 6-hour level of 325 ng/litre, and creatine kinase which was elevated at 964 IU/litre (normal range <150 IU/litre). Differentials on admission included acute coronary syndrome, pulmonary embolism and myocarditis.

She was hospitalised and transthoracic echocardiography showed normal biventricular size and function. As her Well's score was 1.5 (heart rate of >100 bpm), a D-dimer level was measured (to rule out pulmonary embolism) which was 441 ng/ml (normal <500 ng/ml). Invasive coronary angiography showed unobstructed coronary arteries. With traditional acute coronary syndrome ruled out, cardiac magnetic resonance was performed, which showed mildly impaired systolic function (ejection fraction 48%), normal T1 and T2 values and no late gadolinium enhancement, overall suggesting no evidence of myocardial inflammation, scarring or myocarditis (Figure 1).

At this point the most likely diagnosis was troponin-T leak. She was discharged and followed up in cardiology clinic, where further blood tests were performed including repeat creatine kinase and troponin-I. Her creatine kinase level was increasing at 1285 IU/litre but her troponin-I level was normal. The elevated levels of creatine kinase and troponin-T were likely secondary to skeletal muscle inflammation and she was referred to the rheumatology team to rule out a potential underlying myopathy.

In rheumatology clinic, musculoskeletal examination revealed proximal muscle weakness in the hips, and weakness in elbow flexion and wrist extension with a manual muscle testing-8 score of 120/150. A myositis panel of blood tests was performed which showed Ro52 positivity. Nerve conduction studies revealed no evidence of a polyneuropathy and magnetic resonance imaging of the thighs showed patchy mild muscle oedema bilaterally in the quadricep muscles as well as bilateral fatty infiltration, indicating an active inflammatory myopathy (Figure 2). Muscle biopsy of the left lateral vastus lateralis showed multifocal inflammation with dystrophic-like features, with necrotic and regenerating fibres, features associated with an inflammatory myopathy and strongly favouring a diagnosis of inclusion body myositis (Figure 3). She was referred to specialist muscle physiotherapists for exercise rehabilitation.

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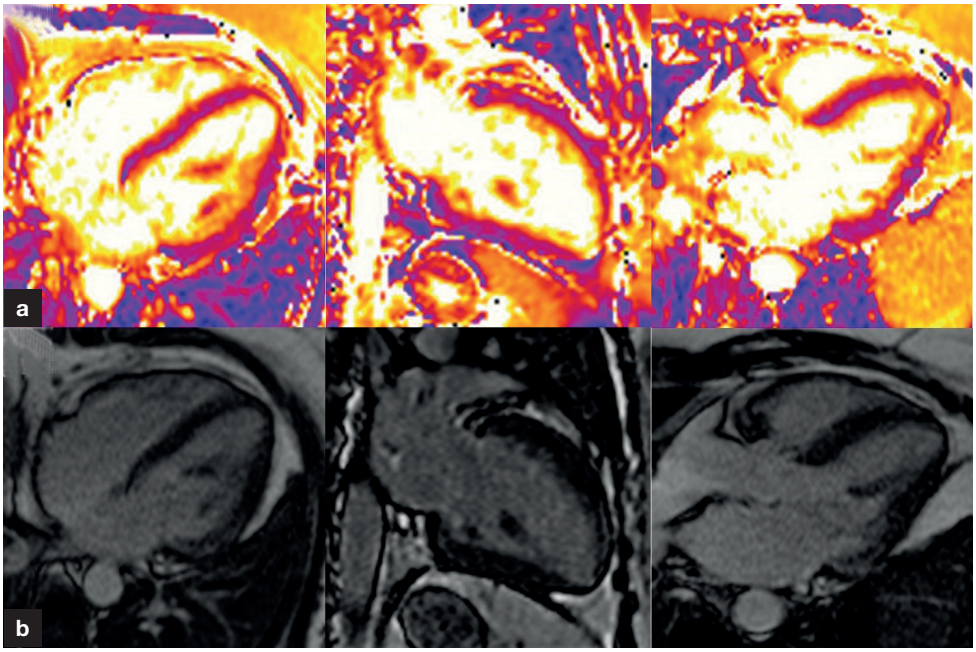

Figure 1. Cardiac magnetic resonance imaging. a. Four-, two- and three-chamber long axis T2-mapping images of the myocardium showed normal values, suggesting no myocardial oedema or inflammation. b. Four-, two- and three-chamber long axis late gadolinium enhancement images showed no evidence of myocardial infarction or focal fibrosis.

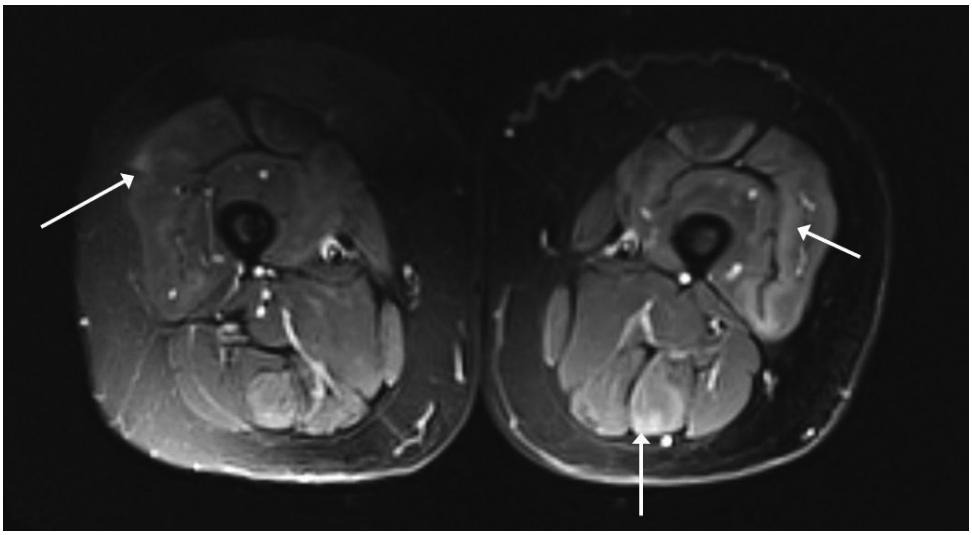

Figure 2. Axial short tau inversion recovery magnetic resonance imaging of the thighs showed mild inflammation and oedema bilaterally in the thighs (arrows indicate high signal showing mild inflammation and oedema).

Discussion

This article has presented a case of a woman investigated for presumed cardiac chest pain with a diagnosis of inclusion body myositis, a type of idiopathic inflammatory myopathy causing elevated troponin-T levels.

Idiopathic inflammatory myopathies are rare systemic inflammatory diseases, with an incidence of up to 19 per 1 000 000 person-years in UK adults (Oldroyd et al, 2022). The hallmark clinical features include progressive proximal muscle weakness, fatigue and myalgia (Lundberg et al, 2021). Diagnosis is made by a combination of clinical examination, detection of elevated levels of skeletal muscle enzymes, magnetic resonance imaging for detection of oedema, and muscle biopsy.

Creatine kinase and troponin-T are used as biomarkers of myocardial injury and for routine screening of chest pain in the emergency department (Mair et al, 2018). However,

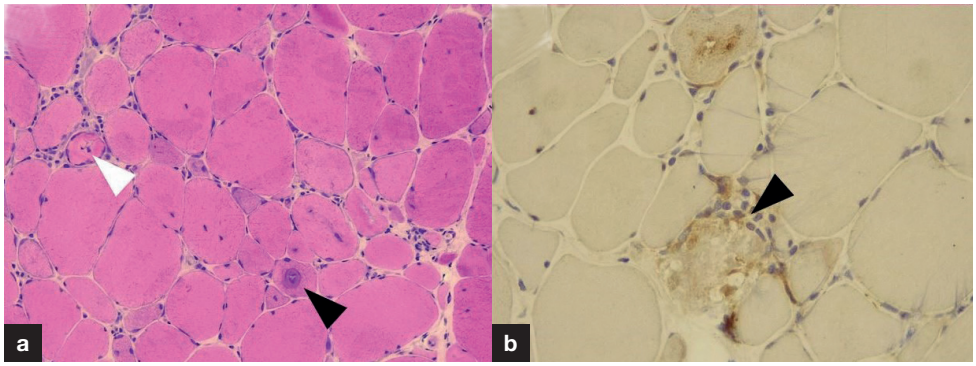

Figure 3. Muscle biopsy histology. a. Left lateral vastus lateralis section stained with haematoxylin and eosin showed characteristic endomysial chronic inflammation with rimmed vacuoles (black arrowhead) and inclusion bodies (white arrowhead) (x400 magnification). b. Left lateral vastus lateralis tissue stained with p62 by immunohistochemistry showed abnormal protein deposition (black arrowhead) (x400 magnification).

there are many non-cardiac conditions where the levels of these biomarkers are falsely interpreted to indicate myocardial injury, such as renal failure, rhabdomyolysis and autoimmune conditions. In patients with idiopathic inflammatory myopathies, enzyme levels can be elevated as a result of constant muscle breakdown (Hughes et al, 2015), and elevation of troponin-T levels can lead to an inaccurate assumption about the presence of myocardial damage (Aggarwal et al, 2009; Schmid et al, 2018). Measurement of troponin-I is useful to delineate if the elevation is the result of inflammatory myositis or myocardial injury, as it is not expressed in regenerating skeletal muscle cells and is more specific to the myocardium (Lilleker et al, 2018). For this reason, troponin-I is increasingly used as a biomarker for myocardial involvement in the idiopathic inflammatory myopathies.

In the present case, if troponin-I had been requested earlier, the patient would not have undergone invasive tests, saving costs, reducing her risk of harm and leading to an earlier diagnosis. The incorrect interpretation of elevated troponin-T levels leading to inappropriate cardiac investigations has been highlighted in other cases (Dhir and Jiang, 2013; Ruperti-Repilado et al, 2022). Clinicians should recognise that elevated troponin-T levels are not always secondary to myocardial injury, and requesting troponin-I measurement can be useful in patients with underlying rheumatological diseases.

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Learning points

- Elevated levels of enzymes such as troponin-T are used as biomarkers of myocardial injury and are part of routine screening for chest pain.
- Elevated levels of troponin-T are not always a marker of myocardial injury as it is also found in skeletal muscle, unlike troponin-I which is much more specific for cardiac myocyte injury.
- It is important to consider an underlying rheumatological diagnosis and requesting a troponin-I level where the cause of a persistently elevated level of troponin-T is not clear.

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