

Letter to the Editor (Matters arising from published papers)

Rheumatology 2021;60:e24–e25

doi:10.1093/rheumatology/kez670

Advance Access Publication 20 January 2020

Comment on: Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis?

Dear Sir, We read with interest the article by Feld *et al.*, who report a retrospective analysis of 2069 patients from two real life, prospective parallel cohorts of AS and axial PsA (axPsA) attending the same tertiary centre in Canada [1]. The authors address an important question of significant clinical relevance, namely the characterization of axial SpA (axSpA) and axPsA and whether these may represent two distinct clinical entities with overlapping features rather than the same disease entity. The understanding, evaluation and timely therapy of axPsA indeed represents an area of unmet need in the study of SpA and poses many clinical challenges in real life where patients with psoriasis and back pain, in the absence of peripheral joint swelling, struggle to get access to appropriate treatment due to the lack of diagnostic criteria or even a consensus definition on what constitutes axPsA.

Axial involvement including sacroiliitis can occur in many musculoskeletal disorders, although it was its higher prevalence and distinct clinical presentation in PsA that led Moll and Wright to incorporate it as one of the main clinical sub-types of PsA [2]. The real prevalence of axial involvement in PsA, however, remains unclear, with reports varying from 25 to 70% [3], which reflects the methodological issues with the different studies and the lack of a standardized definition. Feld *et al.* [1] report an overall prevalence of 36% (477/1303) of axPsA in their overall PsA cohort, based on fulfilment of radiographic criteria for sacroiliitis (at least bilateral grade 2 or unilateral grade 3 or 4) not only at baseline, but at any point over the follow-up period with no requirement of reported back pain. Indeed, their study is the first longitudinal description of axPsA followed up for over a decade. Importantly, they also describe a contemporary AS cohort of which 12% (91/766) had concomitant psoriasis. However, by choosing to define axPsA based on the presence of radiographic sacroiliitis (bilateral grade 2 or unilateral grade 3 or 4) the authors may have missed those cases with isolated spondylitis including cervical spine involvement, estimated to be 35% [4], and who may never develop sacroiliac joint involvement, those presenting with milder asymmetrical or unilateral sacroiliitis [5] not fulfilling the specified radiographic criteria, or those without any radiographic findings that could have been identified by MRI.

One observation from the study is the low prevalence of back pain as found in only 21% of axPsA subjects with radiographic disease. This finding supports previous reports suggesting that axPsA may be more asymptomatic than axSpA [4, 6]. When looking at the radiographs of these patients, Feld *et al.* found milder grades of sacroiliitis in axPsA compared with the AS group. These results are consistent with a previous report from our group showing that patients with axPsA had significantly less inflammation than those with axSpA when assessed by MRI [7]. However, when dividing our study cohort according to HLA-B27 status a clear difference was seen, with more inflammation found in the HLA-B27 positive axPsA patients, which was comparable to the axSpA group [7]. In accordance with other studies and real-life experience, Feld *et al.* report that 80% of their axPsA cohort were HLA-B27 negative. They also observe that the subset of patients in their AS cohort who had concomitant psoriasis (12%) were more likely to be HLA-B27 positive, had higher BASMI and worse sacroiliitis. However, they do not report on their axPsA subset who are HLA-B27 positive (19%) and who may be closer to the axSpA phenotype. Indeed, although this represents a specific, less frequent subtype of axPsA, it closely resembles axSpA with or without psoriasis. This may be supported by genetic studies where HLA-B*0801 is found to be significantly associated with asymmetrical sacroiliitis, typical of axPsA, while HLA-B*2705 in psoriasis subjects is associated with symmetrical sacroiliitis, resembling axSpA [8].

In conclusion, the study by the Toronto group adds to the body of evidence that characterizes axial involvement in PsA and outlines clear differences between the clinical presentation of axPsA and axSpA with or without psoriasis over time. However, there are important limitations such as the retrospective nature of the report and the fact that the axPsA population included was solely based on those with established radiographic sacroiliitis, which may have introduced bias by not encompassing an estimated extra one-third of cases that may present with isolated spondylitis and may never develop sacroiliitis, as well as patients that might only show mild changes on pelvic radiograph but significant lesions when assessed by MRI. The question remains as to whether there are indeed two distinct phenotypes of axPsA and in particular whether the axPsA phenotype that is HLA-B27-determined is equivalent to that of axSpA with skin psoriasis. Further longitudinal studies with robust imaging and immune-genotype characterization are needed to define PsA with predominant axial involvement.

Acknowledgements

The authors are supported by the National Institute for Health Research (NIHR) Leeds Biomedical Research Centre (LBRC). The views expressed are those of the authors and not necessarily those of the (UK) National Health Service, the NIHR or the (UK) Department of Health.

Funding: No specific funding was received from any funding bodies in the public, commercial or not-for-profit sectors to carry out the work described in this manuscript.

Disclosure statement: The authors have declared no conflicts of interest.

Xabier Michelena ^{1,2,3}, **Gabriele De Marco** ^{1,2}, **Sayam Dubash** ^{1,2}, **Dennis McGonagle** ^{1,2}, and **Helena Marzo-Ortega** ^{1,2}

¹NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals Trust, ²Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK and ³Hospital Universitari de Bellvitge-IDIBELL, Hospitalet de Llobregat, Barcelona, Spain
Accepted 11 December 2019

Correspondence to: Helena Marzo-Ortega, LIRMM, Second floor, Chapel Allerton Hospital, Leeds LS7 4SA, UK.
E-mail: medhmo@leeds.ac.uk

References

1 Feld J, Ye JY, Chandran V, Inman RD *et al.* Is axial psoriatic arthritis distinct from ankylosing spondylitis with

and without concomitant psoriasis? *Rheumatology (Oxford)* 2020;59:1340–6.

2 Moll JM, Wright V. Psoriatic arthritis. *Semin Arthritis Rheum* 1973;3:55–78.

3 Baraliakos X, Coates LC, Braun J. The involvement of the spine in psoriatic arthritis. *Clin Exp Rheumatol* 2015;33: S31–5.

4 Jadon DR, Sengupta R, Nightingale A *et al.* Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. *Ann Rheum Dis* 2017;76:701–7.

5 Helliwell PS, Hickling P, Wright V. Do the radiological changes of classic ankylosing spondylitis differ from the changes found in the spondylitis associated with inflammatory bowel disease, psoriasis, and reactive arthritis? *Ann Rheum Dis* 1998;57:135–40.

6 Queiro R, Belzunegui J, González C *et al.* Clinically asymptomatic axial disease in psoriatic spondyloarthropathy. A retrospective study. *Clin Rheumatol* 2002;21:10–3.

7 Castillo-Gallego C, Aydin SZ, Emery P, McGonagle DG, Marzo-Ortega H. Brief report: magnetic resonance imaging assessment of axial psoriatic arthritis: extent of disease relates to HLA-B27. *Arthritis Rheum* 2013;65: 2274–8.

8 Haroon M, Winchester R, Giles JT, Heffernan E, Fitzgerald O. Clinical and genetic associations of radiographic sacroiliitis and its different patterns in psoriatic arthritis. *Clin Exp Rheumatol* 2017;35:270–6.