Author’s response to reviews

Title: Proximal myopathy in lactovegetarian Asian patients responding to Vitamin D and calcium supplement therapy - Report of two cases and literature review

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Author’s response to reviews: see over
Dear Editor,

We would like to thank the reviewers of the above manuscript for their constructive comments and we have now modified the paper in response to these comments. We feel that the paper is significantly strengthened as a result and would like to resubmit it for considerations for publication in the Journal of Medical Case Reports.

The following replies have been made, based on the reviewer’s comments below:

**Reviewer 1**

No comments to be replied.

**Reviewer 2**

While is correct to state that patients with osteomalacia may present with proximal myopathy, it is incorrect to describe the patients as having “osteomalacia-induced myopathy”. That a patient with osteomalacia due privational vitamin D deficiency presents with proximal myopathy does not mean indicate a causal relationship..........The point needs to be corrected throughout the paper – in many instances throughout the text, the word “osteomalacia” should be replaced with “vitamin D deficiency”.

We agree with the reviewer’s comments that the term osteomalacia-induced myopathy is incorrectly used in this context, and that Vitamin D deficiency is the correct pathological definition for the underlying proximal myopathy in both cases. This has been rectified in the revised manuscript.

The pathomechanisms of myopathy due to vitamin D deficiency are not as clear cut. The authors address this in the discussion, but they fail to mention one of the most likely factors – phosphate depletion. Serum phosphate was only reported in case 1 and was only mildly reduced at 0.7 mmol/L. It is important to measure phosphate levels in the fasting state. Was case 1 fasting, and was phosphate measured in case 2?

Unfortunately, the serum phosphate level in the first cases was not measured in the fasting state. In the second case, serum phosphate was measure fasting, and was normal at 1.18 mmol/l (0.87-1.45)]. Based on the available information currently, it is therefore not possible to relate the Vitamin D deficient-induced myopathy in both our cases to phosphate depletion.
Another possible mechanism for proximal myopathy is PTH effect. PTH may be a neurotoxin and may contribute to weakness.

This possible mechanism is noted and has been referenced in the revised manuscript.

Case presentations: Assay methodology for serum 25OHD and serum PTH could be mentioned

The reviewer’s suggestion has been noted and the assay methodology is now mentioned in the revised manuscript.

Discussion, first line: Osteomalacia, as mentioned above, is a disorder of defective bone mineralisation. Osteoid excess is also apparent in high bone turnover states. The failure to mineralise new bone matrix leads to an increase in the both the surface extent and thickness of osteoid seams. A defect on mineralisation can only be detected on bone biopsy.

The definition of osteomalacia has been updated as per the reviewer’s suggestion in the revised manuscript (Discussion section, lines 3 - 5).

Discussion, 1st paragraph: The reasons for privational vitamin D deficiency in their patients warrant further discussion.... In Ireland, milk fortification is common unlike the Britain, so this difference may not apply in Ireland. A dietary factor not mentioned is chapati; diets from the Asian subcontinent often include unleavened bread. Chapati is thought to impair calcium absorption and may account for the severity of the presentation of vitamin D deficiency in both cases. Did the patients eat chapati?

The underlying risk of Vitamin D deficiency for both our patients is now further elucidated in the revised manuscript (Discussion section, paragraph 1), including inclusion in their dietary history of unleavened bread intake, as per the reviewer’s comments.