

The clinical phenotype of inflammatory arthritis correlates with synovial immune cell infiltration: results from the pathobiology of early arthritis cohort

Gloria Lliso Ribera Frances Humby Stephen Kelly Myles LewisMichele
Bombardieri Alessandra Nerviani Rebecca Hands Fabiola BeneChris Buckley Peter C Taylor
Iain B McInnes Costantino Pitzalis

Background: Clinical, histological and molecular heterogeneity in early inflammatory arthritis is well recognised, with differences in qualitative and quantitative degree of immune cell infiltration. Whether synovial pathobiology heterogeneity correlates with diagnostic classification criteria in early inflammatory arthritis is unknown, offering the potential to refine early diagnostic criteria. Therefore, the aim of this study was to examine in a cohort of therapy naïve, early inflammatory arthritis, whether synovial immune cell infiltration differed significantly between diagnostic categories of early inflammatory arthritis (ACR/EULAR 2010 vs ACR 1987 vs undifferentiated).

Methods: A total of 200 consecutive DMARD naïve early arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were categorised according to the following criteria: RA 1987 ACR, RA 2010 ACR/EULAR, and Undifferentiated Arthritis (UA). All patients underwent a baseline US guided synovial biopsy of a clinically active joint along with collection of demographic data. Following H&E staining, degree of synovitis was assessed. Sections underwent immunohistochemical staining and semi-quantitative scoring (0-4) to determine the degree of CD20+Bcells, CD3+T cells, CD68+ lining (l) and sublining (sl) macrophage and CD138+ plasma cell infiltration. Sections were categorised into three pathotypes: fibroid: (CD68 SL < 2 and or CD3, CD20, CD138<1), myeloid: (CD68SL>2, CD20<1 and or CD3>1) and lymphoid: (grade 2-3 CD20+ aggregates, CD20>2). Synovial samples were immersed in RNA-Later for subsequent RNA extraction and synovial gene expression of 238 genes by nanostring analysis was performed.

Results: 128 patients were classified as RA 1987, 25 patients as RA 2010 ACR/EULAR and 47 as UA. 80% of synovial samples were collected from small joints (wrist, MCP, PIP). 166/200 samples were suitable for analysis. Although there were no significant differences in disease duration between diagnostic subgroups, patients classified as RA 1987 criteria had

significantly higher levels of CRP, tender and swollen joints, DAS28 and sero positivity for ACPA and RF. When patients were stratified into pathotypes, a numerically higher proportion of patients within the RA 1987 group were categorised as lymphoid. Further, patients within the RA 1987 group had a significantly higher synovitis score and degree of immune cell infiltration (Table 1). Differential upregulation of genes involved in B and T cell activation/function was observed in RA 1987 group when compared to RA2010 or UA which shared similar clinical and pathobiological features.

Conclusion: Stratifying patients according to baseline clinical diagnosis translates into differences in synovial pathobiology. The capacity to refine early clinical classification criteria through application of synovial pathobiological markers offers the potential to predict disease outcome and stratify therapeutic intervention.

Disclosures: The authors have declared no conflicts of interest