CASE STUDIES

Occurrence of disabling myopathy secondary to hypovitaminosis D

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Abstract

We report a case of severe proximal muscle weakness caused by vitamin D deficiency. Hypovitaminosis D myopathy (HDM) is often misdiagnosed, as the symptoms are non-specific. However, the disease is easily treatable and complete recovery is possible if diagnosed on time.

Introduction

Although the prevalence of vitamin D deficiency is common worldwide, it is often underestimated. Proximal myopathy has been reported to be present in 60-75% of patients with vitamin D deficiency. The weakness usually occurs in proximal muscles and it is often minimal and subclinical. Here we present a case of severe muscle weakness due to vitamin D deficiency, which rendered the patient wheel chair bound. We have discussed the available literature and their implications in identifying the condition early and initiate vitamin D replacement therapy.

Case report

A 42-year-old female visited our outpatient clinic with weakness of all the four limbs, which was gradually deteriorating since one and half years. The patient, who was wheel chair bound since two months, complained of backache, neck muscle weakness, and severe fatigue. Diagnostic test results conducted earlier showed that the blood sugars, electrolytes, and thyroid profile were within the normal limits and the level of alkaline phosphatase (ALP) was 403 U/L. Based on the evaluation and electromyography (EMG) report, the patient was diagnosed with myotonia dystrophica in the previous hospital. The patient was informed that there is no specific treatment for the disease and she was discharged after prescribing calcium supplements and NSAIDs.

Clinical examination conducted in our hospital revealed that she was moderately built and poorly nourished. Her vital signs were stable. She had bilateral pedal edema. Power in all the four limbs was 3/5 (proximal weakness was more than distal). There was no sensory involvement. Other systems examinations did not reveal any abnormality. Results of diverse parameter estimation are given in table 1.

Based on clinical examination and lab investigations, a diagnosis of vitamin D deficiency with secondary hyperparathyroidism was made. The patient was treated with cholecalciferol 60,000 IU IM daily for five days followed by once a week dose. Calcium carbonate 500 mg, folic acid 5 mg, and oral iron preparations were also prescribed for daily administration. Follow-up conducted after three weeks showed a gradual improvement in weakness. She was able to get up from chair and move with support. A significant reduction in fatigue and generalized body aches was noted. ALP was reduced to 275 U/L and the level of phosphorus was 3.55 mg/dl. She was advised to continue the same medications. A second clinical review was conducted after six weeks from her first visit. She was able to get up and walk without support, although with some instability. However, she was not able to get up from squatting position. Levels of various parameters evaluated were hemoglobin-12 gm%, ESR-32 mm at one hour, ALP- 228 U/L, vitamin D- >70.0 ng/

ml, phosphorus- 4.04 mg% and, PTH- 86.70 pg/ml. She was prescribed with oral vitamin D sachets weekly once and daily regimen of oral calcium, iron, and B-complex.

Table 1: Clinical and lab investigation results

Parameters	Values
Hemoglobin	9.0 gm/dl
Total leukocyte count	7290 cells/cu.mm
ESR	33 mm at the end of 1 hour
Random blood sugar	76 mg/dl
Serum glutamic oxaloacetic transaminase (SGOT)	55 U/L
Serum glutamic pyruvic transaminase (SGPT)	52 U/L
ALP	305 U/L
Serum creatinine	0.6 mg/dl
CRP	1.0 mg/L
CPK	76 U/L
Rheumatoid factor	Negative
Antinuclear antibody (ANA)	Negative
HIV/ HBsAg/ HCV	Negative
Sodium	142 mEq/L
Potassium	5.5 mEq/L
Calcium	9.6 mg/dl
Inorganic phosphorus	1.9 mg/dl
Vitamin D	<3.0 ng/ml
PTH	268 pg/ml
TSH	1.25 µIU/ml

Discussion

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.[1] The muscle weakness, which is often minimal, is revealed only on elicitation of history. In infants, myopathy is evident from muscle weakness and hypotonia.[2] Adults may present with predominant proximal muscle weakness with difficulty in getting up from squatting position or climbing stairs. Other clinical characteristics of the disease include uniform generalized muscle wasting with preservation of sensation and deep tendon reflexes, and waddling gait.[3] Symptoms of bone pain may also be present.

The case presented here had disabling muscle weakness and was not able to walk independently. Her serum calcium was normal, but compensatory hyperparathyroidism, elevated ALP, and reduced phosphorus level were noted. Normal serum levels of calcium and phosphorus in healthy individuals are achieved predominantly through interaction between the two hormones: parathyroid hormone (PTH) and calcitriol. In patients with vitamin D deficiency, secondary hyperparathyroidism causes release of calcium stored in bone and resorption of calcium by kidneys to maintain normal serum calcium and phosphorus levels. Hence, vitamin D deficiency is usually accompanied by normal blood levels of calcium and phosphorus, high normal or elevated levels of PTH, normal to elevated levels of ALP, a low 24 hour urine calcium excretion rate, and low levels of total 25-hydroxyvitamin D (25(OH)D). Overt hypocalcemia and /or hypophosphatemia may appear only in patients with severe and long-standing vitamin D deficiency.[4]

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.[4]

A wide 'optimal' range of 25-80 ng/ml has been reported for 25(OH)D and there is no concurrence on the definitions of vitamin D insufficiency (20-30 ng/ml) and deficiency (<20 ng/ml). Mild-to-moderate deficiency of the vitamin is linked to the occurrence of osteoporosis and/or secondary hyperparathyroidism. Severe deficiency can cause rickets in children and osteomalacia in adults.[5]

Clinically, hypovitaminosis D myopathy (HDM) can be confused with other myopathies including late-onset myotonia dystrophica type 2. However, a careful analysis of clinical features will help in distinguishing the disease. In HDM, EMG abnormalities such as polyphasic motor unit potentials with shortened duration and decreased amplitude consistent with a myopathy is also noted. However, such results are not specific to the disease and are, in fact, observed in other muscular diseases such as polymyositis.[6] While for myotonic dystrophy, the EMG shows a myotonic discharge characterized by spontaneous waxing and waning. Hence the descriptive term, the 'divebomber' sound is used to describe the discharge.[7] But, raised ALP and low vitamin D levels should always arouse a suspicion for the former, which is more common and easily treatable. In the present case, a consistent elevation in ALP and a decrease in vitamin D level were noted.

Metabolic myopathies may be often accompanied by secondary hypovitaminosis D. Muscle biopsies can help in differentiating HDM from other myopathies. Muscle biopsies

conducted in adults with profound vitamin D deficiency have demonstrated the predominance of type II muscle fiber atrophy. Thus, the fast-twitching property of type II muscle fibers and their primary role in preventing a fall may better explain the increased falling tendency of vitamin D deficient elderly patients.[8] Histological analysis of vitamin D-deficient subjects shows enlarged interfibrillar spaces and infiltration of fat, fibrosis, and glycogen granules.[9] Whereas, the characteristics of muscle biopsy in myotonic dystrophy are angulated fibers, moderate variations in myofiber diameter, centrally displaced nuclei, ring fibers, scattered atrophic fibers, nuclear chains, increase in endomysial tissue, and type 1 fiber predominance.

It is estimated that vitamin D deficiency or insufficiency affects around one billion worldwide.[10] According to the previously published study reports, the prevalence of varying degrees (50- 90%) of vitamin D deficiency with low dietary calcium intake in Indian population is extensive.[11] However, the exact incidence of myopathy in individuals with hypovitaminosis D is unknown. The mechanism of HDM remains controversial, and it is still not clear whether vitamin D deficiency itself or in association with secondary hyperparathyroidism is the primary cause of muscle tissue and functional abnormalities. PTH production, induced by low vitamin D levels, may confer direct effects on skeletal muscles. Studies conducted in animal models have demonstrated that PTH stimulates muscle catabolism, reduction in calcium transport (calcium–ATPase activity), and impairment of energy availability (decrease in intracellular phosphate and mitochondrial oxygen consumption) and metabolism (decrease in creatinine phosphokinases and oxidation of long-chain fatty acids) in skeletal muscle.[12, 13]

It is important to evaluate vitamin D deficiency as a cause of myopathy in suspected cases. Severe vitamin D deficiency is easily treatable. Generally advocated treated strategy is to prescribe a loading dose (50,000 IU of oral vitamin D once a week for 2-3 months or three times weekly for one month). A previous analysis of multiple loading algorithms indicated that a minimum total dose of 6, 00,000 IU best predicted an end-of-treatment 25(OH)D concentration >30ng/ml. For mild-to-moderate deficiency (11-25 ng/ml), a shorter-term treatment or lower dose may be effective.[14] In cases with recurrent deficiency, maintenance daily dose of 800-2000 IU or more will be required.[15] Treatment using high-dose vitamin D for six months or more may be essential for full normalization of HDM.[16] The present case highlights the significance of considering treatable causes first in patients presenting with musculoskeletal symptoms.[17] A routine test for hypovitaminosis D should be considered in patients with musculoskeletal symptoms such as bone pain, myalgias, and generalized weakness; as there is an increased chance for misdiagnosing hypovitaminosis D-associated symptoms as fibromyalgia, chronic fatigue, age-related weakness or depression.[18] Various anecdotal reports indicate the occurrence of vitamin D deficiency in 80-90% of children and adults with pain, weakness, and myalgias.[19]

Conclusion

It is always worthwhile to look for common and treatable factors causing myopathy. HDM is a common cause for proximal muscle weakness. Raised ALP and PTH levels should always be worked up to diagnose vitamin D deficiency, which is easily treatable. Myopathy linked to vitamin D deficiency is completely reversible.

Competing interests
The authors declare that they have no competing interests.

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