Article:
Michelena, X, De Marco, G orcid.org/0000-0003-2406-161X, Dubash, S et al. (2 more authors) (2020) Comment on: Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis? Rheumatology. kez670. ISSN 1462-0324

https://doi.org/10.1093/rheumatology/kez670

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

Xabier Michelena [1,2,3], Gabriele De Marco[1,2], Sayam Dubash[1,2], Dennis McGonagle[1,2], Helena Marzo-Ortega[1,2]

1.NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds.

2.Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds.

3. Hospital Universitari de Bellvitge-IDIBELL, Hospitalet de Llobregat, Barcelona, Spain.

Address for correspondence

Helena Marzo-Ortega

LIRMM, Second floor

Chapel Allerton Hospital

Leeds LS7 4SA, UK

medhmo@leeds.ac.uk

Word count: 800

References: 10

Sir,

We read with interest the article by Feld et al, who report a retrospective analysis of 2,069 patients from two real life, prospective parallel cohorts of ankylosing spondylitis (AS) and axial psoriatic arthritis (PsA) attending the same tertiary centre in Canada[1]. The authors address an important question of significant clinical relevance namely the characterization of axial spondyloarthritis (axSpA) and axial psoriatic arthritis (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 axial PsA (axPsA) indeed represents an area of unmet need in the study of spondyloarthritis 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 psoriatic arthritis[2]. The real prevalence of axial involvement in PsA however remains unclear with reports varying from 12.5%[3] to 78%[4] 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 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%[5,6], and who may never develop sacroiliac joint involvement, those presenting with milder asymmetrical or unilateral sacroiliitis[7] 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[5,9]. When looking at the radiographs of these patients, Feld et al found milder grades of sacroiliitis in axPsA compared to 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[10]. However, when dividing our study cohort according to HLA-B27 status, a clear difference was seen with more inflammation found in the HLA-B27+ve axPsA patients which was comparable to the axSpA group. 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 (91/766) were more likely to be HLA-B27+, had higher BASMI and worse sacroiliitis. However, they do not report on their axPsA subset who are HLA-B27+ (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, and this may be supported by genetic studies where HLA-B*0801 is found to be significantly associated with asymmetrical sacroiliitis, typical of axPsA; whilst HLA-B*2705 in psoriasis subjects is associated with symmetrical sacroiliitis, resembling axSpA[11].

In conclusion, the study by the Toronto group adds to the body of evidence that characterizes axial involvement in psoriatic arthritis 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 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 axial PsA 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 psoriatic arthritis 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 (NHS), the NIHR, or the (UK) Department of Health.

Conflicts of interest

The authors have declared no conflicts of interest.

References

1 Feld, J. *et al.* Is axial psoriatic arthritis distinct from ankylosing spondylitis with and without concomitant psoriasis? *Rheumatology (Oxford)* https://doi.org/10.1093/rheumatology/kez457 (2019).
2 Moll, J. M. & Wright, V. Psoriatic arthritis. *Semin. Arthritis Rheum.* **3**, 55-78 (1973).
3 Mease, P. J. *et al.* Influence of Axial Involvement on Clinical Characteristics of Psoriatic Arthritis: Analysis from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry. *J. Rheumatol.* **45**, 1389-1396 (2018).
4 Battistone, M. J., Manaster, B. J., Reda, D. J. & Clegg, D. O. The prevalence of sacroilitis in psoriatic arthritis: new perspectives from a large, multicenter cohort. A Department of Veterans Affairs Cooperative Study. *Skeletal Radiol.* **28**, 196-201 (1999).
5 Jadon, D. R. *et al.* Axial Disease in Psoriatic Arthritis study: defining the clinical and radiographic phenotype of psoriatic spondyloarthritis. *Ann. Rheum. Dis.* **76**, 701-707 (2017).
6 Lubrano, E. *et al.* The radiological assessment of axial involvement in psoriatic arthritis: a validation study of the BASRI total and the modified SASSS scoring methods. *Clin. Exp. Rheumatol.* **27**, 977-980 (2009).
7 Helliwell, P. S., 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.* **57**, 135-140 (1998).
8 Rudwaleit, M. *et al.* The development of Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis (part II): validation and final selection. *Ann. Rheum. Dis.* **68**, 777-783 (2009).
9 Queiro, R. *et al.* Clinically asymptomatic axial disease in psoriatic spondyloarthropathy. A retrospective study. *Clin. Rheumatol.* **21**, 10-13 (2002).

10 Castillo-Gallego, C., Aydin, S. Z., Emery, P., McGonagle, D. G. & Marzo-Ortega, H. Brief Report: Magnetic Resonance Imaging Assessment of Axial Psoriatic Arthritis: Extent of Disease Relates to HLA-B27. *Arthritis Rheum.* **65**, 2274-2278 (2013).
11 Haroon, M., Winchester, R., Giles, J. T., Heffernan, E. & Fitzgerald, O. Clinical and genetic associations of radiographic sacroiliitis and its different patterns in psoriatic arthritis. *Clin. Exp. Rheumatol.* **35**, 270-276 (2017).