Bone densitometry in patients with osteomalacia: is it valuable?

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Summary

Osteomalacia is a generalized bone disorder characterized by impairment of mineralization, leading to accumulation of unmineralized matrix or osteoid in the skeleton. The clinical features of osteomalacia include musculoskeletal vague pain and muscle weakness.
In its mild and early stages, osteomalacia may be misdiagnosed with variety of musculoskeletal diseases including osteopenia and osteoporosis, and for early diagnosis high rate of suspicion of osteomalacia is necessary.
Our purpose was to determine the amount of bone mineral density (BMD) in patients with osteomalacia and to evaluate the efficiency of bone densitometry in these patients.
Diagnosis of our patients was based on history, physical, laboratory and radiological findings and in three patients with bone biopsy and histological approval.
BMD (gm/cm^2) at the lumbar vertebrae (L2-L4) and femoral neck were measured by dual X-ray absorptiometry in 20 patients with osteomalacia (16 females and 4 males, age range 20 to 60 years, mean 39 years) before treatment, comparing with 28 matched healthy individuals, and their T scores were evaluated according to WHO criteria for the diagnosis of osteopenia and osteoporosis. 14 patients with osteomalacia (70%) had BMD in amount of osteoporosis in the lumbar spine, and 12 patients with osteomalacia (60%) had BMD in amount of osteoporosis in their femoral neck. 50% of the patients had T≤ -3.
We concluded that bone densitometry may detect osteoporosis in up to 70% of patients with osteomalacia. Middle aged individuals with significant osteoporosis should be evaluated for osteomalacia, beside other causes of secondary osteoporosis. Measurement of BMD in patients with osteomalacia is helpful for assessment of the severity of bone condition and following management.

KEY WORDS: osteomalacia; bone mineral density; densitometry; osteoporosis; Vitamin D.

Introduction

Osteomalacia is an important metabolic bone disease that results from chronic and severe depletion of vitamin D or phosphate of any cause after cessation of growth. Vitamin D or phosphate deficiency lead to defective bone mineralization and generalized or localized vague bone pain in different parts of the skeleton and/or proximal muscle weakness (1). Osteomalacia is more common in regions that sun exposure is low because of long winters with early sunsets or use of traditional long garments. These regions include central and southern areas of Argentina, Middle Eastern and Asian countries (2, 3). Because of various clinical manifestation of this disorder, in its mild and early stages, it may be misdiagnosed with variety of musculoskeletal diseases like osteoporosis, particularly in the elderly and sometimes bone biopsy may be necessary (2-5). For early diagnosis high rate of suspicion of osteomalacia is necessary, and there is no specific single screening blood test for diagnosis (2).
Our purpose in this study was to determine the amount of bone mineral density (BMD) in patients with osteomalacia and to evaluate the efficiency of bone densitometry as a paraclinical modality along with other usual measures in diagnosis of these patients.

Methods

In a prospective study 20 consecutive patients with osteomalacia diagnosed in our rheumatic diseases unit during last four years and 28 matched healthy individuals enrolled for BMD measurements (gm/cm^2) of the lumbar vertebrae (L2-L4) and femoral neck by dual X-ray absorptiometry (LUNAR-DPXIQ machine, USA) and their T- Scores were evaluated before beginning the treatment of the patients. The diagnosis of osteomalacia was based on history, physical examination, radiological findings, and laboratory results including serum calcium, inorganic phosphorus, alkaline phosphates, 25 hydroxy Vitamin D and PTH. In 3 patients bone biopsy was also performed with histological confirmation. The T score of these two groups were evaluated according to the World Health Organization criteria for the diagnosis of osteopenia and osteoporosis (6). The results were statistically analysed by SPSS software version 11.5, and the P value less than 0.05 considered to be significant.

Results

Of 20 patients with osteomalacia 16 were females and 4 were males with mean age of 39 years (ranged 20 to 60 years) and 5 females were in post menopausal years. Of 28 healthy individuals 23 were females and 5 were males with mean age of 39.4 years (ranged 20 to 60 years) and 8 females were in postmenopausal years. The serum bone profile and imaging survey of the patients showed typical biochemical and imaging abnormalities of osteomalacia. The mean serum calcium and phosphorus of the patients were, 8.86 mg/dl (Normal 8.6-11) and 1.78 mg/dl (Normal 2.5-4.5) respectively and the mean alkaline phosphatase was 2.4 times of the mean normal value. The 25 hydroxy Vitamin D mean level was less than 10 ng/ ml (normal 18-45). In patients group the bone density of the lumbar spine and femoral neck was markedly decreased. Mean T score at lumbar vertebrae was -3.005± 1.28, with 70% similar to osteoporosis (T≤-2.5) and at femoral neck was -3.009±1.34, with 60% similar to osteoporosis. 50% of patients had T score ≤-3. A patient with osteomalacia had normal BMD at lumbar spine (T> -1) and another patient had normal BMD at femoral neck. The BMD of other patients at two standard measured areas were in the range of osteopenia. Four patients had other diseases at the time of diagnosis of osteomalacia, one with hyperthyroidism, one with spastic paraparesis, and two patients with malabsorption syndromes. In control group the mean T score at lumbar spine was +0.265±1.08 and at femoral neck was +0.225±0.89. The P value of the BMD results in patients and control group, at lumbar spine and femoral neck was less than 0.001.The results of the BMD measurements in patients with osteomalacia at the time of diagnosis and control group are summarized in Table 1.

Discussion

Osteomalacia is defined as mineralization defect of bone matrix, leading to low mineral content of the skeleton. The main cause of osteomalacia is vitamin D deficiency that can be due to reduced cutaneous production of Vitamin D. It may also occur with nutritional deficiency, malabsorption, chronic liver diseases, long term anticonvulsive therapy, and also phosphate deficiency (5). People who are at risk for Vitamin D deficiency due to lack of exposure to sunlight are housebound elderly and immigrants in northern Europe (4).

Although we live in a country with enough sunlight in most months of the year, the religious dress codes of our women may be effective in their low serum Vitamin D and ultimately osteomalacia. Among 50 veiled young women living in Kuwait, 25- OHD levels were lower than nonveiled women (7). In another study in Turkey veiled women had significantly lower mean 25-OHD concentration than unveiled women (8). In spite of enough sunlight in the region, about 80% of healthy Saudi pre and post menopausal women had vitamin D deficiency (9).

Osteomalacia is not a rare disease. Its importance has increased because of the rising incidence of Vitamin D deficiency (3). Several investigators have shown that osteomalacia accurses in about 4% of elderly people admitted to hospitals (10-12).

A histological study suggested that up to 40% of patients with femoral fracture have evidence of osteomalacia (13). In another study from Finland, osteomalacia was found in 24% of 245 consecutive hip fracture patients (14).

Mild and early manifestations of osteomalacia may be overlooked and misdiagnosed as osteopenia and osteoporosis. Inappropriate use of fluoride (15) and bisphosphonates such as etidronate (16) and pamidronate (17) in patients with undiagnosed osteomalacia may be associated with focal demineralization bone defects.

Although it is reported that BMD may be normal or slightly reduced in patients with osteomalacia (18) many investigators have shown, similar to our results, that bone density is markedly reduced in osteomalacic bone (19, 20).

In the elderly with osteomalacia, the reduction of BMD may be a consequence of an associated osteoporosis (5), but in middle aged and young individuals with a vague bone pain and unexpected low BMD the probability of occurrence of osteomalacia should be considered and the necessary investigation should be carried out to achieve the exact diagnosis. Most of our patients with osteomalacia in this study were young and middle aged individuals (mean age of 39).

Although the most reliable diagnostic test for osteomalacia is bone biopsy, Cosman et al. have demonstrated a significant correlation between quantitative histological measurement and BMD of the spine and proximal femur in patients with various metabolic bone diseases including osteomalacia (21). We had only 4 patients with diseases that may predispose to osteomalacia (hyperthyroidism, spastic paraparesis and two with malabsorption syndromes). Low serum Vitamin D level and BMD have been emphasized recently as a result of malabsorption syndromes (22, 23).

Table 1 - Comparison of T-scores of bone densitometry in our patients with osteomalacia and healthy individuals.

Parameters	Osteomalacia cases	Healthy cases	P Value
No. Investigated	20	28	--
Female/Male	16/4	23/5	0.99
Age range year &(mean)	20-60 (39±14.27)	20-60 (39.27±13.09)	0.94
Lumbar spine (L2-L4) T score range & (mean)	-0.8 to -5.2 (-3.005±1.28)	+2.7 to -1.3 (+0.265±1.08)	0.001
Femoral Neck T score range & (mean)	-1.0 to -5.4 (-3.009±1.34)	+2.1 to -1.7 (+0.225±0.89)	0.001

Getting over the diagnosis of mild or early stages of osteomalacia in middle aged individuals with unexpected low BMD is important, particularly in management intervention. Unlike the management of primary osteoporosis, higher doses of calcium and Vitamin D and avoidance of anti resorptives and other unnecessary medications can improve the condition of osteomalacic patients in few months.

Patients with osteopenia and osteoporosis who feel wellbeing in a few months following treatment with Vitamin D and Calcium, may be the cases of subclinical osteomalacia or pre-osteomalacia.

One of the essential biological activities of Vitamin D in the etiology of osteomalacia is the regulation of intestinal calcium and phosphate absorption (24, 25). The suggestion of increasing doses of Vitamin D for treatment of patients with osteoporosis in recent years (26-28) is also beneficial for accompanying some cases of subclinical osteomalacia.

Serial BMD measurements have been suggested to be of value in monitoring the therapeutic response in osteomalacia (19, 20, 29). It is noted that with proper treatment of osteomalacia, normalization of BMD of vertebrae and hip is expected to be reached in up to 12 months (29, 30).

Conclusions

Based on our investigation, low BMD in amount of osteoporosis results by bone densitometry may be detected in up to 70% of patients with osteomalacia. Middle aged individuals with significant low BMD should be evaluated for osteomalacia, beside other causes of secondary osteoporosis. It is important to distinguish between primary osteoporosis and secondary osteoporosis due to osteomalacia, because management and following its effects is different in these two conditions.

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Conflict of interest

All authors have no conflicts of interest.

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