in the article, several (undefined) criteria are merged under the term BM findings.

On the basis of all the above, we sincerely believe that the recommendations made by Pozdnyakova et al about the potential utility of the newly proposed phenotypic criterion are not supported by our findings, as well as by the authors’ data, and that the observation of a discrete BM MC population should not be viewed as a specific diagnostic criterion for SM. In turn, the recommendations reported in the literature for sensitive flow cytometric evaluation of BM MCs should be strictly followed to prevent false-negative results in the flow cytometry immunophenotypic diagnostic workup of SM patients.

References


The Authors’ Reply

We would like to respond to the points raised by Sánchez-Muñoz et al regarding our article.

First, there are no inconsistencies between the number of patients with systemic mastocytosis (SM) and the number of analyzed specimens. The study included 23 patients with SM. However, 5 patients with SM had sequential flow cytometric studies. Because each sample was analyzed as a separate event, that resulted in a total of 39 SM specimens. Cases of monoclonal mast cell activation syndrome (MMCAS) were analyzed separately. Treatment information was beyond the scope of the study.

Second, we would like to point out that the presence of mast cell clusters by flow cytometry was 100% specific; no false-positive results were observed. All cases with mast cell clusters fulfilled the diagnostic criteria for SM based on biopsy findings and/or other laboratory findings. Discrete populations of mast cells were not observed in cases of MMCAS, cutaneous mastocytosis, anaphylaxis, or mast cell activation syndrome. We performed additional analyses of cases of Waldenström macroglobulinemia (WM; n = 23), myelodysplastic syndrome (MDS; n = 10), and recovering marrow (n = 3), and similarly, none of these cases showed clustering of mast cells or aberrant CD25/CD2 expression.

Sánchez-Muñoz et al wonder whether the presence of a discrete mast cell population on side-scatter and CD117 plots may just reflect an increased number of mast cells in the sample. Based on our findings, this is not the case. For example, in representative specimens from patients with SM, MMCAS, anaphylaxis, and WM with a comparable number of events in the CD117 gate, mast cell clustering is present only in the case of SM, with the number of events in the CD117 gate as low as 396. In cases of MMCAS (304 events in the CD117 gate), WM (996 events in the CD117 gate), MDS (427 events in the CD117 gate), recovering marrow (304 events in the CD117 gate), and anaphylaxis (450 events in the CD117 gate), the cells in the CD117 gate are scattered without cluster formation. In their letter, the authors show 2 representative dot plots from patients with SM and MDS; both images demonstrate clustering of mast cells with side scatter and CD117 characteristics of “a
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discrete population” that we believe to be a phenomenon of SM. Although the authors state that these findings merely represent an increased number of mast cells, on the basis of our experience, in which no mast cell clustering was observed in cases of MDS, we wonder whether the case shown in their Figure 1B may represent a case of SM with associated clonal hematologic non–mast cell lineage disease.

Finally, in our study, we observed a number of SM cases that did not demonstrate aberrant CD25 and/or CD2 expression. All these cases met the diagnostic criteria for SM based on biopsy and other laboratory findings. Although absence of aberrant CD25, CD2 staining by flow cytometry might be explained by lower sensitivity of the fluorochromes employed, these CD25−, CD2− cases may indeed represent a well-differentiated SM variant, as suggested by Sánchez-Muñoz et al. Interestingly, in contrast to the study by Morgado et al,1 which showed that aberrant CD25 expression alone is more informative than CD25 and/or CD2 expression, we identified 2 cases of SM that demonstrated CD2 as the sole aberrant marker in our study.

In conclusion, the phenomenon of mast cell clustering is specific for systemic mastocytosis in our experience but requires confirmation at other institutions.

Figure 1
Mast cell flow cytometric analysis in representative samples. The number of events indicates CD117 bright mast cells to the right of the dotted line. MDS, myelodysplastic syndrome; MMCAS, monoclonal mast cell activation syndrome; PE, phycoerythrin; SSC, side scatter; WM, Waldenström macroglobulinemia.