Comparative Histologic and Molecular Analysis of Synovial Tissue in Early Treatment-Naïve Psoriatic and Rheumatoid Arthritis

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Background/Purpose:

Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) are chronic joint conditions characterised by persistent inflammation of the synovial tissue (ST). Previous reports suggested less marked synovial lining and fewer infiltrating T cells in PsA compared to RA. Several confounders such as disease duration, treatment, sampling techniques and a predominance of large joints samples may have influenced these findings. Here we aimed at comparing the synovial features of RA/PsA early in the disease and prior to treatment intervention to highlight their histologic and molecular individual characteristics.

Methods: 183 consecutive patients with early (<12 months) treatment-naïve arthritis and active synovitis of at least one joint were recruited as part of the multicentre Pathobiology of Early Arthritis Cohort (PEAC) at the Barts Health NHS Trust and underwent a baseline US-guided synovial biopsy of an actively inflamed joint. ST inflammatory infiltrate was evaluated by H&E and semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: Pauci-immune, CD68sublining (SL)<2 and/or CD3-CD20-CD138<1; diffuse-myeloid, CD68SL>2, CD20<2 or CD138<2; lympho-myeloid, CD20>2 or CD138>2. RNA sequencing was performed on 93 RA/15 PsA patients.

Results:

144/183 patients met the 2010ACR/EULAR criteria for RA and 39/183 were diagnosed with PsA (32 polyarticular 7 oligoarticular). PsA patients were significantly younger than RA. Comparison of the age-adjusted clinical variables at baseline showed no significant differences between ESR, CRP and DAS28, despite a significantly higher number of tender

and swollen joints in RA. ST was retrieved from small joints in 74.4% of PsA and 82% of RA. US score of the biopsied joints showed a significantly higher synovial thickening in the PsA group and comparable power-doppler. Histopathology assessment showed a significantly lower infiltration of B/T lymphocytes, plasma cells and SL-macrophages in psoriatic synovitis. The distribution of synovial pathotypes also differed, as the pauci-immune was the most represented in PsA (43.2%) but the least frequent in RA (24.8%). Only in RA, the pauci-immune pathotype associated with significantly lower ESR, CRP and DAS28 in comparison with lympho-myeloid; these differences remained significant also in a subset of 26 RA subjects age- and gender-matched with PsA patients. Conversely, pathotypes did not define less active disease in PsA. Cellular gene modules analysis showed the expression of neutrophil, eosinophil and mast cell gene-sets in PsA but not RA pauci-immune synovitis. Overall, PsA ST differed from RA with a higher expression of the skin fibroblasts, eosinophils and neutrophils gene-sets. Finally, genes significantly up-regulated in PsA clustered in specific modules including neutrophil recruitment/enrichment and cytoskeleton remodelling.

Conclusion:

The demonstration of specific histological and molecular signatures relating to early-untreated PsA and RA will help to shed new light on disease pathogenesis and identify novel therapeutic targets.

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