Mast cells in spondyloarthritis, more than simple inflammatory bystanders?

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Quantitative and qualitative evidences indicate that mast cells (MCs) are important players in spondyloarthritis (SpA) pathogenesis. First, the number of MCs found in the synovial tissue of patients with SpA is higher than the number found in rheumatoid arthritis (RA), which is itself 6–25 times higher than the number in patients with osteoarthritis.[1] Secondly, MCs found in the synovium of patients with peripheral SpA or in the facet joint of axial SpA are high producers/stockers of IL-17.[2,3] IL-17 is a key cytokine mediating inflammation in SpA as demonstrated by the efficacy of anti-IL17 biotherapies in psoriatic or non-psoriatic peripheral SpA and axial SpA.[4,5]

Clinically, patients suffering from mastocytosis, a heterogeneous group of neoplastic conditions characterized by the expansion and accumulation of MCs in one or more organs, have a higher prevalence of SpA than in the general population. Mastocytosis and spondyloarthritis share a same cortege of symptoms and comorbidities (e.g. gastrointestinal manifestations, joint pain and tendinitis, osteoporosis), from which association with MC overactivation or dysfunction is highly suspected or characterized.[6]

The finals proof of MCs involvement in SpA has suffered from the paucity of reliable inducible SpA animal models. Experiments using MC-deficient mice have been performed exclusively on collagen-induced arthritis or K/BxN serum-induced arthritis, two relevant models to study the pathogenesis of RA but not of SpA.

In that respect, the recent study of Regan-Komito *et al.* is of interest since, using arthritis-prone SKG mice in which a single intraperitoneal (IP) injection of a microbial polysaccharide,[7] triggers a SpA-like phenotype, they demonstrate that extramedullary haematopoiesis (EMH) occurs in joints.[8] This EMH was oriented towards myelopoiesis and likely to be granulocyte-macrophage colony-stimulating factor (GM-CSF) driven. Regan-Komito *et al.* found that, besides innate lymphoid cells, MCs contributed greatly to GM-CSF production in this model. Further confirming the importance of MCs in this model, MC blockade by cromolyn dampens SpA severity.

Whether EMH occurs in human SpA is uncertain, but recent studies suggest GM-CSF involvement in the pathophysiology of SpA, since transcriptomic and cytometry studies have revealed GM-CSF expression in lymphocytes from these patients.[9,10]

Tyrosine kinase inhibitors (TKI) like Masitinib, Imatinib or Midostaurin have demonstrated clinical activity in systemic mastocytosis, by blocking MC activation/proliferation.[11,12] Thus, it is tempting to suggest that TKI with high safety profiles may be used in SpA to block joint inflammation as it has been reported in RA.[13,14]

Overall, although fundamental studies are required to clarify the role of MCs in SpA, we can conclude that these innate immune cells are not simple inflammatory bystanders but rather drivers of pain and inflammation.

Key message

Recent findings support an active role for mast cells in SpA, opening new therapeutic insights.

Conflict of interest statement

Masitinib is under clinical development by AB Science. OH is the President of the Scientific Committee of AB Science. All remaining authors have no competing interests.

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