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International Journal of Cardiology 176 (2014) 1118–1119

Contents lists available at ScienceDirect

International Journal of Cardiology

journal homepage: www.elsevier.com/locate/ijcard

Letter to the Editor

Reinforce work-up for myopathy in Takotsubo syndrome

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ARTICLE INFO

Article history:
Received 15 July 2014
Accepted 27 July 2014
Available online 12 August 2014

Keywords:
Apical ballooning
Stress cardiomyopathy
Cardiac involvement
Unclassified cardiomyopathy
Neuromuscular disorder
Myopathy CK-elevation

Sir, we read the article by Bangert et al. [1] about a 61 year old female with Takotsubo syndrome (TTS) triggered by the development of necrotizing myopathy with interest. We have the following comments and concerns.

We doubt the diagnosis of necrotizing myopathy for several reasons. First, the blood sedimentation rate was almost normal (17 mm/h). Second, myofiber necrosis and macrophage infiltration do not unequivocally mean necrotizing myopathy. Muscle fibre necrosis and macrophage infiltration may also occur as an inflammatory response in Duchenne muscular dystrophy (DMD) [2,3] or DMD-carrier state, in muscle injury [4], in experimental Chagas disease [5], in polymyositis [6], in autosomal recessive limb girdle muscular dystrophy 2B (dysferlinopathy) [7], in drug-induced myopathy [8], experimental diabetic myopathy [9], macrophagic myofasciitis [10], or in severe acute respiratory syndrome (SARS) [11]. Muscle fibre necrosis and phagocytosis were even described in metabolic myopathy [12]. Was a DMD-carrier status and all other differentials mentioned above excluded in the presented patient? Was muscle biopsy investigated for immune-histological abnormalities? Were any biochemical investigations carried out? Arguments for a metabolic myopathy are that TTS has been previously reported in metabolic myopathy [13], that the history was positive for bipolar disorder, that she had psoriasis, and that clinical manifestations deteriorated upon administration of statins. Third, the authors themselves mention in their discussion that necrotizing myopathy is characterised by the absence of inflammatory infiltrates [1], which does not comply with the finding of macrophage infiltrates in the presented patient [1]. Fourth, muscle weakness did not necessarily improved upon steroids and azathioprine. Improvement could have occurred spontaneously or could be attributed to successful treatment of heart failure. Usually, azathioprine has a clinical effect not earlier than months but not "a few days" after initiation of treatment. Even steroids may take longer than "a few days" to be effective in necrotizing myopathy. Fifth, so far, necrotizing myopathy has not been reported in association with TTS.

We also disagree with necrotizing myopathy as the trigger of TTS. TTS is usually triggered by physical or psychological stress due to pain, fear, surprise, acute neurological disease, or trauma [14]. Which was the trigger of TTS in the presented patient? The patient is reported to have a history of bipolar disorder [1]. Did she experience an episode of depression, which has been previously reported to trigger TTS [15]? Was the patient shocked by the acute onset of muscle weakness, which she had experienced already in 2010? Did the authors consider a previous seizure? CK of 31241 U/l was relatively high and epilepsy is a frequent and often neglected trigger of TTS [16–19]. Did she report muscle aching, tongue bite, a state of impaired consciousness, or urinary secessus at the day of admission? Was the individual or family history positive for epilepsy? She had fever, which is a well-known trigger of seizures. Did she experience stress from acute dyspnea due to affection of the respiratory muscles?

Further points that need to be addressed are that the authors do not mention if the family history was positive for muscle disease and that they do not provide an explanation for muscle weakness and CK-elevation in 2010. They should also mention the dosage of valproic acid, which has been previously reported to unmask metabolic myopathy [20]. Did the authors look for noncompaction in their patient, since this unclassified cardiomyopathy has been shown to be associated with neuromuscular disease in a large number of patients [21]?

Overall, this interesting case merits reevaluation of the neurological diagnosis and resumption of the TTS trigger. Whether patients with myopathy carry an increased risk to develop TTS is unknown but in each patient with TTS and myopathy the pathogenetic link should be clarified by extensive clinical and instrumental investigations. Particularly important is to establish the correct neuromuscular diagnosis in order not to exhibit the patient towards potentially toxic drugs and to let him profit from adequate treatment.

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[1] JF and CS did not receive an honorarium, grant, or other form of payment for producing the manuscript.

http://dx.doi.org/10.1016/j.ijcard.2014.07.300
0167-5273/

Conflict of interest

There is no financial support or other benefits from commercial sources for the work reported on in the manuscript, or any other financial interest of the authors, which could create a potential conflict of interest or the appearance of a conflict of interest with regard to the work.

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