Indolent systemic mastocytosis without skin involvement *vs.* isolated bone marrow mastocytosis

We have read with great interest the paper by Zanotti *et al.*[1] about the description of "Isolated bone marrow mastocytosis" (BMM) as an underestimated subvariant of indolent systemic mastocytosis (ISM). This is a very interesting paper in which an in depth study was performed in a total of 99 consecutive ISM patients, diagnosed either prospectively or retrospectively according to the 2008 WHO classification.[2] However, the term used to define the series of BMM might not be the most appropriate and may lead to confusion in the field.

In Zanotti's report, after an in depth study, 46 of 84 patients (54.7%) who were referred because of unexplained/recurrent anaphylaxis or severe allergic reactions to hymenoptera sting in the absence of typical skin lesions (e.g. mastocytosis in the skin; MIS), were classified as BMM.

It is noteworthy that, indolent systemic mastocytosis (ISM) in the absence of skin involvement (ISMs-) has been previously recognized and described by several groups. In fact, it was first recognized as a clinical entity in 1991[3] and later, its clinical, biological, morphological, immunophenotypical and KIT mutational characteristics have been established in a large series of cases.[4] In addition, Dr. Zanotti co-authored an elegant paper on hymenoptera venom anaphylaxis and mastocytosis in which patients lacking MIS but fulfilling criteria for SM are classified as ISMs-.[5] Detailed analysis of the reported isolated BM mastocytosis cases[1] shows that most likely they correspond to the previously identified ISMs- patients.

It should be emphasized that ISMs- clearly differs from isolated BM mastocytosis in that the latter is an exceptional subcategory of ISM in the absence of both skin lesions and MC-mediator related symptoms. In addition, subjects with isolated BM mastocytosis typically show a low MC burden[2;6] and their diagnosis is occasionally made during a BM study for pathological conditions other than mastocytosis, due to its clinically silent behavior (only 5 cases in our data base, Spanish Network on Mastocytosis-REMA-, *data not shown*).

Conversely, ISMs- is a "true" systemic disease based on the observation of systemic mast cell-mediator related symptoms, difficult to explain in a BM restricted MC condition. ISMs- is also frequently associated with osteoporosis and presence of multilineal KIT mutations is detected in 3 out of 47 cases (6.7%) in our published series[4] and in a total of 4 out of 62 (6.4%) cases in the updated REMA's data base (REMA, *unpublished data, 2011*) which confers to these patients an increased probability for disease progression.[7]

The term isolated BM mastocytosis may lead the readership not familiar with this disease to consider this condition to be benign and of a localized nature, when in fact it may be associated with life-threatening or even fatal anaphylaxis with possibly around 5% of cases progressing to aggressive disease.

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