Reviewer's report

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

**Version:** 1  **Date:** 27 August 2010

**Reviewer:** Malachi McKenna

**Which of the following following best describes what type of case report this is?:** Other

**If other, please specify:**

First report of such cases in Ireland, but it is still important due to the high prevalence of vitamin D deficiency in immigrant communities living in European countries at high latitude.

**Has the case been reported coherently?:** Yes

**Is the case report authentic?:** Yes

**Is the case report ethical?:** Yes

**Is there any missing information that you think must be added before publication?:** Yes

**Is this case worth reporting?:** Yes

**Is the case report persuasive?:** Yes

**Does the case report have explanatory value?:** Yes

**Does the case report have diagnostic value?:** Yes

**Will the case report make a difference to clinical practice?:** Yes

**Is the anonymity of the patient protected?:** Yes

**Comments to authors:**

Hood et al describe two cases of severe proximal myopathy due to profound vitamin D deficiency. Both patients had a substantial delay in diagnosis with symptoms in case 1 for over 6 months, and in case 2 for 4 years. Case 1 ultimately came to attention with tetany. Both cases had marked abnormalities in the secondary indices of vitamin D deficiency - namely, elevated serum total alkaline phosphatase, low serum calcium and low serum phosphate. In addition,
serum parathyroid hormone (PTH) levels were elevated. Both had marked reduction in serum 25-hydroxyvitamin D (25OHD) levels at 5.5 nmol/L and 16 nmol/L. Following diagnosis and treatment with vitamin D and calcium supplements, the authors noted a marked improvement in both clinical and biochemical findings. The authors attribute the patients presentation to their ethnicity (both being non-Causasians living in Western Europe) that curtails skin production of vitamin D, and to their patients being lactovegetarians.

General Comments:

The patients’ presentation of muscle weakness is not due to osteomalacia. It is a consequence of profound vitamin D deficiency that results in proximal myopathy. Osteomalacia and proximal myopathy are both endpoints of vitamin D deficiency, contemporaneous events but separate. 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 critical aspect about both their cases is that they presented with predominantly with proximal myopathy. Both on further investigation had biochemical evidence that was entirely consistent with osteomalacia. 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”.

For the purist, the definition of privational vitamin D deficiency is as follows: a clinical, radiologoical, biochemical, or histological abnormality that is corrected by vitamin D repletion. The natural history of vitamin-D related bone disease is secondary hyperparathyroidism (that may be of long duration depending on the severity the hypovitaminosis D) that is following by a mineralisation defect in bone, which is only diagnosed on histomorphometric analysis of a bone biopsy. Bone biopsy is rarely performed in clinical practice; it is very likely that their patients had osteomalacia but not proven.

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? Some patients with profound vitamin D deficiency develop an acquired form of PTH resistance that leads to even further fall in serum calcium levels and a paradoxical rise in serum phosphate levels. Given that case 1 presented with tetany with only a mild reduction in serum phosphate, is it possible that this case had some degree of PTH resistance?

Another possible mechanism for proximal myopathy is PTH effect. PTH may be a neurotoxin and may contribute to weakness.

Specific points:

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

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.

Discussion, 1st paragraph: The reasons for privational vitamin D deficiency in their patients warrant further discussion. First, skin production is curtailed due to higher melanin content especially in a high latitude country like Ireland where ultraviolet irradiation of skin is ineffective for nearly 6 months of the year. Second, there are dietary factors. The authors state that lactovegetarians are at greater risk of ovolactovegetarians; this is based on a British study. 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? If they did, then they should be advised to avoid chapatti at least until there is full resolution of vitamin D deficiency, and possible forever.

Quality of written English: Acceptable

Declaration of competing interests:

I declare that I have no competing interests