Myopathy: Effect of Vitamin D Deficiency Beyond Bones

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Abstract

Vitamin D functions as a vitamin as well as a hormone. Its major skeletal actions are complemented by varied extra-skeletal functions. During the past decade, association between Vitamin D and its role in various non-skeletal morbidities have been recognized. It plays a role in decreasing the risk of many chronic illnesses like allergies, asthma, autoimmune diseases, diabetes, cancers, infections and cardiovascular disease. We report the case of a middle aged female with chronic quadriparesis and new onset anemia associated with Vitamin D deficiency. Patient responded to vitamin D supplementation alone.

Introduction

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Case Report

38 year old housewife, came with chief complaints of easy fatiguability and palpitations since 3-4 weeks. She was found to be anaemic and so two units of blood was transfused. Patient improved symptomatically, but 1 week later developed generalised body ache, joint pains and drowsiness. On enquiry, patient gave history of insidious onset gradually progressive weakness of all 4 limbs since 3 years. Weakness initially involved both lower limbs (proximal, then distal), followed by both upper limbs. She also had truncal weakness. There was no diurnal variation, fasciculations, sensory complaints or bowel/bladder involvement. There was no history suggestive of cranial nerve involvement. She did not have bleeding from any site, malena, chronic diarrhea or blood transfusions in the past. She did not have any known co-morbidities.

On examination, patient was conscious, slow in response, well built and well-nourished. She had pallor and Grade III edema. Jugular venous pressure was not raised. Neurological examination revealed quadriparesis with normal muscle tone without cranial nerve or sensory involvement. Power was 3/5 in both upper limbs, while in lower limbs it was 1/5 proximally and 3/5 distally. Deep tendon reflexes were normal.

Routine investigations showed normocytic anemia (Hb-6.6 g/dl, MCV-85 fl) with thrombocytopenia. Iron studies were suggestive of anemia of chronic disease (Serum iron-88 μg/dl, TIBC-87 μg/dl, Transferrin saturation- 101%, Serum ferritin- 1212 μg/L). Hemoglobin electrophoresis was normal. Direct and indirect Coombs’ test, ANA were negative and C3, C4 complement as well as TSH levels were normal. Urine myoglobin levels and CPK levels were normal. 25-hydroxy vitamin D levels were found to be extremely low (<4.2 ng/ml).

Patient was given high dose parenteral vitamin D supplementation daily for 5 days and later was started on oral calcium and vitamin D3 supplements. Patient’s power improved over 1 week and she was able to stand without support. Her hemoglobin also improved during the course of hospital stay without any further blood transfusions or other nutritional supplements (except vitamin D). By the second week, patient was able to walk with support and her haemoglobin had increased to 8.9 g/dl. Patient followed up in the OPD after one month and could walk without support. Although she still had difficulty in getting up from squatting position, she was quite independent in her activities of daily living.

Discussion

Vitamin D is mostly derived from exposure to the sun’s ultraviolet light (80-90%), and to a lesser extent, nutritional intake (10-20%). Vitamin D takes on the predominant circulating form as 25-hydroxyvitamin D or 25(OH) D. The biologically active form, however, is known as calcitriol or 1,25(OH)₂D, and is formed by the hydroxylation of 25(OH)D. Vitamin D carries out a number of pivotal physiological roles in the body. This includes maintaining calcium homeostasis through the kidney, parathyroid gland, bone and intestine. It is also important for cell differentiation as well as regulating the immune response and hence assisting in the defence against pathogens.

Several studies report an association between vitamin D deficiency and proximal myopathy. It has been reported to be seen in 70% of patients with severe osteomalacia. A serum 25-hydroxy vitamin D level below 20 ng/ml causes increased body sway and below 10 ng/ml leads to difficulties in rising from a chair, inability to ascend stairs, and pain and discomfort due to muscular effort.

The actions of vitamin D in muscle are not fully understood, but it appears that at least one of its metabolites, 25-hydroxycholecalciferol, may influence the resting energy state of the muscle and also the protein turnover. It is likely that high levels of parathyroid hormone, hypophosphatemia, and low levels of calcitriol all contribute.

An elevation in serum alkaline phosphatase with a low-normal plasma calcium concentration are clues to the diagnosis. However, the assessment of serum 25 OHD (25 hydroxy vitamin D) is the only reliable test as clinical myopathy may be present before the development of biochemical signs (low calcium and increased alkaline phosphatase) of bone disease. The circulating level of 25(OH)D is the most
suitable indicator of Vitamin D status because it is easily measured, stable and has the longest half life of 3 weeks. Measuring 1,25-dihydroxyvitamin D or serum calcium levels is not generally recommended for diagnosing hypovitaminosis D, as it can impair the accurate interpretation of the patient’s vitamin D status. In patients with vitamin D deficiency, calcitriol levels will be often normal or elevated due to increased PTH levels. Elevation of muscle enzyme creatinine kinase level has been reported in a minority of patients with vitamin D related muscle weakness. Muscle biopsy is not indicated and if done, shows non-specific muscle fiber atrophy and no signs of inflammatory reaction.5

The ultimate evidence of the diagnosis rests on the response to therapy. Proximal muscle strength strikingly improves when 25-hydroxy vitamin D levels increases from 4 ng to 16 ng/ml and continues to improve as the levels increase to more than 40 ng/ml.

There is higher incidence of statin induced myopathy in patients with low vitamin D levels. Myalgia in statin-treated patients may reflect a reversible interaction between vitamin D deficiency and statins.

Vitamin D deficiency is associated with anemia in relatively healthy older persons, particularly among those with anemia of inflammation.6 A cross-sectional study of 554 subjects has demonstrated a greater prevalence and risk of anemia in individuals with 25-hydroxy vitamin D deficiency compared with those with normal levels. Subjects with 25-hydroxy vitamin D deficiency had higher serum iron saturations, ferritin, and lower TIBC levels. The higher levels of ferritin and lower serum albumin suggest that malnutrition and inflammation might be more prevalent in 25-hydroxy vitamin D deficient individuals which introduces a confounder for the association evaluated in the study.7

Conclusion

This case highlights the importance of considering Vitamin D deficiency in differential diagnosis of myopathy, as response to treatment is dramatic if diagnosed promptly.

References