Case Report

Vitamin D deficiency in a man with multiple myeloma

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Abstract

Context: Vitamin D deficiency is extremely common in multiple myeloma, and it represents a surrogate for clinical multiple myeloma disease status. Patients may complain of dull, persistent, generalized musculoskeletal aches and pains with fatigue or decrease in muscle strength. Case Report: A 63 year old male with multiple myeloma on Bortezomib presented with worsening generalized musculoskeletal pain, weakness, and multiple falls. On initial examination he was pale with a depressed affect. He had resting tremor, generalized bony tenderness, worse on movement and weight bearing, muscle weakness, and a waddling gait. His bone studies showed features of osteomalacia with a very low Vitamin D level of less than 20 nmol/L. He was treated with 3000 units of Vitamin D daily and physiotherapy. After 4 months, although his multiple myeloma deteriorated, there was a significant decrease in his generalized musculoskeletal pain. Conclusions: This case highlights that vitamin D deficiency is common in patients with multiple myeloma, and can cause generalized musculoskeletal pain and increase the risk of falls, yet it often goes unrecognized. In patients with non-specific musculoskeletal pain, and inadequate sun-exposure medical practitioners must have a high index of suspicion for vitamin D deficiency.

Keywords: Vitamin D deficiency, musculoskeletal pain, multiple myeloma.

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Introduction

Vitamin D deficiency is endemic in hospitalized patients with multiple myeloma and can predispose to many serious complications. Deficiency can cause osteomalacia and those patients can develop generalized musculoskeletal pain, proximal muscle weakness and increased risk of falls. In many cases, this may not be clinically detectable but are nonetheless present, or “subclinical”, and often go unrecognized.

Case Report

In June 2010, a 63 year old male with multiple myeloma presented with multiple falls and reactivation of herpes zoster. The patient was previously diagnosed with solitary plasmacytoma in 2001, which then progressed to smoldering myeloma in 2004. In 2007 the indolent version of his myeloma transformed to a more aggressive form of myeloma with non-specific musculoskeletal chest pain, anorexia, weight loss, and tumour-lysis requiring hospital admission and plasmapheresis. The patient was treated by Vincristine, Adriamycin, Dexamethasone and completed six induction cycles with an autologous stem cell transplant in June 2008 with high dose Melphalan. In 2009, the patient was treated with Lenalidomide and Dexamethasone salvage; however his disease was resistant to most standard immunomodulatory agents. Salvation presented itself in the form of a phase II study in investigating the role of Bortezomib with a new agent Vorinostat a histone deacetylase inhibitor in heavily pre-treated myeloma. The patient began therapy with Bortezomib in early march 2010. However, in June 2010 the patient was admitted after multiple falls and zoster reactivation including ophthalmic zoster of the right first and second trigeminal branches.
Despite of all the above management, there was a continuing downturn in his overall performance status over the period of 1 to 2 years with generalized musculoskeletal pain, worse on activity and weight bearing, and muscle weakness. His overall functional ability deteriorated markedly such that he became a major falls risk and suffered four falls whilst in hospital.

On examination he was pale with a depressed affect. The patient had resting tremor, generalized bony tenderness (worse on movement and weight bearing), muscle weakness, and a waddling gait. His bone studies showed features of osteomalacia with an elevated alkaline phosphatase at 270 U/L, very low Vitamin D level of less than 20 nmol/L, and a high intact parathyroid hormone at 16.0 pmol/L.

The patient was commenced on 3000 units of Vitamin D supplementation and physiotherapy. After 4 months, although his multiple myeloma deteriorated, there was a significant decrease in his generalized musculoskeletal pain. His bloods showed a normalized level of Vitamin D of 109 nmol/L and decrease in alkaline phosphatase to 182 U/L. He is currently undergoing palliative rehabilitation.

Discussion
Multiple myeloma is a malignant proliferation of plasma cells producing a monoclonal paraprotein and it is associated with end-organ. The cells may cause soft-tissue masses (plasmacytomas) and/or lytic lesions in the skeleton and they impair humoral and cell-mediated immunity [1, 2]. Skeletal complications are a major cause of morbidity in multiple myeloma (MM). These complications include hypercalcemia due to increased bone resorption, generalized bone loss, intractable bone pain. This is due to the lytic bone destruction as a consequence of an increase in osteoclastic lesions, and pathologic fractures at skeletal sites compromised by osteolytic lesions [1]. Bone pain is a common presentation in patients with multiple myeloma, particularly in the back or chest, and less often in the extremities, in approximately 60 percent of patients [2]. The pain is usually induced by movement and does not occur at night except with change of position. The patient's height may be reduced by several inches because of vertebral collapse [1-3].

Vitamin D deficiency is extremely common in multiple myeloma, with 40% of patients having vitamin D levels in the deficient range of levels less than 36 nmol/L and it represents a surrogate for clinical multiple myeloma disease status [3, 4]. Vitamin D and its metabolites have a significant clinical role in these patients because of their interrelationship with calcium homeostasis and bone metabolism and it is best measured using the serum 23-hydroxyvitamin D assay [5].

Vitamin D deficiency causes musculoskeletal pain [7]. It is presumed to begin with hypocalcemia, which stimulates parathyroid hormone secretion and sets in motion a cascade of biochemical reactions negatively affecting bone metabolism. An increase in the parathyroid hormone can diminish bone density (osteopenia) and/or more severely affect bone architecture (osteoporosis) and can lead to osteomalacia which generates pain in the periosteal tissues covering the skeleton [5, 7]. This explains why many patients with vitamin D deficiency may complain of dull, persistent, generalized musculoskeletal aches and pains. Myopathy also is part of the osteomalacic complex, fatigue or decrease in muscle strength, usually in lower limbs, may appear prior to any pain. In many cases involving pain and myopathy, defects of bone metabolism and osteomalacia may not be clinically detectable but are nonetheless present, or “subclinical” [2, 7].

Vitamin D deficiency is also common among hospitalized patients [8], and it is evident that people over age 63 years with low serum 23-hydroxyvitamin D concentrations (<23 nmol/L) are at greater risk for loss of muscle strength and muscle mass and for hip fractures [9]. Muscle biopsy in such people revealed atrophy of the fast twitch (type II) fibers. As type II fibers are first to be recruited to avoid falling, this observation may explain the increased falls risk in vitamin D deficient individuals [10].

Vitamin D supplementation may contribute to improved bone mineral density and muscle function and has shown to reduce falls risk by more than 20% and concentrations less than 40 nmol/L is associated with substantially poorer leg function [11, 12]. The fracture reduction is correlated with the dose of vitamin D, such that doses less than 800 IU are not effective [13, 14]. A randomized trial found a 30 percent reduction in fall incidence over five months comparing subjects taking placebo with those taking...
vitamin D 800 IU daily [13]. These observations suggest that, if used to prevent falls, the daily intake of standard supplemental vitamin D in older adults should be at least 700 to 800 IU and lower intakes of vitamin D are not as effective [13, 14].

While the daily requirement for vitamin D is 400–600 IU, a larger dose is needed to treat patients with deficiency. Larger doses of vitamin D are needed before a change in serum 23-OHD levels is seen [14]. This is due to the fact that vitamin D is distributed in the body fat compartment, which is larger than the plasma and extracellular fluid compartment. This may explain the delay seen with vitamin D supplements before normalization of serum 23-OHD levels. In moderate to severe deficiency supplementation with 3000-5000 IU (73–123 μg) per day for at least 6–12 weeks may be required followed by a maintenance dose of 1000 to 2000 IU to maintain normal physiological needs in otherwise healthy individuals [14]. In addition to falls reduction, there is evidence that vitamin D modulates several other critical cellular processes, including inhibition of carcinogenesis by induction of differentiation, inhibition of proliferation and angiogenesis, and promotion of apoptosis [10], and an increase of 23 nmol/L in 23-hydroxy-vitamin D levels was associated with a 17 percent lower multivariate total cancer risk [15].

Conclusion
This case highlights that vitamin D deficiency is common in patients with multiple myeloma, and can cause generalized musculoskeletal pain and increase the risk of falls, yet it often goes unrecognized. Vitamin D deficiency is also common in hospitalized patients and can have numerous negative effects on their well-being and recovery leading to prolonged hospital stay. Therefore, in patients with non-specific musculoskeletal pain, and inadequate sun-exposure physicians and general practitioners must have a high index of suspicion for vitamin D deficiency.

References
1. Roodman GD. Myeloma bone disease: pathogenesis and treatment. Oncology 2003; 19:983-984.
2. Ng AC, Kumar SK, Rajkumar SV, et al. Impact of vitamin D deficiency on the clinical presentation and prognosis of patients with newly diagnosed multiple myeloma. Am J Hematol 2009; 84(7): 397-400.
3. Diamond T, Golombick T, Manoharan A. Vitamin D status may affect the skeletal complications of multiple myeloma. Am J Hematol 2010; 85 (4): 302-303.
4. Badros A, Goloubeva O, Terpos E, Milliron T, Baer MR, Streeten E. Prevalence and significance of vitamin D deficiency in multiple myeloma patients. Br J Haematol 2008; 142 (3): 492-494.
5. Holick MF. Vitamin D deficiency. N Engl J Med 2007; 357(3): 266-281.
6. Bikle D. Nonclassic actions of vitamin D. J Clin Endocrinol Metab 2009; 94(1): 26-34.
7. Visser M, Deeg DJ, Lips P. Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab 2003; 88: 37-66.
8. Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. N Engl J Med 1998; 338: 777-783.
9. Bischoff-Ferrari HA, Willett WC, Wong JB, et al. Prevention of nonvertebral fractures with oral vitamin D and dose dependency: a meta-analysis of randomized controlled trials. Arch Intern Med 2009: 169 (6): 551-561.
10. Boland R. Role of vitamin D in skeletal muscle function. Endocr Rev 1986;7: 434-448.
11. Souberbielle JC, Friedlander G, Kahan A, et al. Evaluating vitamin D status, implications for preventing and managing osteoporosis and other chronic diseases. Joint Bone Spine 2006; 73: 249-233.
12. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, et al. Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomised controlled trials. BMJ 2009; 339:b3692.
13. Broe KE, Chen TC, Weinberg J, et al. A higher dose of vitamin d reduces the risk of falls in nursing home residents: a randomized, multiple-dose study. J Am Geriatr Soc 2007; 55: 204-209.
14. Sanders KM, Stuart AL, Williamson, EJ, et al. Annual high-dose oral vitamin D and falls and fractures in older women: a randomized controlled trial. JAMA 2010; 303:1815-1822.
15. Giovannucci E, Liu Y, Rimm EB, et al. Prospective study of predictors of vitamin D status and cancer incidence and mortality in men. J Natl Cancer Inst 2006; 98:451-459.