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IL-17A producing mast cells as therapeutic target in spondyloarthritis

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Introduction

We recently observed a remarkably increased synovial infiltration with c-kit-positive mast cells in non-psoriatic and psoriatic spondyloarthritis (SpA) versus rheumatoid arthritis (RA).

Aim

As these mast cells were not degranulated, we investigated whether they could contribute to synovial inflammation by cytokine production, with special focus on IL-17.

Patients and methods

Synovial tissue biopsies from active non-psoriatic and psoriatic SpA (n=10) and RA (n=10) were stained with mouse anti-c-kit, goat anti-IL-17 and mouse anti-mast cell tryptase (MCT) by immunohistochemistry and double immunofluorescence. The effect of inhibition of c-kit tyrosine kinase by imatinib mesylate on proinflammatory cytokine production was tested in vitro on fresh synovial biopsies from 14 SpA patients.

Results

Mast cells were identified in synovial tissue by immunostaining for c-kit or mast cell tryptase. Single immunostaining for IL-17 showed multiple single positive mononuclear cells in all types of arthritis. Double immunofluorescence indicated a striking colocalization of IL-17 and mast cell tryptase in non-psoriatic and psoriatic SpA. Quantification by manual counting confirmed that a median of 65% of the synovial mast cells in SpA express IL-17. In contrast, only 26% of the mast cells expressed IL-17 in RA (p=0.015). Moreover, mast cells were the main IL-17 producing cell subset in SpA (60-70%) but not in RA (20-30%)(p=0.036). In order to investigate the role of cytokine production by mast cells in the synovial inflammation in SpA, we used imatinib mesylate to block c-kit tyrosine kinase in ex vivo synovial tissue cultures. C-kit blockade strongly reduced not only IL-6 and IL-8 but also IL-17A production by SpA synovial biopsies.

Conclusion

The increase in synovial mast cells in SpA synovitis, their augmented production of IL-17, and the downregulation of cytokine production by targeting mast cells ex vivo strongly suggest that mast cells contribute to synovial inflammation in SpA and are an attractive therapeutic target.

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