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Case Report

Nutritional Osteomalacia

Substantial Clinical Improvement and Gain in Bone Density Posttherapy

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Abstract

A 52-yr-old white female presented with worsening low back and hip pain, associated with lower limb proximal muscle weakness and a waddling gait. Her laboratory evaluation revealed hypocalcemia, hypophosphatemia, a very low 25-hydroxyvitamin D level of less than 5 ng/ml, and a bone mineral density in the osteoporotic range. Her laboratory studies were consistent with osteomalacia, although this diagnosis was not established by histomorphometry. She avoided dairy products, spent little time outdoors, and when she went out, she covered her face, arms, and legs. She was on no medications. Her workup for malabsorption including sprue was negative. She was treated with calcium plus high-dose vitamin D 600,000 IU intramuscularly twice within 2 mo and had an impressive clinical improvement. Her difficulty with ambulation improved within 1 wk of start of therapy. Her bone mineral density increased by 40% at the spine and 35% at the hip at 4 mo of therapy, by 63% and 39% at 10 mo, and by 62% and 52% at 15 mo at these sites, respectively. Treatment of osteomalacia is extremely rewarding, with dramatic clinical improvement and normalization of bone mineral density.

Key Words: Vitamin D deficiency; nutritional osteomalacia; bone mineral density, bone pain, weakness.

Introduction

Vitamin D plays a critically important role in the mineralization of the skeleton at all ages. As the body depletes its stores of vitamin D, the efficiency of intestinal calcium absorption decreases from approximately 30% to 50%, to no more than 15%. This results in a decrease in the ionized calcium concentration in the blood, which is sensed by the calcium receptor in the parathyroid glands, thus responding by increasing the synthesis and secretion of parathormone (PTH) *(1,2)*. The increment in PTH levels result in renal calcium conservation and play an active role in mobilizing stem cells to become active calcium-resorbing osteoclasts *(3)*. Thus, chronic increments in PTH levels with either primary or secondary hyperparathyroidism result in bone loss that is more selective at cortical sites, such as the forearm *(4,5)*. Most studies evaluating the effects of parathyroidectomy in hyperparathyroidism on total-body calcium, bone mineral density (BMD), or bone mineral content (BMC) demonstrate increments in spine and hip BMD of 7–13% *(6–8)*. Much higher gains in BMD have been observed with the

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correction of secondary hyperparathyroidism such as is observed in patients with osteomalacia, either secondary to phosphate or vitamin D depletion. Indeed, a patient on a high dose of antacids with secondary phosphate depletion was treated with vitamin D and phosphate and had an increase of BMD of 31% and 23.6% at the spine and hip, respectively *(9)*. Similarly, a 39-yr-old black female with osteomalacia secondary to partial gastrectomy had an increase in her BMD of 23.7% and 36.2% at the spine and femoral neck, respectively, after treatment with vitamin D for 2 yr *(10)*. We describe a case of nutritional osteomalacia who experienced even more substantial and rapid increments in her BMD that actually normalized within 10 mo of therapy with calcium and vitamin D.

Case Report:

A 52-yr-old premenopausal white female presented to the American University of Beirut Medical Center in June 1998 with a 1-yr history of low back pain, hip pain, mainly on weight bearing and walking, and inability to get up from the chair or climb up stairs. The pain and weakness were increasing progressively and interfering with her daily activities, until the last few weeks before admission when she became homebound. She denied any weakness in her upper extremities. The patient claimed that her dietary habits were normal except for a low dairy product intake since she was very young. She was a nonsmoker, did not drink alcohol, and was not taking any calcium or vitamin D supplementation. She avoided dairy products, spent little time outdoors, and when she went out, she covered her face, arms, and legs. She denied any history of amenorrhea, and her menstrual periods were normal. She was G12P6A6; she breast-fed all her children. She denied any history of diarrhea, or intestinal surgery, or nephrolithiasis. She was never on any therapy with thyroid hormone, anticonvulsants, or antacids. Her past medical history revealed a chronic dermatologic problem (dyshidrotic eczema over soles) since 1970, for which she took a steroid injection once yearly.

On physical examination, the patient's vital signs were normal; her height and weight were 58.5 in. and 180.5 lbs, respectively. In general, her appearance was that of a healthy woman with no cushingoid features. She had diffuse musculoskeletal tenderness and was unable to stand from sitting position. She had exaggerated deep tendon reflexes. Bilateral multiple deeply sealed vesicles with exfoliations on the soles were noted.

Nonfasting laboratory studies were as follows: calcium 6.9 mg/dL (8.5–10.5), phosphorus 2.5 mg/dL (2.9–5.0), alkaline phosphatase 820 IU/L (35–120), calculated free calcium 4.0 (4.5–5.5), creatinine 0.2 mg/dL (0.6–1.4), magnesium 1.92 mg/dL (1.6–2.5), total protein 81 g/L (62–83), albumin 38 g/L (36–54), globulin 43 g/L (20–30), sodium 142 meq/L (135–145), potassium 3.7 meq/L (3.5–5.1), chloride 106 meq/L (98–109), CO_2 27 meq/L (24–30); the serum intact parathyroid hormone (PTH) was measured with the use of ELSA-PTH immunoradiometric assay (Cis Bio International, Gif-sur-Yvette, France) and the 25-hydroxyvitamin D [25(OH)D] by a competitive protein binding assay with the use of the Diasoren Incstar kit (Incstar, Stillwater, MN). The PTH was 250 pg/mL (8.0–76.0), 25(OH)D < 5 ng/mL (8–76), repeated < 5 ng/mL. The D-xylose test was normal, stools for Sudan stain were negative, and serum antiendomisial antibodies were negative. Gastroscopy revealed an incompetent lower esophageal sphincter, nonerosive pangastritis, and a biopsy from the distal duodenum revealed no sprue. X-rays of the pelvis, hips, and dorsal spine revealed anterior osteophytes and exaggeration of the dorsal kyphosis but no fractures. Skull X-rays showed multiple lucent areas in the skull vault and parietal areas, and sclerosis and opacification of the mastoid air cells bilateral. The left-hand X-ray revealed no gross abnormalities. Bone densitometry of the spine, hip, and forearm was performed by dual-energy X-ray absorptiometry (DXA) using Lunar DPX-L and revealed osteoporosis in the spine with a BMD of 0.90 g/cm^2 (*T* score = –2.46), osteopenia in the femoral neck with BMD of 0.60 g/cm^2 (*T* score = –2.42), and at the forearm with a BMD of 0.626 g/cm^2 (*T* score = –1.23).

A clinical diagnosis of osteomalacia was made because of the low calcium, low phosphorus, low 25(OH)D, and the high PTH and alkaline phosphatase levels. She was immediately started on calcium carbonate 600 mg po TID, and when the 25-hydroxyvitamin D levels became available, she

Table 1
Response of Biochemical Variables to Calcium and Vitamin D Replacement

	Calcium (mg/dL)	Phosphorus (mg/dL)	Alkaline phosphatase (IU/L)	25(OH)D_3[a] (ng/mL)	PTH[a] (pg/mL)
June 98	6.9	2.5	850	1	250
July 98	9.3	3.9	543	10.8	255.5
March 99	9.4	3.0	227	15	134
Sept. 99	9.4	2.7	128	NA[b]	NA[b]

[a] 25(OH)D denotes 25-hydroxyvitamin D, normal range 16–36 ng/mL; PTH denotes intact parathyroid hormone level, normal range 8–76 pg/mL.
[b] NA: not available.

was given an intramuscular injection of vitamin D (Sterogyl H, 600,000 IU/ampoule, Roussel, France). Within 1 wk of hospitalization, she started to feel much better and stronger, and was able to stand up easily. At discharge, she was able to walk for a short distance in the room without difficulty. The serum calcium level 5 d after admission was 8.0 mg/dL. She was discharged on calcium phosphate 1 tablet TID plus vitamin D 1500 IU daily. A repeat of 25(OH)D_3 done in July 1998 was still low (10 ng/dL), and she was given another injection of vitamin D 600,000IU and continued on the same Ca/vitamin D supplementation daily. The evolution of her laboratory studies are shown in Table 1. Repeat bone mineral densities of her spine and hip revealed substantial increments at 4, 10, and 15 mo of therapy, as shown in Figure 1. The total gain in BMD after 10 mo were 63% and 39%, respectively, and at 15 mo, 62% and 52%, respectively, with complete normalization of the spine and hip bone mass. There was a decrement in forearm BMD of 10.9% at 10 mo and 10.2% at 15 mo.

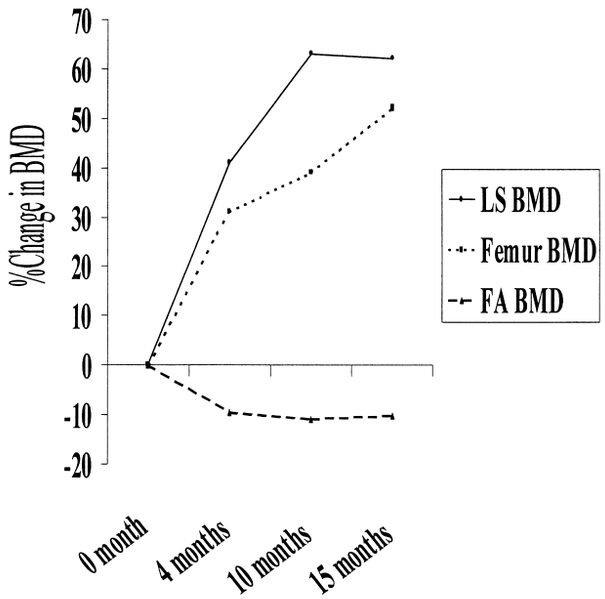

Fig. 1. Serial percentage changes in bone mineral density (BMD) at the lumbar spine (LS), femoral neck (femur), and forearm (FA) after therapy with a high dose of vitamin D.

Discussion

The main natural sources of vitamin D in foods are fatty fish and fish liver oils. Otherwise, fortification of foods such as milk has been necessary to prevent the occurrence of vitamin D deficiency in the United States *(11).* Egg yolks may contain a variable amount of vitamin D, depending on the diet of the laying hens. Consumption of unfortified foods in an environment with reduced exposure to sunlight can lead to vitamin D deficiency in many developing countries, as we have recently reported on in a substantial number of premenopausal healthy women *(12).* This is especially true in Asian women who wear veils, consume unfortified foods when pregnant, do not consume supplements or vitamins containing vitamin D, and nurse their infants. Our case and a previous report *(10)* showed the rapid

improvement and favorable outcome in patients diagnosed with osteomalacia when the vitamin D deficiency is adequately replaced. Our case is unique, however, in the magnitude of bone mineral density gain over a short period of time. Specifically, the increments in bone mineral density observed in our case after 4 mo of initiating therapy exceeded those observed in the previous case report after 2 yr of calcium and vitamin D supplementation *(10)*. Furthermore, the increments in BMD in our case were substantial enough so as to normalize bone mass in less than 1 yr. This emphasizes the importance of seeking secondary causes of bone loss in order to optimize therapy. Significant increments in bone mass were also noted in a recently reported case of treated oncogenic osteomalacia *(13)*.

We recognize that our working diagnosis of osteomalacia is a presumptive one based on the biochemical values of a low calcium, low phosphorus, low 25-hydroxyvitamin D level, and high alkaline phosphatase and PTH levels, all of which improved with treatment with calcium and vitamin D. However, histomorphometry, the established means to confirm such a diagnosis, was not performed in our patient because of the consistent biochemical response to therapy. Bone mineral density cannot differentiate osteomalacia from osteoporosis, as in both entities, the bones are demineralized, and bone mineral density is therefore decreased. The typical bone density findings in primary and secondary hyperparathyroidism are those of selective cortical bone loss with bone density being the lowest at the forearm *(4,5)*. This is different from our case where bone density was the lowest at both the spine and the hip and least affected at the forearm, possibly reflecting axial demineralization resulting from osteomalacia more than peripheral demineralization resulting from hyperparathyroidism. The decrements in forearm bone mass are clinically significant and partially reminescent of what has been observed in patients treated with sodium fluoride (NaF) *(14)*. In such patients, there was an increase in spinal bone mass of 35% over 4 yr, and of 10–12% at the hip with a cumulative decrement of 4% at the forearm *(14)*, leading to the concept that NaF increases spinal bone mass at the expense of peripheral bone mass. It is therefore possible in our patient that the very rapid mineralization of the axial skeleton (spine and hip) occurred at the expense of peripheral skeleton (forearm) despite replacement with calcium at an absolute dose that exceeds the requirement for a premenopausal women *(15)*, hence the potential need for a more generous supplementation with calcium in patients suffering from osteomalacia and/or more gradual correction of the vitamin D deficiency to minimize the observed redistribution phenomenon.

The treatment of osteomalacia is rewarding with rapid clinical response. Whereas standard therapy of osteoporosis results in maintenance or mild increments in bone mass, it usually does not normalize. Our case illustrates that treatment of osteomalacia can result in dramatic clinical improvement in parallel with substantial increments in bone mass that actually normalized within a year of installation of vigorous therapy with calcium and vitamin D.

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