Skeletal implications of isolated bone marrow mastocytosis (reply)
Indolent systemic mastocytosis without skin involvement *vs.* isolated bone marrow mastocytosis (reply)

We are very grateful to Dr. Makras and Dr. Luis Escribano *et al.* for their comments about our letter "Isolated bone marrow mastocytosis: an underestimated subvariant of indolent systemic mastocytosis".[1]

The request of Dr. Makras for more information on skeletal involvement, which was not included in the objectives of our letter, is highly motivated but the response is complex so we decided that these data deserve a separate paper already submitted and under revision. Briefly, a complete bone evaluation (lumbar spine and proximal hip dual X-ray absorptiometry and spine X-ray) was performed in 72 patients with systemic mastocytosis (38 men and 34 women, mean age 46 years, range 20-82 years). After exclusion of concomitant diseases, a diagnosis of osteoporosis according to the World Health Organization (WHO) definition[2] (T-score < -2.5) was made in 14 patients (19.4%) (7 men and 7 women), more frequently at spine (18.1%) than at total hip (2.8%). "Mastocytosis-related osteoporosis" (Z-score at either the spine or the total hip <-2 and/or vertebral fractures) was found in 25 of 72 (34%) patients (24% in women, 45% in men); 13 of them were under 50 years of age. The incidence of osteoporosis and/or vertebral fractures was similar in patients with or without the typical skin lesions (33% *vs.* 36%). In 2 patients radiographic and densitometric osteosclerosis-like characteristics were observed: all had tryptase value more than 200 ug/l and previous long history of urticaria pigmentosa.

The additional observation that only 2% of our patients with osteoporosis had normal serum tryptase suggests that this assay can be confidently used for screening in selected cases of unexplained osteoporosis.

In our report[1] we performed the diagnosis of "bone marrow mastocytosis (BMM)" according to the WHO definition[3] in 46 patients who fulfilled criteria for indolent systemic mastocytosis at bone marrow evaluation and did not show skin lesions or signs or symptoms, other than anaphylactic reaction (mainly after hymenoptera sting), or osteoporosis, suggesting the involvement of other tissues. Moreover, we agree with Dr. Escribano *et al.* that clinical characteristics and incidence of osteoporosis in our "Bone Marrow Mastocytosis" patients are very similar to the classical indolent systemic mastocytosis with skin lesions (ISMs+) and the term of indolent systemic mastocytosis skin negative (ISMs-) well represents these cases, as used in our previous paper.[4] In our series, bone marrow mastocytosis patients mainly differ from the other indolent systemic mastocytosis with skin involvement because of prevalence of males, that probably reflect the epidemiology of hymenoptera venom allergy, and for the lower bone marrow mast cell burden, that could be related to an early phase of disease.

In recent months, there has been great discussion regarding WHO classification of different variants and subvariants of systemic mastocytosis (including bone marrow mastocytosis)[5,6] which will probably lead to their further revision or refinement. Moreover, we believe it is essential that the classification of mastocytosis should include an indolent form without skin lesions, in order to improve the recognition and prognostic evaluation of this underestimated condition.

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