Bone Involvement and Osteoporosis in Mastocytosis

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KEYWORDS

• Mastocytosis • Osteoporosis • Osteosclerosis • Fracture • Bone mineral density
• Bone turnover markers

KEY POINTS

- Bone involvement is frequent in patients with systemic mastocytosis.
- Osteoporosis is the most prevalent bone manifestation, but diffuse osteosclerosis or focal osteolytic or osteosclerotic lesions are not infrequent.
- The risk of osteoporotic fractures is high, especially at the spine and in men.
- Routine measurements of bone mineral density and vertebral morphometry are warranted.
- The bone turnover markers indicate involvement of complex bone metabolism in mastocytosis-related manifestations.
- Bisphosphonates represent the first-line treatment for mastocytosis-related osteoporosis.

EPIDEMIOLOGY

Bone manifestations are one of the frequent symptoms of systemic mastocytosis (SM), particularly in adults. Patients may present with poorly localized bone pain, diffuse osteopenia or osteoporosis with fragility or pathologic fractures, diffuse osteosclerosis, or both focal osteolytic and osteosclerotic bone lesions.

SM has long been identified as a potential cause of osteoporosis. Nevertheless, until recently the bone involvement frequently has been described only in case reports or in small groups of patients.[1–14] In recent years studies on larger numbers of patients[15–18] and use of the dual X-ray absorptiometry (DXA) technique, which is universally accepted as the gold standard for assessing bone mass, have become available.[19]

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According to the traditional World Health Organization (WHO) criteria (T score, standard deviation [SD] below the mean of young healthy adults <−2.5),[19] osteoporosis ranged from 18% to 31% (**Fig. 1**). However, in these studies the reports also included elderly patients, so the real incidence of mastocytosis-related osteoporosis remains unclear. In previous published experience[17] the authors decided, in accord with guidelines of the International Society for Clinical Bone Densitometry,[20] to use the Z score (SD below the age- and gender-matched mean reference value) in addition to the WHO osteoporosis definition based on the T score. The threshold for that value to diagnose mastocytosis-related low bone mineral density (BMD) was set at less than −2, similar, for example, to what has been done for bone mineral classification in cystic fibrosis.[21] Adopting the traditional WHO criteria, osteoporosis was found in 20% of patients with indolent SM (ISM), whereas with the more accurate criteria, mastocytosis-related low BMD was found in 9% of women and 28% of men.[17]

The higher prevalence of osteoporosis in men compared with women, recently confirmed by others,[18] is somewhat consistent with the 9% prevalence of mastocytosis observed in bone biopsies in men with idiopathic osteoporosis.[22]

The percentage of bone involvement in 'the authors' series of ISM was 36%, lower than that reported by Barete and colleagues[16] (46%), who included a higher number of SM variants associated with a poorer prognosis.

Also observed was that patients without skin involvement, 55% versus only 5% in the study of Barete and colleagues,[16] have the same risk of osteoporosis as patients with skin lesions[17]: this is an important issue because in the absence of trigger factors for anaphylaxis, osteoporosis might be the only manifestation of a latent ISM. ISM without mastocytosis in the skin might be a challenge for the physician,[23] and the prevalence is possibly underestimated.[24] The authors' study indicates that osteoporosis of unknown etiology should lead to the suspicion of bone marrow mastocytosis. Moreover, the Z score at the total hip was significantly lower in those patients who did not have previous anaphylaxis when compared with those who did. This finding might simply reflect an earlier diagnosis in the latter group of patients.[25]

A recent update of data from this ISM cohort confirmed the results of the previous analysis carried out on a smaller group. The authors have records from 199 patients (81 women, mean age 53 years, age range 23–84 years; 118 men, mean age 49 years, age range 20–82 years). Among these subjects 65% had anaphylactic reaction to hymenoptera bite or drugs, and skin involvement was evident in 51%. Serum tryptase level higher than 20 μg/L was observed in 70% of cases, whereas in 9 patients it was below the more restrictive threshold of 11.4 μg/L. Osteoporosis, defined by OMS criteria (T score <−2.5), was documented more frequently in women (**Fig. 2**), but on average they were older than the men and most of them were already postmenopausal. Indeed, lower lumbar or femoral BMD, in comparison with age-matched and

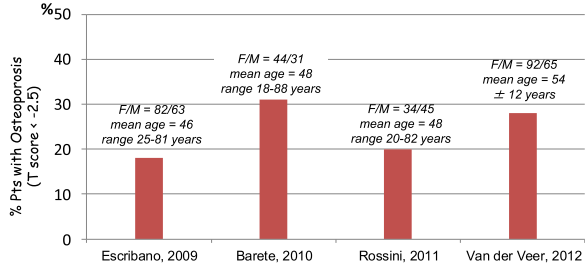

Fig. 1. Prevalence of osteoporosis in the largest available studies.