Reviewer’s report

Title: Nemanline Myopathy and Heart Failure: Role of Ivabradine. A Case Report

Version: 2 Date: 2 December 2014

Reviewer: Carina Wallgren-Pettersson

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Major Clinical Comment:

This manuscript describes a patient who presented at the age of 33-34 years with subacute weakness mainly of the upper limbs. Dysphagia and rapidly progressive heart failure ensued within the following year. He was found to have a monoclonal gammopathy.

What immediately comes to mind is the entity sporadic late-onset subacute nemaline myopathy, SLONM, despite the fact that heart failure has not been an early symptom in previously described patients. Because of the poor prognosis in SLONM, and because it is not clear to me from reading the manuscript how the patient is doing currently in terms of his skeletal muscle strength, I suggest that the patient be re-evaluated with this in mind without further delay, for appropriate treatment to be initiated if this diagnosis is confirmed.

Major Compulsory Revisions:

1) There are a number of publications on adult-onset nemaline myopathy, many of which explicitly describe SLONM, where the presence of a monoclonal gammopathy has been found to carry a poor prognosis. Other case reports, especially those preceding the 2005 paper by Chahin et al., have been less detailed. At least one report (Taglia et al 2012) introduces the use of ivabradine for heart failure. These publications should be cited and careful comparisons made with the patient described herein.

It is true that in some patients with mild nemaline myopathy, the diagnosis may have been delayed into adulthood, and the patient may present in adulthood with respiratory failure without a prior diagnosis of myopathy. In these cases, a careful history may reveal a childhood-onset weakness previously overlooked, or findings on physical examination suggesting a congenital onset, and a genetic cause is then likely to be found to underlie the symptoms.

If, however, the onset of weakness is truly in adulthood, and subacute, and especially if a monoclonal gammopathy is present, the diagnosis of SLONM is more likely.

2) All articles reporting cardiac involvement in nemaline myopathy should be cited, since this is so rare.
3) Did the patient’s postural symptoms amount to camptocormia, reported in a few of the SLONM cases? Would the authors have a profile picture that would be more informative than the dorsal one, in terms of the posture of the spine?

4) Regarding the histological findings, essential details are whether the patient had type 1 fibre hypotrophy or whether it was atrophy, and whether, in addition to this, there was type 1 fibre predominance.

Minor Essential Revisions:

The language requires minor revision. The word nemaline is misspelt in the Title, and the first sentence of the Abstract implies that a wide spectrum of phenotypes is present in the muscle fibres.

I hope these comments will be useful for the improvement of the manuscript.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests