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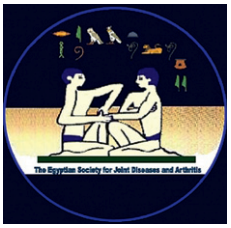

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ORIGINAL ARTICLE

Impaired bone formation and osteoporosis in postmenopausal elderly onset rheumatoid arthritis patients

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KEYWORDS

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Abstract *Introduction:* Bone metabolism may be uncoupled in postmenopausal rheumatoid arthritis (RA). Osteoporotic fracture in RA is highest for the hip especially in elderly women.

Aim of the work: To detect the bone mineral density (BMD) and markers of bone turnover in postmenopausal RA patients and study the influence of age at disease onset. Correlation with clinical and laboratory manifestations and disease activity were considered.

Patients and methods: Sixty postmenopausal RA patients were recruited into two groups, group I: 30 elderly onset (EORA) and group II: 30 young onset (YORA) patients. Thirty age and sex matched healthy subjects served as control. Full history taking, clinical examination, relevant investigations including calcium, phosphorus, total alkaline phosphatase (ALP), bone specific alkaline phosphatase (BALP), osteocalcin (OC), and N-terminal cross-linked telopeptides of type I collagen (NTX) were measured and BMD assessed by DEXA in all patients and control. Disease activity score in 28 joints (DAS-28) was calculated.

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Results: The NTX was remarkably increased and the BMD decreased in RA patients. Osteocalcin in RA was 3.87 ± 1.15 ng/ml being obviously lower in EORA patients compared to YORA and control. In EORA, a significant correlation was present between the ALP and OC (r 0.41, p 0.025) and the NTX and BALP (r 0.46, p 0.011) and a negative correlation between the hip BMD and DAS-28 (r −0.43, p 0.019).

Conclusion: Impaired bone formation and uncoupling of bone turnover are more evident in postmenopausal EORA patients which form a risk predictor of fracture hip in this subgroup of patients.

1. Introduction

Population-growth in the elderly and the development of new therapeutic agents for rheumatoid arthritis (RA) contributes to an increase in the number of elderly patients with RA. Elderly-onset RA (EORA) is defined as RA developing after the age of 60 years [1,2]. With the increasing life expectancy, osteoporosis is becoming a major worldwide health problem being larger in developing countries including Egypt where the prevalence of low bone mass is increased with a very high prevalence of vitamin D insufficiency. Even in a sunny country, hypovitaminosis D is common which is probably explained by a low intake [3]. Little is known about the differences in the immunopathogenesis between EORA and younger-onset RA (YORA) and the factors responsible for their clinical characteristics [4]. At similar disease duration, EORA differs from YORA by a more balanced gender distribution, a higher frequency of acute onset and systemic features, more frequent involvement of the shoulder girdle and higher disease activity [1,5]. In EORA, the disease phenotype is changed compared to YORA highlighting the importance of aging on the immune system [6]. Cause and effect of comorbid diseases such as osteoporosis and cardiovascular disease are points of interest especially in EORA [7].

Osteoporosis is a systemic disease characterized by compromised bone mass and strength, predisposing to an increased risk of fracture [8]. One in 3 women older than 50 years will eventually experience osteoporotic fractures [9]. While the level of bone mass can be estimated by measuring bone mineral density (BMD) using dual energy X-ray absorptiometry (DEXA), its measurement does not capture all the risk factors for fracture. Quantitative changes in skeletal turnover can be assessed easily and non-invasively by the measurement of serum and urinary biochemical markers; the most sensitive markers include serum osteocalcin (OC) and bone specific alkaline phosphatase (BALP) for bone formation and the cross linked N-telopeptides of type I collagen (NTX) for bone resorption [10]. In postmenopausal osteoporosis, abnormal levels of bone markers are associated with an increased risk of fracture. The combined use of BMD measurement and biochemical markers is helpful in risk assessment [10]. Any process that increases the rate of bone remodeling, results in net bone loss over time [11]. Furthermore, in periods of rapid remodeling, as postmenopause, bone is at an increased risk for fracture because the newly produced bone is less densely mineralized, the resorption sites are temporarily unfilled, and the isomerization and maturation of collagen is impaired [12].

Markers of bone formation as OC and ALP are important for promoting vulnerability to hip fracture [13,14]. Bone metabolism may be uncoupled in chronic RA and bone formation appears to be reduced, partly reflecting disease activity, whereas resorption is increased only in steroid users in postmenopausal RA patients [15]. Changes in the levels of bone turnover markers may reflect fracture risk and therapeutic success even before changes in BMD become apparent [16]. Alkaline phosphatase lacks sensitivity and specificity for osteoporosis, because it can be elevated or decreased with many diseases and is increased with aging [16]. In adults with normal liver function, approximately 50% of total ALP activity arises from the liver and 50% from bone. The development of bone-specific ALP improved specificity and sensitivity; however, changes in BALP can lag by several weeks [17]. Serum markers of bone resorption are useful measures in postmenopausal osteoporosis, especially NTX which shows lower variability among patients [18], is the best marker for assessing the bone metabolic state and is the best predictor for the rate of bone loss or fracture risk [19].

The aim of the present study was to detect the BMD and markers of bone turnover; bone formation (OC and ALP both total and bone specific) and bone resorption (serum NTX) and correlate the findings with clinical manifestations, laboratory findings and disease activity in elderly and younger onset RA patients in order to find a possible impact of the age of disease onset on osteoporosis.

2. Patients and methods

Sixty postmenopausal RA patients were included in the current study with definite RA diagnosed according to the 2010 ACR/EULAR classification criteria for RA [20] attending the Rheumatology and orthopedic surgery outpatient clinics of Cairo University Hospitals. Patients were recruited into two groups, group I included 30 elderly onset and group II, 30 young onset RA. Patients who had concurrent medical conditions known to affect bone metabolism (including renal or liver disease, malignancy, thyroid or other endocrine disorders) were excluded. All the patients were veiled house wives that were not sufficiently exposed to the sun and not receiving any vitamin D supplementation. Full history taking, thorough examination, laboratory and relevant radiological investigations as well as DEXA were performed for all patients. The diagnosis of osteoporosis was based on the World Health Organization criteria [21] for osteoporosis. BMD was quantified by DEXA (lunar, prodigy 10041) at lumbar level (L2–L4), at the hip level (femoral neck and total hip) and at the distal forearm (distal radius and ulna). Data were obtained for BMD (g/cm^2), T score (deviation with respect to peak bone mass) and Z score (deviation with respect to age-matched normal values). Complete blood count, Erythrocyte sedimentation rate (ESR), total serum calcium, phosphorus, total alkaline