Commentary

Psoriatic arthritis synovial histopathology: commentary on the article by Kruithof and colleagues

Oliver FitzGerald

Newman Clinical Research Professor, St Vincent's University Hospital, Dublin, Ireland

Corresponding author: Oliver FitzGerald, ofitzger@iol.ie

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Abstract

The clinical features in psoriatic arthritis straddle the divide between rheumatoid arthritis on the one hand and spondyloarthropathy on the other. The paper by Kruithof and colleagues compares synovial immunohistologic features and clearly identifies psoriatic arthritis as being a member of the spondyloarthropathy family.

The excellent article by Kruithof and colleagues stimulates many questions while carefully dissecting differentiating features in synovial histopathology that characterize rheumatoid arthritis (RA) and spondyloarthropathy (SpA), in particular psoriatic arthritis (PsA) [1]. Using a semi-quantitative scoring system, the authors identified a number of features characteristic of RA synovium, including the lining layer thickness, $CD83^+$ dendritic cells, positive staining for intracellular citrullinated proteins (44%) and positive staining for MHC/HC gp-39 peptide complexes (46%). In the SpA group as a whole and in the PsA subgroup alone, increased vascularity and neutrophil numbers distinguished from RA. $CD163^+$ macrophages were also increased in SpA. Interestingly, no significant differences were seen between oligoarticular PsA versus polyarticular PsA. The authors conclude that the synovitis in PsA, both oligoarticular and polyarticular, resembles SpA more than RA.

These observations have a number of important implications. First, although this has been disputed [2], it may be possible to diagnose RA based on the positive staining as already stated. In Kruithof and colleagues' study, positive staining for intracellular citrullinated proteins and positive staining for MHC/HC gp-39 peptide complexes were seen only in RA, although each were present in <50%. Second, the synovitis in PsA shows similar features to other SpA patients, both ankylosing spondylitis and undifferentiated SpA.

Previous studies have compared PsA with RA [3], although Kruithof and colleagues' study is the first to include other SpA patients in the comparison. In the previous study [3], an increase in vessel number was also a distinguishing feature from RA, as were lower macrophage numbers and a reduction in E-selectin expression. Kruithof and colleagues were unable to confirm these findings, which have been confirmed by others [4], but this may relate to issues of patient selection and to methods of quantification of cellular infiltration (semi-quantitative versus quantitative). The interesting additional observation of an increase in neutrophil infiltration in PsA is consistent both with the well-described neutrophil infiltration seen in psoriasis (Ps) skin [5] and with the observation of Flt-1-positive neutrophils in PsA synovium [6]. It is clear that the role of the neutrophil in both Ps and PsA requires further study.

The finding that the synovial immunohistologic features of oligoarticular-type PsA and polyarticular-type PsA are not different and that they both are more like other SpA patients than RA patients answers an important question: is polyarticular PsA really RA in disguise but with coincidental Ps? Indeed, McGonagle and colleagues have proposed a new classification for PsA based on entheseal involvement where patients with predominant synovitis and Ps would be grouped with RA [7]. The results in Kruithof and colleagues' paper would suggest that this proposed classification is not appropriate.

The subject of classification of PsA has been controversial, and many classifications have been proposed since the original Moll and Wright classification in 1974. The Classification of Psoriatic Arthritis initiative led by Philip Helliwell will be reporting later this year on a multicentre prospective case–control study to determine classification

Ps = psoriasis; PsA = psoriatic arthritis; RA = rheumatoid arthritis; SpA = spondyloarthropathy.

criteria in a large number of unselected patients. While the results of this study are eagerly awaited, it is possible that dividing patients up by the number of joints involved has little relevance other than identifying those with a poor prognosis.

Previous studies have identified both the number of inflamed joints and an elevated erythrocyte sedimentation rate to be associated with poor outcome [8]. In addition, classification criteria in established PsA appear to be confounded by the effects of therapy, with 49% of PsA patients who were classified as polyarticular at presentation being reclassified as oligoarticular after 2 years [9]. It may thus be that attempts to classify PsA may have little clinical utility.

PsA belongs to the SpA family, and the focus should be on trying to identify features, perhaps common to the target tissues (skin, synovium and enthesis), which are specific for the disease. To date, efforts have focused on detailed tissue analysis and on studies of T-cell specificity but have largely failed to identify either disease-specific immunohistologic features (cell markers/cytokine expression) [1,3,10] or evidence of T-cell antigen drive [11]. Future studies using detailed differential analysis of gene (genomics) expression or protein (proteomics) expression may be more informative.

Finally, while Kruithof and colleagues' results indicate that PsA belongs to the SpA family, this does not mean that all SpA is the same. There are clinical, genetic and radiological features that are associated with PsA and that together suggest a unique clinical entity. At the very least, the joint disease in PsA is modified by the presence of Ps to produce a form of SpA with easily distinguished clinical features. Again, this supports the final conclusion by Kruithof and colleagues that more detailed studies are required "to unravel pathogenetic and phenotypic differences and similarities".

Competing interests

The author(s) declare that they have no competing interests.

References

1. Kruithof E, Baeten D, De Rycke L, Vandooren B, Foell D, Roth J, Cañete JD, Boots AM, Veys EM, De Keyser F: **Synovial histopathology of psoriatic arthritis, oligo- and polyarticular, resembles more spondyloarthropathy than rheumatoid arthritis.** *Arthritis Res Ther* 2005, **7:**R569-R580.
2. Vossenaar ER, Smeets TJM, Kraan MC, Raats JM, van Venrooij WJ, Tak PP: **The presence of citrullinated proteins is not specific for rheumatoid synovial tissue.** *Arthritis Rheum* 2004, **50:** 3485-3495.
3. Veale D, Yanni G, Rogers S, Barnes L, Bresnihan B, Fitzgerald O: **Reduced synovial membrane macrophage numbers, ELAM-1 expression, and lining layer hyperplasia in psoriatic arthritis as compared with rheumatoid arthritis.** *Arthritis Rheum* 1993, **36:**893-900.
4. Jones SM, Dixey J, Hall ND, McHugh NJ: **Expression of the cutaneous lymphocyte antigen and its counter-receptor E-selectin in the skin and joints of patients with psoriatic arthritis.** *Br J Rheumatol* 1997, **36:**748-757.
5. Ragaz A, Ackerman AB: **Evolution, maturation, and regression of lesions in psoriasis.** *Am J Dermatopathol* 1979, **1:**199-214.
6. Gogarty M, Murphy EP, Bresnihan B, FitzGerald O: **VEGF receptors KDR/Flk-1 and Flt-1 are expressed by distinct cell populations in inflamed synovium [abstract].** *Arthritis Rheum* 2002, **42:**s568.
7. McGonagle D, Conaghan PG, Emery P: **Psoriatic arthritis: a unified concept twenty years on.** *Arthritis Rheum* 1999, **42:** 1080-1086.
8. Kane D, Stafford L, Bresnihan B, FitzGerald O: **A prospective, clinical and radiological study of early psoriatic arthritis: an early synovitis clinic experience.** *Rheumatology* 2003, **42**:1460-1468.
9. Kane D, Stafford L, Bresnihan B, FitzGerald O: **A classification study of clinical subsets in an inception cohort of early psoriatic peripheral arthritis — 'DIP or not DIP revisited'.** *Rheumatology* 2003, **42:**1469-1476.
10. Danning CL, Illei GG, Hitchon C, Greer MR, Boumpas DT, McInnes IB: **Macrophage-derived cytokine and nuclear factor kappaB p65 expression in synovial membrane and skin of patients with psoriatic arthritis.** *Arthritis Rheum* 2000, **43:**1244-1256.
11. Curran SA, FitzGerald OM, Costello PJ, Selby JM, Kane DJ, Bresnihan B, Winchester R: **Nucleotide sequencing of psoriatic arthritis tissue before and during methotrexate administration reveals a complex inflammatory T cell infiltrate with very few clones exhibiting features that suggest they drive the inflammatory process by recognizing autoantigens.** *J Immunol* 2004, **172:**1935-1944.