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CORRESPONDENCE

Mast Cells in Intestinal Motility Disorders: Please Also Look Beyond IBS…

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To the Editor,

Dear Sir,

We read with interest the recent article by Schaeffer et al. [1] commenting our previous article on colonic mast cell increase in patients with obstructed defecation [2]. Although we wholeheartedly agree with their conclusions stating that routine quantification of colonic mast cells in mucosal biopsies and the potential of these cells and their released factors as possible therapeutic targets remain to be defined, we want to point out some misunderstandings.

Firstly, most of Schaeffer and colleagues well-focused discussion is based on features/data described in patients with irritable bowel syndrome [3]. These data, although intriguing, have all been obtained in very selected patients and in an experimental setting; this fact, coupled with the quite-deluding results obtained in therapeutic trials targeting this angle, suggest (as also stated by Schaeffer and colleagues) that routine investigation/quantification of mast cells in irritable bowel syndrome patients is at present not justified.

Secondly, the patients we investigated in this and in a previous study [4] had absolutely no features of irritable bowel syndrome, but belonged to studies investigating various aspects of the various cell populations involved in the neuroimmune environment of constipated patients, in which we tried to obtain cohort patients as homogeneous as possible. Thus, the presence of irritable bowel syndrome was considered as exclusion criteria, in that it would have muddled the waters.

Thirdly, our studies were not limited (as most previous ones conducted on irritable bowel syndrome) only to the mucosal aspects, but were carried out on full-thickness colonic sections obtained from surgical specimens, to have more solid data on mast cell distribution in the whole wall of the viscus. Of course, this might have been a limiting factor in that such specimens are not easily obtained, since the number of such patients undergoing surgery is fortunately low, and the groups' numbers are necessarily limited. However, the rigorous pathologic methodology we employed by using well-defined and validated immunohistochemical markers might be a compensating factor, in that it allowed to define with precision the cell populations under investigation.

Fourthly, we discussed in depth our findings, reporting that an increase of mast cells has been previously described in other clinical conditions characterized by constipation [5, 6] and tried to suggest some pathophysiological implications. For instance, being that mast cells are a source of nerve growth factor, their increase in severely constipated patients might be regarded as: (1) a repairing mechanism toward the neurenteric damage described in these patients [7, 8], (2) a vicariating mechanism trying to maintain an at least feeble colonic propulsive activity when the main propulsive mechanisms (i.e., mass movements) are lost [9], and avoiding as much as possible the appearance of a true colonic inertia [10].

Thus, it is always more apparent that, as for several other so-called "functional" or "idiopathic" gastrointestinal disorders, at least some forms of chronic constipation may actually harbor one or more definite anatomic/

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physiologic abnormalities that justify their inclusion in the complex field of enteric neuropathies [11, 12].

Reply

We would like to thank Drs. Bassotti and Villanacci for clarifying that their patient cohort [2] belonged to the obstructed defecation group, a subgroup of functional constipation (FC) rather than constipation-predominant irritable bowel syndrome (IBS-c). Both are classified among the functional bowel disorders (FBD) and may well represent different ends of the spectrum of severity of FBD [13–15].

Reports of increased mast cell (MC) numbers in mucosal biopsies from patients with diarrhea-predominant IBS (IBS-d) with apparent symptomatic response to MC stabilizers and antagonists [16] have put pressure on pathologists to perform MC counts on biopsies from patients with possible IBS. Thus the study by Bassotti et al. [2] not only raises interesting questions regarding the pathophysiology of FC/obstructed defecation but also provides an opportunity to explore the role of MC in all FBD/IBS irrespective of whether they are the diarrheal or constipation variants. Importantly, the present study suggests that an increase in tissue MC is not specific to the diarrheal forms of FBD. The corollary to this is that well-designed clinical studies are required to resolve the issues of both MC involvement in motility disorders and the role of MC stabilizers and antagonists in treating these disorders.

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Conflict of interest None declared.

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